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Contents

Monthly Volume 16 Number 12 December 15, 2024

EDITORIAL

REVIEW

ORIGINAL ARTICLE

Case Control Study

Retrospective Cohort Study

World Journal of Gastrointestinal Oncology

Monthly Volume 16 Number 12 December 15, 2024

Contents

World Journal of Gastrointestinal Oncology

Monthly Volume 16 Number 12 December 15, 2024

Contents

LETTER TO THE EDITOR

World Journal of Gastrointestinal Oncology

Monthly Volume 16 Number 12 December 15, 2024

Contents

ABOUT COVER

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Oncology* (*WJGO*, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc*.

INDEXING/ABSTRACTING

The *WJGO* is now abstracted and indexed in PubMed, PubMed Central, Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJGO* as 2.5; JIF without journal self cites: 2.5; 5-year JIF: 2.8; JIF Rank: 72/143 in gastroenterology and hepatology; JIF Quartile: Q3; and 5-year JIF Quartile: Q2. The *WJGO*'s CiteScore for 2023 is 4.2 and Scopus CiteScore rank 2023: Gastroenterology is 80/167; Oncology is 196/404.

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https://www.wjgnet.com/bpg/gerinfo/208

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https://www.wjgnet.com/bpg/gerinfo/242

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META-ANALYSIS

Efficacy and safety of transhepatic arterial chemoembolization with drug-loaded microspheres in unresectable primary liver cancer

Jun Deng, Yan-Hong Mi, Le Xie, Xiong-Xing Sun, Dan-Hong Liu, Hua-Jun Long, Li-Yong He, Da-Hua Wu, Hong-Cai Shang

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Jun Deng, Da-Hua Wu, Department of Integrated Traditional Chinese and Western Medicine, Hunan University of Traditional Chinese Medicine, Changsha 410208, Hunan Province, China

Jun Deng, Le Xie, Xiong-Xing Sun, Da-Hua Wu, Department of Neurology, Hunan Provincial Hospital of Integrated Traditional Chinese and Western Medicine, Changsha 410208, Hunan Province, China

Yan-Hong Mi, Department of Prevention Diseases, Hunan Provincial Hospital of Integrated Traditional Chinese and Western Medicine, Changsha 410006, Hunan Province, China

Dan-Hong Liu, Institute of Clinical Pharmacology of Traditional Chinese Medicine, Hunan Provincial Hospital of Integrated Traditional Chinese and Western Medicine, Changsha 410006, Hunan Province, China

Hua-Jun Long, Department of Emergency, Hunan Provincial Hospital of Integrated Traditional Chinese and Western Medicine, Changsha 410006, Hunan Province, China

Li-Yong He, Department of Hepatobiliary Surgery, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou 510062, Guangdong Province, China

Hong-Cai Shang, State Key Laboratory of Internal Medicine of Traditional Chinese Medicine, Beijing University of Chinese Medicine, Beijing 100700, China

Co-first authors: Jun Deng and Yan-Hong Mi.

Co-corresponding authors: Da-Hua Wu and Hong-Cai Shang.

Corresponding author: Hong-Cai Shang, PhD, Professor, State Key Laboratory of Internal Medicine of Traditional Chinese Medicine, Beijing University of Chinese Medicine, No. 5 Sea Warehouse, Dongcheng District, Beijing 100700, China. shanghongcai@126.com

Abstract

BACKGROUND

Transhepatic arterial chemoembolization (TACE), as a local treatment, has been widely used in the treatment of unresectable liver cancer. The introduction of drug carrier microspheres has brought new hope for the therapeutic effect of TACE. Microspheres can realize the slow release and directional delivery of drugs, reduce systemic toxicity and improve local curative effect.

AIM
To compare the effectiveness of traditional transcatheter arterial chemoembolization against microsphere-assisted transcatheter arterial chemoembolization in the treatment of hepatocellular carcinoma that is incurable.

METHODS
We searched the PubMed, Embase, Cochrane Library, and CNKI databases for clinical trials of drug-luting beads TACE (DEB-TACE) *vs* conventional TACE (cTACE) for the treatment of unresectable liver cancer. We screened references based on inclusion and exclusion criteria and then selected valid data for meta-analysis using RevMan 53 software. The complete response (CR) rate, partial response (PR) rate, postoperative stable disease (SD) rate, and 6-month and 12-month survival rates were compared.

RESULTS
A total of 12 articles were included, including 1177 patients, 519 of whom received DEB-TACE and 658 of whom received cTACE. The CR rate in the DEB-TACE group was much greater than that in the cTACE group [relative risk (RR) = 1.42, 95%CI: 1.18–1.72, P = 0.0002]. The 12-month survival rate significantly increased (RR = 1.09; 95%CI: 1.01- 1.17, P = 0.03); the PR rate (RR = 1.13; 95%CI: 0.97-1.30, P = 0.12); the SD rate (RR = 0.82; 95%CI: 0.64-1.05, P = 0.12); and the 6-month survival rate (RR = 1.05; 95%CI: 1.00-1.10, P = 0.07). There was no significant difference (P < 0.05).

CONCLUSION
Compared with those of iodized oil TACE, the drug-loaded microspheres tended to have therapeutic advantages.

Key Words: Transhepatic arterial chemoembolization; Drug-loaded microspheres; Unresectable primary liver cancer; Meta-analysis

Core Tip: This study systematically evaluated the efficacy and safety of transhepatic arterial chemoembolization with drug-loaded microspheres in the treatment of unresectable primary liver cancer. Through a meta-analysis of relevant literature, the effect of this treatment in prolonging survival, relieving symptoms and improving quality of life of patients was discussed, and the incidence of adverse reactions and complications was evaluated, so as to provide more scientific treatment recommendations for clinicians.

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INTRODUCTION

Each year, nearly 500000 hepatocelluar carcinoma (HCC) patients receive a diagnosis, accounting for more than 5% of all cancer cases. The recurrence rate of HCC is as high as 50% within 3 years and 70% at 5 years after hepatectomy[1-4]. Despite recent advances in surgical techniques and preoperative medical treatment, the incidence of postoperative complications in patients with cirrhosis is still as high as 42%[5]. Transhepatic arterial chemoembolization (TACE) is widely used as a treatment for patients with clinically unresectable HCC. It is composed of conventional TACE (cTACE) and the drug-luting beads TACE (DEB-TACE), which use iodide and DEB, respectively, as chemotherapy drug carriers [6]. DEB-TACE, a novel drug delivery and embolization system, delivers local, controlled, and sustained doses of chemotherapeutic agents to the tumor site through the blood vessels of highly vascularized malignancies. Numerous studies[7-9] have shown that DEB-TACE has a significant advantage in terms of overall survival or tumor response and can reduce the occurrence of adverse events. Despite the extensive studies conducted on cTACE and DEB-TACE, the role of DEB-TACE in comparison to that of cTACE remains relatively inconsistent.

MATERIALS AND METHODS

Retrieval strategy

Our search time was July 2023, and we searched the PubMed, Embase, Cochrane Library, and CNKI databases for controlled clinical studies on DEB-TACE and TACE for comparative treatment of unresectable liver cancer. Using a

combination of subject words and free words, we ended the sentence with "DEB" OR "drug eluting" OR "drug eluting microsphere" OR "doxorubicin eluting". The search terms used were "TACE "OR "transcatheterarterial chemoembolization" AND "hepatocellular carcinoma" OR "adenocarcinoma" OR "carcinoma" OR "cancer" OR "neoplasm" OR " tumor".

Inclusion and exclusion criteria

Inclusion criteria: (1) Clinically controlled studies comparing DEB-TACE with cTACE for the treatment of unresectable liver cancer, regardless of age, sex, or nationality; (2) Had confirmed unresectable liver cancer for which a radiological or histopathological diagnosis was made in addition to alpha-fetoprotein levels; and (3) Had complete primary outcomes, including a complete response (CR) rate, a partial response (PR) rate, a stable disease (SD) rate, and 6- and 12-month survival.

Exclusion criteria: (1) Were conference papers, case reports, editorials, and nonhuman studies; and (2) Had repeated publications of the same data or incomplete data in the literature.

Data extraction and quality assessment

Two researchers independently screened the literature, extracted the data and cross-checked the data. Disagreements were resolved through discussion or by discussion with a third party. The following data were extracted: (1) Basic information of the trial, author name, nationality, publication time, sample size, patient sex, age, tumor diameter, and Child-Pugh grade; (2) Main results, namely, the CR rate, PR rate, SD rate, 6-month survival rate, and 12-month survival rate; and (3) The Newcastle-Ottawa Scale (NOS) score, which was used to assess the risk of bias.

Statistical analysis

RevMan 5.3 was used to determine the relative risk in each study [relative risk (RR), 95%CI]. A $P > 0.05$ indicated that there was no significant difference between the DEB-TACE and cTACE groups. Each study used the value of I2, which represents the percentage of total variation, to assess statistical heterogeneity. Generally, we used the fixed-effects model for analysis when I2 was less than 50%, assuming no significant difference in heterogeneity. A random effects model was used to analyze the heterogeneity when the I^2 was greater than 50%. We used a forest plot to graphically represent and evaluate the treatment effect and the symmetry of the funnel plot to visually assess the presence of bias risk.

RESULTS

Literature search results

A total of 1220 pieces of literature were initially retrieved, 865 duplicated pieces were excluded, 105 reviews were excluded, only 32 abstracts were excluded, 12 animal experiments were excluded, 10 case reports were reviewed, 10 reviews were reviewed, and 3 brief investigations were conducted. Upon reviewing the titles and abstracts, we excluded 171 irrelevant studies, resulting in a total of 1208 excluded studies. The final meta-analysis included 12 studies[10-21]. Table 1 displays the characteristics of the included studies (Figure 1). There were 1177 patients (519 patients who received DEB-TACE and 658 patients who received cTACE), and all studies showed no statistically significant differences in age, sex ratio, Child-Pugh grade, tumor stage, or tumor characteristics between the two groups. Of the 12 studies, 7 were prospective, and the remaining 5 were retrospective. Three studies used epirubicin as a drug-carrying microsphere, and four studies used doxubicin.

Meta-analysis results

Postoperative CR rate: We conducted a comparative study on the CR rate based on mRECIST criteria one month after surgery. Eleven studies[10-20] reported the number of CR patients, and there was no significant heterogeneity among the studies. A fixed-effects model was used for analysis. The results of the meta-analysis showed that, compared with that in the cTACE group, the postoperative CR rate in the DEB-TACE group was significantly greater (RR = 1.42, 95%CI: 1.18-1.72, $Z = 3.73$, $P = 0.0002$) (Figure 2A).

PR rate after surgery: One month after surgery, the PR rate was compared according to the mRECIST standard. Eleven studies[10-20] reported the number of PR patients, and there was no substantial heterogeneity among the investigations. The analysis was conducted using a fixed-effects model. There was no significant difference in the PR rate between the cTACE group and the DEB-TACE group (RR = 1.13, 95%CI: 0.97-1.30, $Z = 1.58$, $P = 0.12$) (Figure 2B).

Comparison of the SD rate after surgery: Based on the mRECIST standard eight studies[10-16,18] reported the number of SD patients, and there was no significant heterogeneity among the studies. An analysis was conducted using a fixed-effects model. The meta-analysis results indicated that there was no statistically significant disparity in the SD rate between the cTACE group and the DEB-TACE group (RR = 0.02, 95%CI: 0.64-1). The values for Z and P are 1.57 and 0.12, respectively, as shown in Figure 2C.

Comparison of the 6-month survival rate after surgery: Seven studies[12,13,16-18,20,21] reported 6-month postoperative survival rates, with no significant heterogeneity among the studies. Fixed-effect response model analysis was used. The results of the meta-analysis showed that there was no significant difference in the 6-month survival rate between the

Table 1 Basic features included in the study, mean ± SD

Ref.	Cases		Average age (years)		Gender (male/female)		Tumor size (mm)		Child-Pugh grading (A/B)		Newcastle-Ottawa Scale
	DEB-TACE	cTACE	DEB-TACE	cTACE	DEB-TACE	cTACE	DEB-TACE	cTACE	DEB-TACE	cTACE	
Chen *et al*[10]	22	20	N/A	N/A	19/3	17/3	N/A	N/A	15/7	17/3	6
Chi *et al*[11]	50	50	60.3 ± 12.3		35/15	40/10	42.5 ± 12.3	43.2 ± 11.8	35/15	40/10	8
Ferrer Puchol *et al*[12]	47	25	59.84 ± 11.216	60.01 ± 12.79	34/13	18/7	61.5 ± 38.4	60.4 ± 39.6	30/17	17/8	7
Huang *et al*[13]	30	30	59.2 ± 6.3	58.3 ± 6.4	18/12	20/10					6
Lammer *et al*[14]	93	108	67.3 ± 9.1	67.4 ± 8.8	79/14	95/13	88.9 ± 52.1	89.2 ± 59.3	77/16	89/19	9
Lencioni *et al*[15]	32	188	67.1 ± 10.56		18/14	100/88	67.2 ± 34.2	65.7 ± 33.6	17/15	100/88	8
Malagari *et al*[16]	41	43	70.7 ± 6.9	70.0 ± 7.9	31/10	34/9	83.5 ± 27.5	81.0 ± 28.0	23/18	26/17	7
Sacco *et al*[17]	33	34	70.0 ± 7.7		20/13	21/13	63.1 ± 32.5	60.8 ± 31.1	20/13	22/12	9
Song *et al*[18]	60	69	61.7 ± 9.8	59.4 ± 11.2	42/18	51/18	42.0 ± 28.0	50.0 ± 31.0	56/4	62/6	7
Wiggermann *et al*[19]	22	22	69.02+8.1		18/4	19/3	74.4 ± 33.7	69.8 ± 38.1	22/0	22/0	8
You *et al*[20]	44	43	65	63	30/14	26/17	N/A	N/A	24/20	24/19	8
Dhanasekaran *et al*[21]	45	26	59.96 ± 11.45	58.96 ± 13.30	35/10	19/7	60.7 ± 45.2	54.9 ± 42.9	28/17	15/11	8

DEB-TACE: Drug-luting beads-transhepatic arterial chemoembolization; cTACE: Conventional transhepatic arterial chemoembolization.

cTACE group and the DEB-TACE group (RR = 1.05, 95%CI: 1.00-1.10, Z = 1.81, P = 0.07) (Figure 2D).

Comparison of the 12-month survival rate after surgery: Eight studies[12,13,16-21] reported the survival rate at 12 months after surgery, and there was no significant heterogeneity among the studies. A fixed-effects model was used for analysis. The meta-analysis revealed that the 12-month survival rate was significantly greater in the DEB-TACE group than in the cTACE group (RR = 1.99, 95%CI: 1.01-1.17; Z = 2.11; P = 0.03) (Figure 2E).

Subgroup analysis was performed based on Barcelona clinic liver cancer (BCLC) stage, Child-Pugh grade, and drug delivery status to further evaluate 12-month survival. First, subgroup meta-analyses were performed for the DEB-TACE group and the cTACE group according to BCLC stage, and the results are shown in the table. For HCC patients with BCLC stage A and BCLC stage B disease, the 12-month survival rate was significantly greater in the DEB-TACE group than in the cTACE group (RR = 1.29, 1.42, 95%CI = 1.03-1.61, 1.07-1. Overall, the 12-month survival rate of patients in the DEB-TACE group was significantly greater than that of patients in the cTACE group (RR = 1.18, 95%CI: 1.08-1.29, P = 0.02). Second, a subgroup meta-analysis was conducted between the DEB-TACE group and the cTACE group according to the Child-Pugh classification. For people with Child-Pugh grade A or B liver cancer, there was no significant difference in the 12-month survival rate between the DEB-TACE group and the cTACE group (RR = 1.42). 1.25, 95%CI = 0.79-2.54. The 12-month survival rate of the DEB-TACE group was, however, considerably higher than that of the cTACE group when the two groups were merged (RR = 1.16, 95%CI: 1.06-1.27). Patients in the DEB-TACE group had a significantly higher 12-month survival rate than those in the cTACE group when doxorubicin was administered (RR = 1.15, 95%CI: 1.03–1.28, P = 0.03). Patient in the cTACE group and those in the DEB-TACE group who received epirubicin had different 12-month survival rates. The storage rate did not differ significantly (RR = 1.07, 95%CI: 0.94-1.22, P = 0.06). Overall, the DEB-TACE group's 12-month survival rate was much higher than the cTACE group's (RR = 1.13, 95%CI: 1.01-1.25; P = 0.03). Based on the above subgroup analysis results, the 12-month survival rate of the DEB-TACE group was greater than that of the cTACE group.

Bias risk assessment: A funnel plot was used to observe the bias risk of the five included studies, and the results showed that the risk of bias on the left and right sides of the five groups of images was basically symmetrical (Figure 3). The NOS scores of 12 studies ranged from 6 to 9, indicating that the results of the meta-analysis had good authenticity, so the conclusions were relatively reliable.

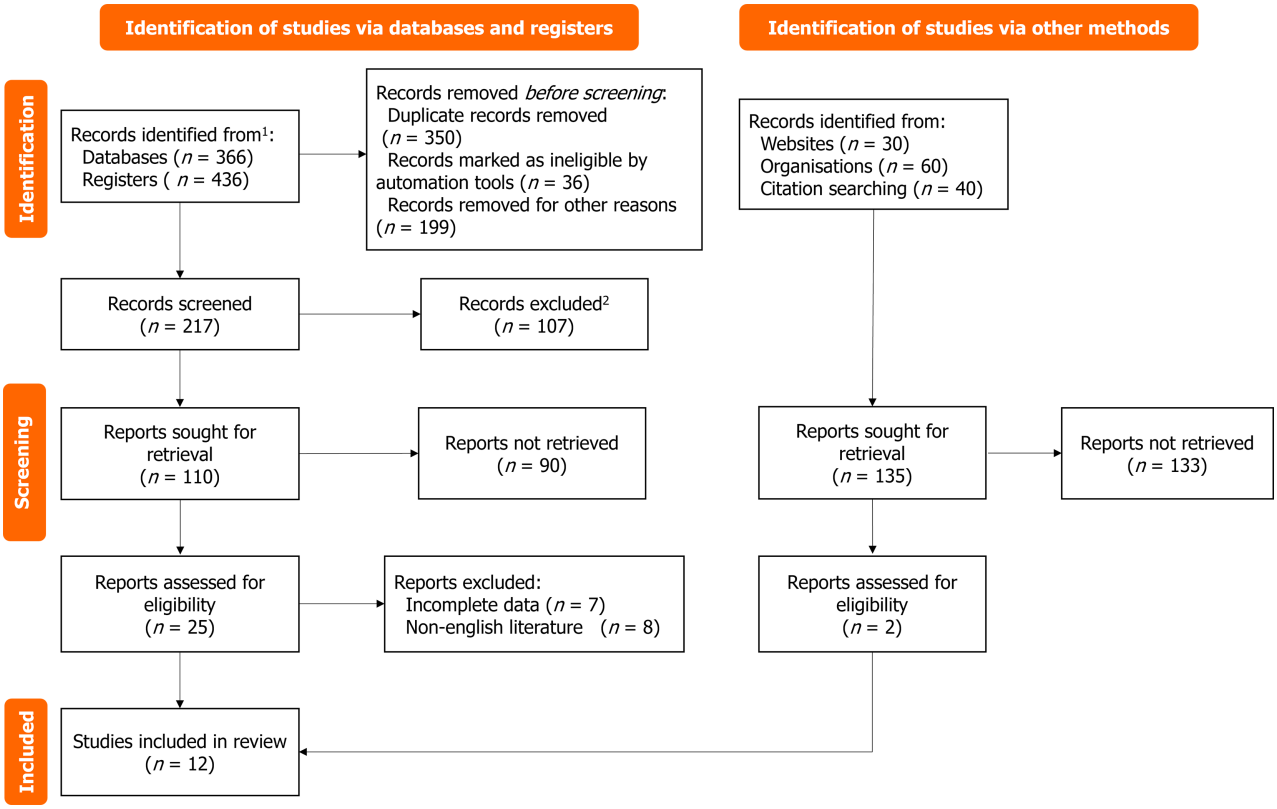


Figure 1 Document screening flow chart. [1]Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers). [2]If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

DISCUSSION

TACE has been used as a standard treatment for patients with unresectable liver cancer. The fundamental idea behind TACE is that the combination of intra-arterial chemotherapy with iodide and chemotherapy drugs, along with selective vascular embolization, produces a potent cytotoxic effect and ischemia, leading to a favorable therapeutic outcome and a high survival rate[22-24]. In recent years, developers have developed DEB-TACE to deliver higher doses of chemotherapeutic agents and extend the contact time with tumors, ensuring controlled and sustained release[25]. Compared with those of regular cTACE, the amount of drug needed to reach the systemic circulation of doxorubicin-loaded microspheres treated with DEB-TACE greatly decreased[26]. They also greatly decreased adverse events related to the drug[27-29]. There was no significant difference in the PR rate, SD rate, or 6-month survival rate between the two groups.

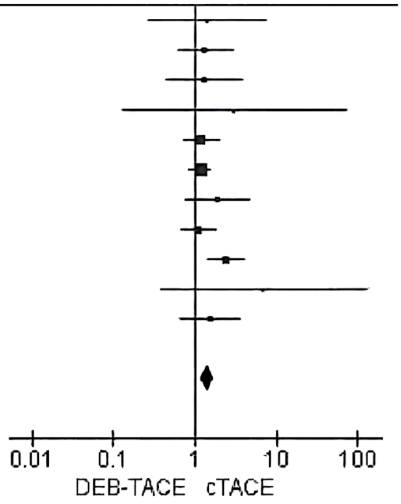
In this meta-analysis, the postoperative CR rate in the DEB-TACE group was significantly greater than that in the cTACE group, which was consistent with the results of one meta-analysis and four retrospective studies. Therefore, DEB-TACE may be an effective treatment for HCC[30]. The pharmacokinetic properties of DEB-TACE, which permits higher doses of chemotherapeutic agents and extended contact time with cancer cells, may account for this difference[31-33]. Malagari *et al*[16] reported that there was more tumor necrosis 7–14 days after DEB-TACE treatment, and during this period, the proportion of damaged and necrotic cells was close to 100%, and the plasma amycin concentration was the lowest. These findings suggest that DEB-TACE is a more effective surgical procedure than cTACE.

In addition, DEB-TACE was superior to cTACE in terms of treatment response and tumor progression[34]. Recently, a meta-analysis revealed three previous studies comparing the efficacy of DEB-TACE and cTACE for the treatment of HCC. In terms of the number of included studies[35-37], the meta-analysis of Gao *et al*[3] included 7 studies, including 693 patients. In contrast, this meta-analysis included a larger number of studies and patients (12 studies, 1177 patients). Previous meta-analyses, based on the quality of the included studies, used the NOS, Egger, and Beger tests for risk assessment, whereas this meta-analysis employed the NOS scale for the same purpose. Previous meta-analyses revealed that patients who underwent DEB-TACE had better 1-year and 2-year survival rates than those who underwent cTACE, while the 6-month and 3-year survival rates were similar. In contrast, this meta-analysis revealed that 12-month survival was significantly greater in the DEB-TACE group than in the cTACE group. A meta-subgroup analysis of the 12-month survival rate after a randomized controlled trial. The results showed that the 1- and 2-year survival rates of the DEB-TTACE group were significantly greater than those of the cTACE group in the randomized controlled trial, but there was no significant difference in the 3-year survival rate after surgery[38]. Several studies[39,40] have shown that the Child-Pugh grade, BCLC stage, Eastern Cooperative Oncology Group score, and serum bilirubin level are associated with survival. Song *et al*'s study showed that in patients with mid-stage HCC, the 1-year survival rate in the DEB-TACE group was significantly greater than that in the cTACE group, while in patients with early-stage HCC, there was no significant

A

Study or subgroup	DEB-TACE Events	DEB-TACE Total	cTACE Events	cTACE Total	Weight	Risk ratio M-H, fixed, 95%CI
Chen 2017	3	17	2	16	1.7%	1.41 [0.27, 7.38]
Chi 2018	12	50	9	50	7.4%	1.33 [0.62, 2.88]
Ferrer 2011	10	47	4	25	4.3%	1.33 [0.46, 3.81]
Huang 2018	1	30	0	30	0.4%	3.00 [0.13, 70.83]
Lammer 2010	25	93	24	108	18.4%	1.21 [0.74, 1.97]
Lencioni 2009	29	52	77	160	31.3%	1.16 [0.87, 1.55]
Malagari 2010	11	41	6	43	4.8%	1.92 [0.78, 4.72]
Sacco 2011	17	33	16	34	13.0%	1.09 [0.67, 1.78]
Song 2012	33	60	16	69	12.3%	2.37 [1.46, 3.86]
Wiggermann 2011	3	22	0	22	0.4%	7.00 [0.38, 128.02]
You 2017	11	44	7	43	5.9%	1.54 [0.66, 3.59]
Total (95% CI)		**489**		**600**	**100.0%**	**1.42 [1.18, 1.72]**
Total events	155		161			

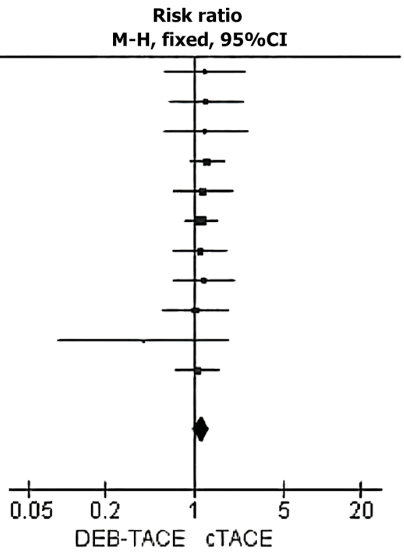
Heterogeneity: Chi² = 9.59, df = 10 (P = 0.48); I² = 0%
Test for overall effect: Z = 3.73 (P = 0.0002)



B

Study or subgroup	DEB-TACE Events	DEB-TACE Total	cTACE Events	cTACE Total	Weight	Risk ratio M-H, fixed, 95%CI
Chen 2017	9	17	7	16	3.9%	1.21 [0.59, 2.47]
Chi 2018	15	50	12	50	6.5%	1.25 [0.65, 2.39]
Ferrer 2011	16	47	7	25	5.0%	1.22 [0.58, 2.56]
Huang 2018	25	30	20	30	10.9%	1.25 [0.93, 1.69]
Lammer 2010	23	93	23	108	11.6%	1.16 [0.70, 1.93]
Lencioni 2009	28	50	80	162	20.5%	1.13 [0.85, 1.52]
Malagari 2010	19	41	18	43	9.6%	1.11 [0.68, 1.79]
Sacco 2011	16	33	14	34	7.5%	1.18 [0.69, 2.01]
Song 2012	16	60	18	69	9.1%	1.02 [0.57, 1.82]
Wiggermann 2011	2	22	5	22	2.7%	0.40 [0.09, 1.85]
You 2017	25	44	23	43	12.7%	1.06 [0.73, 1.55]
Total (95% CI)		**487**		**602**	**100.0%**	**1.13 [0.97, 1.30]**
Total events	194		227			

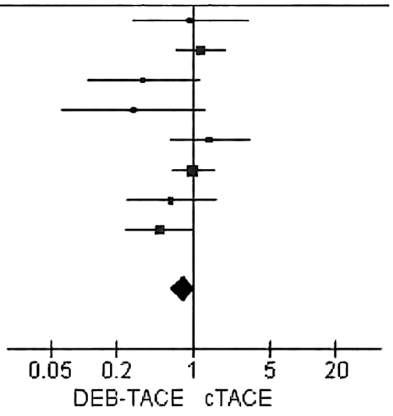
Heterogeneity: Chi² = 2.65, df = 10 (P = 0.99); I² = 0%
Test for overall effect: Z = 1.58 (P = 0.12)



C

Study or subgroup	DEB-TACE Events	DEB-TACE Total	cTACE Events	cTACE Total	Weight	Risk ratio M-H, fixed, 95%CI
Chen 2017	4	17	4	16	4.3%	0.94 [0.28, 3.14]
Chi 2018	20	50	17	50	17.9%	1.18 [0.70, 1.97]
Ferrer 2011	4	47	6	25	8.3%	0.35 [0.11, 1.14]
Huang 2018	2	30	7	30	7.4%	0.29 [0.06, 1.26]
Lammer 2010	11	93	9	108	8.8%	1.42 [0.62, 3.28]
Lencioni 2009	12	24	94	188	22.4%	1.00 [0.65, 1.53]
Malagari 2010	6	41	10	43	10.3%	0.63 [0.25, 1.57]
Song 2012	9	60	21	69	20.6%	0.49 [0.24, 0.99]
Total (95% CI)		**362**		**529**	**100.0%**	**0.82 [0.64, 1.05]**
Total events	68		168			

Heterogeneity: Chi² = 10.72, df = 7 (P = 0.15); I² = 35%
Test for overall effect: Z = 1.57 (P = 0.12)



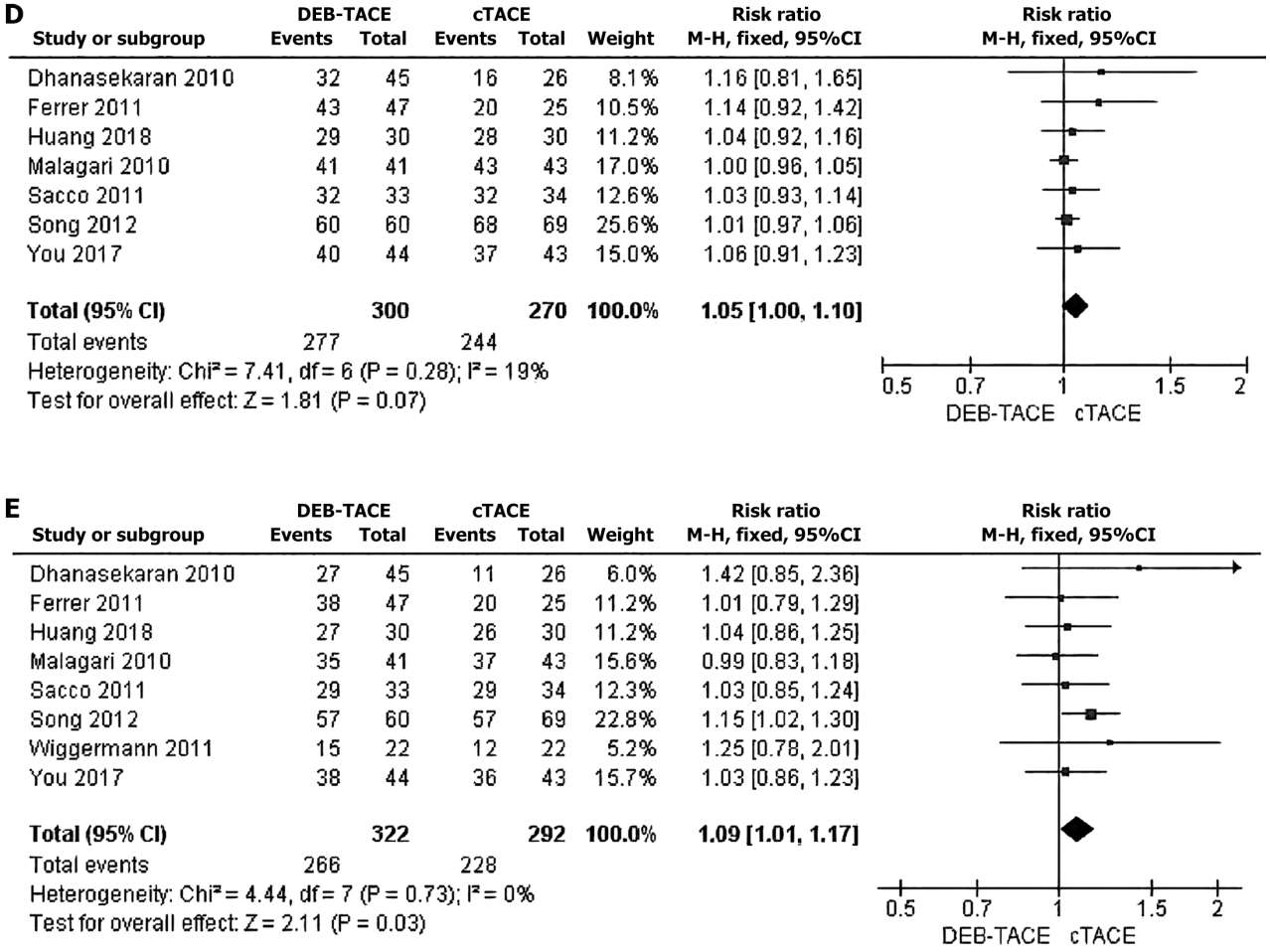


Figure 2 Meta-analysis. A-C: Meta-analysis of postoperative complete response between drug-luting beads-transhepatic arterial chemoembolization (DEB-TACE) and conventional transhepatic arterial chemoembolization (cTACE); D: A meta-analysis of 6-month survival rates between DEB-TACE and cTACE; E: A meta-analysis of 12-month survival after DEB-TACE and cTACE. DEB-TACE: Drug-luting beads-transhepatic arterial chemoembolization; cTACE: Conventional transhepatic arterial chemoembolization.

difference in the survival rate between the two groups[18]. Similarly, Dhanasekaran *et al*[21] reported that among HCC patients with BCLC stage A and BCLC stage B disease, the 1-year survival rate was significantly greater in the DEB-TACE group than in the cTACE group. The results of these two studies were similar to those of this meta-subgroup analysis. Compared with that of patients with early-stage liver cancer, overall survival between the DEB-TACE group and the cTACE group was significantly different only for patients with early-stage liver cancer. Therefore, this paper conducted a subgroup analysis of the 12-month postoperative survival rate according to BCLC stage, Child-Pugh grade, and drugs in drug-loaded microcapsules, resulting in a more substantial and reliable meta-analysis. It is concluded that DEB-TACE is more advantageous for the treatment of HCC.

The limitations of this study include the following: (1) There were fewer studies than DEB-TACE and cTACE, and most of the clinical studies were retrospective studies, suggesting that unmeasured confounding factors and selection bias may have affected the results of these studies; (2) The number of participants is limited, and a large number of samples will increase the accuracy of the results; (3) Heterogeneity of baseline characteristics, such as age, Child-Pugh grade, and tumor diameter, may cause potential bias; (4) Inclusion criteria vary from study to study and may lead to different results; (5) In the selected studies, there were no comprehensive criteria for type, dose, and drug-carrying microsphere size, which may affect the accuracy of the results; and (6) Some studies used the European Society of Hepatology criteria or computed tomography to assess tumor response, which may not take into account the microstructure of necrosis.

CONCLUSION

This meta-analysis compared the efficacy of drug-loaded microspheres and traditional iodized oil in treating unresectable liver cancer *via* hepatic arterial chemoembolization. The results showed that the drug-loaded microsphere treatment had a significant advantage in terms of efficacy, and compared with those in the traditional iodized oil group, the tumor shrinkage rate was greater, survival was significantly longer, and side effects were fewer. Further analysis showed that drug-loaded microspheres had a better local tumor control effect, could release drugs more effectively, reduced damage

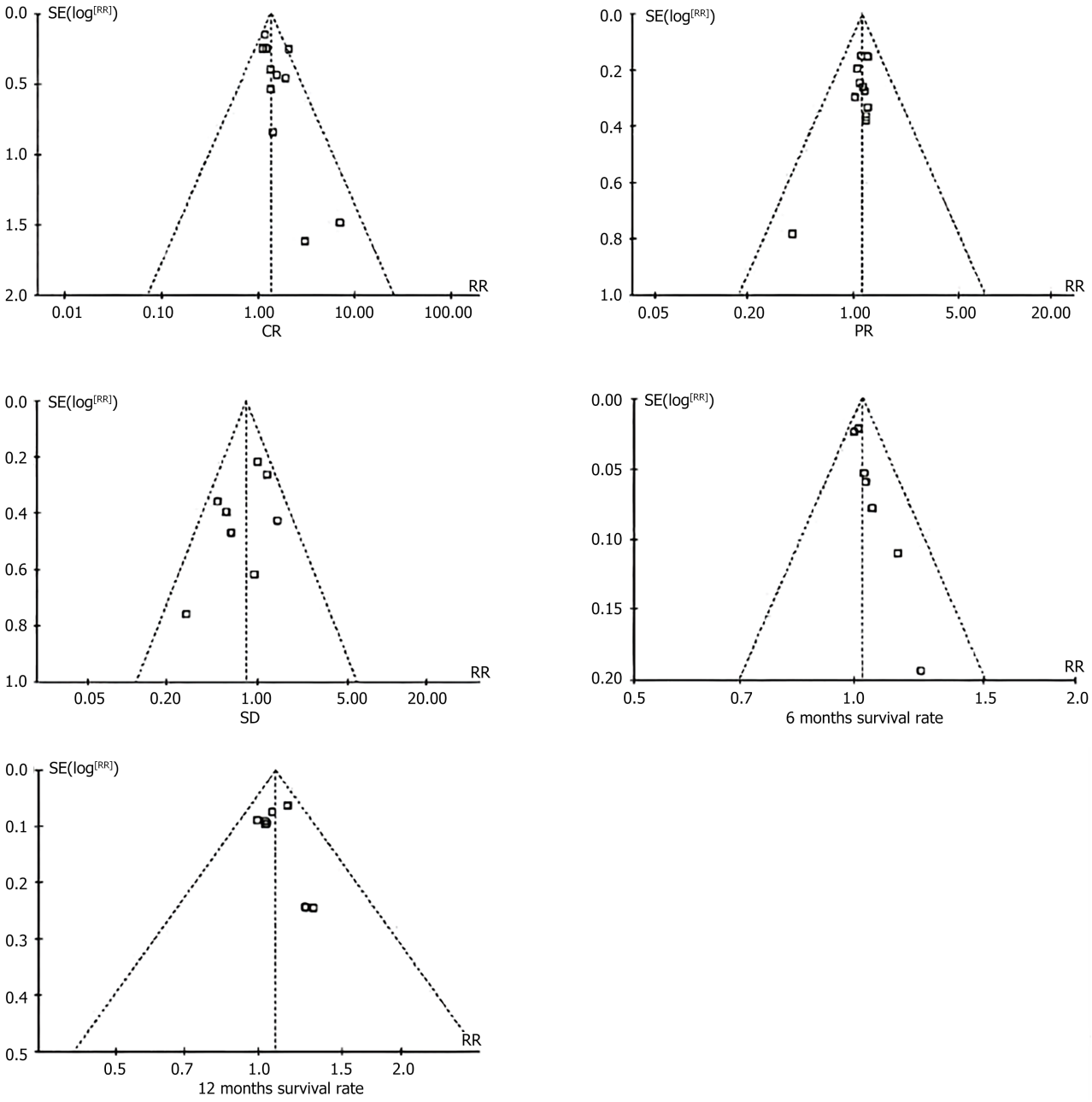


Figure 3 Funnel plot incorporating the results of the study. CR: Complete response rate; PR: Partial response rate; SD: Stable disease.

to normal liver tissue, and improved the safety and tolerability of treatment. Therefore, our results support the idea of using drug-loaded microspheres for hepatic arterial chemoembolization in people with liver cancer that cannot be removed. This should be a better and safer way to treat cancer and provide doctors with important information for their work.

FOOTNOTES

Author contributions: Deng J wrote the manuscript; Mi YH, Xie L, Sun XX, Liu DH, Long HJ and He LY collected the data; Wu DH and Shang HC guided the study; All authors reviewed, edited, and approved the final manuscript and revised it critically for important intellectual content, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

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Country of origin: China

ORCID number: Da-Hua Wu 0000-0002-0943-0037; Hong-Cai Shang 0009-0008-1576-5790.

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