Original Article

Evolution of transarterial chemoembolization-related liver abscess over time: a systematic review and meta-analysis

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Background: Transarterial chemoembolization (TACE) is a primary method for treating malignant liver tumors; however, the occurrence of liver abscesses after TACE has always been a concern. With the evolution of time, TACE techniques and practical experience continue to advance, leading to a deeper understanding of post-TACE liver abscesses. This meta-analysis aimed to comprehensively examine the occurrence of liver abscesses after TACE and focus on its changing trends.

Methods: Two researchers reviewed the databases of PubMed, Embase, and Web of Science to identify articles that reported liver abscess formation after TACE in patients with hepatic malignant tumor. The search was conducted from the date of establishment of each database up to January 2023. After screening the articles and extracting the data, we used Review Manager 5.3 and Stata 16.0 for analysis and processing.

Results: This meta-analysis included a total of 32 studies, comprising 254,408 TACE patients, of whom 642 developed liver abscesses after TACE. The pooled incidence rate of liver abscess formation after TACE was 0.54%. The heterogeneity was considerable and significant. Subgroup analysis revealed a significant impact of the evolution of time on the incidence of liver abscess formation after TACE. The incidence was shown to have decreased from 0.61% in the initial 5 years to 0.47% in the most recent 5 years, with statistical significance. Liver metastasis and type 2 biliary abnormality were significantly associated with the development of liver abscess. Mortality directly associated with liver abscess was 7.73% and was gradually decreasing, from over 50% in the 1990s to 5.48% in the past decade, with a statistically significant difference.

Conclusions: The formation of liver abscess was a relatively low-incidence complication following TACE for malignant liver tumors, with clearly defined risk factors. Moreover, both the incidence and mortality rates of liver abscess were gradually decreasing. These findings provide valuable insights for future clinical practice.

Keywords: Liver abscess; transarterial chemoembolization (TACE); malignant liver tumors; meta-analysis

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Introduction

Transarterial chemoembolization (TACE) is an effective method for the treatment of unresectable malignant liver tumors (1,2). Although this treatment modality is a minimally invasive procedure, it can sometimes lead to serious complications including liver abscess formation that may prolong hospital stay, delay tumor treatment, and even lead to death from severe infection (3-5).

Numerous studies have been conducted on the formation of liver abscesses after TACE, covering aspects such as incidence rates, risk factors, and clinical symptoms (6-11). However, to date, there is still a lack of a comprehensive review and synthesis of these studies. Simultaneously, with the passage of time, the continual maturation of TACE techniques and the accumulation of practical experience may lead to significant variations in the incidence and mortality rates associated with liver abscess formation at different points in time. Prompted by the above issues, we conducted a systematic review and meta-analysis to comprehensively examine the occurrence of liver abscesses after TACE and focus on its changing trends. We present this article in accordance with the PRISMA reporting checklist (12) (available at https://qims.amegroups.com/article/view/10.21037/qims-24-1166/rc) and the guidelines of the Cochrane Handbook for Systematic Reviews of Intervention (13).

Methods

Literature search

Two researchers reviewed the databases of PubMed, Embase, and Web of Science to identify articles regarding liver abscess formation after TACE in patients with hepatic malignant tumors. We included articles from the time each database was established up to January 2023, using combinations of the following keywords: "hepatocellular carcinoma", "liver tumor", "transarterial chemoembolization", "drug-eluting bead transarterial chemoembolization", "conventional transarterial chemoembolization", "liver abscess", "hepatic abscess", "pyogenic liver abscess", "complications", "side effects", and "adverse effects".

Two authors independently reviewed the articles based on the inclusion and exclusion criteria listed below. Any differences in opinion regarding whether to include an article were resolved by discussion with the third author, who made the final decision. Finally, the references of the selected studies were screened to identify any other potentially relevant studies for inclusion.

Selection of studies

The inclusion criteria for the studies were as follows: (I) a minimum of 50 patients with TACE were included; (II) the number of cases of liver abscess in patients with TACE was stated; (III) studies were in English. We used the following exclusion criteria: (I) TACE was combined with other therapies; (II) TACE was performed in specific subgroup; (III) duplicate studies.

Extraction of data

The data from each included study were independently extracted and entered in standardized Microsoft Excel (Microsoft, Redmond, WA, USA) sheets by two authors. The same authors examined the data, and consensus was reached for any discrepancy by reviewing the study. The following information was extracted from each article: characteristics of the study (year, authors, place, study design, setting); assessment of liver abscess formation after TACE (number of liver abscess cases and clinical features).

Quality assessment

Two researchers independently evaluated the risk of bias in the included studies using the Joanna Briggs Institute's Critical Appraisal Checklist for Prevalence Studies (14). This checklist consists of nine items, and for each item, the study received a "yes", "no", or "not applicable". Each "yes" was assigned one point. We defined the following ranges to classify the overall quality of the research qualitatively: 0–3= poor quality; 4–6= fair quality; and 7–9= high quality. Any disagreements were resolved by discussion or through consultation with the third author.

Aim

Our aim was to comprehensively examine the formation of liver abscess after TACE for malignant liver tumors, and we first calculated its incidence rate. For detailed analysis, subgroup analyses were performed using study period, study place, study quality, study design, sample size, and TACE method. We further analyzed the factors related to liver abscess formation after TACE. By including the analyzable data from the studies, we examined factors including male

sex, liver metastasis, type 2 biliary abnormalities, and antibiotic use, which were represented as the odds ratios (ORs). Our study also included the mortality directly associated with liver abscess (liver abscess of the leading causes of death mainly included sepsis and hepatic failure), and analyzed its temporal trends by subgroup analysis.

Relevant definitions

Liver metastasis was defined as the spread of cancer from a primary tumor to the liver. In the studies included in the analysis, the primary tumor types were clearly identified, and these mainly included: colorectal cancer, gastric cancer, pancreatic cancer, esophageal cancer, lung cancer, breast cancer, and neuroendocrine tumors (15-18).

Biliary abnormalities were divided into two types. A type 1 biliary abnormality was defined as a simple biliary abnormality, such as biliary invasion of hepatocellular carcinoma (HCC), biliary stricture, extrinsic compression of the bile duct, or common bile duct stone, without complications on imaging studies, including computed tomography, magnetic resonance imaging, and cholangiography. A type 2 biliary abnormality was defined as a condition prone to ascending biliary infection and included bilioenteric anastomosis, endoscopic papillotomy, percutaneous transhepatic biliary drainage, and T-tube choledochostomy (11).

Statistical analysis

Considering the expected heterogeneity in effect sizes, a pooled estimate of the incidence of liver abscess formation after TACE in patients was performed using a random-effects model based on the method described by DerSimonian and Laird (19). For a study in which no case of liver abscess was detected, a correction of 0.05 was added to allow estimation of the incidence (20). The statistical heterogeneity among the included studies was assessed using the chi-square test, and degrees of heterogeneity were quantified using the I^2 statistic, assuming that $P \leq 0.10$ and $I^2 \geq 50\%$ indicate significant and substantial heterogeneity (21). The pooled estimates were calculated as ORs for dichotomous data and mean differences for continuous data; 95% confidence intervals (CIs) were calculated for effect estimates. The robustness of the pooled estimates was assessed by a leave-one-out sensitivity analysis. Egger's weighted regression was used to confirm publication bias (22). All analyses were performed with the software program RevMan 5.3 (Cochrane, London, UK) and Stata 16.0 software (StataCorp. LLC, College Station, TX, USA).

Results

Study selection and characteristics

The initial search retrieved 2,012 studies in PubMed, 1,176 studies in Embase, and 976 studies in Web of Science. After removal of duplicate studies and review of the abstracts and full texts, 32 studies met the inclusion criteria. *Figure 1* presents a flowchart of study identification and selection. Study characteristics are shown in *Table 1*.

Quality assessment

A total of 17 studies were evaluated as high quality (3-5,10,11,15-18,24,26,27,29,30,32,35,39), 15 as fair quality (6-9,23,25,28,31,33,34,36-38,40,41), and no studies as poor quality (*Figure 2*, Figure S1).

The incidence of liver abscess formation after TACE

In the 32 selected studies, a total of 254,408 TACE patients were included, of whom 642 developed liver abscesses after TACE. Using the random-effects model, the pooled incidence rate of liver abscess formation after TACE was 0.54% (95% CI: 0.41–0.68%). The studies had high (I^2=89%) and significant (P<0.01) heterogeneity of incidence (*Figure 3*). Based on the sensitivity analysis results, none of the studies had an impact on the overall effect, indicating that our meta-analysis was statistically stable (Figure S2).

The incidence of liver abscess formation after TACE according to subgroup analyses

Table 2 shows the results of subgroup analyses. The incidence had decreased from 0.61% in the initial 5 years to 0.47% in the most recent 5 years, with statistical significance (P<0.01). There was also a significant difference in incidence of liver abscess formation in study quality (P<0.01) and sample size (P<0.01). However, there was no significant difference among the studies on the basis of the place of the study (P=0.77), the design of study (P=0.10), or the TACE method (P=0.18).

Related factors for liver abscess formation after TACE

As presented in *Table 3*, factors associated with liver abscess

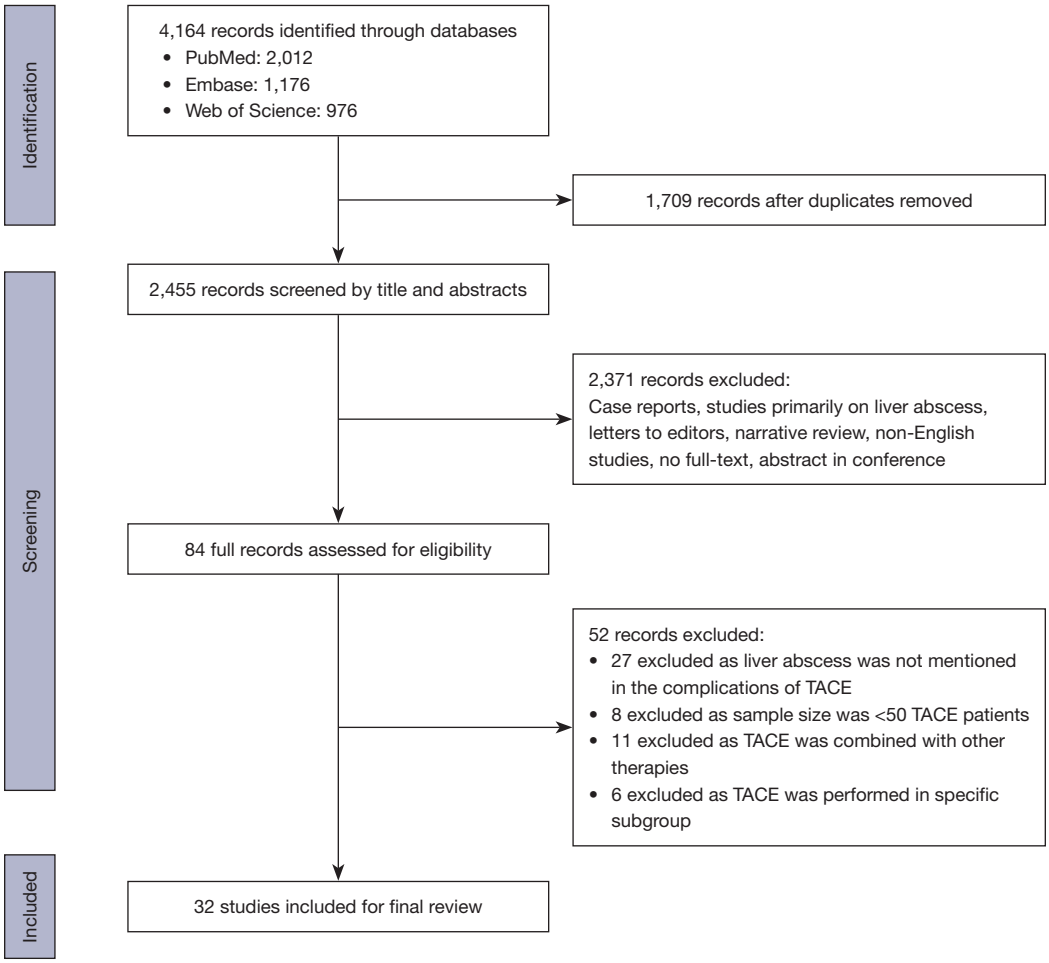

Figure 1 A schematic flowchart of the PRISMA Guidelines. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; TACE, transarterial chemoembolization.

formation after TACE include male sex, liver metastasis, type 2 biliary abnormality, and prophylactic use of antibiotics. There was insufficient comparable information to study other potential risk factors. Male sex (OR =0.71; 95% CI: 0.36–1.38; P=0.31) was not associated with an increased risk of liver abscess. Importantly, liver metastasis (OR =5.09; 95% CI: 2.35–11.01; P<0.01) and type 2 biliary abnormality (OR =133.69; 95% CI: 4.79–3,742.94; P<0.01) were significantly associated with the development of liver abscess. Prophylactic antibiotics (PA) (OR =0.39; 95% CI: 0.29–0.53; P<0.01) were found to be significantly associated with a reduced risk of liver abscess formation after TACE.

Mortality directly associated with liver abscess

In 10 studies, mortality directly associated with liver abscess was 7.73% (95% CI: 1.72–13.74%) (4,5,15,17,27,29,30,35,39,42) (*Figure 4A*). There was a significant difference in temporal trends (1991–2000: 50.49%; 2001–2010: 9.65%; 2011–2022: 5.48%, P<0.05) (*Figure 4B*).

Publication bias

The Egger's test and funnel plot showed significant publication bias for the incidence of liver abscess formation after TACE (P<0.05) (Figure S3). The "trim and fill" method was used for adjusting publication bias and showed potentially missing studies for this meta-analysis (Figure S4).

Discussion

To the best of our knowledge, this study is the first

Table 1 Study characteristics

Study	Year	Place	Design	Setting	No. of patients with TACE	No. of patients with LA after TACE	Patients with LA				
							Mean age (years)	Males (%)	DM (%)	Type 2 biliary abnormality (%)	Mortality (%)
Krieg *et al.* (23)	2022	Germany	Retrospective	Multicenter	49,595	126	NR	NR	NR	NR	NR
Yi *et al.* (6)	2022	South Korea	Retrospective	Single center	72.05	0.05	NA	NA	NA	NA	NA
Zhu *et al.* (24)	2022	China	Retrospective	Multicenter	11,524	84	55.2	74.3	NR	NR	10.7
Ye *et al.* (10)	2022	China	Retrospective	Single center	137	12	55	58.3	16.7	NR	NR
Duan *et al.* (25)	2021	China	Retrospective	Single center	71	1	NR	NR	NR	NR	NR
Yoshihara *et al.* (26)	2021	Japan	Retrospective	Multicenter	167,544	187	NR	NR	NR	NR	NR
Han *et al.* (27)	2020	China	Retrospective	Single center	2,221	35	NR	85.7	NR	NR	5.7
Wang *et al.* (28)	2020	China	Retrospective	Single center	60	2	NR	NR	NR	NR	NR
Arslan *et al.* (29)	2019	Turkey	Retrospective	Single center	163	4	63	25	50	50	25
Wang *et al.* (7)	2018	China	Retrospective	Single center	257.05	0.05	NA	NA	NA	NA	NA
Jia *et al.* (30)	2018	China	Retrospective	Multicenter	3,129	23	52.1	91.3	13	NR	2.1
Sun *et al.* (5)	2017	China	Retrospective	Single center	1,480	5	52	NR	60	40	20
Maruyama *et al.* (31)	2016	Japan	Retrospective	Single center	100	3	NR	NR	NR	NR	NR
Tu *et al.* (32)	2016	China	Retrospective	Single center	1,120	5	42.8	100	NR	NR	NR
Lv *et al.* (15)	2016	China	Retrospective	Single center	3,613	21	54.6	71.4	47.6	57.1	4.8
Shin *et al.* (11)	2014	South Korea	Retrospective	Single center	5,299	72	59.3	79.1	30.5	13.9	NR
Skowasch *et al.* (33)	2012	Germany	Retrospective	Single center	50	1	NR	NR	NR	NR	NR
Shelgikar *et al.* (8)	2009	United States	Prospective	Single center	59.05	0.05	NA	NA	NA	NA	NA
Xia *et al.* (34)	2006	China	Retrospective	Single center	1,348	3	NR	NR	NR	NR	NR
Huang *et al.* (35)	2003	China	Retrospective	Single center	1,347	7	65.7	85.7	NR	NR	7.1
Chan *et al.* (36)	2002	China	Prospective	Single center	59	1	NR	NR	NR	NR	NR
Kim *et al.* (16)	2001	United States	Retrospective	Single center	157	7	46.7	42.9	NR	85.7	NR
Song *et al.* (4)	2001	South Korea	Retrospective	Single center	2,439	14	61.4	78.6	NR	28.6	14.3
Tarazov *et al.* (18)	2000	Russia	Retrospective	Single center	282	6	52	60	NR	NR	NR
Gates *et al.* (37)	1999	United States	Retrospective	Single center	251	1	NR	NR	NR	NR	NR
Sakamoto *et al.* (38)	1998	Japan	Retrospective	Single center	850	5	NR	NR	NR	NR	NR
Chen *et al.* (39)	1997	China	Retrospective	Single center	289	5	68.4	80	20	20	40
de Baère *et al.* (17)	1996	France	Retrospective	Single center	181	3	48.3	33.3	NR	66.7	66.7
Farinati *et al.* (40)	1996	Italy	Retrospective	Single center	72	2	NR	NR	NR	NR	NR
Chung *et al.* (41)	1996	South Korea	Retrospective	Single center	351	1	NR	NR	NR	NR	NR
Castells *et al.* (9)	1995	Spain	Prospective	Single center	61.05	0.05	NA	NA	NA	NA	NA
Reed *et al.* (3)	1994	United States	Retrospective	Single center	227	6	58	16.7	NR	NR	NR

TACE, transarterial chemoembolization; LA, liver abscess; DM, diabetes mellitus; NR, not reported; NA, not applicable (no liver abscess occurred).

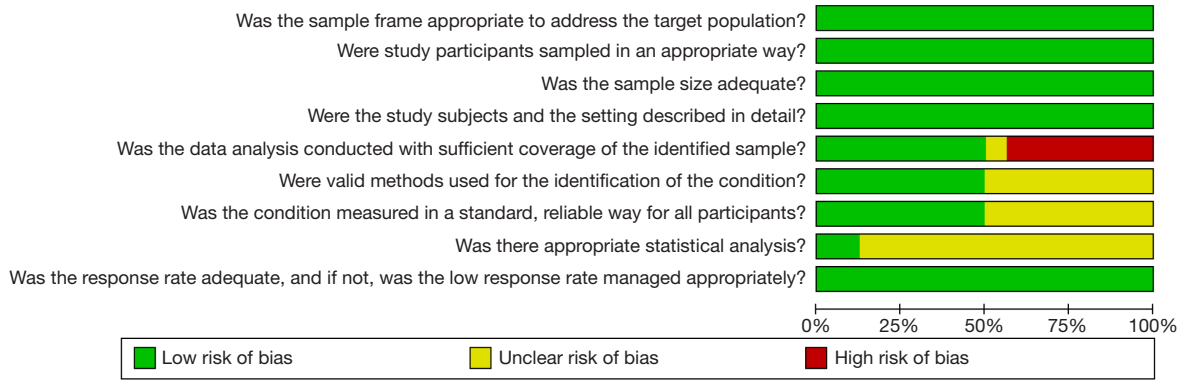

Figure 2 Quality assessment of the included studies (risk bias of graph). Risk bias of graph: judgements about each risk of bias item presented as percentages across all included studies.

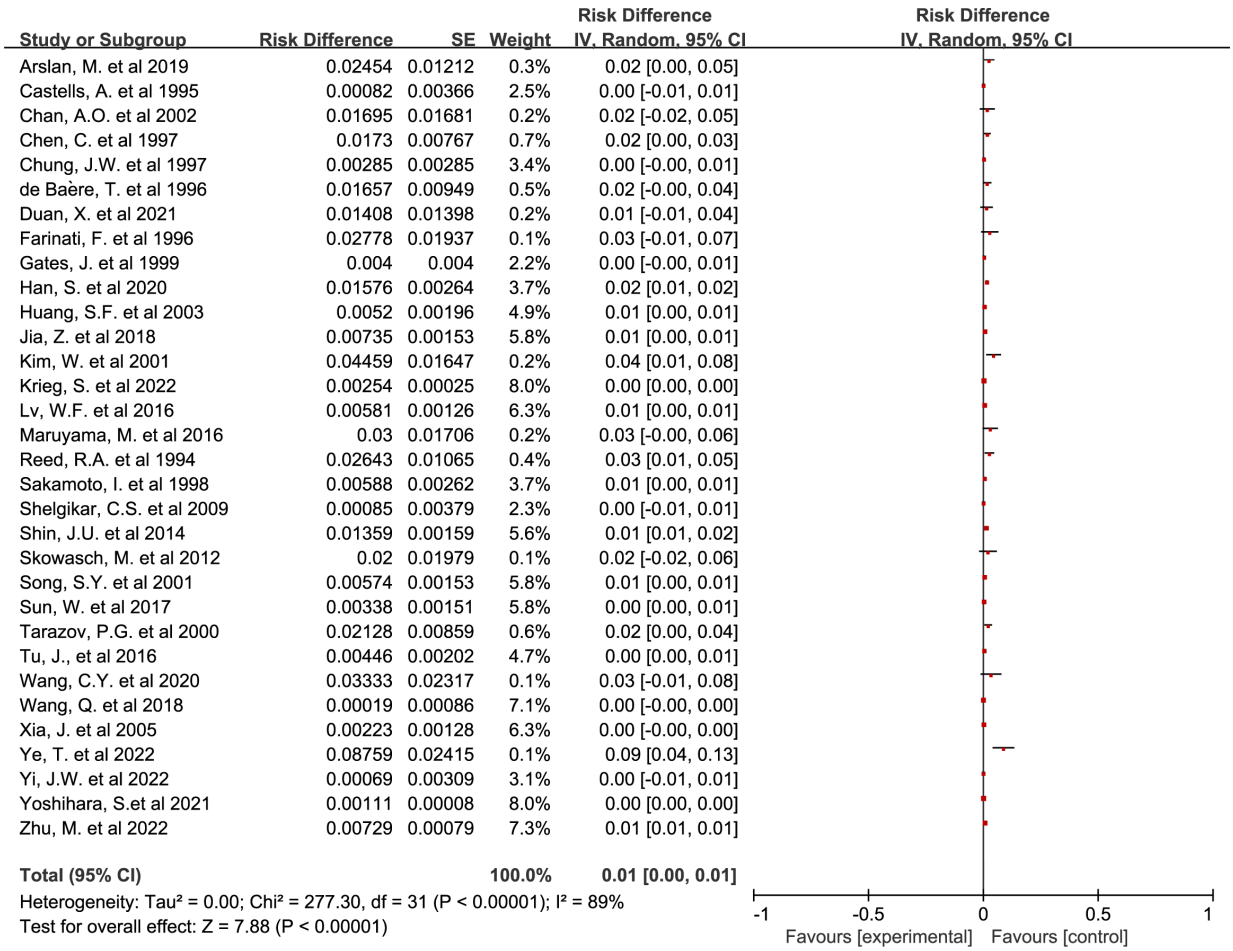

Figure 3 Pooled incidence rate of liver abscess formation after TACE was 0.54% (95% CI: 0.41–0.68%). There was high (I^2=89%) and significant (P<0.01) heterogeneity of incidence. CI, confidence interval; IV, inverse variance; SE, standard error; TACE, transarterial chemoembolization.

Table 2 The incidence of LA formation after TACE on subgroup analyses

Subgroup	No. of studies	Incidence of LA after TACE (%)	95% CI (%)	Heterogeneity		Difference (P)
				P value	I^2 (%)	
Study period						<0.01
1994–1998	7	0.61	0.11 to 1.10	0.15	36	
1999–2003	6	0.55	0.39 to 0.71	0.98	0	
2004–2007	1	0.22	−0.03 to 0.47	–	–	
2008–2012	2	0.15	−0.58 to 0.88	0.34	0	
2013–2017	5	0.72	0.27 to 1.17	<0.01	85	
2018–2022	11	0.47	0.03 to 0.64	<0.01	95	
Study place						0.77
China	14	0.62	0.36 to 0.88	<0.01	84	
Japan	3	0.37	−0.19 to 0.94	0.05	68	
South Korea	4	0.61	0.03 to 01.18	<0.01	87	
United States	4	1.14	−0.09 to 2.38	0.01	73	
Europe	7	0.84	0.16 to 1.52	0.04	54	
Study quality						<0.01
High quality	17	0.89	0.58 to 1.19	<0.01	93	
Fair quality	15	0.21	0.41 to 0.68	0.21	22	
Study design						0.10
Retrospective	29	0.56	0.43 to 0.70	<0.01	90	
Prospective	3	0.54	−0.39 to 0.63	<0.01	89	
Sample size						<0.01
50–100	9	0.29	−0.16 to 0.74	0.34	11	
101–200	4	4.13	1.75 to 6.51	0.12	49	
201–300	5	1.06	0.12 to 1.94	<0.01	77	
301–1,000	2	0.45	0.07 to 0.83	0.43	0	
1,001–2,000	4	0.32	0.18 to 0.50	0.58	0	
2,001–10,000	5	0.93	0.57 to 1.30	<0.01	85	
>10,000	3	0.34	0.15 to 0.53	<0.01	98	
TACE method						0.18
Deb-TACE	4	3.09	−0.55 to 6.73	<0.01	80	
C-TACE	19	0.61	0.38 to 0.84	<0.01	69	

CI, confidence interval; C-TACE, conventional transarterial chemoembolization; Deb-TACE, drug-eluting beads transarterial chemoembolization; LA, liver abscess; TACE, transarterial chemoembolization.

Table 3 Related factors for LA formation after TACE

Related factor	No. of studies	No. of patients with LA/No. of patients with TACE	Odds ratio	95% CI	P value
Male sex	6		0.71	0.36–1.38	0.31
LA/males		35/4,911			
LA/females		22/1,986			
LM	4		5.09	2.35–11.01	<0.01
LA/LM		28/1,175			
LA/HCC		9/3,058			
Type 2 biliary	2		133.93	4.79–3,742.94	<0.01
LA/type 2 biliary abnormality		10/40			
LA/non- type 2 biliary abnormality		11/2,556			
PA	4		0.39	0.29–0.53	<0.01
LA/PA		122/135,001			
LA/non-PA		72/32,899			

CI, confidence interval; HCC, hepatocellular carcinoma; LA, liver abscess; LM, liver metastasis; PA, prophylactic antibiotics; TACE, transarterial chemoembolization.

comprehensive meta-analysis to analyze the formation of liver abscesses after TACE. It includes 32 studies, spanning nearly 30 years and involving multiple countries. Our study revealed that the incidence of liver abscess formation after TACE was 0.54%, and through subgroup analysis, it was gradually decreasing. We believe that with the series of advances in TACE technology, including more precise tumor localization, more effective drug delivery systems, and more refined treatment plans (43); these contribute to reducing damage to normal liver tissue and, consequently, the formation of liver abscesses. Therefore, the incidence of liver abscesses after TACE had been decreasing in recent years. Subgroup analyses also showed that the incidence of liver abscess formation after TACE was lower among studies which were high quality and the difference was statistically significant. We speculated that these literatures studied a wide range of complications after TACE and were not limited to liver abscess, leading to an underestimation of the occurrence of liver abscess.

The mechanism of liver abscess formation after TACE is not yet fully understood and is quite complex. We propose the following hypothesis. The embolization of the hepatic artery during TACE causes localized ischemia and hypoxia in the liver. Additionally, chemotherapy-induced liver dysfunction leads to a decline in systemic immunity. When biliary abnormalities are present, intestinal bacteria can retrogradely enter the liver (44). Meanwhile, gastrointestinal and biliary tract bacteria can enter the venous plexus and, via the bloodstream, ascend to the liver (5). The ischemia and hypoxia caused by TACE create a favorable environment for bacterial growth, thereby increasing the risk of liver abscess formation.

During the process of TACE, the tumor's blood supply arteries are occluded, leading to localized ischemic necrosis. The hepatic arteries/small arteries supplying the bile ducts are likely to be embolized, resulting in ischemic necrosis of the bile ducts, thus predisposing patients to the translocation of bacteria from the colonized biliary tract into the liver parenchyma and into the bloodstream (45). In patients who undergo multiple TACE procedures, varying degrees of stenotic and occlusive disease caused by chemical vasculitis may prevent catheter access, leading to proximal artery embolization rather than tumor-feeding artery embolization. The infusion of an excessive dose of chemoembolic agents into non-tumoral liver parenchyma can cause ischemic damage to the bile ducts, potentially triggering the formation of liver abscess (45). Some high-risk embolization techniques may also increase the risk of liver abscess formation. For example, in the case of large tumors, choosing a higher embolization endpoint during TACE may lead to extensive tumor necrosis due to complete blood flow occlusion (46,47), thereby

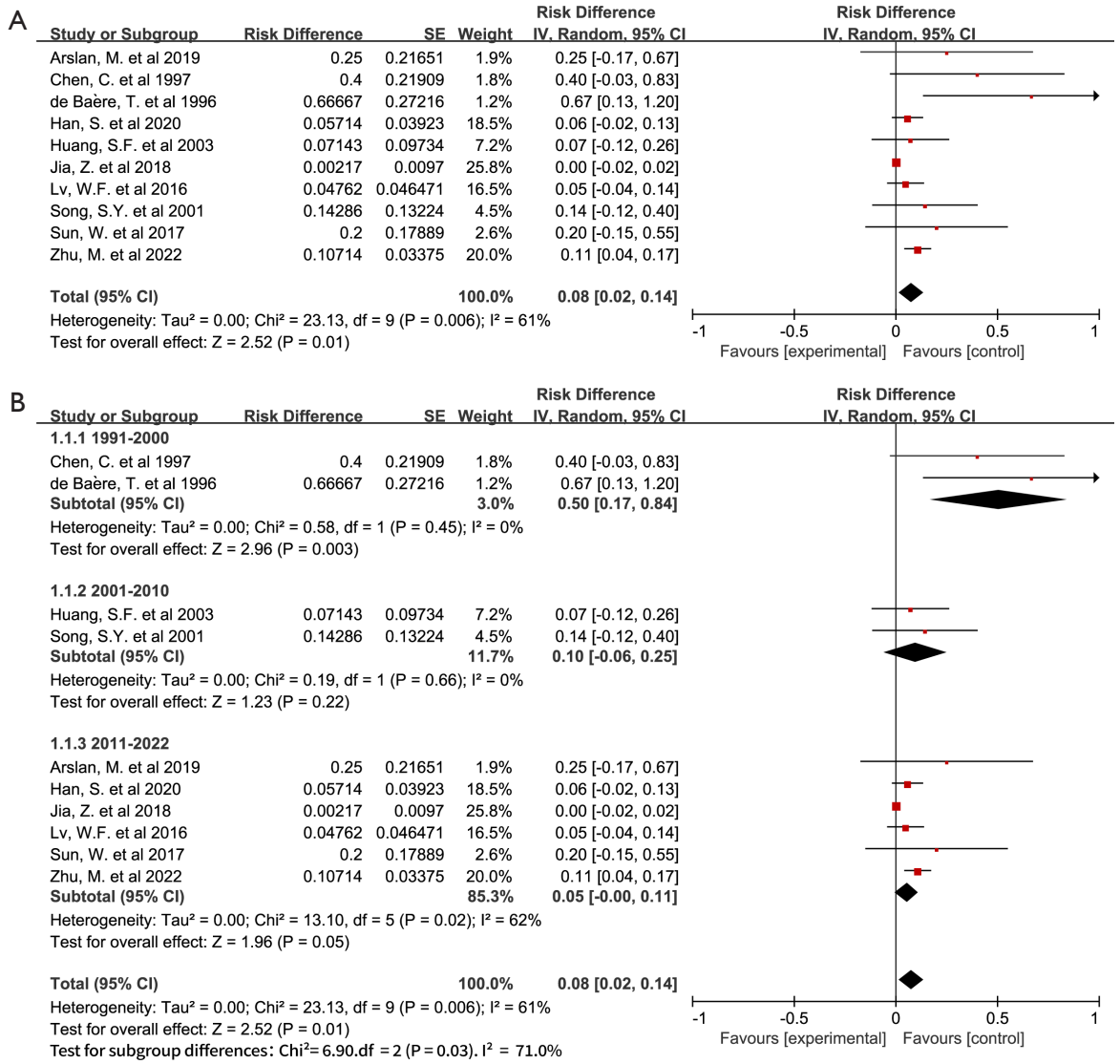

Figure 4 Mortality directly associated with liver abscess after tACE. (A) The mortality directly associated with liver abscess was 7.73% (95% CI: 1.72–13.74%). (B) There was a significant difference in temporal trends (1991–2000: 50.49%; 2001–2010: 9.65%; 2011–2022: 5.48%, P<0.05). CI, confidence interval; IV, inverse variance; SE, standard error.

elevating the likelihood of developing a liver abscess. Some researchers believe that combined hepatic arterial and portal vein embolization, as well as gelatin sponge particle embolization, may improve embolization efficacy, but it may also increase the risk of liver abscess formation (11,44). Therefore, the formation of liver abscess during TACE treatment can be triggered by multiple interacting factors.

We found a higher incidence of liver abscess formation after drug-eluting beads transarterial chemoembolization (Deb-TACE), although the difference was not statistically significant. The higher necrosis rate, greater pathophysiological inflammation responses and higher risk of biliary injury in drug-eluting beads may account for the higher incidence of liver abscess compared with conventional TACE (48-50). Another interesting finding was that the incidence of the disease was higher in Europe and America than in Asia, but the difference also was not statistically significant.

Our study showed that patients with liver metastases had a higher incidence of liver abscess formation after TACE and the difference was statistically significant.

Liver metastases differed from HCC in their blood supply characteristics and liver anatomy. TACE treatment induced local ischemia and necrosis by embolizing the arteries supplying the tumor; however, liver metastases primarily derived their blood supply from the portal venous system. This might have made TACE less effective for metastases compared to primary liver cancer, and the necrotic tissue post-embolization was more difficult to clear, providing an environment favorable for bacterial growth. Moreover, HCC predominantly occurred in cirrhotic livers, where the expansion of the perivascular plexus could compensate for reduced arterial flow by acting as a portal-arterial shunt, offering a certain protective effect (51). Additionally, patients with liver metastases often had compromised systemic immune function, particularly after multiple cycles of chemotherapy, radiotherapy, or immunosuppressive therapy, which reduced their ability to resist infections (38,52). Therefore, in the management of patients with liver metastases after TACE, close monitoring for liver abscess formation was essential, and infections had to be promptly addressed.

Some previous studies had hypothesized that type 2 biliary abnormality was a risk factor for liver abscess formation after TACE (4,11). Our results also supported this view, with the OR value reaching as high as 133.69. Type 2 biliary abnormality could have led to changes in biliary anatomy, potentially causing impaired bile drainage, biliary strictures, or the formation of conditions such as bilioenteric fistulas. These anatomical alterations make it easier for bacteria to retrogradely migrate from the intestines into the bile ducts and spread to the liver, leading to infection. After TACE, the ischemic and necrotic tumor tissue create an environment conducive to bacterial growth, thereby increasing the risk of infection (45,51,53). Additionally, type 2 biliary abnormality might have caused localized tissue damage and inflammation, further altering the immune environment of the liver and biliary system. For example, the function of liver Kupffer cells, biliary epithelial cells, and other immune cells might have been impaired, reducing the ability to clear microorganisms (54). Moreover, the associated inflammation, fibrosis, and changes in bile acid metabolism could have weakened the local immune barrier, all of which might have elevated the risk of liver abscess formation following TACE.

Some studies have reported diabetes mellitus as a potential risk factor for liver abscess formation after TACE (5,11). Diabetic patients often presented with hyperglycemia, which suppressed immune system function, impaired leukocyte phagocytosis and chemotaxis, and diminished the body's ability to combat infections (55). Additionally, hyperglycemia disrupted microcirculation, leading to reduced tissue perfusion and impaired wound healing, thus providing a favorable environment for bacterial growth (56). Consequently, diabetic patients were at a higher risk for bacterial infections and liver abscess formation following TACE.

Furthermore, large tumor size also increased the likelihood of liver abscess formation after TACE (11,16). Larger tumors typically required more extensive embolization, resulting in a broader area of tumor ischemia and necrosis. This extensive necrotic tissue provided ample opportunity and space for bacterial colonization and proliferation, heightening the risk of liver abscess development.

Portal vein thrombosis (PVT) is another potential risk factor for liver abscess formation after TACE (15,57). PVT alters hepatic hemodynamics and exacerbates liver tissue ischemia and necrosis, creating an environment conducive to bacterial colonization. Additionally, PVT promotes the translocation of intestinal bacteria to the liver, and the reduces collateral circulation via the hepatic artery, further increasing the likelihood of abscess formation (58).

Notably, in recent years, with the widespread use of immunotherapy, previous research has reported that immunotherapy could increase the incidence of liver abscess formation after TACE (59). During the immunotherapy process, specific surface proteins on T cells are activated to induce an immune response against tumor cells, thereby enhancing anti-tumor immunity (60). However, this T cell activation might disrupt the immune balance within the tumor microenvironment, leading to an enhanced immune response against liver tissue and potentially causing T cell-mediated liver injury. T cells interact with bacterial polysaccharides, stimulate cytokine release, and promote the recruitment of neutrophils to the site of infection (61). As a result, the process of T cell activation by immunotherapy could disturb immune homeostasis and increase the risk of liver abscess formation. Therefore, for patients with liver cancer undergoing TACE combined with immunotherapy, we should be aware of the potential risk of liver abscess formation and adopt more cautious treatment measures.

Although our study demonstrates that PA can reduce the incidence of liver abscess, the supporting data are primarily based on a large-sample retrospective analysis from Japan (26), which may introduce significant bias and should be interpreted with caution. Therefore, large-scale prospective studies are

needed in the future to explore the issue of prophylactic antibiotic use during TACE, particularly regarding its use in specific high-risk populations.

In the 1990s, liver abscess formation after TACE was identified as an extremely serious complication, with a mortality rate as high as 66.7% (17). However, according to a 2018 study, 23 patients with liver abscess formation after TACE all survived with good prognosis (30). Based on this difference, we examined the mortality and analyzed its temporal trends. The mortality of liver abscess formation after TACE was 7.73%, and the main causes of death included septic shock and acute liver failure (5,17,42). The mortality reached more than 50% in the 1990s, but dropped significantly to 9.65% between 2001 and 2010, and to 5.48% in the last decade, and the difference was statistically significant. We believe that advancements in imaging technologies, such as computed tomography and magnetic resonance imaging, have played a crucial role in improving the early detection of liver abscesses (62). These advanced imaging modalities allow for more accurate identification of lesions, facilitating timely intervention. Progress in blood and pus culture techniques has been instrumental in better understanding the causative agents of liver abscesses (63). Enhanced microbiological diagnostics contribute to targeted and effective antibiotic therapy, reducing the risk of complications and associated mortality. The continuous development of antibiotic therapies has improved the effectiveness of treating liver abscesses. The availability of broader-spectrum antibiotics with increased antimicrobial activity helps enhance treatment success rates. The refinement and widespread adoption of percutaneous drainage (PCD) techniques have revolutionized the management of liver abscesses. PCD allows for precise and minimally invasive drainage of abscess contents, leading to quicker symptom resolution and reduced mortality risk (64,65). The increased awareness and understanding of liver abscesses among healthcare professionals, including intervention in risk factors and early recognition of clinical symptoms, contribute to preventing disease progression. In summary, under the synergistic influence of these factors, the mortality rate associated with liver abscess formation after TACE for malignant liver tumors has significantly decreased. We believe that the future prognosis in this context will continue to improve.

There are several mentionable strengths in our study. Firstly, this is the first comprehensive meta-analysis to globally assess the formation of liver abscess after TACE. Secondly, we pooled the clear risk factors associated with the liver abscess formation after TACE, thereby narrowing the focus on relevant factors that could be recognized and addressed. Finally, we observed a decreasing trend in both the incidence and mortality of liver abscess formation after TACE.

However, our study also has some limitations. Firstly, this study includes two large sample studies, with 167,544 and 49,595 cases, respectively, accounting for a total of 85.3% of the overall sample. Such a high proportion may overly depend on these two studies, reducing the weight of small sample studies and potentially introducing bias, which could affect the generalizability and external validity of the conclusions.

Secondly, there was considerable (I^2=89%) and significant (P<0.01) heterogeneity among the incidences of liver abscess formation after TACE among the various studies. Thirdly, the finding of incidence needs to be interpreted with caution due to the relatively small number of prospective studies, which might present as a potential source of significant bias. Finally, we were unable to study other factors that might have acted as predisposing factors for liver abscess (e.g., size and number of tumor, embolism materials, and whether patients had diabetes) because of insufficient information.

Conclusions

The formation of liver abscess is a relatively low-incidence complication following TACE for malignant liver tumors, with clearly defined risk factors. Moreover, both the incidence and mortality rates of liver abscess are gradually decreasing. These findings provide valuable insights for future clinical practice.

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Footnote

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