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Editorial Board Member of *World Journal of Gastroenterology*, Takuya Watanabe, MD, PhD, Director, Department of Internal Medicine and Gastroenterology, Watanabe Internal Medicine Aoyama Clinic, Aoyama 1-2-21, Nishi-ku, Niigata 950-2002, Japan, nabetaku@dia-net.ne.jp

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T-tube vs no T-tube for biliary tract reconstruction in adult orthotopic liver transplantation: An updated systematic review and meta-analysis

Jun-Zhou Zhao, Lin-Lan Qiao, Zhao-Qing Du, Jia Zhang, Meng-Zhou Wang, Tao Wang, Wu-Ming Liu, Lin Zhang, Jian Dong, Zheng Wu, Rong-Qian Wu

ORCID number: Jun-Zhou Zhao 0000-0003-0365-2568; Lin-Lan Qiao 0000-0003-0405-1588; Zhao-Qing Du 0000-0003-0781-1079; Jia Zhang 0000-0001-7306-3350; Meng-Zhou Wang 0000-0003-3357-656X; Tao Wang 0000-0003-2316-0106; Wu-Ming Liu 0000-0001-5550-0916; Lin Zhang 0000-0003-3927-2997; Jian Dong 0000-0213-0555-6589; Zheng Wu 0000-0002-7102-9543; Rong-Qian Wu 0000-0003-0993-4531.

Author contributions: All authors contributed to the study; Zhao JZ participated in the search strategy design and performed most statistical analyses and paper writing; Qiao LL, Du ZQ, and Zhang J did a literature search of the databases in parallel, built up selection criteria, and selected the potential studies; Wang MZ and Wang T defined the interventions and outcomes; Liu WM, Zhang L, and Dong J assessed the studies' quality and figured out the characteristics of the selected studies; Wu Z assisted with the design of the study; Wu RQ designed and supervised the study and revised the manuscript.

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Jun-Zhou Zhao, Lin-Lan Qiao, Zhao-Qing Du, Jia Zhang, Meng-Zhou Wang, Tao Wang, Wu-Ming Liu, Lin Zhang, Jian Dong, Zheng Wu, Department of Hepatobiliary Surgery, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, China

Jun-Zhou Zhao, Lin-Lan Qiao, Zhao-Qing Du, Jia Zhang, Rong-Qian Wu, National Local Joint Engineering Research Center for Precision Surgery and Regenerative Medicine, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, China

Corresponding author: Rong-Qian Wu, MD, PhD, Professor, National Local Joint Engineering Research Center for Precision Surgery and Regenerative Medicine, First Affiliated Hospital of Xi'an Jiaotong University, No. 76 West Yanta Road, Xi'an 710061, Shaanxi Province, China. rwu001@mail.xjtu.edu.cn

Abstract

BACKGROUND

Whether to use a T-tube for biliary anastomosis during orthotopic liver transplantation (OLT) remains a debatable question. Some surgeons chose to use a T-tube because they believed that it reduces the incidence of biliary strictures. Advances in surgical techniques during the last decades have significantly decreased the overall incidence of postoperative biliary complications. Whether using a T-tube during OLT is still associated with the reduced incidence of biliary strictures needs to be re-evaluated.

AIM

To provide an updated systematic review and meta-analysis on using a T-tube during adult OLT.

METHODS

In the electronic databases MEDLINE, PubMed, Scopus, ClinicalTrials.gov, the Cochrane Library, the Cochrane Hepato-Biliary Group Controlled Trials Register, and the Cochrane Central Register of Controlled Trials, we identified 17 studies (eight randomized controlled trials and nine comparative studies) from January 1995 to October 2020. The data of the studies before and after 2010 were separately extracted. We chose the overall biliary complications, bile leaks or fistulas, biliary strictures (anastomotic or non-anastomotic), and cholangitis as outcomes. Odds

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ratios (ORs) with 95% confidence intervals (CIs) were calculated to describe the results of the outcomes. Furthermore, the test for overall effect (Z) was used to test the difference between OR and 1, where $P \leq 0.05$ indicated a significant difference between OR value and 1.

RESULTS

A total of 1053 subjects before 2010 and 1346 subjects after 2010 were included in this meta-analysis. The pooled results showed that using a T-tube reduced the incidence of postoperative biliary strictures in studies before 2010 ($P = 0.012$, OR = 0.62, 95%CI: 0.42-0.90), while the same benefit was not seen in studies after 2010 ($P = 0.60$, OR = 0.76, 95%CI: 0.27-2.12). No significant difference in the incidence of overall biliary complications ($P = 0.37$, OR = 1.41, 95%CI: 0.66-2.98), bile leaks ($P = 0.89$, OR = 1.04, 95%CI: 0.63-1.70), and cholangitis ($P = 0.27$, OR = 2.00, 95%CI: 0.59-6.84) was observed between using and not using a T-tube before 2010. However, using a T-tube appeared to increase the incidence of overall biliary complications ($P = 0.049$, OR = 1.49, 95%CI: 1.00-2.22), bile leaks ($P = 0.048$, OR = 1.91, 95%CI: 1.01-3.64), and cholangitis ($P = 0.02$, OR = 7.21, 95%CI: 1.37-38.00) after 2010. A random-effects model was used in biliary strictures (after 2010), overall biliary complications (before 2010), and cholangitis (before 2010) due to their heterogeneity ($I^2 = 62.3\%$, 85.4%, and 53.6%, respectively). In the sensitivity analysis (only RCTs included), bile leak ($P = 0.66$) lost the significance after 2010 and a random-effects model was used in overall biliary complications (before 2010), cholangitis (before 2010), bile leaks (after 2010), and biliary strictures (after 2010) because of their heterogeneity ($I^2 = 92.2\%$, 65.6%, 50.9%, and 80.3%, respectively).

CONCLUSION

In conclusion, the evidence gathered in our updated meta-analysis showed that the studies published in the last decade did not provide enough evidence to support the routine use of T-tube in adults during OLT.

Key Words: Orthotopic liver transplantation; T-tube; Biliary tract reconstruction; Biliary complications; Biliary strictures; Meta-analysis

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Core Tip: This is the first meta-analysis that compared the postoperative outcomes with or without a T-tube in biliary reconstruction during orthotopic liver transplantation (OLT) before and after 2010. Before 2010, T-tube was favorable for biliary stricture and had no influence on overall biliary complications, bile leaks, and cholangitis. After 2010, not using a T-tube was good for overall biliary complications and cholangitis; however, using a T-tube was not associated with biliary strictures and showed an unbeneficial trend for bile leaks. Therefore, the studies published in the last decade did not provide enough evidence to support the use of T-tube during adult OLT.

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INTRODUCTION

Orthotopic liver transplantation (OLT) is an effective treatment for end-stage liver diseases^[1,2]. Although the overall outcome of OLT has improved significantly during the last decades, biliary complications, such as biliary strictures and bile leaks, remain the major causes of morbidity and mortality^[3]. Biliary anastomosis was thought to be



the Achilles' heel of liver transplantation^[4].

T-tube has been routinely used for biliary anastomosis during conventional hepatobiliary surgery^[5,6]. However, its use in biliary reconstruction during OLT remains controversial. Several randomized controlled trials (RCTs) and comparative studies have been conducted to evaluate the value of using a T-tube in biliary reconstruction during OLT. The results, however, remained inconclusive. Even meta-analyses on this issue have provided different suggestions; Sun *et al*^[7] indicated that T-tube was an excellent tool for biliary tract reconstruction while Sotiropoulos *et al*^[8] suggested that abandonment of T-tube was better.

Some surgeons chose to use a T-tube during OLT because they believed that it reduces the incidence of biliary strictures. Recent advances in surgical techniques have significantly decreased the overall incidence of postoperative biliary complications. Whether using a T-tube during OLT is still associated with the reduced incidence of biliary strictures needs to be re-evaluated. Therefore, we performed this updated systematic review and meta-analysis to compare biliary complications with and without a T-tube during OLT in studies conducted before and after 2010^[7-27]. We tried to find the current value of using a T-tube for biliary reconstruction during adult OLT.

MATERIALS AND METHODS

Search strategy and selection criteria

To find relevant studies, the electronic databases MEDLINE, PubMed, Scopus, ClinicalTrials.gov, the Cochrane Library, the Cochrane Hepato-Biliary Group Controlled Trials Register, and the Cochrane Central Register of Controlled Trials were used to retrieve papers in English literature from January 1995 to October 2020. The search terms included "OLT" (or "Liver Grafting" or "Liver Transplantations" or "Liver Transplant" or "Hepatic Transplantations") and "T-tube" (or "Stents") and "Biliary Tract Reconstruction" (or "Bile Ducts Reconstruction" or "Bile Duct"). Relevant comparative studies and RCTs on biliary tract reconstruction during OLT were identified. Manual search was still needed to seek further data from the article list.

Inclusion criteria

The inclusion criteria were: (1) Trials including OLT recipients (≥ 18 years); (2) Trials with primary reports of overall biliary complications and at least one biliary complication (bile leaks or fistula, anastomotic or non-anastomotic strictures, and cholangitis); and (3) Trials using choledochostomy (CCS) to reconstruct the bile duct. RCTs and comparative studies were considered, while news, commentaries, and case reports were excluded. The other exclusion criteria were as follows: (1) Liver recipient age less than 18 years; (2) Retransplantations; (3) Significant donor and recipient duct size mismatch; and (4) Diagnosis of some autoimmune diseases (*e.g.*, primary sclerosing cholangitis).

Data extraction

The data of the studies before and after 2010 were separately extracted. Three authors did a literature search of the above databases in parallel and reached consensus on most items. The differences in opinion were discussed by all authors and came to an agreement finally. The following variables were considered: Authors, year of publication, number of patients, sex, mean age of subjects, and cold ischemia time (CIT) (min). The following outcomes were evaluated: Overall biliary complications, bile leaks or fistulas, biliary strictures (anastomotic or non-anastomotic), and cholangitis.

Intervention and outcome definition

In case that a T-tube was used, a T-tube was inserted into the bile duct after the biliary tract reconstruction of end-to-end or side-to-side CCS. In case that T-tube was not used, there was not any T-tube used in the end-to-end or side-to-side CCS. The main outcomes were defined as bile leaks, biliary strictures, and cholangitis. Bile leaks were suspected in patients with abdominal pain and fever. Biliary strictures were indicated by the biochemical elevations of alkaline phosphatase and total bilirubin levels in patients without allograft rejection or hepatic artery thrombosis^[28]. Bile leaks and biliary strictures were diagnosed by percutaneous transhepatic cholangiography, endoscopic retrograde cholangio-pancreatography, and T-tube cholangiogram^[29]. In

addition, biliary strictures can also be diagnosed by computed tomography and magnetic resonance imaging. Cholangitis was suspected when the infectious symptoms with cholestatic parameters occurred, and the Charcot triad (right upper quadrant pain, jaundice, and fever) was also a characteristic of cholangitis^[30].

Quality assessment

The quality of the studies in the systematic review and meta-analysis was determined using the Jadad composite scale^[31]. The following parameters were evaluated: Randomized study, description of randomization, description of withdrawals and dropouts, double-blinded study, and description of double blinding. Each of these was scored as one point. The maximum of points was five. A greater score indicated better quality of selected studies.

Data analysis

This systematic review and meta-analysis were performed with STATA software (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC.). Outcomes evaluated were: Overall biliary complications, bile leaks or fistulas, biliary strictures, and cholangitis. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to describe the results of dichotomous outcomes. Furthermore, the test for overall effect (Z) was used to test the difference between OR and 1, where $P \leq 0.05$ indicated a significant difference between OR value and 1. Statistical heterogeneity was assessed with the statistics I^2 , where $P \leq 0.05$ or $I^2 > 50\%$ were considered as having significant heterogeneity^[32]. A fixed-effects model was suitable to estimate the cases with homogeneity ($I^2 \leq 50\%$) while a random-effects model should be used when significant heterogeneity ($I^2 > 50\%$) was detected. The Egger test (bias, P) was used to detect the publication bias, where $P \leq 0.05$ indicated a significant publication bias^[33]. Sensitivity analysis based on ten RCTs was used to test the stability of the results of meta-analysis including all studies.

RESULTS

Characteristics of selected studies

There were 267 studies published between 1995 and 2020, of which 109 were excluded because they did not mention the use of a T-tube during OLT. Fourteen reviews, five case reports, and one letter were also excluded. After the full texts of the potential studies had been retrieved, only 20 studies met the inclusion criteria. A study was excluded because it was the preliminary result of a RCT while the final result of the RCT was already included^[34]. Two studies were excluded because of the lack of no reference to patient selection or confounding variables^[35] or the use of a T-tube in patients without a T-tube^[36]. Finally, eight RCTs and nine comparative studies with 2199 subjects were included in our meta-analysis (Figure 1). Among them, 1053 subjects were from studies conducted before 2010 and 1146 were from studies conducted after 2010. Five RCTs got 3 points on the Jadad scale while three RCTs got only 2 points. The mean Jadad score of RCTs was 2.63 points. Seven comparative studies are retrospective, whereas two comparative studies are prospective. The observation period was at least 3 mo except for one with only 2 mo. In most studies, the T-tube was removed 3 mo after the biliary reconstruction operation, but in one comparative study, the T-tube was removed only 9 wk after operation. One study had selection bias for the use of a T-tube and another study was biased on the intention-to-treat^[13]. There were no significant differences in age, CIT, and gender (data not shown). Detailed data and results are summarized in Tables 1 and 2, respectively.

Results of meta-analysis including all studies

The pooled result showed that in studies conducted between 1995 and 2010, the use of a T-tube appeared to reduce the incidence of biliary strictures ($P = 0.012$, OR = 0.62, 95%CI: 0.42-0.90, Figure 2A and Table 3), while for studies conducted after 2010, there was no significant difference between the “with T-tube” group and the “without T-tube” group in the occurrence of biliary strictures ($P = 0.60$, OR = 0.76, 95%CI: 0.27-2.12, Figure 2B). No significant differences in the incidences of overall biliary complications ($P = 0.37$, OR = 1.41, 95%CI: 0.66-2.98, Figure 3A), bile leak ($P = 0.89$, OR = 1.04, 95%CI: 0.63-1.70, Figure 4A), and cholangitis ($P = 0.27$, OR = 2.00, 95%CI: 0.59-6.84, Figure 5A) were observed between using and not using a T-tube in studies conducted before 2010. However, using a T-tube appeared to increase the incidences of

Table 1 Characteristics of all studies

Ref.	Study design	Year	T-tube	Number of patients	Gender ¹	Mean age (year) ³	Mean CIT ^{2,3} (min)	Jadad score
López-Andújar <i>et al</i> ^[25]	CS	2019	Y	240	139/101	58 ± 18	268 ± 109	1
			N	165	89/76	63 ± 14	265 ± 105	
Ong <i>et al</i> ^[24]	CS	2018	Y	88	64/24	55	327	1
			N	37	27/10	51	316	
Santosh Kumar <i>et al</i> ^[23]	RCT	2017	Y	31	NR	43.4 ± 11.1	NR	2
			N	33	NR	48.5 ± 11.6	NR	
García Bernardo <i>et al</i> ^[22]	CS	2016	Y	23	21/2	55.3 ± 9.7	321 ± 108	1
			N	23	20/3	57.7 ± 6.6	343 ± 100	
T. Anila <i>et al</i> ^[21]	RCT	2015	Y	13	NR	NR	73.3 ± 25.1	2
			N	13	NR	NR	74.9 ± 31.5	
López-Andújar <i>et al</i> ^[20]	RCT	2013	Y	95	75/20	53.7 ± 7.68	316 ± 157	3
			N	92	66/26	53.2 ± 8.68	297 ± 143	
Weiss <i>et al</i> ^[19]	RCT	2009	Y	99	69/30	53.3 ± 9.8	597 ± 159	3
			N	95	60/35	55.3 ± 6.7	559 ± 178	
Lin <i>et al</i> ^[17]	CS	2007	Y	51	45/6	50.1 ± 10.0	NR	1
			N	53	47/6	52.0 ± 10.0	NR	
Li <i>et al</i> ^[18]	CS	2007	Y	33	30/3	47.2 ± 9.4	479 ± 98	1
			N	51	46/5	42.5 ± 13.5	457 ± 89	
Amador <i>et al</i> ^[16]	RCT	2005	Y	53	21/32	51.8 ± 9.4	362	3
			N	54	24/30	50.6 ± 10.6	390	
Elola-Olaso <i>et al</i> ^[15]	CS	2005	Y	50	29/71	51.93 ± 9.8	NR	1
			N	50			NR	
Scatton <i>et al</i> ^[14]	RCT	2001	Y	90	62/28	48.3 ± 9.9	604 ± 194	3
			N	90	58/32	49.2 ± 9.5	570 ± 153	
Shimoda <i>et al</i> ^[13]	CS	2001	Y	76	33/43	51.8 ± 11.7	NR	1
			N	71	32/39	52.9 ± 12.3	NR	
Rabkin <i>et al</i> ^[12]	CS	1998	Y	118	43/75	47.7	610	1
			N	44	7/37	48.0	522	
Nuño <i>et al</i> ^[11]	RCT	1997	Y	50	NR	NR	NR	2
			N	48	NR	NR	NR	
Vougas <i>et al</i> ^[10]	RCT	1996	Y	30	12/18	42.0	678	3
			N	30	13/17	45.0	696	
Randall <i>et al</i> ^[9]	CS	1996	Y	59	NR	NR	NR	1
			N	51	NR	NR	NR	

¹Female/Male.²Mean ± standard deviation or mean.³Cold ischemia time.

NR: No reference; Y: Yes; N: No; CS: Comparative study; RCT: Randomized control trial; CIT: Cold ischemia time.

overall biliary complications ($P = 0.049$, OR = 1.49, 95%CI: 1.00-2.22, **Figure 3B**), bile leak ($P = 0.048$, OR = 1.91, 95%CI: 1.01-3.64, **Figure 4B**), and cholangitis ($P = 0.02$, OR = 7.21, 95%CI: 1.37-38.00, **Figure 5B**) in studies conducted after 2010. A random-effects model was used in biliary strictures (in studies after 2010), overall biliary

Table 2 Measurements of outcomes provided in all studies

Outcome	Ref.	Year	With T-tube	Without T-tube
Total biliary complications	López-Andújar <i>et al</i> ^[25]	2019	31/240	20/165
	Ong <i>et al</i> ^[24]	2018	26/88	3/37
	García Bernardo <i>et al</i> ^[22]	2016	7/23	5/23
	López-Andújar <i>et al</i> ^[20]	2013	24/95	18/92
	Weiss <i>et al</i> ^[19]	2009	27/99	50/95
	Li <i>et al</i> ^[18]	2007	10/33	6/51
	Lin <i>et al</i> ^[17]	2007	5/51	9/53
	Amador <i>et al</i> ^[16]	2005	32/53	6/54
	Scatton <i>et al</i> ^[14]	2001	30/90	14/90
	Shimoda <i>et al</i> ^[13]	2001	25/76	11/71
	Rabkin <i>et al</i> ^[12]	1998	43/118	11/44
	Nuño <i>et al</i> ^[11]	1997	5/50	16/48
	Vougas <i>et al</i> ^[10]	1996	5/30	6/30
	Randall <i>et al</i> ^[9]	1996	13/59	7/51
Bile leak	López-Andújar <i>et al</i> ^[25]	2019	10/240	2/165
	Ong <i>et al</i> ^[24]	2018	2/88	1/37
	Santosh Kumar <i>et al</i> ^[23]	2017	11/31	4/33
	García Bernardo <i>et al</i> ^[22]	2016	4/23	2/23
	T. Anila <i>et al</i> ^[21]	2015	0/13	1/13
	López-Andújar <i>et al</i> ^[20]	2013	4/95	5/92
	Weiss <i>et al</i> ^[19]	2009	5/99	9/95
	Li <i>et al</i> ^[18]	2007	4/33	1/51
	Lin <i>et al</i> ^[17]	2007	1/51	1/53
	Amador <i>et al</i> ^[16]	2005	2/53	3/54
	Elola-Olaso <i>et al</i> ^[15]	2005	3/47	0/50
	Scatton <i>et al</i> ^[14]	2001	2/90	2/90
	Shimoda <i>et al</i> ^[13]	2001	4/76	5/71
	Rabkin <i>et al</i> ^[12]	1998	3/118	1/44
	Nuño <i>et al</i> ^[11]	1997	3/50	8/48
Biliary stricture	Vougas <i>et al</i> ^[10]	1996	1/30	0/30
	Randall <i>et al</i> ^[9]	1996	5/59	0/51
	López-Andújar <i>et al</i> ^[25]	2019	11/240	14/165
	Ong <i>et al</i> ^[24]	2018	11/88	2/37
	Santosh Kumar <i>et al</i> ^[23]	2017	7/31	2/33
	García Bernardo <i>et al</i> ^[22]	2016	2/23	3/23
	T. Anila <i>et al</i> ^[21]	2015	1/13	2/13
	López-Andújar <i>et al</i> ^[20]	2013	2/95	14/92
	Weiss <i>et al</i> ^[19]	2009	7/99	8/95
	Li <i>et al</i> ^[18]	2007	5/33	4/51
	Lin <i>et al</i> ^[17]	2007	5/51	8/53
	Amador <i>et al</i> ^[16]	2005	6/53	3/54

Cholangitis	Elola-Olaso <i>et al</i> ^[15]	2005	6/44	4/46
	Scatton <i>et al</i>^[14]	2001	3/90	6/90
	Shimoda <i>et al</i> ^[13]	2001	5/76	6/71
	Rabkin <i>et al</i> ^[12]	1998	7/118	10/44
	Nuño <i>et al</i>^[11]	1997	1/50	8/48
	Vougas <i>et al</i>^[10]	1996	2/30	6/30
	Randall <i>et al</i> ^[9]	1996	8/59	7/51
	López-Andújar <i>et al</i> ^[25]	2019	6/240	0/165
	Ong <i>et al</i> ^[24]	2018	1/88	0/37
	López-Andújar <i>et al</i>^[20]	2013	6/95	0/92
	Weiss <i>et al</i>^[19]	2009	5/99	11/95
	Li <i>et al</i> ^[18]	2007	1/33	1/51
	Amador <i>et al</i>^[16]	2005	8/53	0/54
	Elola-Olaso <i>et al</i> ^[15]	2005	5/45	1/49
	Scatton <i>et al</i>^[14]	2001	4/90	3/90
	Vougas <i>et al</i>^[10]	1996	2/30	0/30

Bold typed studies indicate randomized control trials.

Table 3 Meta-analysis of outcomes (all studies included)

Period	Outcome	Studies	Participants	Effect size OR, 95%CI (fixed/random)	Heterogeneity	Test for overall effect (fixed/random)	Publication bias	Study quality ¹	Favors
1995-2010	Overall biliary complications	10	1246	1.41 [0.66, 2.98]	$I^2 = 85.4\%$ ($^bP = 0.001$)	$Z = 0.89/(P = 0.37)$	Egger: Bias = 1.92; $P = 0.60$	$3 \times 4, 2 \times 1, 1 \times 5$	None
	Bile leak	11	1346	1.04 [0.63, 1.70]	$I^2 = 16.7\%$ ($P = 0.29$)	$Z = 0.14/(P = 0.89)$	Egger: Bias = 2.43; $^bP = 0.003$	$3 \times 4, 2 \times 1, 1 \times 6$	None
	Biliary stricture	11	1346	0.62 [0.42, 0.90]	$I^2 = 26.6\%$ ($P = 0.19$)	$Z = 2.51/(^aP = 0.012)$	Egger: Bias = -1.09; $P = 0.56$	$3 \times 4, 2 \times 1, 1 \times 6$	With T-tube
	Cholangitis	6	725	2.00 [0.59, 6.84]	$I^2 = 53.6\%$ ($P = 0.06$)	$Z = 1.11/(P = 0.27)$	Egger: Bias = 2.97; $^aP = 0.02$	$3 \times 4, 1 \times 2$	None
2010-2020	Overall biliary complications	4	763	1.49 [1.00, 2.22]	$I^2 = 31.9\%$ ($P = 0.22$)	$Z = 1.97/(^aP = 0.049)$	Egger: Bias = 2.50; $P = 0.22$	$3 \times 1, 1 \times 3$	Without T-tube
	Bile leak	6	853	1.91 [1.01, 3.64]	$I^2 = 6.0\%$ ($P = 0.38$)	$Z = 1.98/(^aP = 0.048)$	Egger: Bias = -1.69; $P = 0.30$	$3 \times 1, 2 \times 2, 1 \times 3$	Without T-tube
	Biliary stricture	6	853	0.76 [0.27, 2.12]	$I^2 = 62.3\%$ ($^aP = 0.02$)	$Z = 0.53/(P = 0.60)$	Egger: Bias = 0.84; $P = 0.70$	$3 \times 1, 2 \times 2, 1 \times 3$	None
	Cholangitis	3	717	7.21 [1.37, 38.00]	$I^2 = 0.0\%$ ($P = 0.52$)	$Z = 2.33/(^aP = 0.02)$	Egger: Bias = -12.51; $P = 0.12$	$3 \times 1, 1 \times 2$	Without T-tube

¹Jadad scores \times study number.

^a $P < 0.05$.

^b $P < 0.01$.

Odds ratio < 1 indicates the use of a T-tube. OR: Odds ratio; CI: Confidence interval.

complications (in studies before 2010), and cholangitis (in studies before 2010) due to their heterogeneity ($I^2 = 62.3\%$, 85.4% , and 53.6% , respectively). Unfortunately, we failed to figure out the source of heterogeneity. Sensitivity analysis failed to reveal the main cause of the heterogeneity. Funnel plots detected a publication bias for bile leaks (Egger: Bias = 2.43, $P = 0.003$) and for cholangitis (Egger: Bias = 2.97, $P = 0.02$).

Results of sensitivity analysis including only RCTs

The meta-analysis with only RCTs showed that except for bile leaks which lost the significance in studies after 2010 ($P = 0.66$), the rest outcomes remained unchanged. Overall biliary complications and cholangitis were not evaluated because only one RCT was available to provide the information and the publication bias tests were not applicable (Table 4). A random-effects model was used in overall biliary complications (in studies before 2010), cholangitis (in studies before 2010), and biliary strictures (in studies after 2010) because of their heterogeneity ($I^2 = 92.2\%$, 65.6% , 50.9% , and 80.3% , respectively). Funnel plots did not detect any publication bias among the outcomes.

DISCUSSION

Whether to use a T-tube or not during OLT remains a challenging question for today's transplant surgeons. The advantages of using a T-tube are the real-time monitoring of the color and quantity of bile. Therefore, using a T-tube can get the condition of transplanted liver and an access of the radiographic imaging of the biliary tree^[10,12,14]. And the use of a T-tube has been thought to reduce intraductal pressure to protect biliary anastomosis^[12,37]. However, the use of a T-tube may also contribute to the development of biliary leaks and cholangitis^[15,16,25]. Although, in the period from 1995 to 2010, the data showed that the use of a T-tube could reduce the incidence of biliary strictures, the use of a T-tube had no influence on the occurrence of overall biliary complications, cholangitis, and bile leak. However, in the current updated (from 2010 to 2020) meta-analysis, we documented that the use of a T-tube did not reduce the incidence of biliary strictures and it appeared to increase the development of overall biliary complications and cholangitis and showed an unfavorable trend for bile leaks.

Reduction of the postoperative development of anastomotic or non-anastomotic strictures is considered an inherent trait of using a T-tube during OLT. Indeed, inserting a T-tube is still a useful way to decrease the use of invasive diagnostic techniques like endoscopic retrograde cholangiography^[26,38], when a patient is suspected with bile leaks, just as the past decade data showed. However, unlike most studies, there was no significant difference between the "with T-tube" group and the "without T-tube" group in the occurrence of biliary strictures in the period from 2010 to 2020 in our analysis. Biliary stricture could occur in the non-anastomotic part due to the lack of the blood supply^[39,40]. And bile leak, infection, and wound contraction may contribute to anastomotic biliary stricture^[41-43]. The inflammatory reaction and fibrosis processes may occur in the biliary tract wall contacting with the T-tube due to the foreign body reaction to a T-tube^[44,45]. If a T-tube was placed on the biliary tract for a long time, T-tube will alter the local host defense mechanism to increase the susceptibility to infection which may induce biliary fibrosis^[46,47]. Fortunately, the recent advancement in surgical techniques has significantly improved the short-term outcomes after OLT^[48,49].

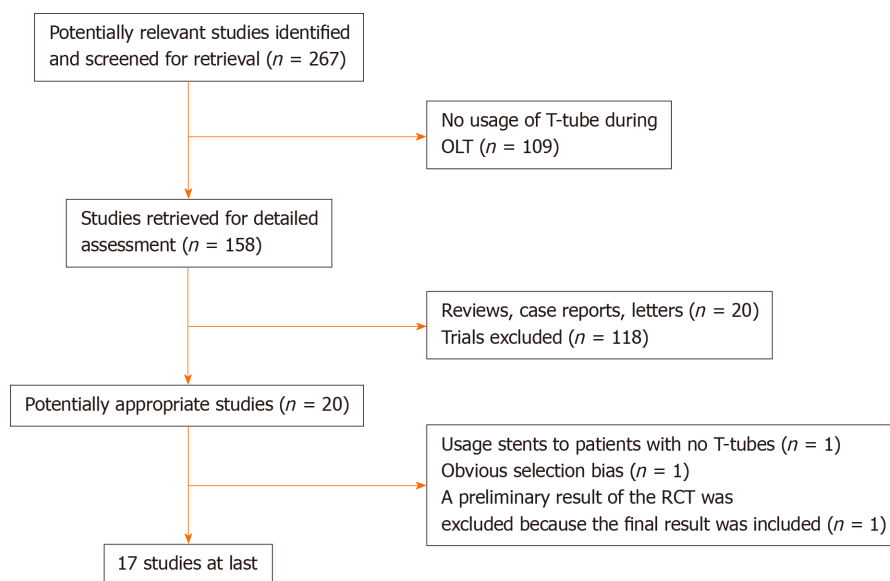
Bile leaks commonly complicate liver transplantation. They usually occur in the early postoperative period or after the T-tube removal. And bile leaks prolonged the hospital stay, increased the medical costs, and disturbed the postoperative recovery^[50]. Some physicians thought that the use of a T-tube plays an important role in development of bile leaks in recipients^[51]. In the results of our study, there was no significant difference in the incidence of bile leaks between the "with T-tube" group and the "without T-tube" group in the period from 1995 to 2010. Nevertheless, we found that the use of a T-tube increased the risk of developing bile leaks in biliary reconstruction during OLT in the period from 2010 to 2020. Unfortunately, in the sensitivity analysis, bile leaks lost the significance, which lowered the statistic power of the results. Therefore, at least in part, our data demonstrated that T-tube showed an unbeneficial trend for bile leaks. Previous studies showed that 5% to 15% of patients suffered from bile leaks after T-tube removal^[52,53]. And the biliary anastomosis or T-tube exit site was a major source of the bile leakage^[54,55]. The delayed formation of a fibrous trajectory to allow safe removal of T-tube may play an important role in the incidence of bile leak^[56]. In addition, multiple biliary reconstructions also contributed to the occurrence of the bile leaks and were associated with a poor prognosis of

Table 4 Sensitivity analysis of outcomes (only randomized control trials included)

Period	Outcome	Studies	participants	Effect size OR, 95%CI (fixed/random)	Heterogeneity	Test for overall effect (fixed/random)	Publication bias	Study quality ¹	Favors
1995-2010	Overall biliary complications	5	639	1.15 [0.28, 4.72]	$I^2 = 92.2\%$ ($^bP = 0.001$)	$Z = 0.19/(P = 0.85)$	Egger: Bias = 2.63; $P = 0.71$	3 × 4, 2 × 1	None
	Bile leak	5	639	0.56 [0.28, 1.13]	$I^2 = 0.0\%$ ($P = 0.72$)	$Z = 1.62/(P = 0.11)$	Egger: Bias = 1.72; $P = 0.08$	3 × 4, 2 × 1	None
	Biliary stricture	5	639	0.45 [0.24, 0.85]	$I^2 = 0.0\%$ ($P = 0.46$)	$Z = 2.47/(^aP = 0.014)$	Egger: Bias = -2.78; $P = 0.10$	3 × 4, 2 × 1	With T-tube
	Cholangitis	4	541	1.83 [0.36, 9.41]	$I^2 = 65.6\%$ ($^aP = 0.03$)	$Z = 0.72/(P = 0.47)$	Egger: Bias = 3.39; $P = 0.054$	3 × 4	None
2010-2020	Bile leak	3	277	1.38 [0.34, 5.65]	$I^2 = 50.9\%$ ($P = 0.13$)	$Z = 0.45/(P = 0.66)$	Egger: Bias = -1.94; $P = 0.62$	3 × 2, 2 × 1	None
	Biliary stricture	3	277	0.63 [0.06, 6.99]	$I^2 = 80.3\%$ ($^aP = 0.01$)	$Z = 0.38/(P = 0.71)$	Egger: Bias = 1.08; $P = 0.92$	3 × 2, 2 × 1	None

¹Jadad scores × study number.^a $P < 0.05$.^b $P < 0.01$.

Odds ratio < 1 indicates the use of a T-tube. OR: Odds ratio; CI: Confidence interval.

**Figure 1 Flowchart of selection process of randomized control trials and comparative studies.** RCT: Randomized control trials; OLT: Orthotopic liver transplantation.patients^[57].

Cholangitis always seems to be a direct outcome of usage of T-tube in biliary reconstruction during OLT. Our study documented that the development of cholangitis had a significant difference between the “with T-tube” group and the “without T-tube” group in the period from 2010 to 2020. However, in the period from 1995 to 2010, we found that cholangitis did not reach the significance between the two groups. There was a trend that T-tube increased the risk of cholangitis. A T-tube was a bridge between the abdominal cavity and external environment to facilitate entry of bacteria into human body. And the surface of a T-tube is a good platform for bacteria to implant so bacteria could form biofilm which help bacteria proliferate better^[58,59]. The biofilm in T-tube plays an important role in occurrence of cholangitis^[60,61]. If the T-tube was broken by the patient carelessly, the bile may flow out of the biliary tree to induce bacterial infection. Most patients were immunocompromised because of immunosuppressors after OLT, which made patients vulnerable to bacterial or viral infection. In another words, it is fatal for some patients suffering from infections such

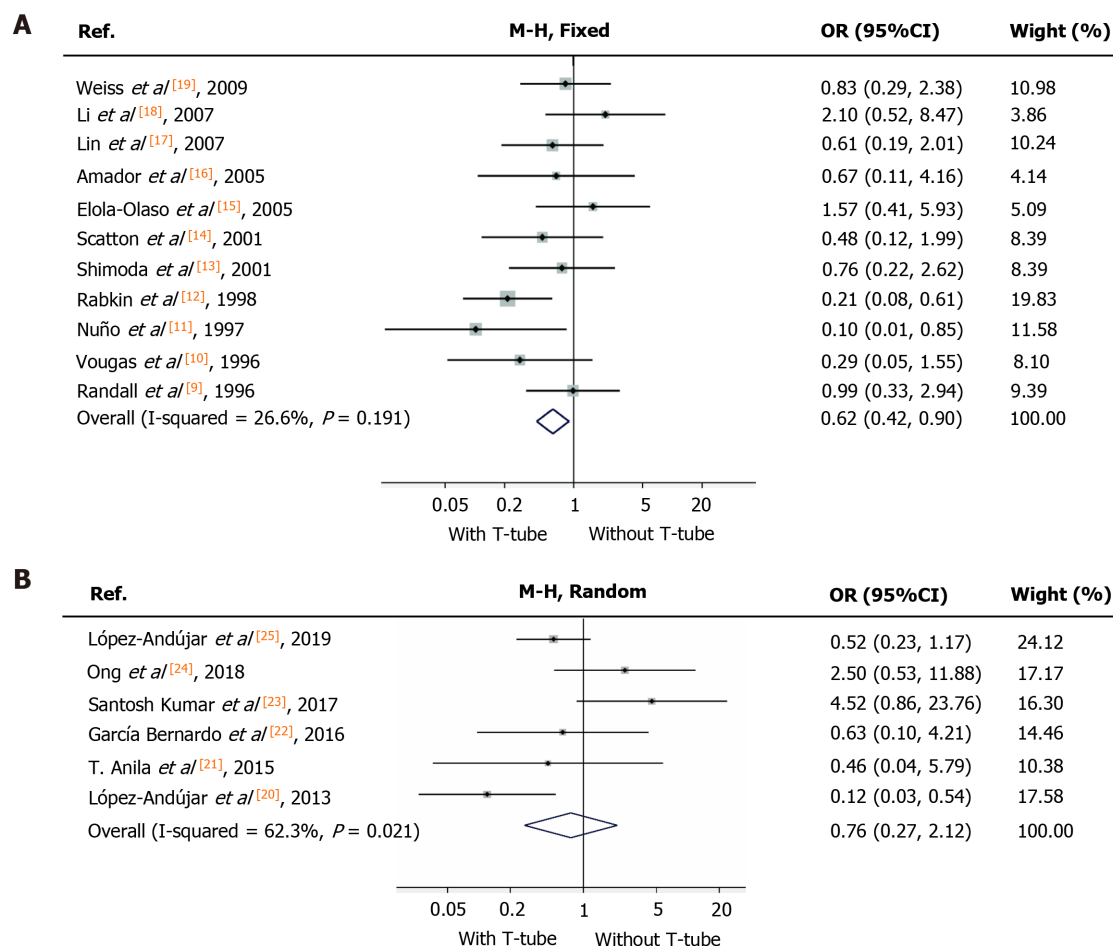


Figure 2 Biliary strictures. A: In the period from 1995 to 2010, odds ratio (OR) for biliary strictures between “T-tube” group and “without T-tube” group was calculated with a fixed-effects model. The shape of diamond represents the overall effect of OR with 95% confidence interval (CI). The use of T-tube decreased the incidence of biliary strictures; B: In the period from 2010 to 2020, OR for biliary strictures between “T-tube” group and “without T-tube” group was calculated with a random-effects model. The shape of diamond represents the overall effect of OR with 95%CI. There was no significant difference between the two groups. OR: Odds ratio; CI: Confidence interval.

as cholangitis. T-tube inserting also increased the risk of long-term biliary inflammation and biliary tract fibrosis^[47].

As for overall biliary complications, there was no significant difference between the two groups in the period from 1995 to 2010. Interestingly, our document showed that the use of a T-tube did play a role in development of all kinds of biliary complications in the period from 2010 to 2020. The modern diagnostic devices and the advanced endoscopic technique revealed many latent complications (small thrombosis, local infections, mild internal hemorrhage, and so on), which were difficult to be detected in the past^[10,13,14].

There may be a potential bias because several outcomes had significant publication bias. Since our meta-analysis contained nonrandomized studies and some comparative studies that had selection bias, both contributed to the article’s limitation. Although we reduced the heterogeneity of the selected studies *via* using random-effects models, the inherent bias still partially existed. And almost all the comparative studies got just 1 point on the Jadad scale; however, the five RCTs got 3 points on the Jadad scale while three RCTs got 2 points, which indicated that the quality of the selected studies was not very high. In addition, the retrospective design of the comparative studies may introduce recall bias and reporting bias.

CONCLUSION

In conclusion, the data in our study showed that the use of a T-tube is a beneficial factor for biliary strictures before 2010, whereas no benefit was observed for overall biliary complications, biliary leak, and cholangitis in the same period. According to the

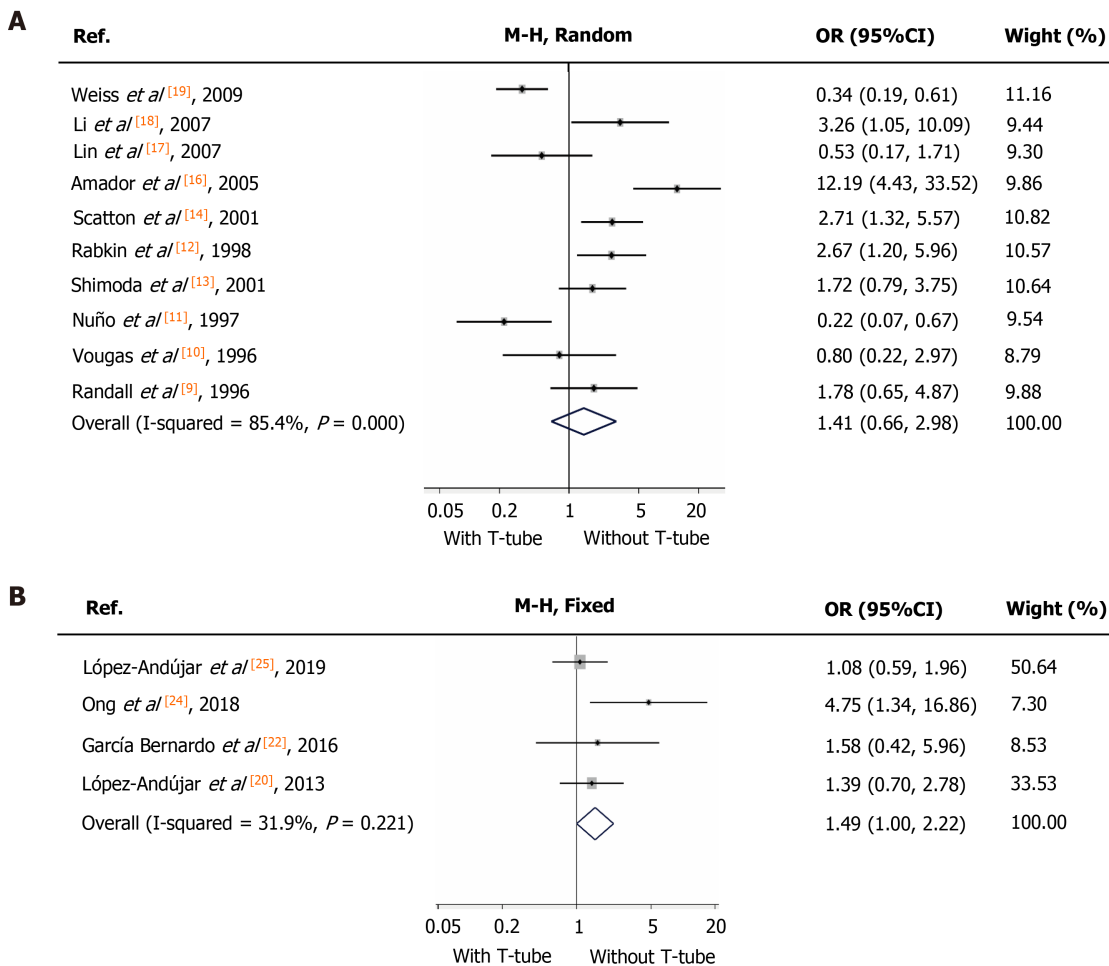


Figure 3 Overall biliary complications. A: In the period from 1995 to 2010, odds ratio (OR) for overall biliary complications between “T-tube” group and “without T-tube” group was calculated with a random-effects model. The shape of diamond represents the overall effect of OR with 95% confidence interval (CI). The use of T-tube had no influence on occurrence of overall biliary complication; B: In the period from 2010 to 2020, OR for overall biliary complications between “T-tube” group and “without T-tube” group was calculated with a fixed-effects model. The shape of diamond represents the overall effect of OR with 95%CI. The occurrence of overall biliary complications was significantly higher in “T-tube” group. OR: Odds ratio; CI: Confidence interval.

studies after 2010, not using a T-tube is beneficial in terms of overall biliary complications and cholangitis; however (after sensitivity analysis), the use of a T-tube is not associated with biliary strictures and shows an unbeneficial trend for bile leaks. Therefore, the evidence gathered in our updated meta-analysis showed that the studies published in the last decade did not provide enough evidence to support the routine use of T-tube in adults during OLT.

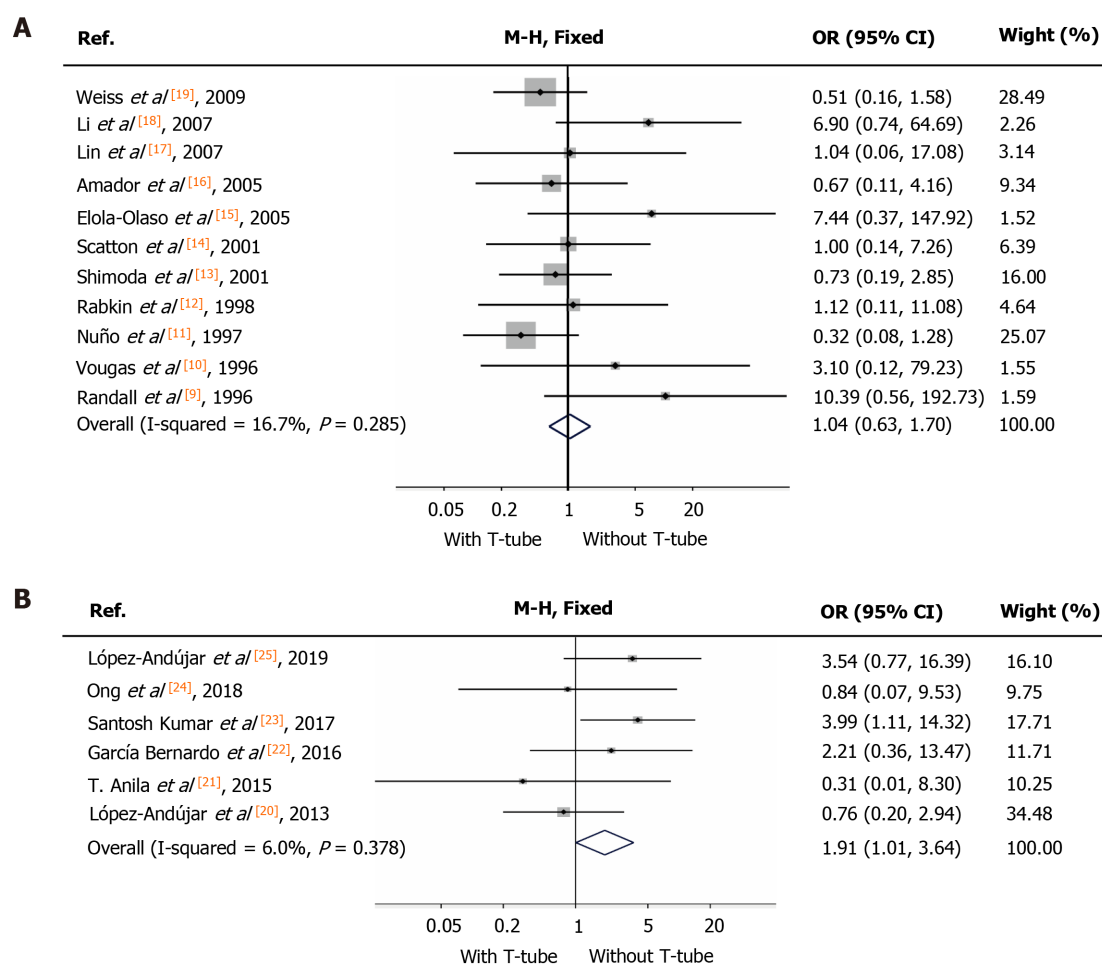


Figure 4 Bile leaks. A: In the period from 1995 to 2010, odds ratio (OR) for peritonitis between “T-tube” group and “without T-tube” group was calculated with the fixed model. The shape of diamond represents the overall effect of OR with 95% confidence interval (CI). There was no significant difference between the two groups; B: In the period from 2010 to 2020, OR for peritonitis between “T-tube” group and “without T-tube” group was calculated with the fixed model. The shape of diamond represents the overall effect of OR with 95%CI. The incidence rate of bile leaks was significantly higher in “T-tube” group. OR: Odds ratio; CI: Confidence interval.

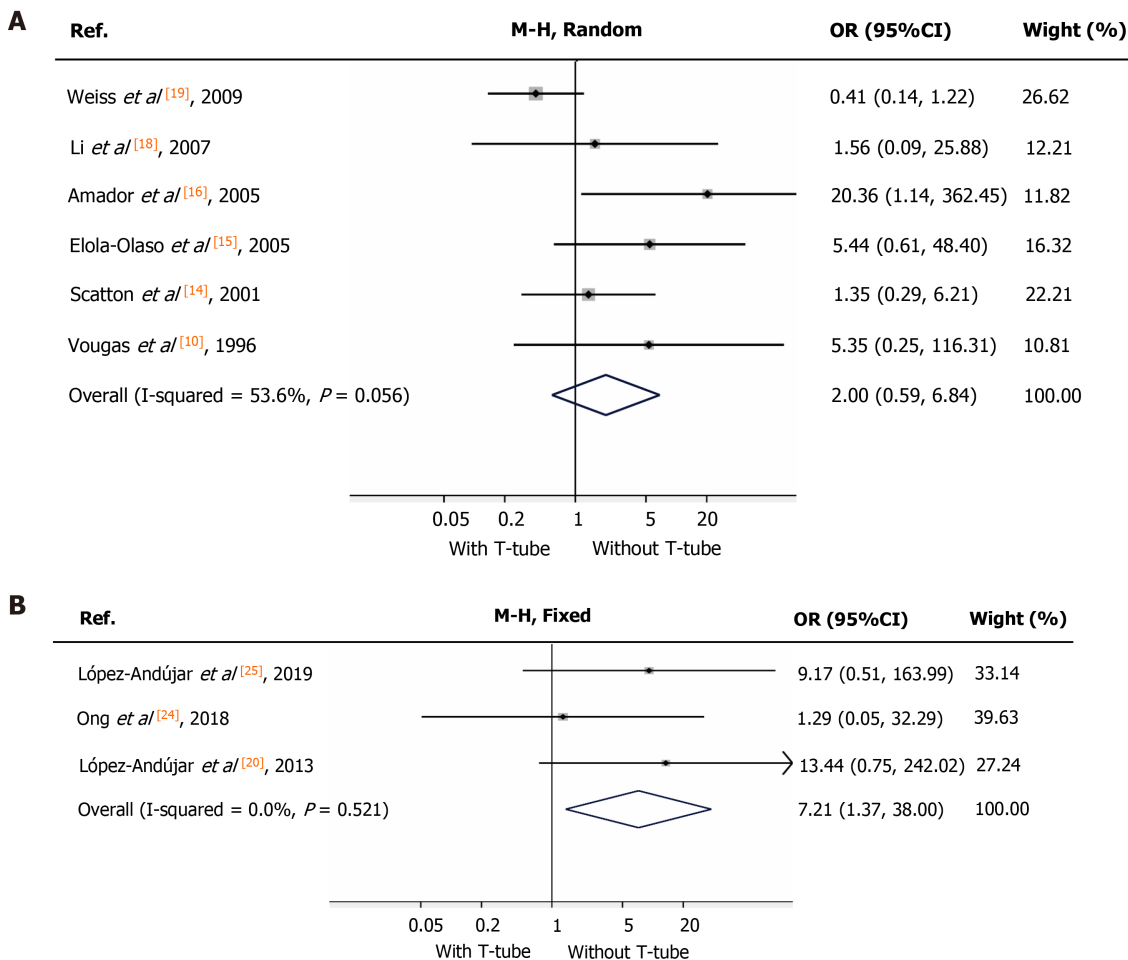


Figure 5 Cholangitis. A: In the period from 1995 to 2010, odds ratio (OR) for cholangitis between “T-tube” group and “without T-tube” group was calculated with a random-effects model. The shape of diamond represents the overall effect of OR with 95% confidence interval (CI). There was no significant difference between the two groups; B: In the period from 2010 to 2020, OR for peritonitis between “T-tube” group and “without T-tube” group was calculated with a fixed-effects model. The shape of diamond represents the overall effect of OR with 95%CI. The incidence rate of bile leaks was significantly higher in “T-tube” group. OR: Odds ratio; CI: Confidence interval.

ARTICLE HIGHLIGHTS

Research background

The use of the T-tube in the reconstruction of the biliary tree during orthotopic liver transplantation (OLT) is still debatable.

Research motivation

Biliary complications after OLT, including bile leaks, cholangitis, and biliary strictures, prolonged the hospital stay, impaired the postoperative recovery, and increased the medical costs. T-tube was involved in the occurrence of these biliary complications. Therefore, it is helpful to identify the role of T-tube in the incidence of the biliary complications.

Research objectives

We performed a meta-analysis to evaluate whether patients benefit from the use of a T-tube during OLT.

Research methods

We calculated odds ratios with 95% confidence intervals to identify the role of a T-tube in the incidence of the overall biliary complications, bile leaks, cholangitis, and biliary strictures.

Research results

We discovered that T-tube had no influence on the risk of the overall biliary complications, bile leaks, and cholangitis and reduced the incidence of biliary strictures in the period from 1995 to 2010. However, in the recent decade (from 2010 to 2020), we found that T-tube did not affect the occurrence of biliary strictures and increased the incidence of overall biliary complications and cholangitis. And the use of a T-tube showed an unbeneficial trend for bile leak after 2010.

Research conclusions

In conclusion, the evidence gathered in our updated meta-analysis showed that the studies published in the last decade did not provide enough evidence to support the routine use of T-tube in adults during OLT.

Research perspectives

More T-tube-related outcomes should be included in the future meta-analysis so the advantages and disadvantages would be evaluated better.

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