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A Meta-Analysis of the Effect of Preoperative Biliary Stenting on Patients With Obstructive Jaundice

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Abstract: The goal of this study was to systematically review the effects of biliary stenting on postoperative morbidity and mortality of patients with obstructive jaundice. PubMed, Embase, Cochrane Library, and other relevant databases were searched by computer and manually for published and unpublished studies on the impact of preoperative biliary drainage on patients with obstructive jaundice from 2000 to the present day. Two investigators independently selected the studies according to the inclusion and exclusion criteria, extracted the data, and assessed the quality of the selected studies. Meta-analysis was performed to compare postoperative morbidity and mortality of patients between the drainage and nondrainage groups.

Compared with the nondrainage group, the overall mortality, overall morbidity, infectious morbidity, incidence of wound infection, intraabdominal abscess, pancreatic fistulas, bile leak, and delayed gastric emptying in the drainage group were not significantly different. Compared with the nondrainage group, the drainage group had a drainage time of <4 weeks with an increased overall morbidity by 7% to 23%; however, the overall morbidity of the drainage group with a drainage time >4 weeks was not significantly different. Compared with the nondrainage group, the overall morbidity of the drainage group using metal stents and plastic stents as internal drainage devices was reduced by 0.5% to 6%, whereas that of the drainage group using plastic stent devices was not significantly different.

In summary, preoperative drainage should be applied selectively. The drainage time should be >4 weeks, and metal stents should be used for internal drainage.

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Abbreviations: CI = confidence interval, MOOSE = meta-analysis of observational studies in epidemiology, NRCT = nonrandomized controlled trial, OR = odds ratio.

BACKGROUND

The postoperative mortality and postoperative morbidity of patients with malignant obstructive jaundice was 5% to 27% and \sim 50%, respectively^{1,2}; in view of high mortality and

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morbidity, a large number of studies have been carried out to explore the main risk factors. It has been reported that hyperbilirubinemia (serum bilirubin >170 µmoL/L) in patients who underwent obstructive jaundice surgery might increase their postoperative morbidity and mortality,^{3–5} given that hyperbilirubinemia would lead to impairment of liver function, decreased clearance of endotoxin, coagulation disorders, decreased immune function, and impaired gastrointestinal mucosal barrier.^{6,7} Therefore, to reduce the level of serum bilirubin, preoperative biliary drainage was performed before obstructive jaundice surgery. The earliest report of preoperative biliary drainage was published by Whipple et al⁸ in 1935, in which 4 weeks after the first operation, a cholecystogastrostomy, pancreatectomy was performed.⁸ With the development and application of radiological and endoscopic technologies, the methods of minimally invasive preoperative drainage gradually emerged, they include percutaneous transhepatic cholangiography, nasobiliary drainage, and biliary stenting (percutaneous transhepatic approach, endoscopic retrograde approach), with the former serving as external drainage and the latter serving as internal drainage. Despite that preoperative biliary drainage has been suggested to exert positive effect on jaundice patients, such as improving their liver function and reducing the incidence of perioperative complications $^{9-12}$; it was not proved to be capable of improving prognosis. The supporters of preoperative biliary drainage have argued that in those studies, the applied drainage methods mostly included external drainage devices or even bypasses, whereas actually, internal drainage adapts better to human physiology; hence, they deemed that those conclusions might be biased.¹³ Metaanalyses of preoperative biliary drainage have been carried out by several researchers; however, a specific meta-analysis targeting internal drainage has not yet been published. Therefore, the goal of our study was to perform a meta-analysis on the effects of preoperative biliary stenting on patients with obstructive jaundice and to explore the impact of preoperative internal drainage on postoperative complications and mortality.

MATERIALS AND METHODS

Materials

All published and unpublished journal articles regarding the impact of preoperative biliary drainage on patients with obstructive jaundice from 2000 to present day were searched by both computer and manual procedures. We followed the meta-analysis of observational studies in epidemiology (MOOSE) guidelines for searching and reporting, and this investigation was approved by the ethics committee of the Affiliated Hospital of Guiyang Medical College. Computer research was done in databases of PubMed, Embase, Cochrane Library, and other relevant databases, with the following keywords: preoperative biliary drainage, preoperative biliary stenting, malignant obstructive jaundice, ampullary carcinoma, pancreatic cancer, and pancreaticoduodenectomy. No language restrictions were set; mesh

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words and free words were combined. In this way, the search range was maximized to select articles that met the requirements.

Methods

Inclusion Criteria

Patients were mainly those suffering from obstructive jaundice; cancer patients who had no local invasion, distant metastasis or cholangitis, and whose condition still allows operations were also included. The primary surgical method was pancreaticoduodenectomy. The intervention measure was biliary stent placement for internal drainage, and there were no restrictions regarding the surgical approach for stent placement, drainage time, or stent material. The outcomes included postoperative morbidity and/or postoperative mortality. The hypotheses of all the included studies were similar.

Exclusion Criteria

The patient had local invasion or distant metastasis, or concomitant cholangitis; the drainage method was external drainage or a combination of external and internal; the outcomes did not include postoperative complications and mortality; repeated reports; the design was flawed, and the quality of the study was poor.

Literature Screening, Quality Assessment, and Data Extraction

The literature was screened by 2 investigators independently, the quality of the studies were assessed afterwards based on the quality assessment criteria recommended by the *Cochrane Handbook for Systematic Reviews* (Higgins JPT, Green S, eds. Cochrane handbook for systematic reviews of interventions: version 5.0.1. Cochrane Collaboration, 2008), namely whether the included studies involved randomly assigned groups, allocation concealment, blind design, description of dropped follow-ups, intention to treat (ITT) analysis on dropped follow-ups, and consistent baselines. The data in all studies were then extracted before a cross-check of the results. If there was disagreement, a discussion or consultation with a third party was needed.

Statistical Analysis

Meta-analysis was performed on RevMan 5.2 (The Cochrane Collaboration, Oxford, UK) software provided by the Cochrane Collaboration. A χ^2 test was performed to test the heterogeneity between target studies. If there was no significant heterogeneity ($P \ge 0.05$), the fixed effect model was applied for follow-up analysis; if there was significant heterogeneity (P < 0.05), the random effects model was applied. The outcome variables were the ratio of postoperative morbidity and mortality of the group with preoperative drainage to that of the group without preoperative drainage, that is, the corresponding odds ratio (OR). STATA 12.0 (Stata, StataCorp, College Station, TX, USA) software was used to analyze publication bias through Begg test. Subgroup analysis was used to evaluate the effect of drainage material and time to the results.

RESULTS

Characteristics of the Included Studies and Quality Assessment

According to the inclusion and exclusion criteria, a total of 14 articles were included in the present study. The total number of patients was 2248, of whom 1305 had undergone

preoperative drainage and 943 had not. Among the 14 articles, 11 (quality assessment for class C) of them were retrospective cohort studies except for 3 (quality assessment for class B) randomized controlled trials. Two studies out of the 14 involved pancreatic cancer patients and 1 study involved an ampullary cancer patient; the other studies were all about patients with obstructive jaundice who once underwent pancreaticoduode-nectomy. In 1/14 articles, patients who had preoperative drainage were divided into 2 subgroups based on the stent material, that is, metal or plastic, to compare the effects of stent material on the outcome; in another article, the drainage group was divided into 3 subgroups based on the preoperative serum bilirubin levels that were low, medium, or high. The result of quality assessment of the included literature is shown in Table 1.

Meta-Analysis

Overall Mortality

All studies reported the overall mortality. There was no significant heterogeneity among the studies (P = 0.63); therefore, the fixed effects model was used. The result of metaanalysis showed that the overall mortality did not differ significantly between the 2 groups (OR = 0.74, 95% confidence interval [CI] [0.52, 1.05]) (see Figure 1A).

Overall Morbidity

Twelve studies reported the overall morbidity. There was significant heterogeneity between the studies (P = 0.002), and therefore, the random effects model was used. The metaanalysis showed that the overall morbidity did not differ significantly between the 2 groups (OR = 1.11, 95% CI [0.76, 1.64]) (see Figure 1B).

Incidence of Infectious Morbidity

Seven studies reported the incidence of infectious morbidity. There was significant heterogeneity among the studies (P < 0.001), and therefore, the random effects model was used. The meta-analysis showed that the incidence of infectious morbidity did not differ significantly between the 2 groups (OR = 1.62, 95% CI [0.70, 3.77]) (see Figure 1C).

Incidence of Wound Infection

Ten studies reported the incidence of wound infection. There was significant heterogeneity among the studies (P = 0.009), and therefore, the random effects model was used. The meta-analysis showed that the incidence of wound infection morbidity did not differ significantly between the 2 groups (OR = 1.46, 95% CI [0.69, 3.10]) (see Figure 1D).

Incidence of Intra-abdominal Abscess

Seven studies reported the incidence of intra-abdominal abscess. There was no significant heterogeneity among the studies (P = 0.04), and therefore, the fixed effects model was used. The meta-analysis showed that the incidence of intra-abdominal abscess did not differ significantly between the 2 groups (OR = 0.77, 95% CI [0.30, 1.93]) (see Figure 1E).

Incidence of Pancreatic Fistula

Six studies reported the incidence of pancreatic fistula. There was no significant heterogeneity among the studies (P = 0.44), and therefore, the fixed effects model was used.

Authors	Study Type	Study Quality	Group	Number of Patients	Male/ Female	Age, y	Drainage Time, d	Drainage Material
Abdullah et al ¹⁴	NRCT	С	Stent	35	14/21	65	39	Plastic
			No stent	47	26/21	62		
Bhati et al ³	NRCT	С	Stent	21	10/11	50		Plastic
			No stent	27	15/12	48		
Coates et al ¹⁵	NRCT	С	Stent	56	31/25	66 ± 12	39	_
			No stent	34	17/17	85 ± 15		
Eshuis et al ¹⁶	RCT	В	Stent	95	51/44	64.7 ± 10.3	28 - 42	Plastic
			No stent	90	63/27	64.6 ± 9.5		
Gaag et al ¹⁷	RCT	В	Stent	102	53/49	64.7 ± 10.5	28-42	Plastic
0			No stent	94	66/28	64.7 ± 9.5		
Hodul et al ⁷	NRCT	С	Stent	154	95/59	66 ± 11	_	_
			No stent	58	33/25	64 ± 10		
Howard et al ¹⁸	NRCT	С	Stent	86	52/34	61 ± 13	_	_
			No stent	52	61 ± 13	59 ± 14		
Jagannath et al ¹⁹	NRCT	С	Stent	74	50/24	50	42	Plastic
C			No stent	70	48/22	50		
Mezhir et al ¹³	NRCT	С	Stent	94	48/46	68 ± 10	27	Plastic + meta
			No stent	94	47/47	69 ± 9		
Lermite et al ²⁰	RCT	В	Stent	28	22/6	64.8 ± 9.3	24	Plastic
			No stent	28	17/11	64.4 ± 9.5		
Mullen et al ²¹	NRCT	С	Stent	170	_	_	43	Plastic + meta
			No stent	92		_		
Pešková et al ⁴	NRCT	С	Stent	144	_	63	18	_
			No stent	160		53.2		
Santos et al ²²	NRCT	С	Stent	14	6/8	69.6	_	_
			No stent	39	21/18	60.1		
Sewnath et al ⁵	NRCT	С	Stent	232	118/114	66	41	Plastic
		-	No stent	58	30/28	65		

TABLE 1. Patient Information of the Included Studies

NRCT = nonrandomized controlled trial, RCT = randomized controlled trial.

The meta-analysis showed that the incidence of pancreatic fistula did not differ significantly between the 2 groups (OR = 0.95, 95% CI [0.56, 1.61]) (see Figure 1F).

Incidence of Bile Leak

Six studies reported the incidence of pancreatic bile leak. There was no significant heterogeneity among the studies (P = 0.79), and therefore, the fixed effects model was used. The meta-analysis showed that the incidence of bile leak did not differ significantly between the 2 groups (OR = 1.61, 95% CI [0.74, 3.51]) (see Figure 1G).

Incidence of Delayed Gastric Emptying

Eight studies reported the incidence of delayed gastric emptying. There was no significant heterogeneity among the studies (P = 0.82), and therefore, the fixed effects model was used. The meta-analysis showed that the incidence of delayed gastric emptying did not differ significantly between the 2 groups (OR = 1.07, 95% CI [0.75, 1.54]) (see Figure 1H).

Publication Bias Analysis

A funnel plot was applied for publication bias analysis (Figure 2), which resulted in a symmetric inverted funnel shape in all plots. The results of Begg test indicate that there were no publication bias in all studies (P > 0.252).

Subgroup Analysis

Group Analysis Based on Drainage Time

Ten studies reported the duration of preoperative drainage, including 3 studies discussing a duration of <4 weeks (group I) and 7 discussing a duration of >4 weeks (group II). As shown in Figure 3, the overall mortalities of groups I and II were (OR = 0.66, 95% CI [0.28, 1.58]) and (OR = 0.75, 95% CI [0.50, 1.13]), respectively, which indicate that they did not differ from each other significantly. Besides, in groups of I and II, the overall morbidities were (OR = 1.90, 95% CI [1.33, 2.70]) and (OR = 1.61, 95% CI [0.68, 3.82]), respectively. When compared with nondrainage patients of group I, the overall morbidity of drainage patients increased by 7% to 23%, which was greater than that of nondrainage patients; whereas, the overall morbidity of group II was not obviously different between drainage and nondrainage patients. We speculated that longer drainage duration, for instance, >4 weeks, might help reduce the overall morbidity.

Group Analysis Based on Stent Material

Nine studies discussed the stent material (metal/plastic). In 7 studies, plastic stents were used and in the remaining 2, both metal and plastic stents were used. As shown in Figure 4, the overall mortalities of plastic and metal–plastic group were (OR = 0.88, 95% CI [0.58, 1.34]) and (OR = 0.14, 95% CI

	Study or subgroup	Ster Events	nt Total	No s Events	stent Tota	al Weight	Odds ratio M-H. Fixed 95% Cl		M-	Odds	ratio d 95% CI		
	Abdullah et al	10	35	13	47	10.8%	1.05 [0.40, 2.77]				<u> </u>		
	Bhati et al	3	21	5	27	5.1%	0.73 [0.15, 3.49]			-			
	Coastes et al	3	56	8	34	12.9%	0.18 [0.05, 0.75]	-					
	Eshuis et al	77	95	76	90	20.2%	0.79 [0.37, 1.70]				<u>+-</u>		
	Gaag et al	15	102	12	94		1.18 [0.52, 2.67]						
	Hodul et al	3	154	1	58		1.13 [0.12, 11.11]				-		
	Howard et al	2	86	1	52		1.21 [0.11, 13.73]			_	•		
	Jagannath et al	3	74	6	60		0.45 [0.11, 1.88]	4					
	James et al Lermite et al	0 1	94 28	5 2	94 28	7.5% 2.6%	0.09 [0.00, 1.58]	` -	_	_			
	Mullen et al	1	170	2	92		0.48 [0.04, 5.64] 0.27 [0.02, 2.98]			_	<u> </u>		
	Peskova et al	7	144	6	160		1.31 [0.43, 4.00]				 -		
	Santos et al	0	14	3	39	2.5%	0.36 [0.02, 7.41]			-			
	Sewnath et al	3	232	0	58	1.1%	1.78 [0.09, 35.03]				-		_
	Total (95% CI)		1305		943	100.0%	0.74 [0.52, 1.05]			•	•		
	Total events Heterogeneity: $\xi^2 = 10.75$			=0%				+				+	-+
A	Test for overall effect: Z =	1.70 (<i>P</i> = 0.09	9)					0.02	0.1	Stent	1 No Ster	10 nt	50
		Ster	nt	No S	Stent		Odds Ratio			Odds	Ratio		
	Study or Subgroup	Events	Total	Events	Tota	al Weight	M-H. Random, 95%	CI	M-H	. Rand	om 95% C		
	Hodul et al	51	154	25	58	12.2%	0.65 [0.35, 1.21]				t		
	Howard et al	37	86	19	52	11.1%	1.31 [0.65, 2.66]			_			
	Jagannath et al	30	74	30	70	11.6%	0.91 [0.47, 1.76]			_			
	James et al	48	94	39	94	12.7%	1.47 [0.83, 2.62]			-			
	Lermite et al	21	28	16	28	7.0%	2.25 [0.72, 7.01]			-			
	Mullen et al	100	170	69	92	12.8%	0.48 [0.27, 0.84]						
	Peskova et al	61	144	40	160	13.8%	2.20 [1.35, 3.59]						
	Santos et al	9	14	18	39	6.2%	2.10 [0.59, 7.41]				•	-	
	Sewnath et al	117	232	32	58	12.7%	0.83 [0.46, 1.47]				-		
	Total (95% CI)		996		651	100.0%	1.11 [0.76, 1.64]			•			
	Total events	474					[· · · ·]						
	Heterogeneity: $\tau^2 = 0.22$ &		8 (P - 0	1 002). R=	67%			+				+	+
В	Test for overall effect: $Z=0.22$			J.002), I	07 /0			0.02	0.1	-	1	10	50
			,							Stent	No Sten	t	
		Ster	nt	No S	Stent		Odds Ratio			Odds	Ratio		
	Study or Subgroup	Ster Events	nt Total	No S Events		al Weight	Odds Ratio M-H. Random 95% (21	M-H		Ratio om 95% (CI	
	Study or Subgroup						M-H. Random 95% (21	M-H			CI	
	Abdullah et al	Events 11	Total 35	Events 26	Tota 47	15.7%	M-H. Random 95% (0.37 [0.15, 0.93]	3	M-H				
	Abdullah et al Bhati et al	Events 11 9	Total 35 21	Events 26 1	Tota 47 27	15.7% 8.4%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86]	<u>)</u>	M-H				
	Abdullah et al Bhati et al Coastes et al	Events 11 9 10	Total 35 21 56	Events 26 1 7	Tota 47 27 34	15.7% 8.4% 14.6%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46]		<u>M-H</u>			<u></u>	
	Abdullah et al Bhati et al Coastes et al Jagannath et al	Events 11 9 10 22	Total 35 21 56 74	Events 26 1 7 29	Tota 47 27 34 70	15.7% 8.4% 14.6% 17.0%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19]	<u>, </u>	M-H				>
	Abdullah et al Bhati et al Coastes et al	Events 11 9 10	Total 35 21 56	Events 26 1 7	Tota 47 27 34	15.7% 8.4% 14.6%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46]	21	M-H -				
	Abdullah et al Bhati et al Coastes et al Jagannath et al	Events 11 9 10 22	Total 35 21 56 74	Events 26 1 7 29	Tota 47 27 34 70	15.7% 8.4% 14.6% 17.0%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19]		<u>M-H</u>			<u>-</u>	
	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al	Events 11 9 10 22 30	Total 35 21 56 74 94	Events 26 1 7 29 12	Tota 47 27 34 70 94	15.7% 8.4% 14.6% 17.0% 16.7%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75]	21	<u>M-H</u>			<u>-</u>	
	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI)	Events 11 9 10 22 30 14 7	Total 35 21 56 74 94 28	Events 26 1 7 29 12 6 11	Tota 47 27 34 70 94 28 39	15.7% 8.4% 14.6% 17.0% 16.7% 14.0%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79]		<u>M-H</u>			<u>-</u>	_
	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al	Events 11 9 10 22 30 14 7	Total 35 21 56 74 94 28 14	Events 26 1 7 29 12 6	Tota 47 27 34 70 94 28 39	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96]		<u>M-H</u>			<u>-</u>	
	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.96$ 5	Events 11 9 10 22 30 14 7 103 ² = 28.52, <i>df</i> =	Total 35 21 56 74 94 28 14 322 $\in 6 (P = 0)$	Events 26 1 7 29 12 6 11 92	Tota 47 27 34 70 94 28 39 339	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96]	+		<u>I. Rand</u>	om 95% (→
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events	Events 11 9 10 22 30 14 7 103 ² = 28.52, <i>df</i> =	Total 35 21 56 74 94 28 14 322 $\in 6 (P = 0)$	Events 26 1 7 29 12 6 11 92	Tota 47 27 34 70 94 28 39 339	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96]	0.02	<u>M-H</u>	<u>I. Rand</u>	om 95% (<u>-</u> - 10	→ 50
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.96$ 5	Events 11 9 10 22 30 14 7 103 ² = 28.52, <i>df</i> =	Total 35 21 56 74 94 28 14 322 $\in 6 (P = 0)$	Events 26 1 7 29 12 6 11 92	Tota 47 27 34 70 94 28 39 339	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96]	+		<u>I. Rand</u>	om 95% (- 10	→ 50
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.96$ 5	Events 11 9 10 22 30 14 7 103 ² = 28.52, <i>df</i> =	Total 35 21 56 74 94 28 14 322 $\in 6 (P = 0)$	Events 26 1 7 29 12 6 11 92	Tota 47 27 34 70 94 28 39 339	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96]	+		<u>I. Rand</u>	om 95% (- 10	→ 50
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.96 \xi$ Test for overall effect: Z=	Events 11 9 10 22 30 14 7 103 $S^2 = 28.52, df =$ 1.13 ($P = 0.26$ Ster	$ \begin{array}{r} Total \\ 35 \\ 21 \\ 56 \\ 74 \\ 94 \\ 28 \\ 14 \\ 322 \\ 6 (P = 0) \\) \end{array} $	Events 26 1 7 29 12 6 11 92 0.0001); <i>F</i>	Tota 47 27 34 70 94 28 39 339 339 2=79%	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77]	-+		I. Rand	om 95% (- - 10 ent	
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.96 \xi$ Test for overall effect: $Z =$	Events 11 9 10 22 30 14 7 103 $s^2 = 28.52, df = 1.13 (P = 0.26)$ Ster Events	Total 35 21 56 74 94 28 14 322 $e \in (P = 0)$ ont Total	Events 26 1 7 29 12 6 11 92 0.0001); <i>f</i> Events	Tota 47 27 34 70 94 28 39 339 339 2=79%	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] Odds Ratio M-H. Random 95% (-+		I. Rand	om 95% (- - 10 ent	
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.96 \xi$ Test for overall effect: $Z =$ Study or Subgroup Abdullah et al	Events 11 9 10 22 30 14 7 103 ² = 28.52, df = 1.13 (P = 0.26 Ster Events 1	Total 35 21 56 74 94 28 14 322 : 6 ($P = 0$) nt Total 35	Events 26 1 7 29 12 6 11 92 0.0001); <i>F</i> 0.0001); <i>F</i> No S Events	<u>Tota</u> 47 27 34 70 94 28 39 339 339 339 2≥=79%	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 0.009 [0.01, 0.70	-+		I. Rand	om 95% (- - 10 ent	→ +- 50
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.96 \xi$ Test for overall effect: $Z =$ Study or Subgroup Abdullah et al Bhati et al	Events 11 9 10 22 30 14 7 103 $\zeta^2 = 28.52, df =$ 1.13 (P = 0.26) Ster Events 1 5	$ \frac{\text{Total}}{35} \\ 21 \\ 56 \\ 74 \\ 94 \\ 28 \\ 14 \\ 322 \\ 6 \\ (P = 0) \\ 14 \\ 322 \\ 14 \\ 322 \\ 35 \\ 21 \\ 35 \\ 21 $	Events 26 1 7 29 12 6 11 92 0.0001); <i>F</i> 0.0001); <i>F</i> <u>Events</u> 12 1	<u>Tota</u> 47 27 34 70 94 28 39 339 339 2≥=79% Stent <u>Tota</u> 47 27	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% <u>100.0%</u>	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 0.62 [0.70, 3.77] 0.0405 Ratio M-H. Random 95% (0.09 [0.01, 0.70 8.13 [0.87, 75.98]	-+		I. Rand	om 95% (- - 10 ent	
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% Cl) Total events Heterogeneity: $r^2 = 0.96$ E Test for overall effect: $Z = 1000$ Study or Subgroup Abdullah et al Bhati et al Coastes et al	Events 11 9 10 22 30 14 7 103 ² = 28.52, df = 1.13 (P = 0.26 Ster Events 1	Total 35 21 56 74 94 28 14 322 : 6 ($P = 0$) nt Total 35	Events 26 1 7 29 12 6 11 92 0.0001); <i>F</i> 0.0001); <i>F</i> No S Events	<u>Tota</u> 47 27 34 70 94 28 39 339 339 339 2≥=79%	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 0.009 [0.01, 0.70	-+		I. Rand	om 95% (- - 10 ent	
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.96 \xi$ Test for overall effect: $Z =$ Study or Subgroup Abdullah et al Bhati et al	Events 11 9 10 22 30 14 7 103 $\zeta^2 = 28.52, df =$ 1.13 (P = 0.26) Ster Events 1 5	$ \frac{\text{Total}}{35} \\ 21 \\ 56 \\ 74 \\ 94 \\ 28 \\ 14 \\ 322 \\ 6 \\ (P = 0) \\ 14 \\ 322 \\ 14 \\ 322 \\ 35 \\ 21 \\ 35 \\ 21 $	Events 26 1 7 29 12 6 11 92 0.0001); <i>F</i> 0.0001); <i>F</i> <u>Events</u> 12 1	<u>Tota</u> 47 27 34 70 94 28 39 339 339 2≥=79% Stent <u>Tota</u> 47 27	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% <u>100.0%</u>	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 0.62 [0.70, 3.77] 0.0405 Ratio M-H. Random 95% (0.09 [0.01, 0.70 8.13 [0.87, 75.98]	+		I. Rand	om 95% (- - 10 ent	→ + 50
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% Cl) Total events Heterogeneity: $r^2 = 0.96$ E Test for overall effect: $Z = 1000$ Study or Subgroup Abdullah et al Bhati et al Coastes et al	Events 11 9 10 22 30 14 7 103 $g^2 = 28.52, df =$ 1.13 (P = 0.26) Ster Events 1 5 3		Events 26 1 7 29 12 6 11 92 0.0001); <i>F</i> No S Events 12 1 3	<u>Tota</u> 47 27 34 70 94 28 39 339 339 339 2≥=79% Stent <u>Tota</u> 47 27 34	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% 100.0% <u>100.0%</u> 7.9% 7.3% 10.3%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 0.070 [0.01, 0.70 8.13 [0.87, 75.98 0.58 [0.11, 3.08]	-+		I. Rand	om 95% (- - 10 ent	→ + 50
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $r^2 = 0.96 \xi$ Test for overall effect: $Z =$ Study or Subgroup Abdullah et al Bhati et al Coastes et al Hodul et al	Events 11 9 10 22 30 14 7 103 $S^2 = 28.52, df =$ 1.13 (P = 0.26) Ster Events 1 5 3 12	$ \frac{\text{Total}}{35} $ 21 56 74 94 28 14 322 6 (P = 0) 156 154	Events 26 1 7 29 12 6 11 92 0.0001); <i>F</i> Events 12 1 3 0	Tota 47 47 27 34 70 94 28 39 339 339 339 339 339 339 339 339 22=79% Stent Tota 47 58	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% 100.0%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 1.62 [0.70, 3.77] 0.09 [0.01, 0.70 8.13 [0.87, 75.98 0.58 [0.11, 3.08 10.26 [0.60, 176.20]	+- 0.02		I. Rand	om 95% (- - 10 ent	→ 50
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С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.96 \xi$ Test for overall effect: $Z =$ Study or Subgroup Abdullah et al Bhati et al Coastes et al Hodul et al Jagannath et al Jagannath et al James et al	Events 11 9 10 22 30 14 7 103 ² = 28.52, df = 1.13 (P = 0.26 Ster Events 1 5 3 12 12 15 19	$ \frac{\text{Total}}{35} $ 21 56 74 94 28 14 322 66 ($P = 0$) t $\frac{\text{Total}}{56} $ 154 86 74 94	Events 26 1 7 29 12 6 11 92 0.0001); <i>f</i> No S Events 12 1 3 0 1 16 7	$\begin{array}{r} \hline \text{Tota} \\ 47 \\ 27 \\ 34 \\ 70 \\ 94 \\ 28 \\ 39 \\ 339 \\ 339 \\ 339 \\ 339 \\ 339 \\ 339 \\ 47 \\ 27 \\ 34 \\ 58 \\ 52 \\ 70 \\ 94 \\ 94 \\ \end{array}$	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% 100.0% 100.0% 100.0% 100.3% 5.2% 8.0% 16.8% 15.8%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 1.62 [0.70, 3.77] 0.09 [0.01, 0.70 8.13 [0.87, 75.98 0.58 [0.11, 3.08 10.26 [0.60, 176.20 8.27 [1.04, 65.60 0.86 [0.39, 1.90 3.15 [1.25, 7.90	+		I. Rand	om 95% (- - 10 ent	→ + 50
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С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $r^2 = 0.96$ § Test for overall effect: $Z = 100$ Study or Subgroup Abdullah et al Bhati et al Coastes et al Hodul et al Howard et al Jagannath et al James et al Mullen et al Sewnath et al	Events 11 9 10 22 30 14 7 103 $j^2 = 28.52$, $df =$ 1.13 ($P = 0.26$ Ster Events 1 5 3 12 15 19 11 17	$\frac{\text{Total}}{35}$ 21 56 74 94 28 14 322 66 (P = C) 154 86 74 94 170 232	Events 26 1 7 29 12 6 11 92 0.0001); <i>F</i> Events 12 1 3 0 1 16 7 4	Tota 47 27 34 70 94 28 39 339 2=79% Stent Tota 47 27 34 52 70 94 52 70 94 92 58	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 1.62 [0.70, 3.77] 0.99 [0.01, 0.70 8.13 [0.87, 75.98 0.58 [0.11, 3.08 10.26 [0.60, 176.20 8.27 [1.04, 65.60 0.86 [0.39, 1.90 3.15 [1.25, 7.90) 1.52 [0.47, 4.92 0.84 [0.30, 2.37	+		I. Rand	om 95% (- - 10 ent	→ 50
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $r^2 = 0.96$ § Test for overall effect: $Z =$ Study or Subgroup Abdullah et al Bhati et al Coastes et al Hodul et al Howard et al Jagannath et al James et al Mullen et al Sewnath et al Total (95% CI)	Events 11 9 10 22 30 14 7 .103 $j^2 = 28.52$, $df =$ 1.13 ($P = 0.26$ Ster Events 1 5 3 12 15 19 11 17	$ \frac{\text{Total}}{35} $ 21 56 74 94 28 14 322 66 ($P = 0$) 7 $ \frac{1}{35} $ 21 56 154 86 74 94 170	Events 26 1 7 29 12 6 11 92 0.0001); <i>F</i> No S Events 12 1 3 0 1 16 7 4 5	Tota 47 27 34 70 94 28 39 339 2=79% Stent Tota 47 27 34 52 70 94 92 58	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 1.62 [0.70, 3.77] 1.62 [0.70, 3.77] 0.813 [0.87, 75.98 0.58 [0.11, 3.08 10.26 [0.60, 176.20 8.27 [1.04, 65.60 0.86 [0.39, 1.90 3.15 [1.25, 7.90 1.52 [0.47, 4.92]	+		I. Rand	om 95% (- - 10 ent	→ + 50
С	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.96 \xi$ Test for overall effect: $Z =$ Study or Subgroup Abdullah et al Bhati et al Coastes et al Hodul et al Howard et al Jagannath et al James et al Mullen et al Sewnath et al Total (95% CI) Total events	Events 11 9 10 22 30 14 7 103 i ² = 28.52, df = 1.13 (P = 0.26) Ster 1 5 3 12 15 19 11 17 95	$\begin{array}{c} \hline {\rm Total} \\ 35 \\ 21 \\ 56 \\ 74 \\ 94 \\ 28 \\ 14 \\ 322 \\ \hline 6 \ (P=0) \\ \hline \\ \hline \\ 10 \\ 10 \\ 154 \\ 86 \\ 74 \\ 94 \\ 170 \\ 232 \\ 922 \\ \end{array}$	Events 26 1 7 29 12 6 11 92 0.0001); <i>F</i> No S Events 12 1 3 0 1 16 7 4 5 49	Tota 47 27 34 70 94 28 39 34 352 36 37 38 39 39 39 39 39 39 <td< td=""><td>15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%</td><td>M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 1.62 [0.70, 3.77] 0.99 [0.01, 0.70 8.13 [0.87, 75.98 0.58 [0.11, 3.08 10.26 [0.60, 176.20 8.27 [1.04, 65.60 0.86 [0.39, 1.90 3.15 [1.25, 7.90) 1.52 [0.47, 4.92 0.84 [0.30, 2.37</td><td>+</td><td></td><td>I. Rand</td><td>om 95% (</td><td>- - 10 ent</td><td>→ + 50 </td></td<>	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 1.62 [0.70, 3.77] 0.99 [0.01, 0.70 8.13 [0.87, 75.98 0.58 [0.11, 3.08 10.26 [0.60, 176.20 8.27 [1.04, 65.60 0.86 [0.39, 1.90 3.15 [1.25, 7.90) 1.52 [0.47, 4.92 0.84 [0.30, 2.37	+		I. Rand	om 95% (- - 10 ent	→ + 50
	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.96$ E Test for overall effect: $Z =$ Study or Subgroup Abdullah et al Bhati et al Coastes et al Hodul et al Jagannath et al Jagannath et al Sewnath et al Sewnath et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.71$	$\begin{tabular}{c} \hline Events \\ \hline 11 \\ 9 \\ 10 \\ 22 \\ 30 \\ 14 \\ 7 \\ 103 \\ 14 \\ 7 \\ 130 \\ e^2 = 28.52, \ df = 100 \\ 1.13 \ (P = 0.26) \\ \hline Events \\ \hline 113 \ (P = 0.26) \\ \hline 113 \ (P = 0.26) \\ \hline 123 \\ 123$	$\begin{array}{c} \hline {\rm Total} \\ 35 \\ 21 \\ 56 \\ 74 \\ 94 \\ 28 \\ 14 \\ 322 \\ 6 \\ (P=0) \\ \hline \\ \hline \\ \hline \\ 15 \\ 6 \\ 154 \\ 86 \\ 74 \\ 94 \\ 170 \\ 232 \\ 922 \\ = 8 \\ (P=-1) $	Events 26 1 7 29 12 6 11 92 0.0001); <i>F</i> No S Events 12 1 3 0 1 16 7 4 5 49	Tota 47 27 34 70 94 28 39 34 352 36 37 38 39 39 39 39 39 39 <td< td=""><td>15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%</td><td>M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 1.62 [0.70, 3.77] 0.99 [0.01, 0.70 8.13 [0.87, 75.98 0.58 [0.11, 3.08 10.26 [0.60, 176.20 8.27 [1.04, 65.60 0.86 [0.39, 1.90 3.15 [1.25, 7.90) 1.52 [0.47, 4.92 0.84 [0.30, 2.37</td><td>+ 0.02</td><td></td><td>I. Rand</td><td>om 95% (</td><td></td><td></td></td<>	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 1.62 [0.70, 3.77] 0.99 [0.01, 0.70 8.13 [0.87, 75.98 0.58 [0.11, 3.08 10.26 [0.60, 176.20 8.27 [1.04, 65.60 0.86 [0.39, 1.90 3.15 [1.25, 7.90) 1.52 [0.47, 4.92 0.84 [0.30, 2.37	+ 0.02		I. Rand	om 95% (
C	Abdullah et al Bhati et al Coastes et al Jagannath et al James et al Lermite et al Santos et al Total (95% CI) Total events Heterogeneity: $\tau^2 = 0.96 \xi$ Test for overall effect: $Z =$ Study or Subgroup Abdullah et al Bhati et al Coastes et al Hodul et al Howard et al Jagannath et al James et al Mullen et al Sewnath et al Total (95% CI) Total events	$\begin{tabular}{c} \hline Events \\ \hline 11 \\ 9 \\ 10 \\ 22 \\ 30 \\ 14 \\ 7 \\ 103 \\ 14 \\ 7 \\ 130 \\ e^2 = 28.52, \ df = 100 \\ 1.13 \ (P = 0.26) \\ \hline Events \\ \hline 113 \ (P = 0.26) \\ \hline 113 \ (P = 0.26) \\ \hline 123 \\ 123$	$\begin{array}{c} \hline {\rm Total} \\ 35 \\ 21 \\ 56 \\ 74 \\ 94 \\ 28 \\ 14 \\ 322 \\ 6 \\ (P=0) \\ \hline \\ \hline \\ \hline \\ 15 \\ 6 \\ 154 \\ 86 \\ 74 \\ 94 \\ 170 \\ 232 \\ 922 \\ = 8 \\ (P=-1) $	Events 26 1 7 29 12 6 11 92 0.0001); <i>F</i> No S Events 12 1 3 0 1 16 7 4 5 49	Tota 47 27 34 70 94 28 39 34 352 36 37 38 39 39 39 39 39 39 <td< td=""><td>15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%</td><td>M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 1.62 [0.70, 3.77] 0.99 [0.01, 0.70 8.13 [0.87, 75.98 0.58 [0.11, 3.08 10.26 [0.60, 176.20 8.27 [1.04, 65.60 0.86 [0.39, 1.90 3.15 [1.25, 7.90) 1.52 [0.47, 4.92 0.84 [0.30, 2.37</td><td>+</td><td></td><td>I. Rand</td><td>om 95% (</td><td></td><td>→ + 50 </td></td<>	15.7% 8.4% 14.6% 17.0% 16.7% 14.0% 13.5% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	M-H. Random 95% (0.37 [0.15, 0.93] 19.50 [2.21, 171.86] 0.84 [0.29, 2.46] 0.60 [0.30, 1.19] 3.20 [1.52, 6.75] 3.67 [1.14, 11.79] 2.55 [0.72, 8.96] 1.62 [0.70, 3.77] 1.62 [0.70, 3.77] 0.99 [0.01, 0.70 8.13 [0.87, 75.98 0.58 [0.11, 3.08 10.26 [0.60, 176.20 8.27 [1.04, 65.60 0.86 [0.39, 1.90 3.15 [1.25, 7.90) 1.52 [0.47, 4.92 0.84 [0.30, 2.37	+		I. Rand	om 95% (→ + 50

FIGURE 1. (A) Overall mortality, (B) overall morbidity, (C) infectious morbidity, (D) wound infection, (E) intra-abdominal abscess, (F) pancreatic fistula, (G) bile leak, (H) delayed gastric emptying.

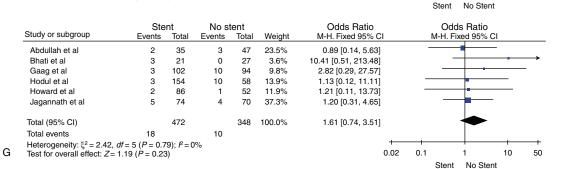
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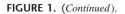
Study or subgroup	Ste Events		No s Events		Weight	Odds Ratio M-H. Random 95% (CI		Odds Rat Random 9		
Abdullah et al	1	35	8	47	11.2%	0.14 [0.02, 1.21]		-			
Gaag et al	2	102	3	94	13.5%	0.61 [0.10, 3.71]			-	-	
Hodul et al	10	154	3	58	17.7%	1.27 [0.34, 4.80]					
Howard et al	2	86	4	52	14.1%	0.29 [0.05, 1.62]					
James et al	11	84	3	94	17.9%	4.02 [1.08, 14.91]				-	
Mullen et al	4	170	6	92	18.1%	0.35 [0.09, 1.26]					
Sewnath et al	38	232	0	9	7.6%	3.53 [0.20, 61.98]		_		•	
Total (95% CI)		873		446	100.0%	0.77 [0.30, 1.93]			•		
Total events	66		27								
Heterogeneity: $\tau^2 = 0.80$ Test for overall effect: $Z=$			0.04); <i>I</i> ²=	54%			0.02	0.1	1	10	50

Study or subgroup		ent ts Total		stent ts Total	Weight	Odds Ratio M-H. Random 95% CI	Odds Ratio M-H. Random 95% Cl
Abdullah et al	2	35	2	47	5.7%	1.36 [0.18, 10.19]	
Bhati et al	6	21	2	27	4.4%	5.00 [0.89, 28.02]	
Hodul et al	15	154	8	58	37.2%	0.67 [0.27, 1.69]	
Howard et al	2	86	2	52	8.6%	0.60 [0.08, 4.36]	
Jagannath et al	11	74	12	70	37.2%	0.84 [0.35, 2.06]	
Lermite et al	1	28	2	28	6.8%	0.48 [0.04, 5.64]	
Total (95% CI)		398		282	100.0%	0.95 [0.56, 1.61]	•
Total events	37		28				
Heterogeneity: $\xi^2 = 4.80$, Test for overall effect: Z=			6				0.02 0.1 1 10 50

F Test for overall effect: Z = 0.20 (P = 0.84)



Study or subgroup	St Events	ent Total	No s Events	tent Total	Weight	Odds Ratio M-H. Fixed 95% CI			ds Ratio	-	
Abdullah et al	6	35	10	47	12.4%	0.77 [0.25, 2.35]			-		
Gaag et al	18	102	9	94	13.5%	2.02 [0.86, 4.76]				_	
Hodul et al	7	154	2	58	4.9%	1.33 [0.27, 6.61]					
Howard et al	2	86	1	52	2.1%	1.21 [0.11, 13.73]			-		
Jagannath et al	5	74	5	70	8.4%	0.94 [0.26, 3.41]			-		
James et al	7	94	7	94	11.3%	1.00 [0.34, 2.97]			-		
Mullen et al	13	170	10	92	21.0%	0.68 [0.29, 1.62]			•+-		
Sewnath et al	50	232	12	58	26.4%	1.05 [0.52, 2.14]		-	-		
Total (95% CI)		947		565	100.0%	1.07 [0.75, 1.54]			•		
Total events	108		56								
Heterogeneity: $\xi^2 = 3.67$,			%				0.02	0.1	1	10	
Test for overall effect: Z=	0.38 (P = 0.7))					0.02	Stent	No St		50



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[0.02, 0.89]), respectively, and the overall morbidities of the 2 groups were (OR = 2.48, 95% CI [0.91, 6.77]) and (OR = 1.16, 95% CI [0.72, 1.86]), respectively. The overall morbidity was not affected by the stent material.

When compared with the nondrainage group, the overall mortality of the drainage group using metal-plastic stents was reduced by 0.5% to 6%; yet, the rates of the drainage group using plastic stents only were not significantly different. We conjectured that metal stents could reduce the overall mortality and possibly are superior to plastic ones.

DISCUSSION

It still remains controversial whether to perform preoperative biliary drainage on obstructive jaundice patients with indications for surgery routinely.^{4,13,23} Previous retrospective and prospective randomized controlled trials have drawn different conclusions. Some studies have reported that preoperative biliary drainage could reduce the length of a hospital stay, the proceeding $^{24-26}$ postoperative infection rate, renal damage, and bleeding.^{24–26} Lygidakis et al²⁷ suggested that preoperative biliary drainage

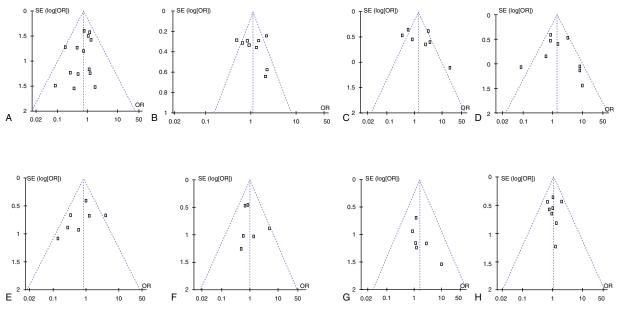


FIGURE 2. (A) Overall mortality, (B) overall morbidity, (C) infectious morbidity, (D) wound infection, (E) intra-abdominal abscess, (F) pancreatic fistula, (G) bile leak, (H) delayed gastric emptying.

could reduce the pressure within the biliary tract, improve liver function, and reduce perioperative bleeding and postoperative complications. Abdullah et al¹⁴ reported that preoperative biliary drainage could reduce the rate of wound infections and did not affect the overall mortality. However, some studies declared that preoperative biliary drainage can increase the chances of biliary infection and infectious complications.^{3,19,20} Pešková et al⁴ indicated that preoperative biliary drainage could also increase the overall morbidity. Studies have shown that

many severe complications were caused by improper drainage.¹⁷ Despite the improvements in drainage technology, surgical conditions, and perioperative care, it is still unclear whether the outcome of preoperative drainage has caused any improvements. Hence, in the current study, articles from the past decade were selected for meta-analysis.

Preoperative drainage methods include external and internal drainage. External drainage can lead to insufficient bile in the intestines, and thus, weakened inhibition of intestinal

Study or subgroup	Ste Events	nt Total	No st Events	ent Total	Weight	Odds Ratio M-H. Fixed 95% Cl			Odds Ratio		
James et al	48	94	39	94	42.5%	1.47 [0.83, 2.62]			+-		
Lermite et al	21	28	16	28	8.9%	2.25 [0.72, 7.01]			+		
Peskova et al	61	144	40	160	48.6%	2.20 [1.35, 3.59]					
Total (95% CI)		266		282	100.0%	1.90 [1.33, 2.70]			•		
Total events	130		95								
Heterogeneity: $\xi^2 = 1.20$, Test for overall effect: Z=			%				0.02	0.1 Ste	1 ent No St	10 ent	50

Study or subgroup	Ste Events	nt Total	No s Events	tent Tota	I Weight	Odds Ratio M-H. Random 95% C	I		s Ratio dom 95% Cl	
Coastes et al	21	56	16	34	16.5%	0.68 [0.28, 1.60]			+	
Eshuis et al	72	95	35	90	17.8%	4.92 [2.61, 9.26]				
Gaag et al	100	102	67	94	12.6%	20.15 [4.64, 87.57]				
Jagannath et al	30	74	30	70	17.7%	0.91 [0.47, 1.76]			-	
Mullen et al	21	170	16	92	17.4%	0.67 [0.33, 1.36]		-	t	
Sewnath et al	117	232		58	18.1%	0.83 [0.46, 1.47]		-	-	
Total (95% CI)		729		438	100.0%	1.61 [0.68, 3.82]				
Total events	361		196							
Heterogeneity: $\tau^2 = 0.99$ Test for overall effect: Z=			0.00001); <i>P</i>	^e =88%		(0.02 0.		1 10	50
								Stent	No Stent	

FIGURE 3. (A) Comparison of total morbidity between the nondrainage and drainage groups with drainage times <4 weeks. (B) Comparison of total morbidity between the nondrainage and drainage groups with drainage time >4 weeks.

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Study or subgroup	Ste Events	nt Total	No st Events	tent Total	Weight	Odds Ratio M-H. Fixed 95% Cl			lds Ratio Fixed 95% Cl	
James et al	0	94	5	94	68.0%	0.09 [0.00, 1.58]			-	
Mullen et al	1	170	2	92	32.0%	0.27 [0.02, 2.98]			+	
Total (95% CI)		264		186	100.0%	0.14 [0.02, 0.89]		\bullet		
Total events	1		7							
Heterogeneity: $\xi^2 = 0.37$, a	f = 1 (P = 0.5)	4); <i>I</i> ²=0°	%				+		1 10	
Test for overall effect: $Z=2$	2.09 (<i>P</i> = 0.04)					0.02	0.1 Stent	1 10 No Stent	50
Study or subgroup	Ste Events	nt Total	No st Events	tent Total	Weight	Odds Ratio M-H. Fixed 95% Cl			lds Ratio Fixed 95% Cl	

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Study or subgroup	Events	Total	Events	Total	Weight	M-H. Fixed 95% CI	M-H. Fixed 95% CI
Abdullah et al	10	35	13	47	17.3%	1.05 [0.40, 2.77]	
Bhati et al	3	21	5	27	8.2%	0.73 [0.15, 3.49]	
Eshuis et al	77	95	76	90	32.3%	0.79 [0.37 1.70]	
Gaag et al	15	102	12	94	23.3%	1.18 [0.52, 2.67]	
Jagannath et al	3	74	6	70	12.9%	0.45 [0.11, 1.88]	
Lermite et al	1	28	2	26	4.2%	0.48 [0.04, 5.64]	
Sewnath et al	3	232	0	58	1.7%	1.78 [0.09, 35.03]	
Total (95% CI)		587		414	100.0%	0.88 [0.58, 1.34]	•
Total events	1		7				
Heterogeneity: $\xi^2 = 2.04$,	$df = 6 \ (P = 0.9)$	2); <i>P</i> =0	%				
Test for overall effect: Z=	0.59 (P = 0.55						0.02 0.1 1 10 50
							Stent No Stent

FIGURE 4. (A) Comparison of total mortality between the nondrainage and drainage groups using plastic and metal as stent material. (B) Comparison of total mortality between the nondrainage and drainage groups using plastic as stent material.

bacteria causing endotoxemia.⁵ It may also cause malnutrition because of lipid malabsorption and fluid balance disorders because of bile loss. In contrast, internal drainage can significantly improve these drawbacks of external drainage. Materials used for internal drainage include plastic and metal stents. Plastic stents are inexpensive and easy to operate for repeated placement; however, its major disadvantage is the presence of 3 to 6 internal obstructions,²⁸ which may result in recurrence of jaundice and increase the incidence of cholangitis.^{29–31} Compared with plastic stents, metal stents have a larger diameter when expanded, and the expansion time is notably longer.^{32–34} Wasan et al³⁵ showed that metal stents could reduce the occurrence of cholangitis and intraoperative and postoperative complications. However, metal stents may also become obstructed through tumor ingrowth or overgrowth.36,37 We performed a meta-analysis on drainage subgroups using different stent materials and found that the overall mortality and morbidity of the subgroups using plastic stents were not significantly different from the nondrainage group. Compared with the nondrainage group, the overall morbidity of the drainage subgroup using plastic and metal stents was not significantly different, yet its overall mortality was significantly lower. Compared with using plastic stents only, the use of metal and plastic stents can reduce the overall mortality. This suggests that compared with plastic stents, metal stents can reduce mortality. However, there were only 2 studies that have used plastic and metal stents for internal drainage. The small number of available studies makes this conclusion unreliable.

Drainage time is still a rather controversial issue. The supporters of preoperative biliary drainage believe that the reason why preoperative biliary drainage did not have any benefits in some cases was that the drainage time was too short. As liver function recovery requires 4 to 6 weeks, even if the bilirubin level may have returned to normal prior to 4 weeks, the drainage time should last 4 to 6 weeks.^{4,20} However, an overly long drainage time may increase infectious morbidity. In the present study, a meta-analysis on studies with drainage times

 \geq 4 weeks showed that the overall mortality and morbidity were not significantly different from that of the nondrainage group. A meta-analysis on studies with drainage times <4 weeks showed that the overall mortality was not significantly different from that of the nondrainage group, yet the overall morbidity of the former group was significantly higher than that of the latter group. This suggests that a drainage time \geq 4 weeks can reduce overall morbidity compared with a drainage time <4 weeks. However, studies with drainage times \geq 4 weeks showed relatively large heterogeneity. Sensitivity analysis revealed that the results obtained from the fixed effects and random effects models were different. Hence, this conclusion is not very reliable.

Thus, we believe that preoperative biliary drainage should not be routinely applied. However, for patients with severe jaundice (serum bilirubin level \geq 150 µm/L), concomitant cholangitis, or severe malnutrition and patients who need a relatively long preoperative assessment and wait for a relatively long time before the surgery, preoperative drainage may be selectively applied.³⁸ We suggest that the drainage time should >4 weeks, and metal stents should be used for drainage.

This study has limitations. First, the quality of the included studies was not high. Second, there was a relatively large heterogeneity among different studies regarding the comparison of overall morbidity, infectious morbidity, and wound infection, and the results obtained from using the fixed effects and random effects models were different, thereby leading to unreliable conclusions. The main cause of the heterogeneity was that different studies defined the complications differently, and the evaluation criteria were different. Hence, future large-scale, large-sample, multicenter randomized controlled trials using standardized assessment indicators are still needed.

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