Metal stents versus plastic stents for the management of pancreatic walled-off necrosis: a systematic review and meta-analysis

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Background and Aims: Endoscopic transluminal drainage of symptomatic walled-off necrosis (WON) is a good management option, although the optimal choice of drainage site stent is unclear. We performed a systematic review and meta-analysis to compare metal stents (MSs) and plastic stents (PSs) in terms of WON resolution, likelihood of resolution after 1 procedure, and adverse events.

Methods: An expert librarian queried several databases to identify studies that assessed WON management, and selection was according to a priori criteria. Publication bias, heterogeneity, and study quality were evaluated with the appropriate tools. We performed single and 2-arm meta-analyses for noncomparative and comparative studies using event rate random-effects model and odds ratio (OR)/difference in means, respectively.

Results: We included 41 studies involving 2213 patients. In 2-arm study meta-analysis, WON resolution was more likely with MSs compared with PSs (OR, 2.8; 95% confidence interval, 1.7-4.6; $P < .001$). Resolution with a single endoscopic procedure was similar between stents (47% vs 44%), although for those cases requiring more than 1 intervention, the MS group had fewer interventions, favored by a mean difference of –.9 procedures (95% CI, –1.283 to –.561). In single-arm study meta-analysis, when compared with PSs, MS use was associated with lower bleeding (5.6% vs 12.6%; $P = .02$), a trend toward lower perforation and stent occlusion (2.8% vs 4.3%, $P = .2$, and 9.5% vs 17.4%, $P = .07$), although with higher migration (8.1% vs 5.1%; $P = .1$).

Conclusion: Evidence suggests that MSs are superior for WON resolution, with fewer bleeding events, trend toward less occlusion and perforation rate, but increased migration rate compared with PSs. (Gastrointest Endosc 2018;87:30-42.)

Abbreviations: CI, confidence interval; LAMS, lumen-apposing metal stent; MS, metal stent; NOS, Newcastle Ottawa scale; OR, odds ratio; PS, plastic stent; WON, walled-off necrosis.

DISCLOSURE: *All authors disclosed no financial relationships relevant to this publication.*

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0016-5107/$36.00
https://doi.org/10.1016/j.gie.2017.08.025

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Acute pancreatitis is the third most common GI-related hospital discharge diagnosis and costs about 2.6 billion dollars a year because of the high morbidity and appreciable mortality.[1] Almost one fifth of patients with acute pancreatitis develop pancreatic or peripancreatic necrosis, which is associated with high rates of morbidity and mortality.[2] Encapsulation of the necrotic tissue by a fibrous shell occurs during the first month of illness and denotes the progression from an acute necrotic collection to walled-off necrosis (WON). It is now accepted that intervention for fluid collection in the early stage should be avoided until a perceptible wall develops, usually after 4 weeks.[3]

Treatment of symptomatic WON with endoscopic transluminal drainage and endoscopic transluminal necrosectomy have become popular, given their efficacy and lower morbidity and mortality rates compared with surgery or percutaneous methods.[4] Stents are used to maintain

patency of endoscopic transluminal drainage sites, and the best choice of prosthesis remains undefined. Larger-caliber metal stents (MSs) may facilitate spontaneous drainage of necrotic debris but may entail increased risks of isolated peripheral collections or erosion into vessels once the central portion of the collection resolves.[5] Previous studies have not fully assessed the comparative benefits of plastic stents (PSs) versus MSs, because of relatively small size, lack of comparative arms, and conflicting findings.

In this meta-analysis we aimed to detect differences between MSs and PSs in terms of WON resolution, the likelihood of resolution after a single intervention session, and rates of clinically important adverse events to provide evidence-based recommendations for WON management. We also sought to analyze the performance of lumen-apposing MSs (LAMSs), a subset of MSs, compared with PSs in terms of these endpoints.

METHODS

Search strategy and study selection

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement guidelines to perform the current meta-analysis.[6] Several databases were queried (from 1990 to December 20, 2016) by an expert librarian with input from the study's principal investigator to identify studies that assessed stenting for pancreatic WON without a language restriction, excluding duplicates, reviews, and animal/in vitro studies. We performed a comprehensive search from 1990 to December 20, 2016 of Ovid Medline In-Process & Other Non-Indexed Citations, Ovid Medline, Ovid Embase, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and Scopus. Actual search strategies are available (Supplementary Table 1, available online at www.giejournal.org).

Reference lists from selected articles and review articles were examined. We also excluded studies that did not follow the revised Atlanta criteria for diagnosis of WON, did not provide sufficient data to allow application of the revised Atlanta criteria to their data, or used concomitant percutaneous or surgical drainage simultaneously with endoscopic treatment. Thus, studies were included in the systematic review and meta-analysis if they were randomized clinical trials or either prospective or retrospective controlled studies or case series reporting stenting for revised Atlanta criteria–defined pancreatic WON.

Data extraction

Two investigators (F.B. and T.S.) independently reviewed the abstracts and extracted data (discrepancies resolved by B.K.A.). For the selected studies, characteristics were abstracted, including publication year, country, and study design. In addition, patient characteristics (age, sex, number of WONs, WON size, and the presence of infected necrosis), type of the stent, resolution rate, resolution with a single procedure, number of procedures, occlusion, migration, bleeding and perforation rates were also extracted.

Study methodologic quality assessment

The Newcastle Ottawa scale (NOS)[7] was used to assess the quality of comparative cohort studies.[8] Each study was assessed independently across 3 areas of potential bias: patient selection, comparability, and outcome reporting (Supplementary Tables 2 and 3, available online at www.giejournal.org). We applied a previously used tool to assess the risk of bias (ie, methodologic quality) of noncomparative case series, derived from the NOS, and used items that were appropriate for this systematic review.[9,10] This tool had removed from the NOS items that relate to comparability and adjustment and kept items that focused on selection and representativeness of cases and ascertainment of outcome and exposure. The tool consisted of 5 items each requiring a binary response to indicate whether bias was likely, and these items were applied to single-arm studies. We considered the quality of the study good when all 5 criteria were fulfilled, moderate when 4 were fulfilled, and poor when 3 or less were fulfilled. The same 2 reviewers assessed the methodologic quality of included studies with discussion between them in case of disagreement (Supplementary Table 3).

Outcomes assessment

WON was defined based on the revised Atlanta criteria as a mature, encapsulated pancreatic, or peripancreatic necrosis with a well-defined inflammatory wall.[2] We considered patients to have WON if the study clearly stated that the revised Atlanta criteria were used or described the presence of defined wall around the pancreatic fluid collection and solid necrosis within it.

Our primary comparison was between MSs and PSs. We subsequently performed a subgroup analysis comparing LAMSs with PSs. The primary outcome was WON clinical resolution. Secondary outcomes were number of endoscopic procedures and adverse events, including stent occlusion, bleeding during drainage and postdrainage, perforation, and migration. We also captured, when reported, rate of infected WON, hospital stay, and intensive care unit stay. WON resolution definition varied between studies, and we provide the definitions as they appear in each study in Supplementary Table 4, available online at www.giejournal.org. We considered surgical intervention or percutaneous drainage subsequent to endoscopic treatment as stent treatment failure in achieving WON resolution. Perforation was defined as either that of the WON wall or of the adjacent GI tract lumen.

Statistical methods

We performed separate 1-arm and 2-arm analyses. For analysis of adverse events we performed 1-arm analyses by evaluating data from all included studies regarding either PSs or MSs without regard to comparisons between

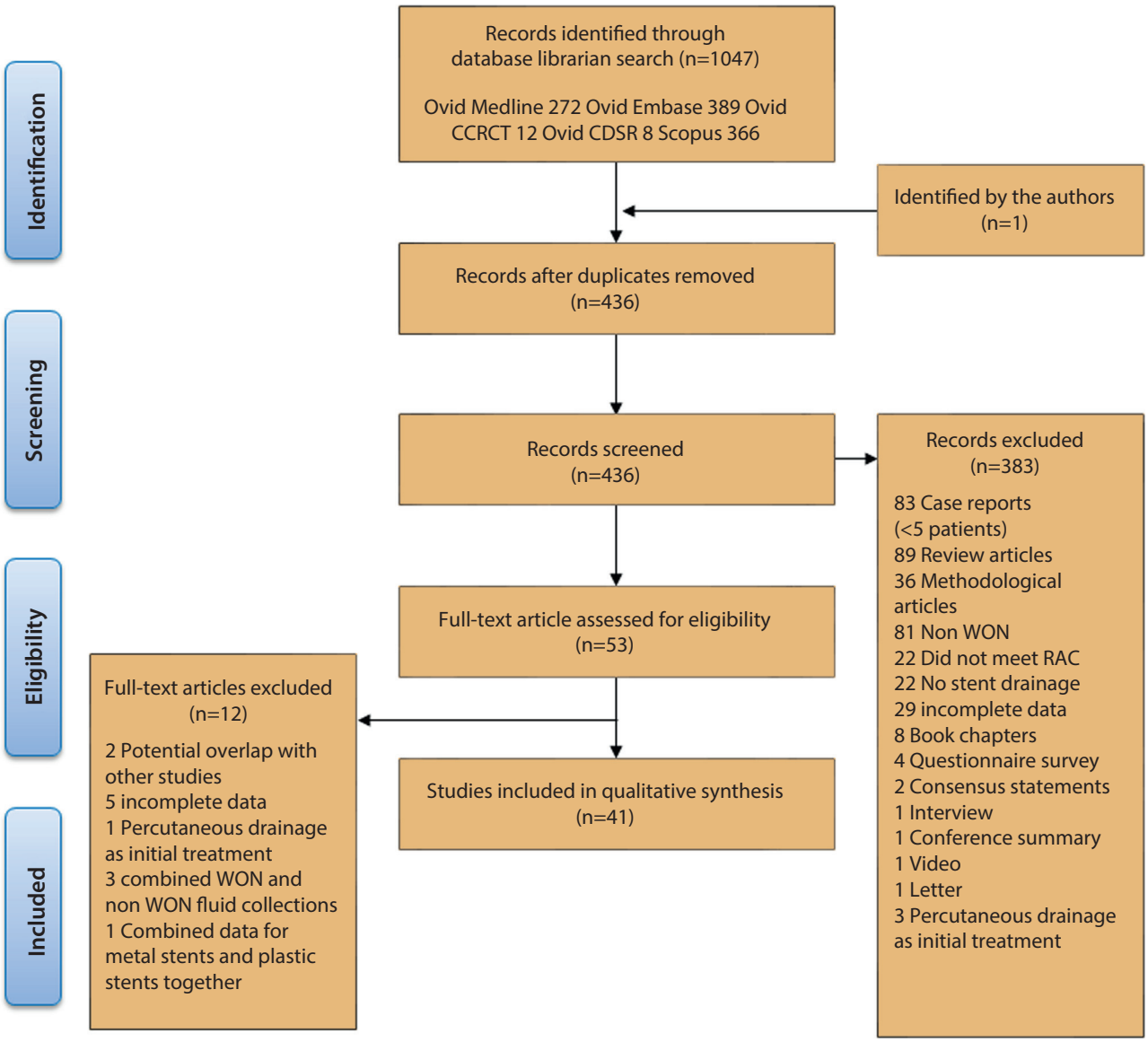

Figure 1. Flow diagram depicting study search and selection.

the 2 stent types. We did not attempt to compare resolution outcome differences between stent types in this analysis because of differences in definition of WON (with pseudocysts possibly included in some studies), definition of WON resolution across studies, and differences in endoscopic technique between centers.

For comparison of outcomes between PSs and MSs, we included all studies that directly compared PS and MS arms and evaluated both the overall WON resolution rate and how often resolution occurred after a single endoscopic procedure. These comparisons likely have higher integrity despite differences in WON resolution definitions and endoscopic technique across studies and centers, because the integrity of the comparison is likely preserved in each individual study (ie, between stents). We provided data regarding WON resolution outcomes as it pertains to LAMS and non-LAMS cohorts. We also separately analyzed the adverse events reported in these studies.

Overall meta-analysis summaries were created using random-effects models of the event rate for the single-arm analysis and the odds ratio (OR) and difference in means for the 2-arm analysis. We evaluated the individual studies heterogeneity with the I^2 test. We used the software package Comprehensive Meta-Analysis (version 3.3.070; Biostat Inc, Englewood, NJ, USA) for all meta-analysis random-effects modeling and SAS (version 9.3; SAS Inc, Cary, NC) for all other analyses.

To assess publication bias, we considered Egger's linear regression and the Begg-Mazumdar test (Kendall's tau) and elected to use Egger's linear regression method and associated funnel plots.[11,12] The selection of this test

was based on our impression that Egger's linear regression method is a widely applied method for publication bias analysis in medical systematic literature reviews of the type we conducted.

RESULTS

Description of included studies

A flow diagram showing study selection is shown in Figure 1. Included studies presented 2213 patients. Sixteen studies evaluated PSs only and included 891 patients, whereas 15 studies evaluated MSs only and included 604 patients. Ten studies were comparative, examining PS (total of 311) versus MS (total of 407) performance. Of the 1011 patients receiving MSs, 871 received LAMS (86%; 439/871 [50.5%] received AXIOS [Boston Scientific, Natick, Mass], 64/871 [7.3%] received Hot AXIOS [Boston Scientific], and 368/871 [42.2%] received Nagi [Taewoong Medical, Goyang, Korea]), whereas 140 (14%) received non-LAMS. One study included WON in the setting of gastric varices only, 2 included only children, 1 included WONs with disconnected pancreatic duct only, 2 included combined PS followed by MS technique, and 1 compared direct necrosectomy with step-up approach. Twenty-seven studies were retrospective case series[13-36] (22 single center, 5 multicenter), 8 studies were cohort retrospective studies[37-43] (5 single center, 3 multicenter), 3 were prospective case series[44-46] (2 single center, 1 multicenter), 1 was a prospective cohort registry[47] (single center), 1 was a randomized controlled trial[5] (single center), and 1 was an observational open-label study[48] (single center). The follow-up period after therapy varied from 6 weeks up to 6 years.

Patient characteristics, study parameters, and outcomes are summarized in Table 1. Summary data from PS studies and MS studies are found in Supplementary Tables 5 and 6 (available online at www.giejournal.org), respectively.

Studies evaluating PSs

Twenty-six studies included drainage of WON with PSs. There was heterogeneity between the studies regarding follow-up (Supplementary Table 5). To evaluate publication bias, we created funnel plots examining overall WON resolution, resolution after a single endoscopic procedure, and individual adverse event types (Supplementary Fig. 1A-F, available online at www.giejournal.org). No publication bias was detected by visual inspection of funnel plots. When applying Egger's linear regression method, potential publication bias was possibly present regarding reports of bleeding events ($P = .006$) and perforation events ($P = .03$). No other quantifiable publication bias was detected.

Studies evaluating MSs

Twenty-five studies involved drainage of WON with MSs. There was heterogeneity between the studies regarding follow-up (Supplementary Table 6). To evaluate publication bias, we created funnel plots examining overall WON resolution, resolution after a single endoscopic procedure, and individual adverse event types (Supplementary Fig. 2A-F, available online at www.giejournal.org). No publication bias was detected on visual inspection of funnel plots. When applying Egger's linear regression method, no quantifiable publication bias was detected.

Studies comparing PSs and MSs (2-arm studies)

Ten studies compared MS and PS in WON drainage.[5,19,20,31,37-42] There was heterogeneity between the studies regarding follow-up. For this meta-analysis we excluded 5 studies because of low total number of patients in 4 studies (<10 for MS and PS groups, combined)[20,31,38,40] and significant disproportion of PS versus MS patients in 1 study (43 vs 3, respectively).[19] No publication bias was detected on visual inspection of funnel plots. When applying Egger's linear regression method, no quantifiable publication bias was detected.

Meta-Analyses

Averse events. *Bleeding.* Eighteen studies evaluated bleeding in 935 patients receiving MSs with an event rate of 5.6% (95% confidence interval [CI], 3.6%-8.6%), and 19 studies evaluated bleeding in 1083 patients receiving PSs with an event rate of 12.6% (95% CI, 9.5%-16.5%; MS vs PS; $P = .002$) (Supplementary Fig. 3A, available online at www.giejournal.org). Heterogeneity in MS studies was 38.3 ($P = .055$) and 52.6 in PS studies ($P = .004$). A subanalysis looked at bleeding with LAMSs (total of 15 studies, 784 patients), and the event rate was 6.2% (95% CI, 3.9%-9.6%; LAMS vs PS; $P = .007$), with heterogeneity of 40.3 ($P = .053$).

Stent migration. Nineteen studies evaluated migration in 899 patients receiving MSs with an event rate of 8.1% (95% CI, 5.1%-12.6%), and 11 studies evaluated migration in 676 patients receiving PSs with an event rate of 5.1% (95% CI, 2.6% - 10.1%; MS vs PS; $P = .2$) (Supplementary Fig. 3B, available online at www.giejournal.org). Heterogeneity in MS studies was 59 ($P < .001$) and in PS studies 70.1 ($P < .0001$). A subanalysis looked at migration with LAMSs (total of 16 studies, 748 patients), and the event rate was 7.8% (95% CI, 4.7%-12.5%; LAMS vs PS; $P = .3$), with heterogeneity of 56.6 ($P = .003$).

Perforation. Eleven studies evaluated perforation in 673 patients receiving MSs with an event rate of 2.8% (95% CI, 1.6%-5%), and 13 studies evaluated perforation in 911 patients receiving PSs with an event rate of 4.3% (95% CI, 3.1% - 6%; MS vs PS; $P = .2$) (Supplementary Fig. 3C, available online at www.giejournal.org). Heterogeneity in MS studies was 14.2 ($P = .3$) and in PS studies 0 ($P = .7$). A subanalysis looked at perforation with LAMSs, and the

TABLE 1. Study characteristics

Author (Year)	Study design	Country	Age (mean ± SD)	Gender (male)	No. of WON
Abu Dayyeh (2017)[37]	Cohort retrospective (single center)	USA	55.4 ±16.9	77.6%	94
Lakhtakia (2016)[13]	Retrospective case series (single center)	India	34.8 ± 12.8	88.3%	205
Ang (2016)[38]	Cohort retrospective (multicenter)	Thailand	N/A	N/A	18
Sharaiha (2016)[14]	Retrospective case series (multicenter)	USA	54.2 ± 15.5	60%	124
Siddiqui (1) (2016)[39]	Cohort retrospective (multicenter)	USA	52.9 ± 15.1	76.7%	313
Siddiqui (2) (2016)[15]	Retrospective case series (multicenter)	USA	51.7 ± 14.3	60.3%	68
Smoczyński (1) (2016)[16]	Retrospective (single center)	Europe	50.68	N/A	22
Storm (2016)[17]	Retrospective case series (single center)	USA	47.1 (27-62)	60%	15
Thompson (2016)[44]	Prospective case series (single center)	USA	52.8 ± 2	60%	60
Sharma (2016)[18]	Retrospective case series (single center)	India	N/A	N/A	35
Keane (2016)[19]	Retrospective case series (multicenter)	UK	60 (22-84)	N/A	46
Gornals (2016)[45]	Prospective case series (single center)	Europe	52.5 ±14.3	N/A	12
Bang (1) (2016)[20]	Retrospective case series (single center)	USA	13.5 ± 3.1	16%	6
Bang (2) (2016)[40]	Cohort retrospective (single center)	USA	N/A	N/A	39
Bang (3) (2016)[5]	RCT	USA	N/A	N/A	21
Albers (2016)[21]	Retrospective case series (single center)	Europe	49.8 ±18.3	66%	13
Walter (2015)[46]	Prospective case series (multicenter)	Europe	N/A	N/A	46
Smoczyński (2) (2015)[52]	Retrospective Case Series (single center)	Europe	N/A	N/A	64
Smith (2015)[22]	Retrospective case series (single center)	USA	52.6 (24-69)	88%	17
Rana (1) (2014)[23]	Retrospective case series (single center)	India	36.0 ± 10.1	83.7%	43
Schmidt (2015)[53]	Retrospective case series (single center)	Europe	N/A	64.1%	81
Rinninella (2015)[24]	Retrospective case series (multicenter)	Europe	N/A	N/A	52
Rana (2) (2015)[25]	Retrospective case series (single center)	India	37 ± 7.6	82.8%	35
Mukai (1) (2015)[26]	Retrospective case series (single center)	Japan	N/A	N/A	19
Bapaye (2017)[54]	Cohort retrospective (single center)	India	42.2 ± 12.8	87%	133
Nabi (2017)[27]	Retrospective case series (single center)	India	14.9 ± 2.3	95%	21
Mukai (2) (2015)[42]	Cohort retrospective (single center)	Japan	54.9 ± 15.5	82.8%	70
Jagielski (2015)[28]	Retrospective case series (single center)	Europe	52.7 ± 13.2	71%	176
Hugget (2015)[48]	Open label observational (multicenter)	UK	Median 60 (11-81)	73.6%	19
Chandran (2015)[29]	Retrospective case series (single center)	Australia	Median 55 (10-87)	66%	9
Smoczyński (3) (2014)[30]	Retrospective case series (single center)	Europe	Median 53.7 (28-86)	74.1%	112
Saxena (2014)[32]	Retrospective case series (single center)	USA	60.6 ±12.7	80%	5
Mukai (3) (2014)[31]	Retrospective (single center)	Japan	55.6 ± 22.4	80%	5
Lin (2014)[33]	Retrospective case series (multicenter)	China	Median 53 (32-79)	47%	17
Kumar (2014)[47]	Cohort prospective registry (single center)	USA	58.9 ±3.9	66%	12
Attam (2014)[34]	Retrospective case series (single center)	USA	52.7 ±18.6	80%	10
Yamamoto (2013)[49]	Retrospective case series (multicenter)	Japan	51.8 ± 12.2	75%	4
Varadarajulu (2011)[35]	Retrospective case series (single center)	USA	52.1 ±16.4	75%	60
Gardner (2011)[36]	Retrospective case sereis (multicenter)	USA	58.1 (95% CI, 55.1-61.1)	67%	104
Gardner (2009)[43]	Cohort retrospective (multicenter)	USA	61.8 ± 13	62%	45
Papachristou (2007)[54]	Retrospective (single center)	USA	Median 61 (12-79)	52.8%	53

RCT, randomized controlled trial; *WON,* walled-off necrosis; *LAMS,* lumen-apposing metal stent; *N/A,* not applicable.

TABLE 1. Continued

WON size (cm) (mean ± SD or [range])	No. plastic stents	No. metal stents	No. LAMS	No. infected necrosis	Follow-up length (median [range])
13.2 ± 6.2	36	58	46	Plastic 16 (44%) Metal 23 (40%)	8 weeks [6–12]
10.87 ± 2.81	0	205	203	N/A	12 months [3 months-3 years]
N/A	10	8	.	N/A	N/A
9.5 [4-30]	0	124	124	N/A	4 months [1-34]
10.2 [2-51]	106	207	86	N/A	6 months
12.12 ± 5.32	0	68	68	N/A	2 months [1-3]
8.03 [5.5-17.3]	22	0	0	N/A	1 year
N/A	15	0	0	N/A	N/A
N/A	60	0	0	N/A	67.8 weeks ± 9.9
13.22 ± 3.47	35	0	0	N/A	N/A
11.9 [7.6-20]	43	3	0	N/A	11 [0–131]
12.4 ± 2.94	0	12	12	Metal 7 (58%)	Mean 13 ± 11.4 months
13.3 ± 6.28	5	1	1	N/A	781 days [133-2359]
N/A	26	13	13	N/A	Median 20.3 months
N/A	9	12	12	N/A	N/A
N/A	.	13	13	13 (100%)	Mean 8.5 months ± 5.9
N/A	0	43	43	N/A	N/A
14.6 [10.6-22]	64	0	0	N/A	6 months
9.5 [8-26]	0	17	0	N/A	Mean 7.3 weeks ±12.7
9.95 ±2.75	43	0	0	N/A	N/A
Median 15 [4-42]	81	0	0	Metal 71%	41 months [14-91]
N/A	0	52	52	N/A	11 months ± 5
N/A	35	0	0	N/A	Mean 28.2 months [6-50]
N/A	0	19	0	Metal 10 (53%)	N/A
10.8 ±3.2	61	72	72	N/A	8 weeks
Median 8.8 [range 5.5-14.8]	0	21	.	N/A	Median 360 days [30-1020]
9.5 ± 3.9	27	43	43	Plastic 16 (59%) Metal 23 (53%)	At least 24 months
12 ±4.9	176	0	.	Plastic 49 (28%)	At least 6 months
Median 15 [7-29]	0	19	19	Metal 16 (84%)	At least 3 months
Median 8 [range 6-17]	0	9	9	Metal 4 (44%)	At least 6 months
Median 11.6 [range 4.5-26.7]	112	0	0	Plastic 38 (34%)	31 months [range 2-85]
12.3	0	5	5	N/A	mean 184 days
10.4 ± 3.7	2	3	3	Metal 3 (100%) Plastic 2 (100%)	Mean 21 months, [5-44]
Median 11.9 ± 5.2	17	0	0	N/A	48 months [26–126]
13 ±5.1	12	0	0	Plastic 8 (67%)	Mean 1.9 years ± 0.3
18.3 ± 5.5	0	10	10	Metal 5 (50%)	N/A
20 ±12.7	0	4	4	Metal 3 (75%)	8 weeks
10.8 ±2.6	60	0	0	N/A	Group 1 (48 pts) 169 days [IQR 60-228] Group 2 (12 patients) 159.5 days [IQR 112-228]
15 [13.9-16.2]	104	0	0	Plastic 40 (38.4%)	Mean 19.5 months (1-53)
15.6	45	0	0	N/A	N/A
16 [3-46]	53	0	0	Plastic 26 (49%)	Mean 25 weeks (3-416)

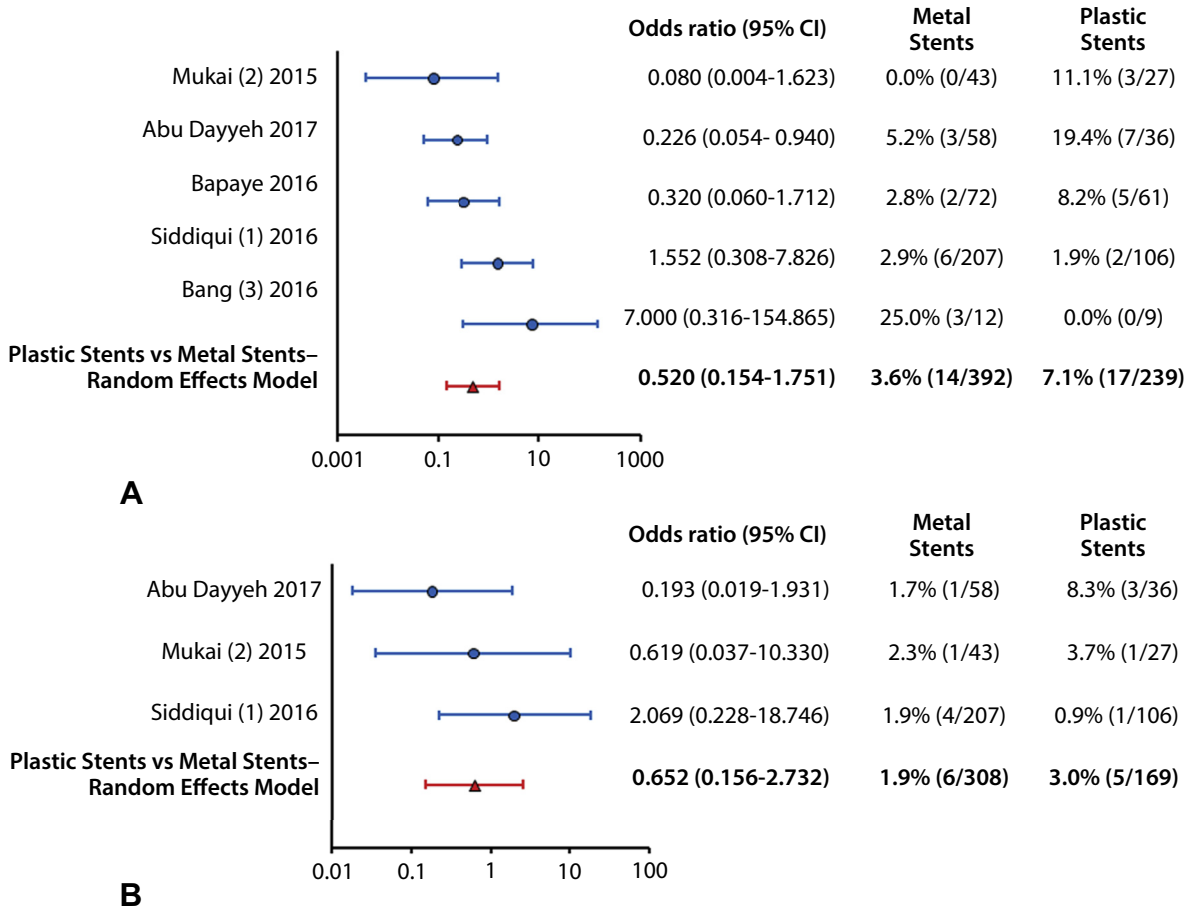

Figure 2. Adverse event odd ratios for plastic stents vs metal stents analysis: bleeding (A) perforation (B) stent migration (C) stent occlusion (D).

event rate was 3.8% (95% CI, 2.1%-6.9%; LAMS vs PS; $P = .7$), with heterogeneity of 24.5 ($P = .22$).

Stent occlusion. Thirteen studies evaluated stent occlusion in 775 patients receiving MSs with an event rate of 9.5% (95% CI, 7.5%-12.1%), and 4 studies evaluated 182 patients receiving PSs with an event rate of 17.4% (95% CI, 9.4%-29.9%; MS vs PS; $P = .07$) (Supplementary Fig. 3D, available online at www.giejournal.org). Heterogeneity in MS studies was 5.1 ($P = .39$) and in PS studies 44.5 ($P = .14$). A subanalysis looked at LAMS occlusion (11 studies, 629 patients), and the event rate was 7.5% (95% CI, 5.6%-9.9%; LAMS vs PS; $P = .015$), with heterogeneity of 0 ($P = .7$).

A separate adverse event analysis was performed limited to studies that compared PSs and MSs. In this analysis bleeding occurred in 3.6% of MS patients, compared with 7.1% in the PS group (OR, .5; 95% CI, .15-1.7; $P = .2$; heterogeneity = 47, $P = .1$). Perforation occurred in 1.9% of MS patients, compared with 3% in PS group (OR, .6; 95% CI, .15-2.7; $P = .5$; heterogeneity = 6, $P = .3$). Stent migration occurred in 6.7% of MS patients, compared with 5.3% in the PS group (OR, 1.3; 95% CI, .6-2.6; $P = .4$; heterogeneity = 0, $P = .8$). Finally, stent occlusion occurred in 11.7% of MS patients, compared with 17% in the PS group (OR, .6; 95% CI, .34-1.1; $P = .1$; heterogeneity = 0, $P = .5$) (Figs. 2A-D).

Patient outcomes. *Overall WON resolution.* For PS versus MS, overall resolution was evaluated in 5 studies and was more likely to occur when using MSs (92.1%) compared with PSs (80.9%; OR, 2.8; 95% CI, 1.7-4.6; $P < .001$; heterogeneity = 0, $P = .4$) (Fig. 3A). For PS versus LAMS, overall resolution was evaluated in 5 studies and was more likely to occur when using LAMSs (91.5%) compared with PSs (80.9%; OR, 2.5; 95% CI, 1.4-4.3; $P = .001$; heterogeneity = 0, $P = .4$) (Fig. 3B). In our systematic review no studies directly compared LAMSs versus non-LAMSs. However, indirect comparison showed no statistically significant difference in overall WON resolution in those who received LAMS (87.7%; 95% CI, 81.8%-91.8%) versus non-LAMS (77.6%; 95% CI, 30.3%-96.5%).

Resolution after a single endoscopic procedure. For PS versus MS, the success of treatment after a single session was evaluated in 5 studies and was similar whether using MSs (47.1%) or PSs (43.4%; OR, 1.3; 95% CI, .7-2.4; $P = .2$;

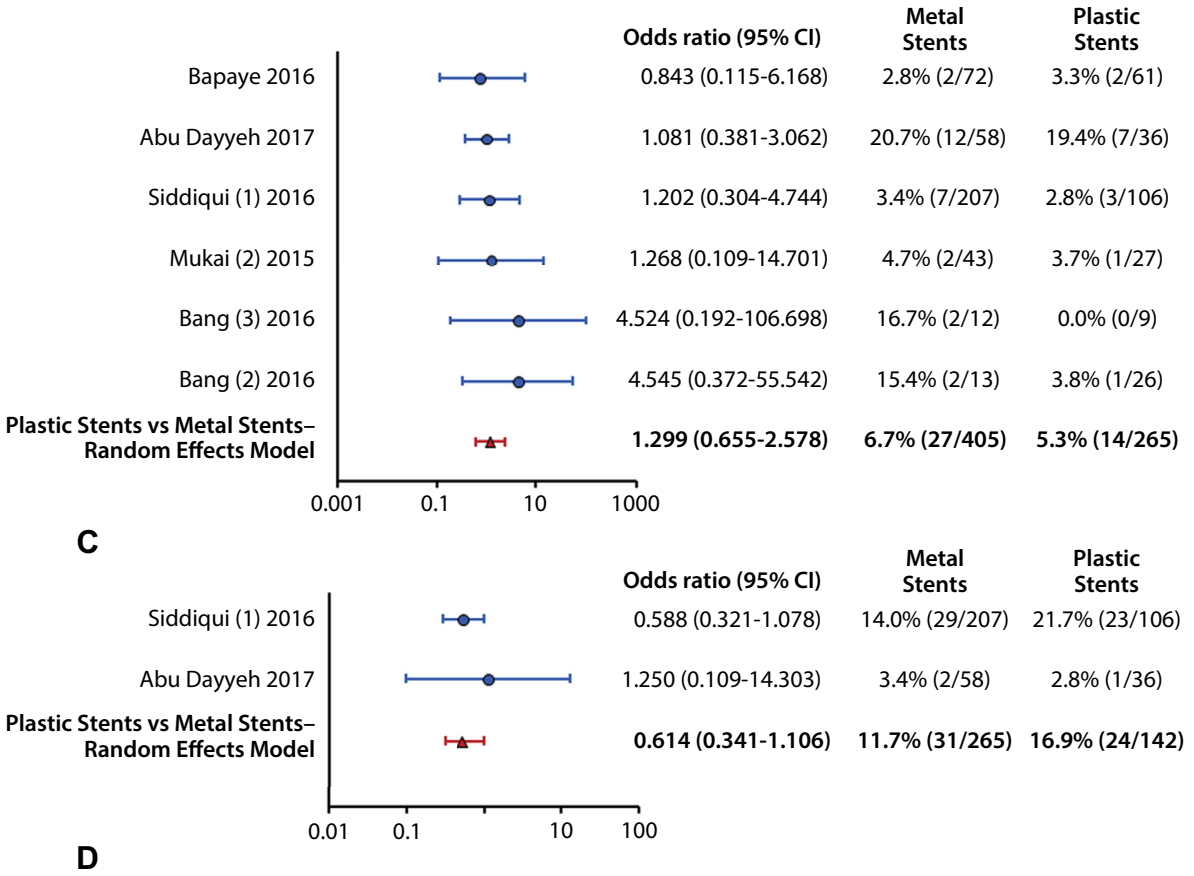

Figure 2. continued.

heterogeneity = 60.2, P = .03) (Fig. 3C). For PS versus LAMS, similarly, no difference was found in resolution after a single endoscopic procedure when using LAMSs (52.3%) versus PSs (43.4%; OR, 1.4; 95% CI, .56-3.6; P = .4; heterogeneity = 81.6, P < .001) (Fig. 3D). Indirect comparison showed no statistically significant difference in resolution after a single endoscopic procedure in those who received LAMSs (49%; 95% CI, 33.2%-65%) versus non-LAMSs (21.7%; 95% CI, 4.7%-61%).

Cumulative need for reintervention (total number of endoscopic sessions to achieve resolution). A meta-analysis of 4 studies showed that the MS group had fewer interventions compared with the PS group, with an overall reintervention mean difference of –.9 in favor of MS (95% CI, –1.283 to –.561; heterogeneity = 0, P = .4) (Supplementary Table 7). In Table 2 the outcome measures for which a statistically significant difference (P < .05) was established between MS and PS WON drainage were bleeding (in 1-arm studies) and overall WON resolution (in 2-arm studies).

Quality Assessment

Thirty-five case series were assessed for bias using the modified NOS. Seventeen studies were deemed to have high methodologic quality, 13 moderate methodologic quality, and 5 low methodologic quality. Seven studies were deemed inclusive of patients not representative of the general WON population.[17,20,21,25,27,34,49] All studies used medical record review to collect the data. Outcome assessment was not performed by an independent blinded assessment in any of the studies. The randomized controlled trial study and 6 cohort studies were assessed using the NOS. Six studies were awarded a maximum of 4 stars on selection. Five studies did not report controlling for important confounders in the analysis. All 7 studies were awarded only 2 stars on outcome assessment because of lack of blinded assessment (Supplementary Tables 2 and 3, available online at www.giejournal.org).

Sensitivity Analysis

In the 2-arm analyses we performed sensitivity analysis by excluding 1 study at a time. Our results remained statistically significant in terms of MSs, as well as LAMSs, superiority in overall WON resolution. No statistically significant changes in adverse events outcomes were observed with the sensitivity analysis (Supplementary Table 8, available online at www.giejournal.org).

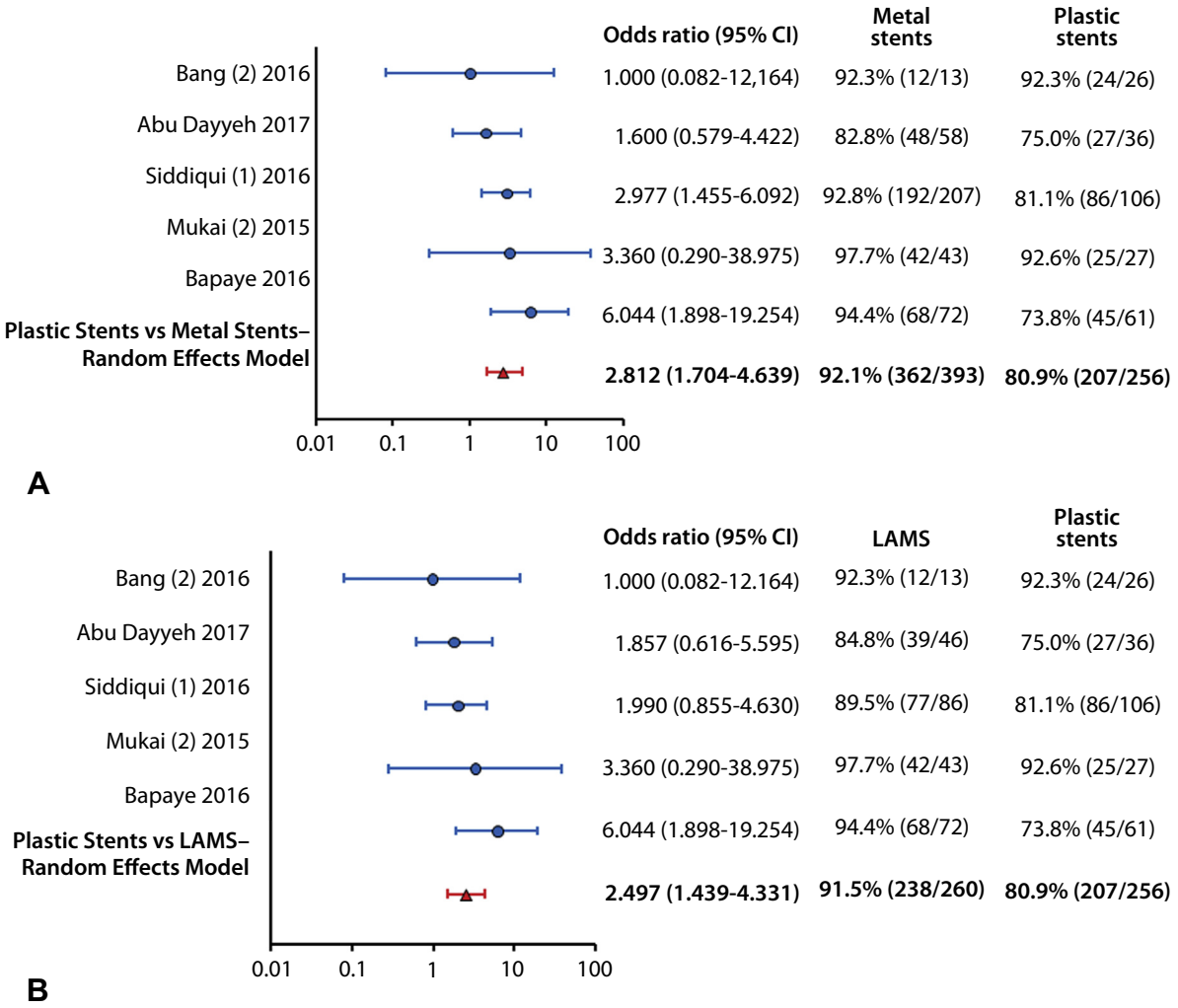

Figure 3. Odds ratios for overall WON resolution in **A,** plastic stents vs metal stents, **B,** plastic stents vs LAMS; and resolution after a single endoscopic procedure in **C,** plastic stents vs metal stents, **D,** plastic stents vs LAMS. *LAMS,* lumen-apposing metal stent.

DISCUSSION

Although endoscopic approaches to WON management are usually favored over surgery, the best stent choice for cystenterostomy creation remains unclear. A recent systematic review did not find a difference in resolution rates of pancreatic fluid collections between PSs and MSs.[50]. However, that systematic review included a large number of patients with pseudocysts and did not include many of the larger comparator studies published in the literature more recently that exclusively evaluated WON resolution rates between PSs and MSs. In this systematic review and meta-analysis we focused on WON and sought to minimize sources of heterogeneity, grade the quality of the evidence based on the risk of bias, and follow established guidelines to conduct a high-quality systematic review and meta-analysis that can inform clinical practice and future research. We found that MSs are superior to PSs with regard to overall WON resolution rate and that for those patients who required multiple sessions, fewer endoscopic procedures were needed. Moreover, less bleeding occurs when MSs are used.

In our study we divided the analysis of published literature into single-arm and 2-arm studies with different inferences drawn from a meta-analysis of each group. We pooled outcome results from comparative studies, whereas we pooled adverse events from all studies. The rationale behind this methodology is that adverse events are likely to be related to the endoscopic procedure rather than the WON, whereas resolution outcomes are largely dictated by the characteristics of the fluid collection because it is known that pseudocysts are more responsive to endoscopic treatment than WON. Therefore, it is methodologically and clinically rational to pool the outcomes from comparative studies that likely compared similar collections. Furthermore, we have counted the need for

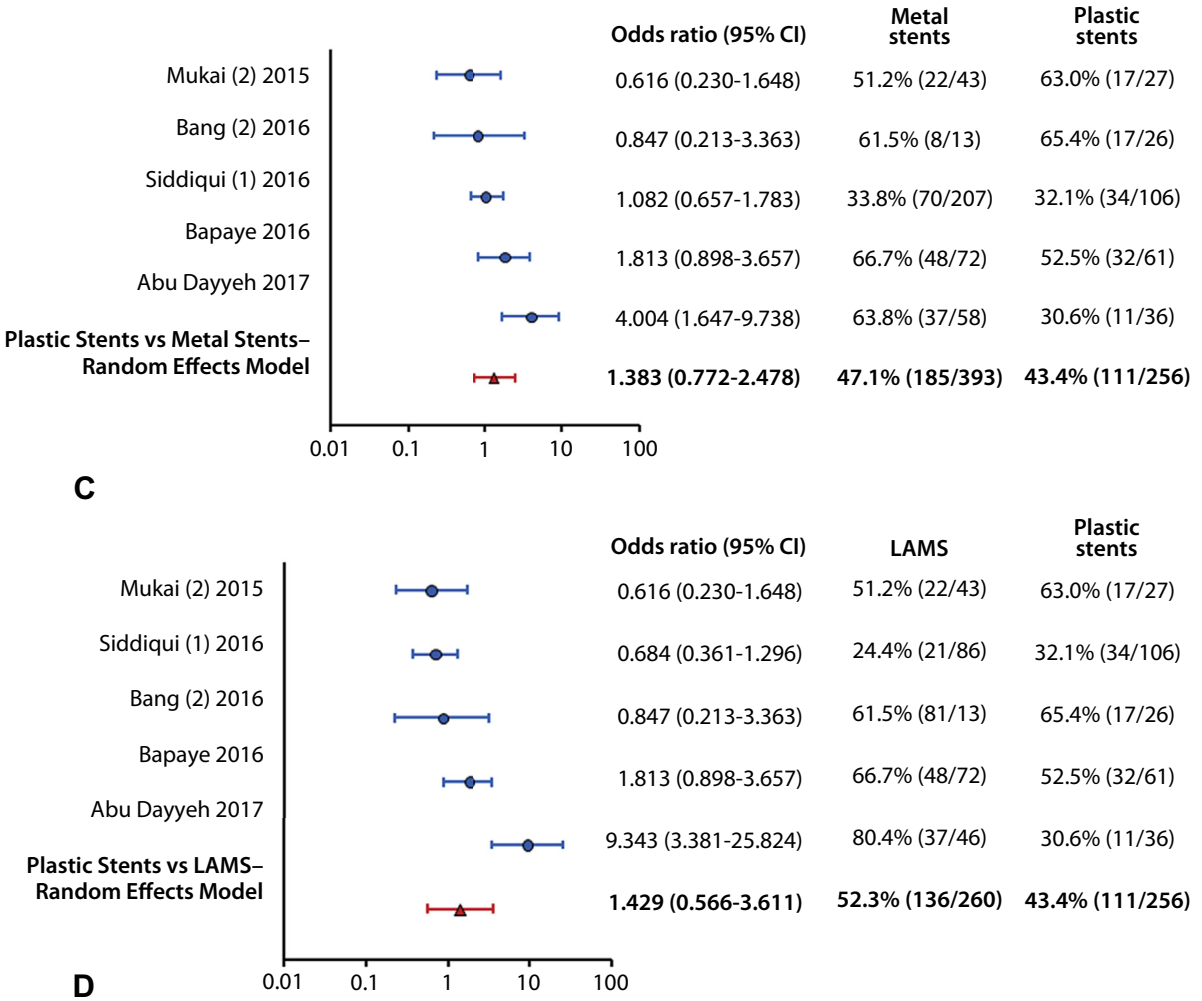

Figure 3. continued.

percutaneous drainage and/or surgery as failure of prosthesis.

Recently, there were concerns regarding increased risk of bleeding when using regular MSs because of abutment of the end of the stent against the luminal wall[51] or LAMSs because of friction against vasculature as collection resolves.[5] We demonstrate in our study that the bleeding risk is actually higher in PSs. This may be related to the more robust radial forces that allow for tamponade and hemostasis of ruptured vessels after deployment, a quality that is absent in PSs. However, we cannot exclude the possibility that bleeding might occur long after WON resolution if MSs are left in place.

On the other hand, we found a trend toward increased rates of stent migration with MSs. This could be explained by the large caliber, which allows for the passage of larger blocks of necrotic material, potentially dislodging the stent or occluding it. This is less of a problem in smaller-caliber PSs that remain in place when the WON cavity collapses around them.

We found higher PS success rates in single-arm studies than in 2-arm studies. One possible explanation for this discrepancy is the possibility of misclassification of pseudocysts as WON in single-arm studies. This would be more consistent with previous studies that showed that pseudocysts have better outcomes than WON after endoscopic drainage, for instance by creation of multiple transluminal drainage sites in some studies. Results from the 2-arm study meta-analysis might reflect a more homogenous cohort to extrapolate more accurate comparison between PSs and MSs. Indeed, our meta-analysis of 2-arm studies showed superiority of MSs in terms of overall WON resolution and with lower heterogeneity. Another explanation could be that those patients who did well with a single procedure using PSs had concomitant endoscopic necrosectomy during that procedure.

Our study has several inherent and unavoidable limitations, such as the heterogeneity between included studies. Although our methodology is not perfect in

TABLE 2. Summary of meta-analysis metrics results

Metric	Plastic stents	Metal stents	Lumen-apposing metal stents
Two arm-studies			
Overall resolution	80.9%	92.1% (OR: 2.8; 95% CI, 1.7-4.6; $P < .001$)	91.5% (OR, 2.5; 95% CI, 1.4-4.3; $P = .001$)
Rate of resolution with a single procedure	43.4%	47.1% (OR: 1.3; 95% CI, 0.7-2.4; $P = .2$)	52.3% (OR, 1.4; 95% CI, 0.56-3.6; $P = .4$)
Number of procedures to achieve resolution	Mean difference –.92 (95% CI, –1.283-.561, $p < 0.001$) (favoring metal stents)		
Bleeding	7.1%	3.6% (OR: 0.5; 95% CI, 0.15-1.7; $P = .2$)	5% (OR, 0.64; 95% CI, 0.13-3.1; $P = .5$)
Perforation	3%	1.9% (OR: 0.6; 95% CI, 0.15-2.7; $P = .5$)	4% (OR, 1.2; 95% CI, 0.24-6.18; $P = .8$)
Stent migration	5.3%	6.7% (OR: 1.3; 95% CI, 0.6-2.6; $P = .4$)	6.3% (OR, 1.12; 95% CI, 0.51-2.47; $P = .7$)
Stent occlusion	16.9%	11.7% (OR: 0.6; 95% CI, 0.34-1.1; $P = .1$)	3.8%(OR, 0.36; 95% CI, 0.03-4; $P = .4$)
One-arm studies			
Bleeding	12.6% [95% CI, 9.5%-16.5%]	5.6% [95% CI, 3.6%-8.6%] ($P = .002$)	6.2% [95% CI, 3.9%-9.6%] ($P = .007$)
Perforation	4.3% [95% CI, 3.1%-6%]	2.8% [95% CI, 1.6%-5%] ($P = .2$)	3.8% [95% CI, 2.1%-6.9%] ($P = .7$)
Stent migration	5.1% [95% CI, 2.6%-10.1%]	8.1% [95% CI, 5.1%-12.6%] ($P = .2$)	7.8% [95% CI, 4.7%-12.5%] ($P = .3$)
Stent occlusion	17.4% [95% CI, 9.4%-29.9%]	9.5% [95% CI, 7.5%-12.1%] ($P = .07$)	7.5% [95% CI, 5.6%-9.9%] ($P = .015$)

ensuring homogeneity of comparative studies, there was less heterogeneity compared with that noted with 1-arm studies. Second, the studies were heterogeneous, consisting of variable patient selection, study protocols, and endpoints/adverse events. Third, most included studies were retrospective with inherent confounders and heterogeneity. Consequently, this exploratory analysis will require further adequately randomized controlled trials to confirm it. We did not implement a cost-effectiveness analysis considering of lack of substantive information in most articles extracted. Fourth, we were unable to account for differences in endoscopic methods (eg, multigated transgastric gateway approach, placement of PSs inside MSs). Fifth, although we analyzed studies that reported resolution with a single procedure versus those with multiple sessions, the data regarding the exact timing of necrosectomy were unavailable. Because of this limitation, we could not draw a conclusion whether large-diameter LAMs might facilitate easier and earlier endoscopic necrosectomy. Finally, we did not examine the rate of secondary infections with use of each stent.

Although a signal may be inferred from our 2-arm study meta-analysis regarding the superiority of MSs, prospective randomized controlled trials are needed to answer this question. However, we are able to provide an objective evaluation of adverse events, as they relate to each type of stents.

In conclusion, evidence suggests that MSs are superior for WON resolution, with fewer bleeding events, trend toward less occlusion and perforation rate, but increased migration rate compared with PSs. A randomized prospective trial is needed to definitively answer these questions.

ACKNOWLEDGMENT

We acknowledge the assistance of Mr Edmund McMullen from Boston Scientific in providing the statistical analysis support for this project.

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Received March 25, 2017. Accepted August 20, 2017.

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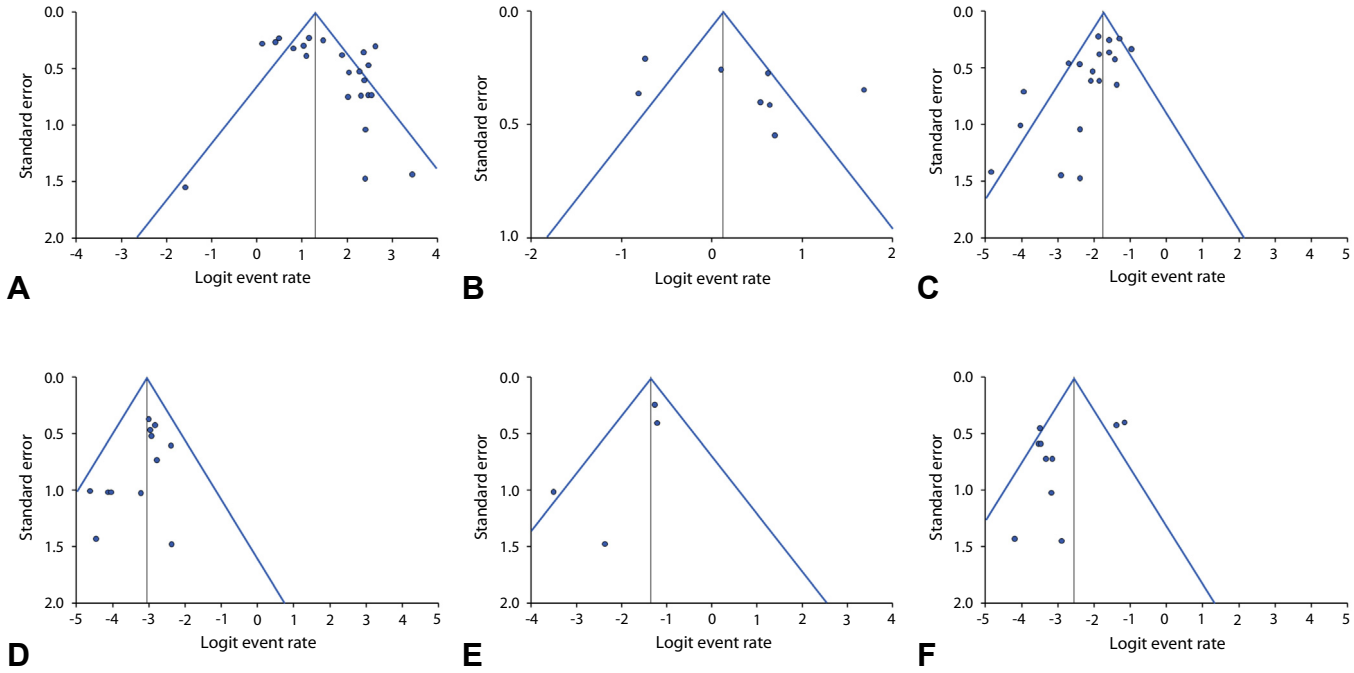
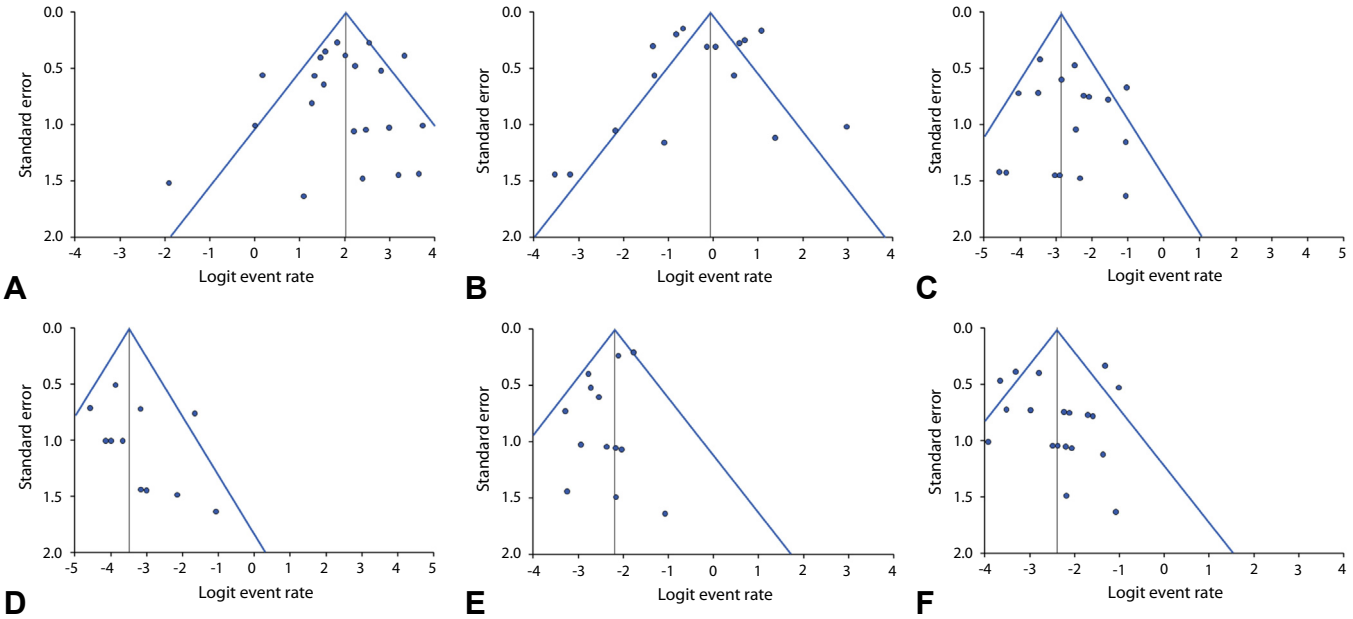
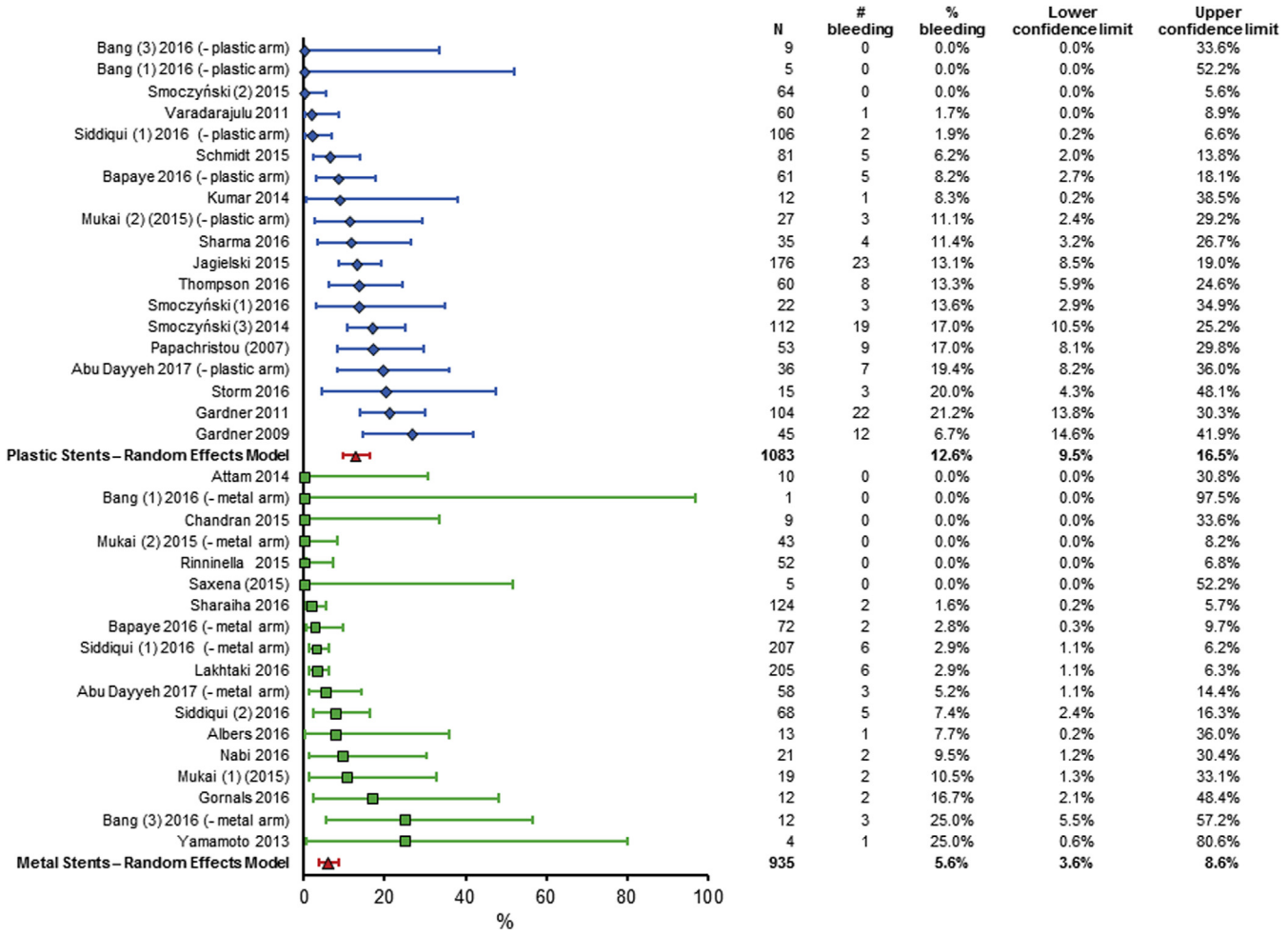


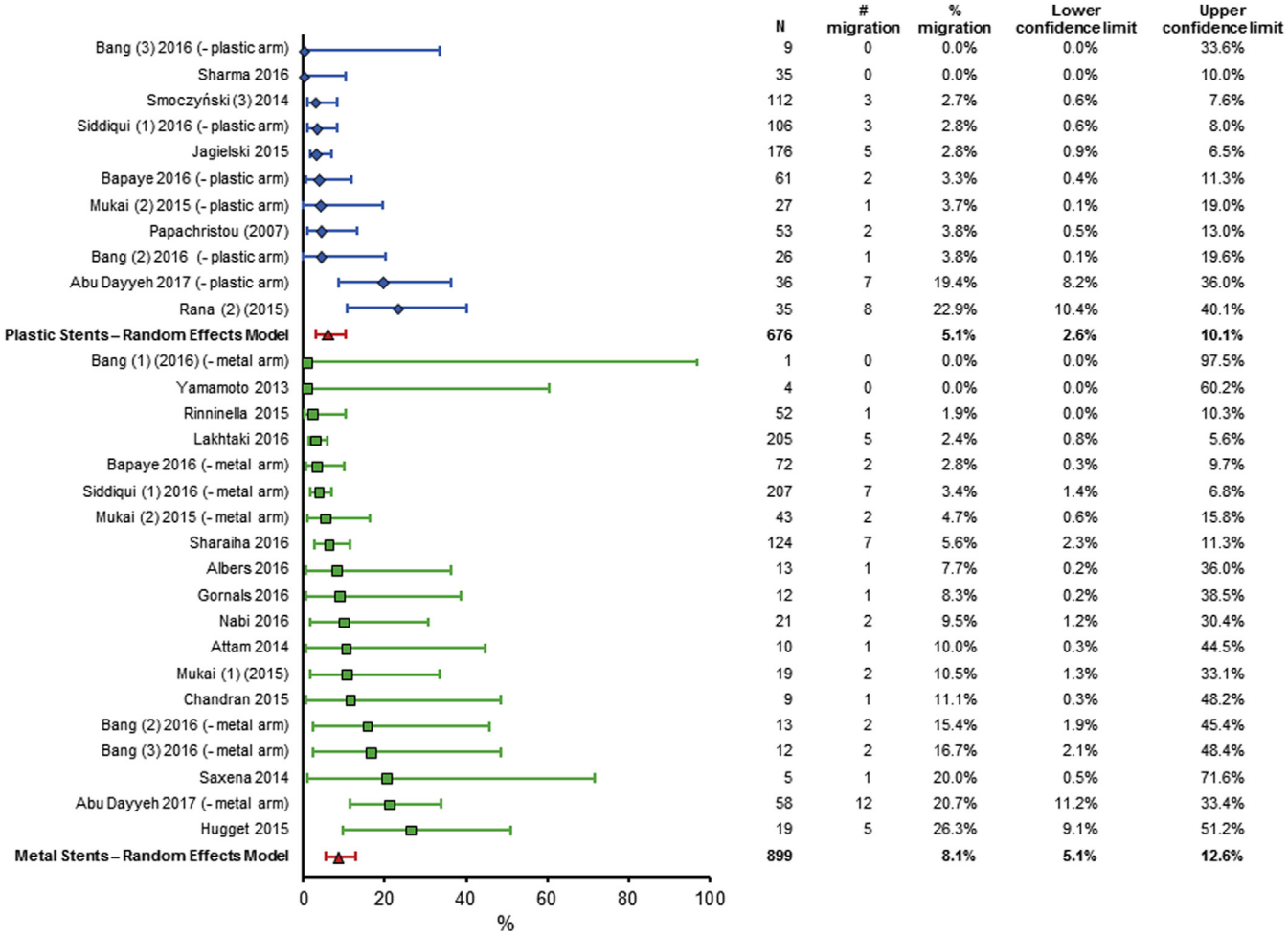
Supplementary Figure 1. Funnel plots for studies involving plastic stents (PSs): overall WON resolution (A), resolution after a single endoscopic procedure (B); and individual adverse events: bleeding (C) stent migration (D) perforation (E) stent occlusion (F).



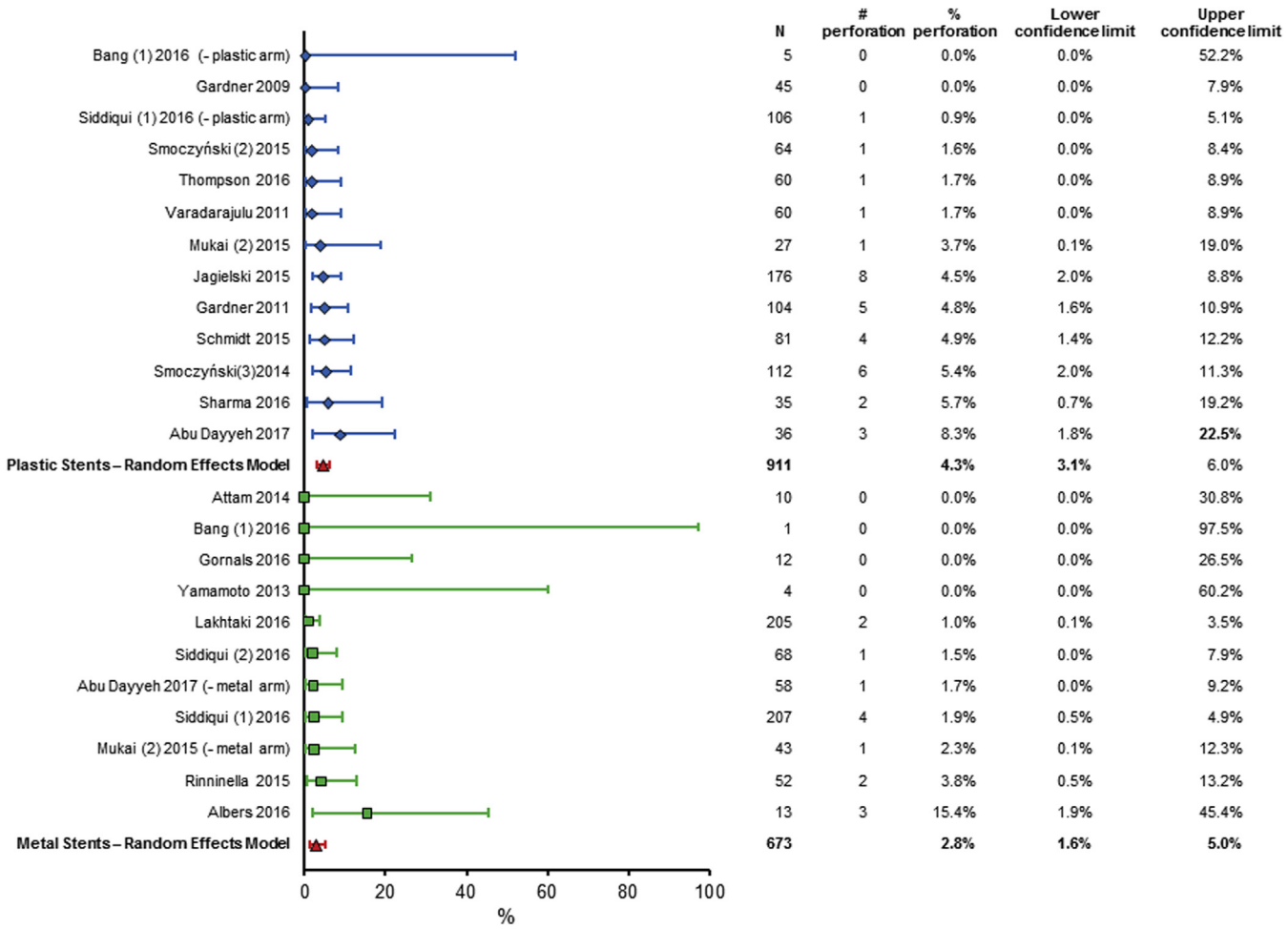
Supplementary Figure 2. Funnel plots for studies involving metal stents(MSs): overall WON resolution (A), resolution after a single endoscopic procedure (B); and individual adverse events: bleeding (C), stent migration (D), perforation (E), stent occlusion (F).



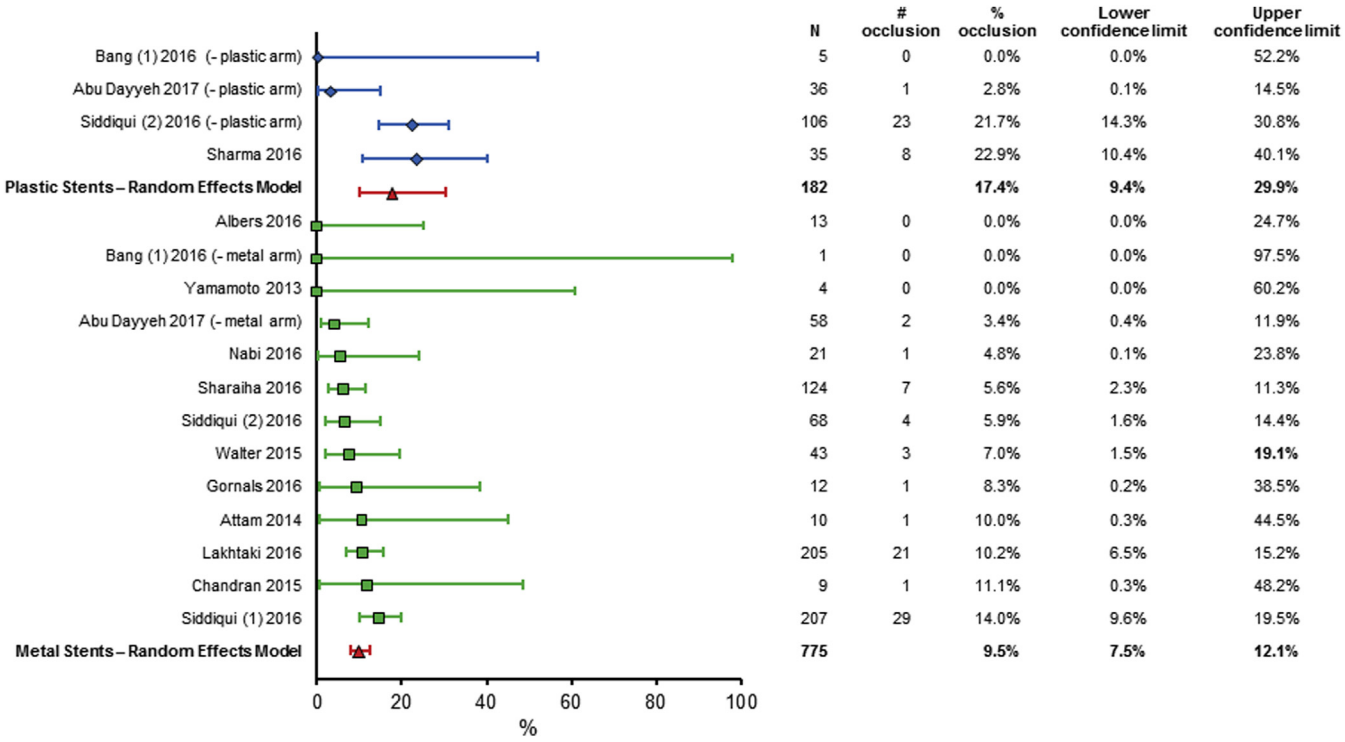
Supplementary Figure 3. Meta analysis of adverse events in plastic and metal stents. Individual and pooled rates are shown.



Supplementary Figure 3. continued.



Supplementary Figure 3. continued.



Supplementary Figure 3. continued.

SUPPLEMENTARY TABLE 1. Actual search strategy

	Ovid
Database(s): Embase 1988 to 2016 Week 51, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present, EBM Reviews–Cochrane Central Register of Controlled Trials December 2016, EBM Reviews–Cochrane Database of Systematic Reviews 2005 to December 20, 2016	
Search strategy:	
#	**Searches**
1	exp Necrosis/
2	exp Pancreas/or exp Pancreatitis/
3	1 and 2
4	((pancrea* adj3 (necros* or necroti*)) or (pancrea* adj3 fluid* adj3 collection*) or "walled-off necros*" or "walled-off necroti*").mp.
5	3 or 4
6	(((endoscop* or transmural*) adj3 drain*) or ((metal* or plastic*) adj3 stent*) or "AXIOS stent*" or "double pigtail plastic stent*" or "endoscopic necrosectom*" or "lumen apposing metal stent*" or "metal stent*" or "plastic stent*" or "self-expanding metal stent*").mp.
7	5 and 6
8	limit 7 to english language [Limit not valid in CDSR; records were retained]
9	limit 8 to yr="1990 -Current"
10	9 not "conference abstract".pt.
11	(exp animals/or exp nonhuman/) not exp humans/
12	((alpaca or alpacas or amphibian or amphibians or animal or animals or antelope or armadillo or armadillos or avian or baboon or baboons or beagle or beagles or bee or bees or bird or birds or bison or bovine or buffalo or buffaloes or buffalos or "c elegans" or "Caenorhabditis elegans" or camel or camels or canine or canines or carp or cats or cattle or chick or chicken or chickens or chicks or chimp or chimpanze or chimpanzees or chimps or cow or cows or "D melanogaster" or "dairy calf" or "dairy calves" or deer or dog or dogs or donkey or donkeys or drosophila or "Drosophila melanogaster" or duck or duckling or ducklings or ducks or equid or equids or equine or equines or feline or felines or ferret or ferrets or finch or finches or fish or flatworm or flatworms or fox or foxes or frog or frogs or "fruit flies" or "fruit fly" or "G mellonella" or "Galleria mellonella" or geese or gerbil or gerbils or goat or goats or goose or gorilla or gorillas or hamster or hamsters or hare or hares or heifer or heifers or horse or horses or insect or insects or jellyfish or kangaroo or kangaroos or kitten or kittens or lagomorph or lagomorphs or lamb or lambs or llama or llamas or macaque or macaques or macaw or macaws or marmoset or marmosets or mice or minipig or minipigs or mink or minks or monkey or monkeys or mouse or mule or mules or nematode or nematodes or octopus or octopuses or orangutan or "orang-utan" or orangutans or "orang-utans" or oxen or parrot or parrots or pig or pigeon or pigeons or piglet or piglets or pigs or porcine or primate or primates or quail or rabbit or rabbits or rat or rats or reptile or reptiles or rodent or rodents or ruminant or ruminants or salmon or sheep or shrimp or slug or slugs or swine or tamarin or tamarins or toad or toads or trout or urchin or urchins or vole or voles or waxworm or waxworms or worm or worms or xenopus or "zebra fish" or zebrafish) not (human or humans)).mp.
13	10 not (11 or 12)
14	limit 13 to (editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CCTR,CDSR; records were retained]
15	from 14 keep 1-93
16	13 not 15
17	remove duplicates from 16
	Scopus
1	TITLE-ABS-KEY((pancrea* W/3 (necros* or necroti*)) OR (pancrea* W/3 fluid* W/3 collection*) OR "walled-off necros*" OR "walled-off necroti*")
2	TITLE-ABS-KEY(((endoscop* or transmural*) W/3 drain*) OR ((metal* or plastic*) W/3 stent*) OR "AXIOS stent*" OR "double pigtail plastic stent*" OR "endoscopic necrosectom*" OR "lumen apposing metal stent*" OR "metal stent*" OR "plastic stent*" OR "self-expanding metal stent*")
3	PUBYEAR AFT 1989 AND LANGUAGE(english)
4	1 and 2 and 3
5	TITLE-ABS-KEY((alpaca OR alpacas OR amphibian OR amphibians OR animal OR animals OR antelope OR armadillo OR armadillos OR avian OR baboon OR baboons OR beagle OR beagles OR bee OR bees OR bird OR birds OR bison OR bovine OR buffalo OR buffaloes OR buffalos OR "c elegans" OR "Caenorhabditis elegans" OR camel OR camels OR canine OR canines OR carp OR cats OR cattle OR chick OR chicken OR chickens OR chicks OR chimp OR chimpanze OR chimpanzees OR chimps OR cow OR cows OR "D melanogaster" OR "dairy calf" OR "dairy calves" OR deer OR dog OR dogs OR donkey OR donkeys OR drosophila OR "Drosophila melanogaster" OR duck OR duckling OR ducklings OR ducks OR equid OR equids OR equine OR equines OR feline OR felines OR ferret OR ferrets OR finch OR finches OR fish OR flatworm OR flatworms OR fox OR foxes OR frog OR frogs OR "fruit flies" OR "fruit fly" OR "G mellonella" OR "Galleria mellonella" OR geese OR gerbil OR gerbils OR goat OR goats OR goose OR gorilla OR

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

	gorillas OR hamster OR hamsters OR hare OR hares OR heifer OR heifers OR horse OR horses OR insect OR insects OR jellyfish OR kangaroo OR kangaroos OR kitten OR kittens OR lagomorph OR lagomorphs OR lamb OR lambs OR llama OR llamas OR macaque OR macaques OR macaw OR macaws OR marmoset OR marmosets OR mice OR minipig OR minipigs OR mink OR minks OR monkey OR monkeys OR mouse OR mule OR mules OR nematode OR nematodes OR octopus OR octopuses OR orangutan OR "orang-utan" OR orangutans OR "orang-utans" OR oxen OR parrot OR parrots OR pig OR pigeon OR pigeons OR piglet OR piglets OR pigs OR porcine OR primate OR primates OR quail OR rabbit OR rabbits OR rat OR rats OR reptile OR reptiles OR rodent OR rodents OR ruminant OR ruminants OR salmon OR sheep OR shrimp OR slug OR slugs OR swine OR tamarin OR tamarins OR toad OR toads OR trout OR urchin OR urchins OR vole OR voles OR waxworm OR waxworms OR worm OR worms OR xenopus OR "zebra fish" OR zebrafish) AND NOT (human OR humans))
6	4 and not 5
7	DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh) OR DOCTYPE(ab)
8	6 and not 7
9	PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)
10	8 and not 9

SUPPLEMENTARY TABLE 2. Quality assessment of comparative studies using the NOS

	NOS score		
First author, year	**Selection**	**Comparability**	**Outcome**
Abu Dayyeh 2017	****	*	**
Ang 2016	***	*	**
Siddiqui (1) 2016	****	**	**
Bang (2) 2016	****	*	**
Bang (3) 2016*	****	**	**
Bapaye 2016	****	*	**
Mukai (2) 2015	****	*	**

NOS, Newcastle Ottawa scale.
*Randomized controlled trial.

SUPPLEMENTARY TABLE 3. Quality assessment of non-comparative studies using modified NOS

	Question 1		Question 2		Question 3		Question 4		Question 5		
First author, year	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Methodologic quality
Lakhtakia 2016	X		X		X		X		X		High
Sharaiha 2016	X		X		X		X		X		High
Siddiqui (2) 2016	X		X		X		X		X		High
Smoczyński (1) 2016	X		X		X			X	X		Moderate
Storm 2016		X	X		—	—		X	X		Low
Thompson 2016	X		X		—	—		X	X		Low
Sharma 2016	X		X		X			X	X		Moderate
Keane 2016	X		X		X			X	X		Moderate
Gornals 2016	X		X		X		X		X		High
Bang (1) 2016		X	X		X		X		X		Moderate
Albers 2016		X	X		X		X		X		Moderate
Walter 2015	X		X		X		X		X		High
Smoczyński (2) 2015	X		X		X		X		X		High
Smith 2015	X		X		X			X		X	Low
Rana (1) 2014	X		X		X			X		X	Low
Shmidt 2015	X		X		X		X		X		High
Rinninella 2015	X		X		X		X		X		High
Rana (2) 2015		X	X		X			X	X		Low
Mukai (1) 2015	X		X		X			X	X		Moderate
Nabi 2016		X	X		X		X		X		Moderate
Jagielski 2015	X		X		X		X		X		High
Hugget 2015	X		X		X		X		X		High
Chandran 2015	X		X		X		X		X		High
Smoczyński (3) 2014	X		X		X		X		X		High
Saxena 2014	X		X		X		X		X		High
Rana (3) 2014	X		X		X		X			X	Moderate
Mukai 2014	X		X		X			X	X		Moderate
Lin 2014	X		X		X			X	X		Moderate
Kumar 2014*	X		X		X			X	X		Moderate
Attam 2014		X	X		X		X		X		Moderate
Yamamoto 2013		X	X		X		X		X		Moderate
Varadarajulu 2011	X		X		X		X		X		High
Gardner 2011	X		X		X		X		X		High
Gardner 2009*	X		X		X		X		X		High
Papachristou 2007	X		X		X		X		X		High

Questions 1: Did the patient(s) represent the whole case(s) of the medical center? Cases included represented the general population of walled-of-necrosis; question 2: Was the diagnosis correctly made? Based on the revised Atlanta criteria; question 3: Was follow-up long enough for outcomes to occur? Reported adequate follow-up time; question 4: Were all important data cited in the report? Reported resolution and at least 2 outcomes; question 5: Was the outcome correctly ascertained? Provided definition of resolution.
—, Not available.
*Cohort study but evaluated as case series because reported 2 different techniques of drainage rather than 2 types of stents.

SUPPLEMENTARY TABLE 4. Definition of WON resolution in included studies

Definition	CRR	CRR+SR	Absent	SR	<3 cm+SR	≤2 cm+SR	≤2 cm	↓>50% +SR	↓≥80%	↓≥90%	RI+SR
Studies	Sharaiha 2016	Abu Dayyeh 2017	Smith 2015	Storm 2016	Smoczyński (1)2016	Ang 2016	Keane 2016	Lakhtaki 2016	Hugget 2015	Gardner 2011	Varadarajulu 2011
	Albers 2016	Bapaye 2016	Rana (1) 2014	Thompson 2016	Bang (3)2016	Bang (1) 2016		Gornals 2016			
	Rinninella 2015	Siddiqui (1) 2016	Rana (2) 2014	Mukai (1) 2015	Smoczyński (2)2015	Bang (2) 2016		Nabi 2016			
	Chandran 2015	Siddiqui (2) 2016		Mukai (2) 2015	Jagielski 2015	Walter 2015					
	Attam 2014	Sharma 2016		Mukai (3) 2014	Smoczyński (3) 2014	Lin 2014					
	Yamamoto 2013	Schmidt 2015		Kumar 2014	Saxena 2014						
	Gardner 2009	Papachristou 2009									

WON, Walled-off necrosis; *CRR*, complete radiologic resolution; *SR*, symptoms resolution; *RI*, radiologic improvement; +, with.

SUPPLEMENTARY TABLE 5. Plastic stent group: patient demographics and characteristics

First author (year)	Number of WONs	Size of WON (cm) (mean ± SD)	Patient age (mean ± SD)	Male gender (n)	Age at WON (mean ± SD)	No. of infected necrosis	Paracolic WON	Median follow-up time [range]
Abu Dayyeh (2017)	36	12.8 ± 5.8	59.7 ± 16	28		16	10	8 weeks [IQR 6-12]
Ang (2016)	10							
Siddiqui (1) (2016)	106	10.6	56.3	68	.	.	.	6
Smoczyński (1) (2016)	22	Median 8.03 [5.5-17.3]	50.68	15	.	.		1 year
Storm (2016)	15	.	Median 47.1 [27-62]	9				.
Thompson (2016)	60	.	52.8 ± 2	36				
Sharma (2016)	35	13.22 ± 3.47	.	.				
Keane (2016)	43	.	.	.				11 [0–131]
Bang (1)(2016)	5	.	.	.	.	.	.	
Bang (2) (2016)	26	.	.	.				570 days
Bang (3) (2016)	9	.	.	.				
Smoczyński (2) (2016)	64	Median 14.6 [10.6-22]	.	.				6 month
Rana (1) (2014)	43	9.95 ± 2.75	36.04 ± 10.1	36				
Schmidt (2015)	81	.	.	52				
Rana (2) (2015)	35	.	37 ± 7.6	29				28 months ± 14
Bapaye (2016)	61	11.7 ± 3	43.89 ± 15.1	54				8 weeks
Mukai (2) (2015)	27	7.71 ± 3.3	55.9 ± 14.2	21		16		at least 24 months
Jagielski (2015)	176	12 ± 4.9	52.7 ± 13.2	125	17.8 ± 15.6 weeks	49		at least 6 months
Chandran (2015)								at least 6 months
Smoczyński (3) (2016)	112	Median 11.6 [4.5-26.7]	Median 53.7 [28-86]	83	Median 16.3 weeks [3-78]	38		31 months [2-85]
Rana (2) (2014)	43	9.95 ± 2.75			10.95 ± 2.45			
Mukai (3) (2014)	2	8.8 ± 2.2	61 ± 7.07	2				Mean 601 days, [150-1240]
Lin (2014)	17	11.9 ± 5.2	Median 53 [IQR 32-79]	8				48 months [26–126]
Kumar (2014)	12	13.1 ± 5.1	58.9 ± 3.9	8		8		Group 1 (DEN group) 1.9 ± .3 group 2 (SUA) 2.5 ± 0.8
Varadarajulu (2011)	60	10.7 ± 2.6	52.09 ± 16.4	42				Group 1 (48 patients) 169 [IQR 60-228]

(*continued on the next page*)

SUPPLEMENTARY TABLE 5. Continued

First author (year)	Number of WONs	Size of WON (cm) (mean ± SD)	Patient age (mean ± SD)	Male gender (n)	Age at WON (mean ± SD)	No. of infected necrosis	Paracolic WON	Median follow-up time [range]
								Group 2 (12 patients) 159.5 [IQR 112-228]
Gardner (2011)	104	15	58.1	67	46	40		Mean 19.5 months [1-53]
Gardner (2009)	45	15.6	62	28				
Papachristou (2007)	53	16	61	28	49	26		Mean 178 days [21-8]

cm, centimeter; *DEN*, direct endoscopic necrostectomy; *IQR*, interquartile range; *SD,* standard deviation; *SUA*, step-up approach; *WON,* Walled-off necrosis.

SUPPLEMENTARY TABLE 6. Metal stent group: patient demographics and characteristics

First author (year)	Age (yr) (mean ± SD)	Males gender (n)	No. of stents (LAMS and regular)	No. of LAMS	No. of non-LAMS	WON size (cm) (mean ± SD)	Median age at WON [range]	No. of infected necrosis	Paracolic WON	Median follow-up time [range]
Abu Dayyeh (2017)	52.7 ± 17	45	58	46	12	13.4 ± 6.5		23	9	8 weeks [IQR 6-12]
Lakhtakia (2016)	34.8 ± 12.8	1 81	205	203	2	10.87 ± 2.81	42 days	.		8 weeks
Ang (2016)			8	8	0					
Sharaiha (2016)	54.2 ± 5.5	75	124	124	0	9.5 [4-30]	.	.	12	4 [1-35]
Siddiqui (1) (2016)	51.7	172	207	86	121	10	.	.	.	6
Siddiqui (2) (2016)	51.7 ± 14.3	41	68	68	0	12.1 ± 5.3				2 months [1-3]
Keane (2016)	.	.	3	0	3	.				11 [0-131]
Gornals (2016)	52.5 ± 14.3	9	12	12	0	12.4 ± 2.9		7		Mean 13 ± 11.4 months
Bang (1) (2016)	.	.	1	1	0	.	.	.	.	
Bang (2) (2016)	.	.	13	13	0	.				570 days
Bang (3) (2016)	.	.	12	12	0	.				
Albers (2016)	49.8 ± 18.3	9	13	13	0	.				8.5 months
Walter (2015)	.	.	43	43	0	.				
Smith (2015)	52.6 [24-69]	15	17	0	17	9.5 [8-26]				Mean 7.3 weeks ± 12.7
Rinninella (2015)	.	.	52	52	0	.				320 ± 142
Mukai (1) (2015)	.	.	19	19	0	.				
Bapaye (2016)	40.69 ± 10.2	62	72	72	0	10.1 ± 3.2				8 weeks
Nabi (2016)	14.9 ± 2.34	20	21	21	0	Median 8.8 [5.5-14.8]	58 days [30-288]			360 days [30-1020]
Mukai (2) (2015)	54.4 ± 16.2	37	43	43	0	10.6 ± 4		23		At least 24 months
Hugget (2015)	Median 60 [11-81]	14	19	19	0	Median 15 cm [7-29]	7 wks [3-27]	16		At least 3 months
Chandran (2015)	Median 55 [10-87]	Ratio 2:1 (therefore males = 6)	9	9	0	8 [6-17]				At least 6 months
Saxena (2014)	60.6 ± 12.7	4	5	0	5	12.3				Mean 184 days
Mukai (3) (2014)	52 ± 27.82	2 of 3	3	3	0	11.5 ± 4.6				Mean 601 days, [150-1245]
Attam (2014)	52.7 ± 18.6	8	10	0	0	18.3 ± 5.5	30 [12-117]	5	6 of 10	Unknown
Yamamoto (2013)	51.75 ± 12.2	3	4	4	0	20 ± 12.7	Mean 23 ± 12.8	3		8 weeks

WON, Walled-off necrosis; *IQR*, interquartile range.

SUPPLEMENTARY TABLE 7. Meta-analysis of continuous variables (total number of endoscopic interventions to achieve WON resolution) as reported in 4 studies

Comparison	Outcome	No. of Std	No. of PSs	No. of MSs	Difference in mean	SE	Variance	Lower limit	Upper limit	z-value	*P* value
PS vs MS	No. of procedures	4	230	380	−.922	.184	.034	−1.283	−.561	−5.007	.000

Study	Comparison	Outcome	Difference in mean	SE	Variance	Lower limit	Upper limit	z-value	*P* value
Abu Dayyeh (2017)	PS vs MS	No. of procedures	−1.143	.239	.057	−1.612	−.675	-4.780	.000
Siddiqui (1) (2016)	PS vs MS	No. of procedures	−.966	.265	.070	−1.486	−.446	−3.638	.000
Bapaye (2016)	PS vs MS	No. of procedures	−.807	.212	.045	−1.222	−.392	−3.809	.000
Mukai (2) (2015)	PS vs MS	No. of procedures	−.880	.198	.039	−1.269	−.491	-4.432	.000
Random-effects model			−.922	.184	.034	−1.283	−.561	−5.007	.000

WON, Walled-off necrosis; *Std*, studies; *PS*, plastic stent; *MS*, metal stent; *SE*, standard error.

SUPPLEMENTARY TABLE 8. Sensitivity analysis of 2-arm studies (plastic stent versus metal stent)

Study	Endpoint	Odds ratio	CI lower limit	CI upper limit	z-value	*P* value
Abu Dayyeh (2017)	Single session for resolution	1.124	.752	1.680	.571	.568
Siddiqui (1) (2016)	Single session for resolution	1.490	.665	3.340	.968	.333
Bang (2) (2016)	Single session for resolution	1.480	.762	2.871	1.158	.247
Bapaye (2016)	Single session for resolution	1.268	.587	2.740	.604	.546
Mukai (2) (2015)	Single session for resolution	1.640	.885	3.041	1.571	.116
Total (random-effects model)	**Single session for resolution**	**1.383**	**.772**	**2.478**	**1.089**	**.276**
Abu Dayyeh (2017)	Bleeding	.714	.153	3.322	–.429	.668
Siddiqui (1) (2016)	Bleeding	.356	.094	1.350	–1.519	.129
Bang (3) (2016)	Bleeding	.383	.129	1.139	–1.726	.084
Bapaye (2016)	Bleeding	.621	.121	3.192	–.571	.568
Mukai (2) (2015)	Bleeding	.668	.184	2.426	–.613	.540
Total (random-effects model)	**Bleeding**	**.520**	**.154**	**1.751**	**–1.056**	**.291**
Abu Dayyeh (2017)	Migration	1.496	.602	3.713	.867	.386
Siddiqui (1) (2016)	Migration	1.334	.605	2.940	.714	.475
Bang (2) (2016)	Migration	1.174	.576	2.394	.442	.659
Bang (3) (2016)	Migration	1.222	.606	2.465	.560	.576
Bapaye (2016)	Migration	1.377	.664	2.857	.860	.390
Mukai (2) (2015)	Migration	1.302	.638	2.658	.725	.468
Total (Random-effects model)	**Migration**	**1.299**	**.655**	**2.578**	**.749**	**.454**
Abu Dayyeh (2017)	Occlusion	.588	.321	1.078	–1.718	.086
Siddiqui (1) (2016)	Occlusion	1.250	.109	14.303	.179	.858
Total (Random-effects model)	**Occlusion**	**.614**	**.341**	**1.106**	**–1.624**	**.104**
Abu Dayyeh (2017)	Perforation	1.308	.231	7.416	.303	.762
Siddiqui (1) (2016)	Perforation	.308	.052	1.831	–1.295	.195
Mukai (2) (2015)	Perforation	.648	.063	6.618	–.366	.714
Total (random-effects model)	**Perforation**	**.652**	**.156**	**2.732**	**–.585**	**.559**
Abu Dayyeh (2017)	Overall resolution	3.368	1.895	5.987	4.137	.000
Siddiqui (1) (2016)	Overall resolution	2.669	1.204	5.917	2.418	.016
Bang (2) (2016)	Overall resolution	2.936	1.761	4.894	4.131	.000
Bapaye (2016)	Overall resolution	2.358	1.354	4.109	3.029	.002
Mukai (2) (2015)	Overall resolution	2.772	1.549	4.961	3.433	.001
Total (random-effects model)	**Overall resolution**	**2.812**	**1.704**	**4.639**	**4.047**	**.000**