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Risk of recurrence with or without plastic stent after EUS-guided treatment of peripancreatic fluid collections: A systematic review and meta-analysis

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Bibliography

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ABSTRACT

Background and study aims Recent advances in endoscopic transmural treatment have improved the clinical outcomes of patients with pancreatic fluid collections (PFCs). However, there is still a debate about the preventive effect of long-term placement of a transmural plastic stent (PS) on recurrence after successful endoscopic ultrasound (EUS)-guided treatment of PFCs. We conducted a systematic review and meta-analysis to evaluate PFC recurrence rates with and without a transmural PS after EUS-guided treatment.

Patients and methods A systematic literature search of PubMed, Embase, and the Cochrane database was conducted to identify clinical studies comparing outcomes with and without transmural PS published until September 2022. Data on PFC recurrence and adverse events (AEs) were pooled using a random-effects model.

Results Nine studies including 380 patients with long-term transmural PS and 289 patients without PS were identified. The rate of PFC recurrence was significantly lower in patients with transmural PS (pooled odds ratio [OR] = 0.23, 95% confidence interval [CI] [0.08-0.65], P = 0.005). In a subgroup analysis limited to studies focusing on patients

with disconnected pancreatic duct syndrome, which has been reported to be a risk factor for PFC recurrence, the OR was numerically lower than that for the entire cohort (OR = 0.14, 95% CI [0.04-0.46]). The rate of AEs was significantly higher with long-term transmural PS (OR = 14.77, 95% CI [4.21-51.83]).

Conclusions In this meta-analysis, long-term PS placement reduced the risk of PFC recurrence. Given the potential AEs of indwelling PS, further research is required to evaluate the overall benefits of long-term PS placement.

Introduction

Pancreatic fluid collections (PFCs) are one of the common complications of severe acute pancreatitis and are classified into four distinct subtypes based on the presence of necrotic contents and elapsed time after the onset of pancreatitis as follows: acute peripancreatic fluid collections (APFC) and pseudocysts occurring in interstitial edematous pancreatitis, and acute necrotic collections (ANC) and walled-off necrosis (WON) occurring after necrotizing pancreatitis [1]. APFC and ANC are fluid collections within 4 weeks from the onset of severe acute pancreatitis and may develop into pseudocysts or WON with a matured wall, respectively. These PFCs may resolve spontaneously, but can be persistent and symptomatic, requiring treatment. In particular, if PFC is associated with an infection, it could be a fatal complication. Endoscopic ultrasound (EUS)-guided transmural drainage is a minimally invasive and clinically effective method for managing symptomatic PFCs refractory to conservative treatment [2, 3, 4]. When PFC is not resolved by drainage alone, endoscopic necrosectomy through the transmural fistula has been reported as an effective step-up method to achieve resolution, specifically in WON with abundant necrotic materials [5, 6, 7, 8, 9, 10]. More recently, a lumen-apposing metallic stent (LAMS), which has a large caliber and allows endoscope passage, has made endoscopic necrosectomy more feasible and effective [11, 12, 13, 14]. These developments in techniques and devices and the comprehension of disease pathology have made endoscopic transluminal drainage a more reliable and essential treatment for the management of PFCs.

Despite the improved efficacy of endoscopic transluminal drainage of PFC, many issues remain to be addressed in the management of PFC [15, 16, 17, 18]. One of these issues is reducing the recurrence rate of PFC after resolution using endoscopic transmural drainage. PFC recurrence requiring further treatment may occur at a certain rate after resolution with endoscopic management [19, 20]. Especially in disconnected pancreatic duct syndrome (DPDS), which commonly occurs as a result of necrosis of the main pancreatic duct [21], the disconnection between the upstream and downstream pancreatic ducts may sustain the leakage of pancreatic juice into the PFC cavity, which might increase the risk of recurrence [15]. Recently, several studies have evaluated whether long-term transmural plastic stent (PS) placement could reduce the risk of PFC recurrence after the resolution of PFC by endoscopic transmural drainage [22, 23], although there is no robust evidence supporting this. However, attention should be paid to the adverse events (AEs0 associated with long-term PS, including stent occlusion and migration. To date, there have been no comprehensive data on the drawbacks of long-term stent placement.

Therefore, we conducted a systematic review and meta-analysis to assess the efficacy and safety of long-term transmural PS placement after resolution of PFC by endoscopic transmural drainage, compared with that without stenting.

Patients and methods

Study overview

This meta-analysis summarizes the current evidence to evaluate the efficacy of long-term PS placement at the fistula after resolution of PFC using endoscopic drainage, in comparison with that without stenting. This study was performed in accordance with the PRISMA (the Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. This study was conducted by the WONDERFUL (WON anD pERipancreatic FlUid coLlection) study group which consists of expert endoscopists, gastroenterologists, interventional radiologists, and epidemiologists at high-volume centers in Japan.

Selection criteria

We included prospective or retrospective studies that contained the following information: 1) patients: successful resolution of PFC including pseudocysts and WON achieved with endoscopic transmural drainage; 2) intervention: a long-term transmural PS placed at the fistula after resolution of PFC; 3) control: no stent placement at the fistula after resolution of PFC; and 4) outcome: recurrence of PFC. Studies were excluded if only percutaneous or surgical interventions were examined, the overall cohort size was less than 10 patients, not fully published, not English articles, or not human studies.

Literature search

A comprehensive literature search of PubMed, Embase, and the Cochrane Library (Central) was performed to identify clinical studies published between January 1990 and September 2022 that met the aforementioned selection criteria. Two authors (T.I. and T.Sat.) independently performed the literature search, study selection, assessment of study quality, and data extraction. Disagreements were resolved through discussions with another author (T.M.). The search terms included ("pancreatic fluid collection" or "walled-off necrosis" or "pseudocyst" or "pancreatic necrosis" or "necrotizing pancreatitis") AND ("endoscopy" or "endoscopic ultrasound" or "endoscopic ultrasonography" or "endosonography") AND ("stent" or "drainage") with the settings "not review", "English only" and "hu-

man only". Word variations were also included. The bibliographies of the selected articles were further screened for additional eligible articles.

Quality assessment

The risk of bias for each included study was assessed using the Newcastle-Ottawa Scale (NOS) for observational cohort studies and Cochrane risk of bias assessment for randomized controlled trial. NOS has a scale of 0 to 9 with 0 indicating poor quality and 9 indicating good quality [24]. The scores were summarized into the following three categories: selection of intervention and control cohorts (4 points), comparability of cohorts (2 points), and assessment of outcome (3 points). According to the total score (the number of stars), the quality of data reporting was categorized as poor (0–2 points), fair (3–6 points), and good (≥ 7 points).

Data extraction

Data from studies were extracted into a standardized form by two authors (T.I. and T.Sat.) independently. The collected data included study setting, study design, patient characteristics, treatment protocols, treatment outcomes, and outcome definitions.

Study outcomes

The primary endpoint was recurrence of PFC after resolution with endoscopic transmural drainage. Subgroup analysis for PFC recurrence was also performed using study type (prospective or retrospective), and the cohort with DPDS alone. As the secondary outcome, adverse events (AE) other than recurrence of PFS (e.g., stent occlusion, stent migration, or pain) were also evaluated. The devices used for endoscopic transmural drainage and the definition of PFC recurrence were heterogeneous across the studies and are summarized in ▶ **Table 1**. Therefore, a uniform definition of PFC recurrence was not applied, and the original definition in each study was used in this analysis.

Statistical analysis

Pooled odds ratios (ORs) and 95% confidence intervals (CIs) for each outcome variable were computed based on the data reported in the pooled studies. Given the heterogeneity of the study cohorts and procedures, a random-effects model was used for the analysis using the Mantel-Haenszel method. Heterogeneity between study specific estimates was assessed using the inconsistency index (I^2), in which cut-offs of 0% to 40%, 30% to 60%, 50% to 90%, and 75% to 100% were applied to suggest minimal, moderate, substantial, and considerable heterogeneity, respectively [25]. Potential publication bias was evaluated based on visual inspection of the funnel plot. A leave-one-out meta-analysis was performed to investigate influence of each study on the primary outcome. All tests were two-sided and $P < 0.05$ was considered statistically significant. All analyses were performed using RevMan 5.4. (The Cochrane Collaboration, UK).

Results

Through a systematic review of the literature, 2,100 articles were initially identified. Among them, 15 studies were reviewed, and nine studies were finally included in this analysis (▶ **Fig. 1**) [22, 23, 26, 27, 28, 29, 30, 31, 32]. A total of 669 patients (380 with and 289 without PS placement) were included in this analysis. Overall, five studies were conducted in the USA, and one study was conducted in each of Germany, Belgium, India, and Japan; two studies were randomized controlled trials, one was a prospective cohort study, and six were retrospective cohort studies. Summarized information regarding the stent type used for long-term PS placement, definition of PFC recurrence, and presence of DPDS in each study is shown in ▶ **Table 1**. The NOS scores of the included studies are presented in ▶ **Table 2**.

As the primary outcome, recurrence of PFC after successful resolution using endoscopic transmural drainage was evaluated, including subgroup analysis stratified by study design and presence of DPDS (▶ **Table 3**). Based on the results of nine studies, the pooled OR for recurrence after resolution of PFC using endoscopic transmural drainage between long-term PS placement and that with no PS was 0.23 (95% CI [0.08–0.65]), which indicated long-term PS placement significantly reduced the risk of recurrence compared to that without PS. The pooled recurrence rates were 5.8% (22/380) in the long-term PS placement group and 20.8% (60/289) in the no PS group. (▶ **Fig. 2**) The data were substantially heterogeneous among the studies (I^2 = 66%), and the funnel plots also showed an asymmetrical scatter of points, which might indicate the presence of a possible publication bias (▶ **Fig. 3**). However, leave-one-out analysis did not differ the pooled ORs ranging 0.17 to 0.28. The pooled OR for recurrence stratified by study design showed a significantly lower risk of recurrence in the PS placement group with a pooled OR 0.14 (95% CI 0.02–0.85) in the prospective studies but only a tendency of lower risk in the PS placement group in the retrospective studies with a pooled OR 0.29 (95% CI 0.07–1.24), compared with that of the no PS group (▶ **Fig. 4**). In the analysis of the studies including only patients with DPDS, long-term PS placement significantly reduced the risk of recurrence compared with no stenting, with a pooled OR 0.14 (95% CI 0.04–0.46), although substantial heterogeneity was again seen with the study data (I^2 = 54%) (▶ **Fig. 5**).

In the five studies that reported AE other than recurrence of PFC, the pooled OR for AE after resolution of PFC with endoscopic transmural drainage was 14.77 (95% CI 4.21–51.83) with minimal heterogeneity in the study data (I^2 = 0%) (▶ **Fig. 6**). Long-term PS placement was associated with a higher risk of AE compared with no PS placement. The pooled incidence rates of AE were 26.1% (37/142) and 0.5% (1/183) in the long-term PS placement and no PS groups, respectively. The reported AEs related to deployed PS were mostly spontaneous PS migration (32 of 37 events), which occurred with the pooled incidence rate of 22.5% (32/142) and did not cause serious health problems except for possible PFC recurrence.

▶ **Table 1** Overview of seven studies included in meta-analysis.

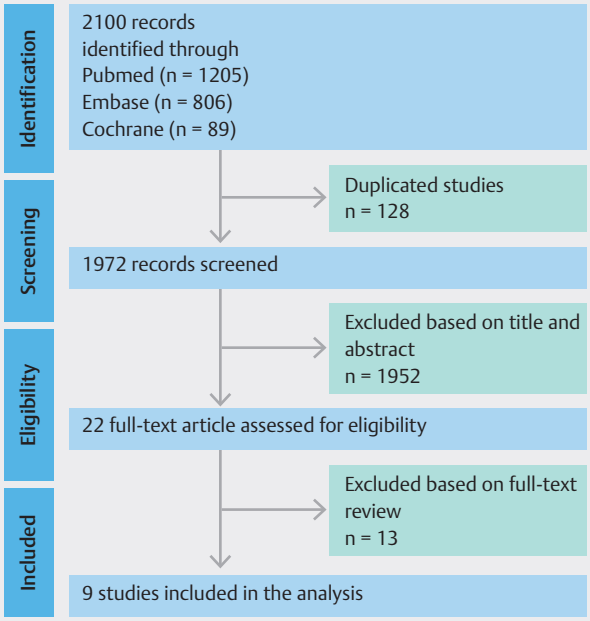
Author, year	Country	Study design	Study subject	Initial stent	Presence of DPDS	Type of PS for long-term placement	Definition of recurrence
Arvanitakis M, 2007	Belgium	RCT	Successful endoscopic transmural drainage of PFC	DPS	Partial cohort	One or two, 7–10 F, 3–12 cm length DPS	A recurrence of the same symptomatic PFC after initial successful resolution
Kato S, 2013	Japan	Retrospective cohort	EUS-guided transmural drainage for pancreatic pseudocyst	DPS	No information	7F DPS	Not defined specifically
Bang JY, 2013	USA	Retrospective cohort	Endoscopic transmural drainage of WON	DPS	Partial cohort	Two, 7F, DPS	Symptomatic peripancreatic fluid collection diagnosed on CT imaging
Ruckert A, 2017	Germany	Retrospective cohort	EUS-guided transmural drainage for acute or chronic pancreatic pseudocysts	DPS	No information	One, 10F, DPS	The presence of a pancreatic pseudocyst on imaging after successful treatment
Bang JY, 2018	USA	Retrospective cohort	Endoscopic transmural drainage for PFC	DPS	Entire cohort	Two, 10F, 4 cm DPS or two to three, 7F, 4 cm DPS	Not defined specifically
Wang L, 2021	USA	Retrospective cohort	EUS-guided transmural drainage for PFCs secondary to acute pancreatitis	DPS or LAMS	Partial cohort	DPS	A fluid collection that developed in the same location after prior successful resolution
Bang JY, 2021	USA	Prospective cohort	EUS-guided transmural drainage for PFC using LAMS	LAMS	Entire cohort	Two, 7F, 4 cm DPS	Not defined specifically
Pawa R, 2022	USA	Retrospective cohort	EUS-guided transmural drainage for PFC using LAMS	LAMS	Entire cohort	Two, 7F, 4 cm or 10F 4 cm DPS	Reaccumulation of PFC (> 2 cm) in the same location on follow-up imaging
Chavan R, 2022	India	RCT	EUS-guided transmural drainage for WON using LAMS	LAMS	Entire cohort	One or two, 7F, 5 cm, DPS	Occurrence of a new fluid collection at the same location after prior resolution

RCT, randomized controlled study; PFC, pancreatic fluid collection; WON, walled-off necrosis; EUS, endoscopic ultrasound; DPS, double-pigtail stent; LAMS, lumen-apposing metallic stent; DPDS, disconnected pancreatic duct syndrome

Discussion

This meta-analysis of nine studies involving 669 patients with PFC evaluated the significance of long-term transmural PS placement for PFC recurrence after resolution via endoscopic transmural drainage compared to that without PS. Long-term PS placement reduced the risk of PFC recurrence by 76%, and a modestly stronger preventive effect was suggested in an analysis limited to studies that included only patients with DPDS (86% reduction). However, the AE rate, except for PFC recurrence, was approximately 14-fold higher in the long-term transmural PS placement group, although most AEs involved stent migration without symptoms. These findings on the advantages and disadvantages of long-term PS placement highlight the importance of conducting a study that compares the overall benefits of this treatment strategy while considering patients' quality of life.

In the current meta-analysis, long-term transmural PS placement at the fistula was associated with a low risk of recurrence after resolution of PFC was achieved using endoscopic transmural drainage. Recently, DPDS is known to be associated with a higher risk of PFC recurrence and a recent meta-analysis confirmed a 7-fold higher risk of PFC recurrence in patients with DPDS (pooled OR 6.72, 95% CI 2.72–16.6) compared with patients without DPDS [15]. In our subgroup analysis including only patients with DPDS, long-term PS placement significantly



▶ **Fig. 1** Flow diagram of study selection in a meta-analysis for recurrence of pancreatic fluid collections after resolution using endoscopic transmural drainage in patients with and without long-term plastic stent (PS) placement.

reduced the risk of PFC recurrence with a pooled OR 0.14 (95% CI 0.04–0.46), and the preventive effect appeared to be greater than that for the overall population of PFC patients. Therefore, patients with DPDS are thought to be good candidates for long-term PS placement after the successful resolution of PFCs. Additional concurrent management options should be explored to further improve clinical outcomes in patients undergoing EUS-guided treatment of PFCs. A retrospective study by Ni et al. [33] which evaluated the effect of transpapillary PS placement on recurrence of PFC in 153 patients, reported that PFC recurrence was more common in patients with DPDS (19% vs. 1.4%, $P < 0.001$), the same as previous study results. The recurrence rate of combined transmural and transpapillary drainage was significantly lower than that with transmural or transpapillary drainage alone (6.5% vs 15.4% vs 22.7%, respectively; $P < 0.01$). Concurrent treatment with long-term transmural drainage might further improve the recurrence rate of PFC after successful management using endoscopic transmural drainage. However, this treatment modality has been associated with a low technical success rate and a higher risk of procedure-induced infections [34]. Therefore, the appropriate timing of transpapillary stent placement in the context of EUS-guided PFC treatment should be investigated in future research considering the risk-benefit balance.

Several points should be addressed before the long-term placement of a transmural PS is routinely performed in patients

▶ **Table 2** The Newcastle-Ottawa Scale and Cochrane quality assessment score for assessment of data reporting quality of each study included in a meta-analysis. + low risk of bias; - unclear risk of bias; x high risk of bias

The Newcastle-Ottawa Scale									
	Selection				**Comparability (up to 2 stars)**	**Outcome**			**Total**
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	
Kato S, 2013	★		★	★	★	★			5
Bang JY, 2013	★		★	★	★	★			5
Ruckert A, 2017	★		★	★	★	★			5
Bang JY, 2018	★		★	★	★	★			5
Wang L, 2021	★		★	★	★	★	★	★	7
Bang JY, 2021	★	★	★	★	★	★			6
Pawa R, 2022	★		★	★	★	★	★	★	7
Cochrane risk of bias assessment									
	Random sequence allocation	Allocation concealment	Blinding of investigators	Blinding outcome data	Incomplete outcome data	Selective reporting	Other bias		
Arvanitakis M, 2007	○, +	○, +	○,-	○, +	○, +	○, +	○, +		
Chavan R, 2022	○, +	○, +	○,-	○, +	○, +	○, +	○, +		

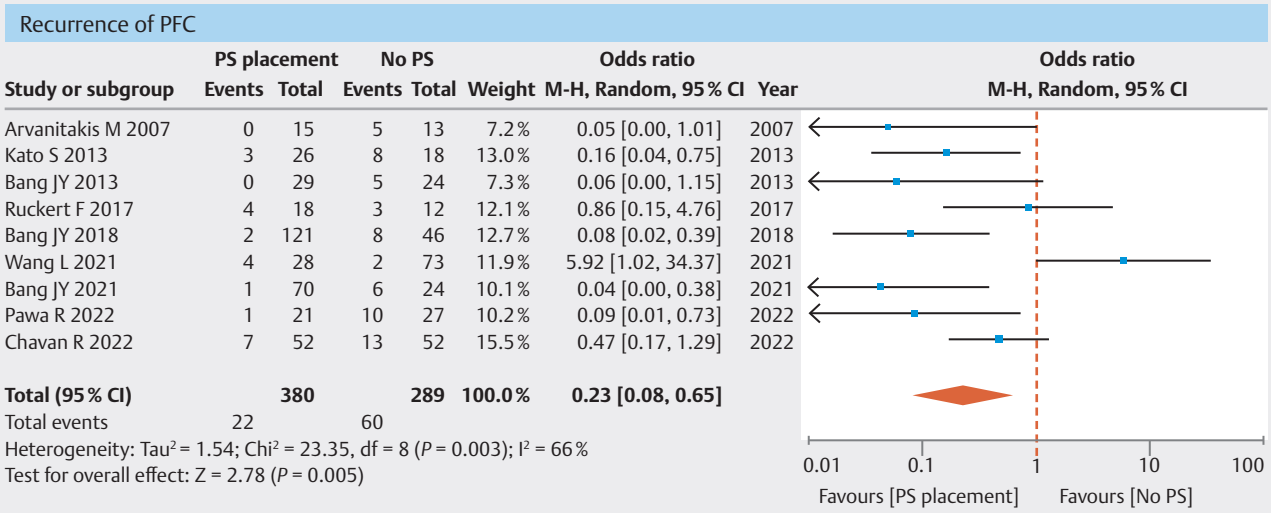
▶ **Table 3** Study outcomes.

Author, Year	Group	No. of patients	DPDS	No. of recurrences	Follow-up period	AEs	Details of AEs
Arvanitakis M, 2007	PS placement	15	6	0	Median 12 mo (IQR 7–18)	5	Stent migration in 3 (asymptomatic in 3), Pain in 1, removal for ERCP in 1
	No PS	13	2	5	Median 9 mo (IQR 4.5–18)	1	New PFC in 1
Kato S, 2013	PS placement	26	NA	3	NA	16	Stent migration in 16 (asymptomatic in 14)
	No PS	18	NA	8	NA	0	
Bang JY, 2013	PS placement	29	29	0	NA	NA	
	No PS	24	13	5	NA	NA	
Ruckert A, 2017	PS placement	18	NA	4	NA	NA	
	No PS	12	NA	3	NA	NA	
Bang JY, 2018	PS placement	121	121	2	NA	NA	
	No PS	46	46	8	NA	NA	
Wang L, 2021	PS placement	28	NA	4	Median 555 day (IQR 116–899)	3	Stent migration in 2 (asymptomatic in 1), Stent obstruciton in 1
	No PS	73	NA	2	NA	0	
Bang JY, 2021	PS placement	70	70	1	NA	NA	
	No PS	24	24	6	NA	NA	
Pawa R, 2022	PS placement	21	21	1	Median 17.2 mo	1	Stent migration in 1
	No PS	27	27	10	Median 20.2 mo	0	
Chavan R, 2022	PS placement	52	52	7	Median 19 mo (IQR 14.75–23.25)	12	Stent migration in 10 (asymptomatic in 10), Self-limiting pain in 2
	No PS	52	52	13	Median 18 mo (IQR 14.5–20.5)	0	

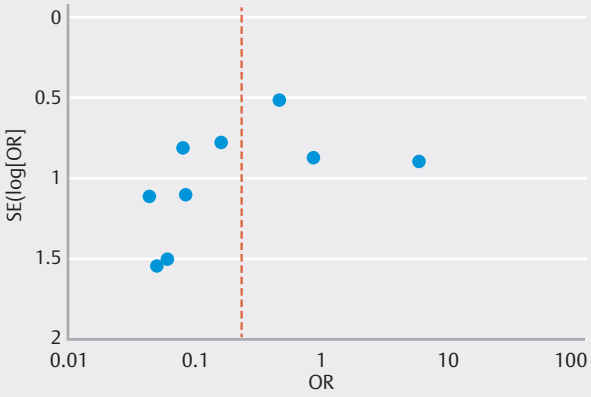
DPS, double-pigtail stent; DPDS, disconnected pancreatic duct syndrome; AE, adverse event; IQR, interquartile range; ERCP, endoscopic retrograde cholangiopancreatography; PFC, pancreatic fluid collection; PS, plastic stent; NA, not applicable.

with successful transmural endoscopic management of PFCs. First, data are required to optimize the timing of switching to a PS in patients receiving LAMS-based interventions. Recently, LAMSs have been increasingly used for EUS-guided PFC drainage because their larger caliber allows quicker drainage and direct endoscopic insertion through the stent into the PFC for necrosectomy. However, for long-term PS placement, LAMS must be replaced with PS. LAMS is also known to be related to several late AEs, such as bleeding and buried LAMS syndrome [35, 36]. The mechanism of LAMS causing bleeding is assumed to be persistent contact of the edges of LAMS with the adjacent vasculature of the PFC wall, which could cause erosion of vessels, precipitating a bleeding event [37]. A prospective study by Bang et al. [37] evaluated AEs related to LAMS and showed that AEs were observed in 6.4% of patients (12/188) including delayed bleeding in 4.3% (8 patients) and buried LAMS syndrome in 2.1% (4 patients); factors predicting AEs were stent removal after four weeks (OR 4.60, 95% CI 1.30–16.3, P = 0.018) and a PFC size of ≤ 7 cm (OR 4.33, 95% CI 1.10–17.0, P = 0.036). From the perspective of prevention of late AEs, the preferable exchange timing from LAMS to PS could be within four weeks after the resolution of PFC. In addition, it might be technically challenging to replace an existing LAMS with a PS when the cavity of the PFC collapses as a result of successful treatment. In the prospective studies included in this analysis, the technical failure rates of exchanging LAMS with PS were reported to be 11.5% (6/52) [23] and 25.5% (24/94) [31] because of collapsed PFC cavities. Taken together, these results suggest that it may be reasonable to convert to a PS within four weeks of LAMS placement.

The risk of stent-related AEs during long-term follow-up should be considered. In our study, the rate of AEs other than recurrence of PFC was approximately 14-fold higher with long-term PS placement (OR 14.77, 95% CI 4.21–51.83) and most of



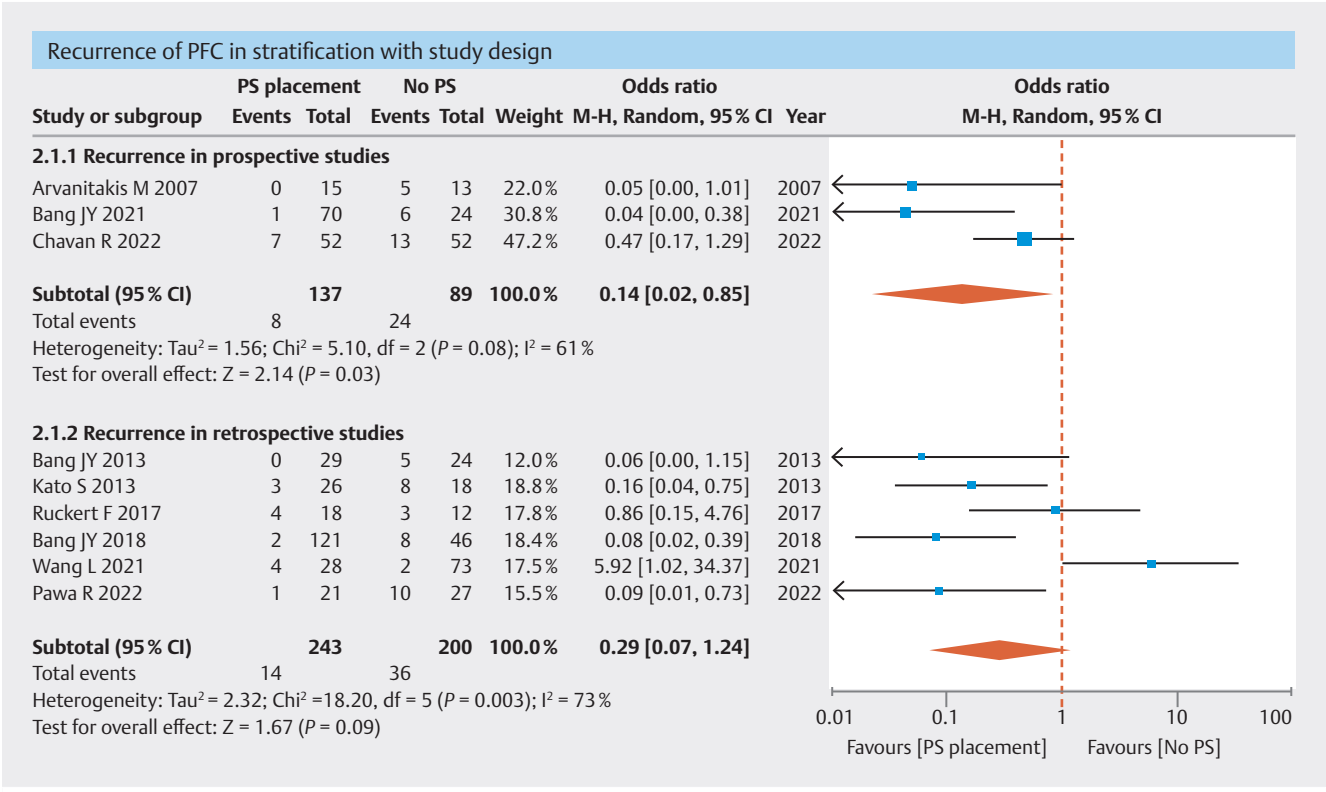
▶ **Fig. 2** Meta-analysis for recurrence of pancreatic fluid collections after resolution using endoscopic transmural drainage in patients with and without long-term plastic stent (PS) placement.



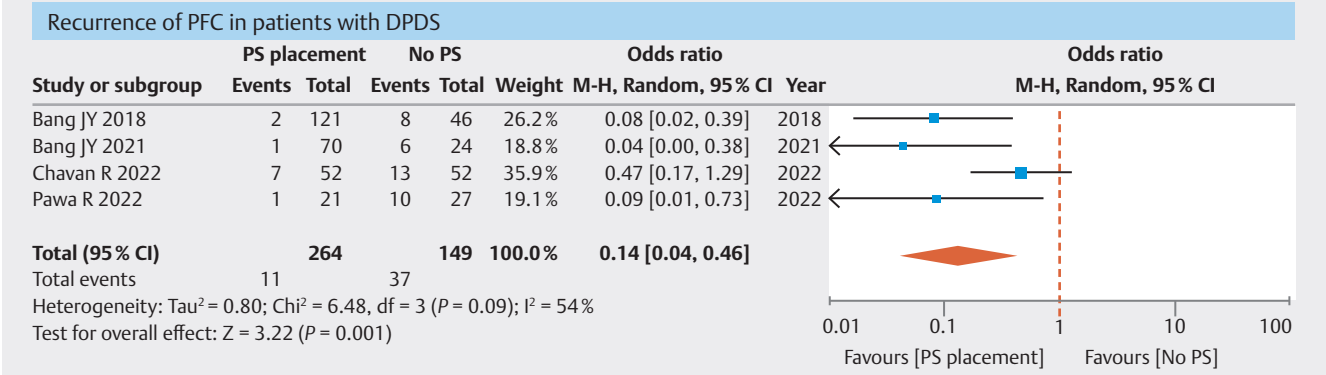
▶ **Fig. 3** Funnel plot to assess a publication bias in reporting of odds ratios of recurrence of pancreatic fluid collection in patients with and without long-term stent placement.

the AEs were spontaneous PS migration. In the studies included in this analysis, stent migration did not cause any additional events related to the migrated stent itself, such as perforation, bleeding, or ulceration. However, a retrospective study by Yamauchi et al. [38] including 36 patients with long-term double-pigtail stent (DPS) placement, reported that colon perforation occurred in three patients (8.3%) due to a migrated DPS. Colon perforation was managed with surgical intervention in one patient, but endoscopic removal of the stent successfully managed the events in the remaining two patients. Another retrospective study by Gkolfakis et al. [39] evaluated the incidence rate of late (> 30 days) AEs associated with long-term DPS placement for the management of PFC with DPDS and showed that 17 late AEs occurred in the included 116 patients with a mean follow-up of 80.6 months (standard deviation 34.4) and the incidence rate was 2.18 (95% CI [1.27–3.49]) per 100 patient-years. The detailed late AEs were DPS-associated pain in 10 events, fistula formation in three events, upper gastrointestinal bleeding in two events, biliary stenosis in one event, and retroperitoneal stent migration in one event; these were managed with conservative treatment in three events, stent removal in 10 events, endoscopic treatment in one event, angiographic treatment in one event and surgical treatment in two events. Furthermore, although asymptomatic PS migration or intentional removal was not counted as an AE in the study by Gkolfakis et al. [39], the stent migration rate, including asymptomatic and symptomatic, occurred in approximately three-quarters (72%) of their cohort (95% CI [64.1–79.9]). Although an indwelling or migrated PS itself does not frequently cause AE, we should be aware of and concerned about the high migration rate of PS and the possible symptoms related to indwelling or migrated PS. Further research with a cost-effectiveness evaluation is warranted to compare the clinical outcomes of permanent PS placement, periodic PS exchange, and PS placement with a prespecified long-term duration.

This meta-analysis with a systematic review has several limitations. First, although we systematically collected and evaluated the currently available evidence using a spectrum of data sources, the limited evidence has made this analysis include studies other than randomized controlled trials, which might have caused bias in treatment selection and the resultant between-group heterogeneity in patient characteristics, although the leave-one-out analysis did not differ the pooled OR. In addition, we conducted the analysis based on the pooling of aggregated data reported in published studies and did not utilize individual patient data. Some of the included studies compared long-term PS placement with no PS placement as a secondary analysis, and detailed data on basic characteristics and clinical outcomes stratified by treatment strategy were not available in these studies. Nonetheless, these biases might

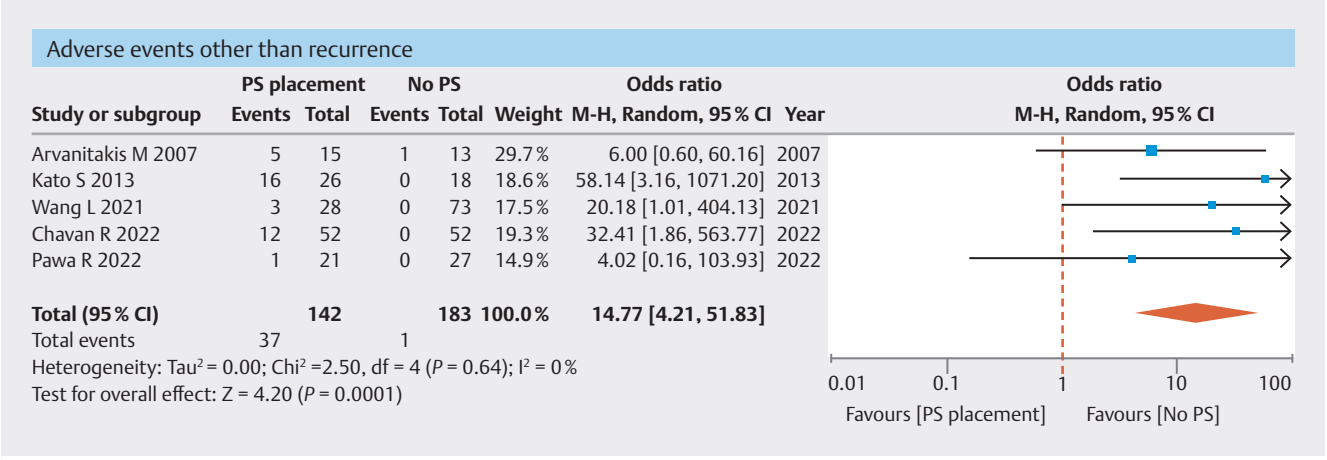


▶ **Fig. 4** Meta-analysis for recurrence of pancreatic fluid collections after resolution using endoscopic transmural drainage in patients with and without long-term plastic stent (PS) placement, stratified by the study design with prospective or retrospective studies.



▶ **Fig. 5** Meta-analysis of the studies included only patients with DPDS for recurrence of pancreatic fluid collections after resolution using endoscopic transmural drainage in patients with and without long-term plastic stent (PS) placement.

have driven our findings toward the null hypothesis because patients at a higher risk of PFC recurrence (e. g., those with DPDS) might be more likely to receive long-term PS placement, potentially underestimating the beneficial effect of long-term PS placement. Second, there might be publication bias based on the results of the funnel plot; therefore, an updated meta-analysis based on prospectively collected data is needed to draw a definite conclusion on the preventive effect of long-term PS placement on post-treatment PFC recurrence. Third, detailed treatments, such as the number of PS, size of PS, or timing of exchange, varied between studies, and further studies are required to find optimal methods for these points. Fourth, we could not standardize the classification and definition of recurrence or AE, because each study has different classification for these outcomes. Finally, the follow-up period for long-term transmural PS placement was limited to up to several years based on current evidence. Because an indwelling stent might cause further AEs if placed permanently, longer follow-up information is required.



▶ **Fig. 6** Meta-analysis for adverse events other than recurrence in patients with and without long-term plastic stent (PS) placement.

Conclusions

In conclusion, based on a meta-analysis of nine studies, we observed that long-term PS placement reduced the risk of PFC recurrence compared with no PS after achieving resolution of PFC by endoscopic transmural drainage. In the subgroup analysis of PFC complicated with DPDS, long-term PS placement reduced the risk of recurrence. AEs other than recurrence, mainly stent migration, frequently occurred with long-term PS placement, and attention should be paid to possible symptomatic AEs related to indwelling and migrated stents. Future trials are warranted to determine the optimal timing of stent exchange, type and number of PS, and other concurrent treatments for further improvement of clinical outcomes after resolution of PFC by endoscopic transmural drainage.

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Conflict of Interest

YN received research grants from Boston Scientific Japan, Fujifilm Corporation, and HOYA Corporation, and honoraria from Boston Scientific Japan, Fujifilm Corporation, Olympus Corporation, and Gadelius Medical. HI received research grants from Boston Scientific Japan, Fujifilm Corporation, Fujifilm Health Care Corporation, Gadelius Medical KK, and Zeon Medical Inc., and honoraria from Boston Scientific Japan, Fujifilm Corporation, Taewoong Medical Devices, Olympus Corporation, Century Medical Inc., and Cook Medical Japan G.K. Other authors have no conflicts of interest to declare.

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