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# Efficacy and safety of endoscopic drainage versus percutaneous drainage for pancreatic fluid collection; a systematic review and meta-analysis

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#### ABSTRACT

**Background/Aims:** Pancreatic fluid collections (PFC) are debris or fluid of the pancreas that needs to be drained out. This may result from surgery or necrotizing pancreatitis. This meta-analysis compared the outcomes of PFC through endoscopic and percutaneous interventions.

**Methods:** A medical database was searched up to June 2022, comparing the outcomes of endoscopic drainage (ED) and percutaneous drainage (PD) for the PFC. Eligible studies reporting clinical and technical success and adverse events were selected.

**Results:** Seventeen studies with 1170 patients were included for meta-analysis, of which 543 patients underwent ED and 627 underwent PD. The odd ratio (OR) of technical success was 0.81 (95% confidence interval (CI) 0.31, 2.1) and clinical success was in the favor of the ED group at OR 2.23 (95% CI 1.45, 3.41). Adverse events OR 0.62 (95% CI 0.27, 1.39) and stent migration OR 0.61 (95% CI 0.10, 3.88) were the same in both groups, but hospital stay pooled mean difference of 15.02 days (95% CI 9.86, 20.18), mortality OR 0.24 (95% CI 0.09, 0.67), and re-interventions OR 0.25 (95% CI 0.16, 0.40) favored ED.

**Conclusions:** ED is safe and efficient for PFC with higher clinical success, lower mortality rate, hospital stay, and re-interventions compared with PD.

#### ARTICLE HISTORY

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#### **KEYWORDS**

Pancreatic fluid collections; endoscopic drainage; percutaneous drainage; post-operative pancreatic drainage; infected pancreatic necrosis; Meta-analysis

# **1. Introduction**

Pancreatic fluid collections (PFCs) are accumulations of debris or fluid from the pancreas that are encircled by a wall of granulation tissue. They can develop as a result of acute pancreatitis, surgery of the pancreas, abdominal trauma, or chronic obstructive disease of the pancreatic duct [1–3]. According to the recent Atlanta classification [1], there are four unique forms of pancreatic fluid collections, which can be split down as follows: The collections that last for more than four weeks are referred to as pancreatic pseudocysts, while the collections that last for less than four weeks are referred to as acute peripancreatic collections (APC). On the other hand, collections that occur in the context of pancreatic necrosis

and last for less than four weeks or more than four weeks are referred to as acute necrotic collections (ANC) and walled-off necrosis (WON), respectively. Patients who have symptomatic, mature PFCs that are transitioning to infectious PFCs or who have maintained a rise in size throughout follow-up should be evaluated for possible intervention therapy. Patients whose PFCs have continued to grow in size throughout the follow-up should also be evaluated. This is because these patients have a higher risk of encountering complications overall [4–6]. Pain, gastrointestinal obstruction, fistulas, and even septic shock might result from some PFCs, whereas others do not cause any symptoms at all. Long-term feeding through the jejunum, total parenteral nutrition, and

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antibiotics are all possible conservative therapeutic options for patients with PFCs. However, some PFCs may necessitate extra therapies. For example, ERCP with trans-papillary stent insertion, endoscopic ultrasound-guided drainage (EUSD), surgery for cysto-gastrostomy with or without debridement, or percutaneous drainage (PD) is some of the procedures that can help.

Surgery is only performed as a last option when other treatments have failed or when severe issues arise [7,8]. Symptomatic PFCs can be drained percutaneously under local anaesthesia, but an external catheter can decrease quality of life (QOL). Percutaneous catheters require frequent fluid output monitoring, continual flushing to maintain patency, interval catheter changes, skin problems, and visiting nursing services [9–11]. Endoscopic treatment reduces fluid and electrolyte loss and reduces the need for a pancreatic fistula and external drainage catheter.

Endoscopic drainage and percutaneous drainage have not yet been shown to be better for patients with PFCs in terms of how well they work or how safe they are. Studies that compare these two interventions often have small sample sizes, which makes it hard to conclude. Our meta-analysis of the relevant literature was performed to find out whether endoscopic drainage (ED) or percutaneous drainage (PD) was better for PFCs.

# 2. Materials and methods

This study followed the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) [12].

#### 2.1. Search strategy

To find relevant papers, electronic databases were searched such as PubMed, MEDLINE, Web of Science, and the Cochran Library. The publishing period of the search strategy was limited to June 2022, and only available in English. Mesh keywords such as 'percutaneous', 'endoscopic', 'endoscopic-ultrasound-guided', 'pancreatic drainage', 'pancreatic walled-off necrocisis', 'pancreatic pseudocysts', 'pancreatic fluid collection', and 'acute necrotic collection' and their different combinations were used for the search. All results were inspected, and duplicates were eliminated.

# 2.2. Studies selection

Studies were included or excluded according to the following criteria.

# 2.2.1. Studies selection criteria

This analysis included studies that met the following criteria:

- 1. All of the patients in the study have pancreatic fluid or debris collections.
- 2. All kinds of studies such as; randomized control trials, cohort studies, and retrospective studies (observational studies) were included.
- 3. Studies comparing the outcomes of ED and PD modes for PFCs.
- 4. Studies only on adult patients (More than 18 years old).
- 5. Human studies in English.

# 2.2.2. Studies exclusion criteria

- 1. Studies comparing outcomes other than ED and PD.
- 2. Duplicates, case studies, review articles, abstracts, and letters were excluded.
- 3. Studies focusing solely on ED or PD outcomes.
- 4. Studies that do not provide adequate results or miss our primary outcome.
- 5. Animal research or publications in other languages.

# 2.3. Data extraction

Two authors extracted data from the studies that were selected. Specifically, collected information from each study about the following factors: publication year, country, design of the study, overall number of patients, mean age of the patients, sex proportion of patient populations, number of patients who had undergone ED or PD, clinical success, technical success, 30 days morality, stent migration, type of fluid, re-interventions, hospital stay, and adverse events. Different coefficients were converted into the same units of measurement. Each study was subdivided into two groups: the ED group and the PD group.

# 2.4. Quality assessment of studies

The technique for assessing the risk of bias published by the Cochrane Collaboration was used in this study [13]. It received a grade of 'low' when there was a low risk of bias, a grade of 'high' when there was a high risk of bias and a grade of 'some concerns' when the information offered was insufficient to make a risk of bias judgment [14]. When analysing research, a variety of aspects were taken into account, including missing outcome data, timeliness of participant identification or recruitment, measurement of outcome, deviations from the intended treatments, and selection of the reported outcomes (Supplementary risk of bias table).

# 2.5. Outcome and definitions

Our primary outcomes were a clinical success (defined as improvement in the clinical condition of the patients with resolution of sepsis after AP and no need for any kind of surgical intervention being necessary) and technical success (defined as success in stenting and catheterizing PFCs and the capacity to drain them out). Secondary outcomes include adverse events (defined as any type of procedure-related complication occurring during the follow-up period), stent migration (defined as stent occlusion or migration), hospital stay (duration of hospital stay after receiving treatment), and 30-day mortality (number of patients dying within a specific 30-day period). In sub-group analysis, studies were divided into two groups: the POPFC group (post-operative pancreatic fluid collection patients) and the WON group (walled-off necrosis and pancreatic pseudocysts patients).

# 2.6. Publication bias and study effect

A funnel plot of the results was used for the estimation of the potential for publication bias in this meta-analysis. To figure out how each study affected the overall result, each one was removed one at a time.

#### 2.7. Statistical analysis

This study used the Cochrane Review Manager Software (version 5.4.1) to calculate odds ratios (ORs) for outcomes. By utilizing the Mantel-Haenszel technique of the random effect model the pooled odds ratio (OR) and 95 percent confidence intervals (CI) were calculated for each outcome. To calculate the mean difference, employed the continuous inverse variance approach with a random effect model. Whereas Cochrane x2 and I<sup>2</sup> statistics were used to quantify statistical heterogeneity. Heterogeneity is represented by the following criteria; values of 25%–49% indicate less heterogeneity, whereas values of 50%–74% indicate a moderate level of heterogeneity, and values greater than 75% indicate a higher level of heterogeneity [15]. A funnel plot was applied to figure out whether or not there was any sort of publication bias. For the data to be considered statistically significant, the p-value needed to be lower than 0.05.

#### 3. Results

# **3.1.** Search results, study characteristics, and evaluation

318 articles were identified following the elimination of all of the duplicate search results and papers that were not related to our investigation. At the end of the process of assessment, a total of 95 papers were looked into for possible inclusion in the final selection. A total of 17 [16-32] papers were considered for inclusion in the analysis in the end. A detailed PRISMA flow chart on the selection of studies is shown here (Figure 1). In these studies, a total of 1170 patients participated, 543 of whom received endoscopic pancreatic fluid drainage and 627 of whom underwent percutaneous fluid collection. There were a total of ten studies that reported post-operative pancreatic fluid collections (POPFC), and the remaining seven included either WON fluid collections or a mix of WON and PP collections. The eleven studies that were conducted in Asia (China, Japan, and India), four studies that were

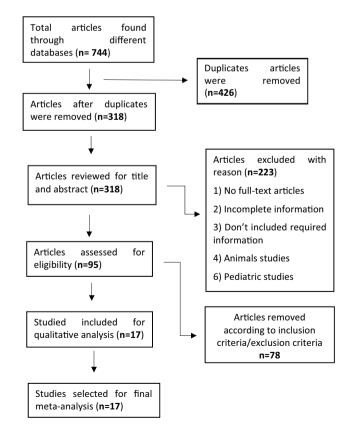


Figure 1. PRISMA flow chart for studies selection.

conducted in the United States, one study that was conducted in Germany, and one study that was conducted in the United Kingdom were all observational cohort studies. According to the inclusion criteria, the features of the studies that were taken into consideration for the analysis are presented in the tables (Tables 1 and 2). The results of the test of the risk of bias showed that every study had a moderate risk of bias (Supplementary Table 1). He et al. [21] and Jurgenson et al. [24] reported only clinical success. Whereas Kwon et al. [19] and Grobmyer et al. [16] did not report any adverse events.

#### 3.2. Primary outcomes

#### 3.2.1. Technical success

In total, fifteen studies reported technical success. He et al. and Jurgenson et al. did not report technical success. Only six studies were included in the calculation of the odd ratio (OR), while the remaining nine studies achieved 100% technical success for both drainage procedures. There was no significant difference in technical success OR between the two procedures: 0.81 (95% CI

Table 1. Characteristics of included studies.

0.31, 2.1),  $I^2 = 0\%$ , p = 0.66 (Figure 2(a)). Whereas in subgroup analysis POPFC studies had an OR of 1.97 (95% CI 0.38, 10.29)  $I^2=0\%$ , p=0.42 and WON studies had an OR of 0.49 (95% CI 0.12, 2.05)  $I^2=33\%$ , p=0.33. Subgroup analysis also revealed no significant differences between the two procedures.

#### 3.2.2. Clinical success

Clinical success was reported in all seventeen studies. Tamura et al. achieved 100% clinical success for both procedures. The OR for the other sixteen studies was 2.23 (95% Cl 1.45, 3.41), l<sup>2</sup>=28%, p=0.0002. For PFCs, the OR result was significantly in favor of endoscopic intervention. The data from the included studies had low heterogeneity. However, in the subgroup analysis, POPFC studies revealed an OR of 1.38 (95% Cl 0.72, 2.63) l<sup>2</sup>=0%, p=0.33, indicating that there is no significant difference in clinical success between ED and PD patients (Figure 2(b)). WON studies revealed an OR of 2.74 (95% Cl 1.56, 4.81) l<sup>2</sup>=50%, p=0.0005, indicating a significant difference in clinical success in favour of ED with moderate heterogeneity.

Study	Number of patients	Mean age (x±SD)	Sex(Male/Female	Type of PFCs	Clinical Success	Technical success
Grobmyer 2009 USA	ED 2	55±	1/1	POPFC	2/2	2/2
,	PD 6	55±	4/2		4/6	6/6
Onodera 2012 Japan	ED 6	67±	6/0	POPFC	6/6	6/6
·	PD 18	66.9±	11/7		15/18	18/18
Azeem	ED 15	52±	8/7	POPFC	12/15	15/15
2012 China	PD 33	52.25±	14/33		26/33	32/33
Kwon 2013	ED 9	62.6±	4/5	POPFC	9/9	9/9
USA	PD 11	55.6±	5/6		8/11	11/11
Akshintala2013 USA	ED 41	47±	28/13	PP	29/41	37/41
	PD 40	52±	26/14		29/40	39/40
He 2016 China	ED 11	44.5±	5/6	WON	8/11	N/A
	PD 13	49.5±	7/6		9/13	
Keane 2016 UK	ED 109	54±	60/49	WON + PP	89/109	100/109
	PD 55	51.75±	37/18		30/55	54/55
Futagawa	ED 12	60±	5/7	POPFC	11/12	11/12
2017 Japan	PD 21	64±	17/4		21/21	18/21
Jurgenson 2018 Germany	ED 39	60±	21/18	POPFC	38/39	N/A
· · ·	PD 59	66±	29/20		54/59	
Tamura	ED 13	64.2±	10/3	POPFC	13/13	13/13
2019 Japan	PD 28	67±	16/12		28/28	28/28
Xie 2019 China	ED 18	45±	10/8	WON + PP	16/18	18/18
	PD 17	47.5±	9/8		9/17	17/17
Watanabe 2019 Japan	ED 11	66±	9/2	POPFC	3 / 4	4/4
	PD 4	53±	3/1		10/11	11/11
Efishat 2019 USA	ED 39	58.75±	19/20	POPFC	26/39	39/39
	PD 39	61.25±	19/20		23/39	38/39
Kuwatani 2020 Japan	ED 17	64.4±	N/A	POPFC	17/17	23/23
	PD 73	39.68±			72/73	41/41
Rana 2020 India	ED 23	36.13±	19/4	WON	20/23	23/23
	PD 41	39.68±	29/12		27/41	41/41
Wan 2020	ED 62	47±	39/23	WON + PP	53/62	62/62
China	PD 67	47.6±	41/26		51/67	67/67
Jayanta S. 2022 India	ED 116	39.1±	97/19	WON	105/116	114/116
-	PD 102	40.8±	78/24		64/102	99/102

ED: Endoscopic drainage; PD: Percutaneous drainage; WON: Walled-off necrosis; POPFC: Post-operative pancreatic fluid collection; PP: Pancreatic pseudocysts; x ± SD: mean ± standard deviation; N/A: No information available.

Table 2. Characteristics of included studies table 1 continue.

Study	Mortality	<b>Re-intervention</b>	Hospital stay	Stent migration	Other adverse events
Onodera 2012 Japan	N/A	N/A	5.65±0.87	N/A	N/A
			$33 \pm 10.5$		
Azeem	N/A	2	N/A	1	2
2012 China		6		0	2
Akshintala2013 USA	N/A	4	$6.5 \pm 6.7$	N/A	6
		17	$14.8 \pm 14.4$		6
He 2016 China	3	N/A	$40 \pm 25$	N/A	6
	3		66±37		10
Keane	0	N/A	11±6	4	6
2016 UK	4	-	$17 \pm 15.7$	0	2
Futagawa	0	N/A	$21 \pm 10.40$	N/A	N/A
2017 Japan	6		$22.75 \pm 7.2$		
Jurgenson 2018 Germany	0	N/A	N/A	N/A	N/A
	4				
Tamura	N/A	2	N/A	N/A	N/A
2019 Japan		14		-	
Xie 2019 China	N/A	2	$9 \pm 2.75$	2	2
		9	$21 \pm 11.5$	5	5
Watanab 2019 Japan	N/A	N/A	$39.8 \pm 17$	N/A	N/A
indianal 2015 Sapan	,,,		$73 \pm 36$		,,,
Efishat 2019 USA	N/A	12	N/A	2	7
	14/74	16	14/74	0	3
Kuwatani 2020 Japan	N/A	N/A	$14.25 \pm 4.73$	N/A	2
	14/74	14/71	$28.5 \pm 2.09$	14/74	4
Rana 2020 India	2	N/A	N/A	N/A	5
	5	14/74	14/14		12
Wan 2020	3	6	$20.25 \pm 17.35$	0	12
China	7	35	$40.53 \pm 20.9$	4	53
Jayanta S. 2022 India	3	25	$40.55 \pm 20.9$ 7.5 ± 1.66		6
Jayanta J. 2022 mula	30	51	$28 \pm 3.9$	22	28

N/A: Not available; other adverse events: adverse events including bleeding, abdominal pain, perforation, pancreatic fistula etc.

#### 3.3. Secondary outcomes

# 3.3.1. Adverse events

Ten studies reported adverse events for both drainage procedures. The OR for adverse events was 0.62 (95% CI 0.27, 1.39),  $I^2 = 72\%$ , p = 0.25, indicating that there were fewer adverse events in the ED group, but statistically there was no significant difference in adverse events between the two interventions and moderate heterogeneity of the included data (Figure 3(a)). Only three studies in the POPFC group reported adverse events, with an OR of 2.47 (95% CI 0.92, 6.60)  $I^2=0\%$ , p=0.25. In the WON group, seven studies produced an OR of 0.37 (95% CI 0.17, 0.81)  $I^2=64\%$ , p=0.01. This indicates that adverse events for ED procedures are lower in the WON group with moderate heterogeneity, but there is no difference in the POPFC group.

#### 3.3.2. Stent migration

Only six studies have noted stent migration events. There were fewer stent migration events in the ED procedure, but the difference was not statistically significant and showed moderate heterogeneity. The OR for stent migration was 0.61 (95% CI 0.10, 3.88),  $I^2 = 68\%$ , p = 0.60 (Figure 3(b)). Only two POPFC studies reported stent migration, yielding an OR of 5.99 (95% CI 0.64, 55.97)  $I^2 = 0\%$ , p = 0.12, and four

WON studies yielded an OR of 0.23 (95% Cl 0.03, 1.59)  $I^2 = 63.9\%$ , p = 0.14. In POPFC studies, stent migration incidents were greater in ED than in PD, but this difference was not statistically significant because only two studies were included, whereas, in WON studies, stent migration events were lower in the ED group, although not statistically significant. The study by Jayanta et al. had a significant impact on the final result, reporting 22 stent migration events in the ED group leading to higher heterogeneity.

#### 3.3.3. Hospital stay

Eleven studies reported hospital stays after the interventions for both groups. The pooled mean difference in hospital stay was 15.02 days (95%CI 9.86, 20.18),  $l^2=94\%$ , p=0.00001, indicating that the ED and PD groups had a 15-day difference in hospital stay that is statically significant but presenting higher heterogeneity (Figure 4(a)). POPFC studies had a pooled mean difference of 17.86 days (95% CI 6.91, 28.80),  $l^2 = 93\%$ , p=0.001, whereas WON studies had a pooled mean difference of 14.10 days (95% CI 6.75, 21.45),  $l^2 = 95\%$ , p=0.0002. In terms of length of hospital stay, subgroup analysis also shows that the ED intervention is better than PD but it showed higher heterogeneity.

a)

	ED		PD			Odds Ratio			Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year		M-H, Rando	om, 95% Cl	
1.1.1 POPFC											
Azeem 2012	15	15	32	33	8.6%	1.43 [0.06, 37.17]	2012	-		•	_
Futagawa2017	11	12	18	21	16.0%	1.83 [0.17, 19.89]	2017			•	
Efishat 2019	39	39	38	39	8.7%	3.08 [0.12, 77.91]	2019				
Subtotal (95% CI)		66		93	33.3%	1.97 [0.38, 10.29]					
Total events	65		88								
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup>	= 0.11	, df = 2 (F	9 = 0.94	); l <sup>2</sup> = 0%						
Test for overall effect:	Z = 0.80 (F	P = 0.43	2)								
1.1.2 WON											
Akshintala 2013	37	41	39	40	18.2%	0.24 [0.03, 2.22]	2013		•		
Keane 2016	100	109	54	55	20.8%	0.21 [0.03, 1.67]	2016	5	•	<u> </u>	
Jayanta S.2022	114	116	99	102	27.8%	1.73 [0.28, 10.55]	2022			-	
Subtotal (95% CI)		266		197	66.7%	0.49 [0.12, 2.05]					
Total events	251		192								
Heterogeneity: Tau <sup>2</sup> =	0.52; Chi <sup>2</sup>	= 2.97	, df = 2 (F	P = 0.23	3);   <sup>2</sup> = 33%	, 0					
Test for overall effect:	Z = 0.98 (F	P = 0.3	3)								
Total (95% CI)		332		290	100.0%	0.81 [0.31, 2.10]			-		
Total events	316		280								
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup>	= 4.79	, df = 5 (F	e = 0.44	);   <sup>2</sup> = 0%					1	+
Test for overall effect:	Z = 0.44 (F	P = 0.6	6)					0.02	0.1 1	10 Equation (ED)	50
Test for subaroup diffe	rences: C	hi² = 1.	56. df = 1	(P = 0)	21). I <sup>2</sup> = 3	5.9%			Favours [PD]	Favours [ED]	

b)

Study or Subaroup	ED Events	Total	PD Events	Total	Weight	Odds Ratio M-H, Random, 95% C	Odds Ratio M-H. Random, 95% Cl
2.1.1 POPFC	Lventa	Total	Lvento	Total	weight	M-11, 1(d)(d)(1, 3376 C)	
Azeem 2012	12	15	26	33	6.0%	1.08 [0.24, 4.90]	
Efishat 2019	26	39	23	39	11.7%	1.39 [0.55, 3.50]	
-utagawa2017	11	12	21	21	1.6%	0.18 [0.01, 4.74]	· · · · · · · · · · · · · · · · · · ·
Grobmyer 2009	2	2	4	6	1.5%	2.78 [0.09, 83.84]	
Jurgenson 2018	38	39	54	59	3.3%	3.52 [0.40, 31.34]	
Kuwatani 2020	17	17	72	73	1.6%	0.72 [0.03, 18.54]	
Kwon 2013	9	9	8	11	1.8%	7.82 [0.35, 174.42]	
Onodera 2012	6	6	15	18	1.8%	2.94 [0.13, 65.26]	· · · · ·
Watanab 2019	3	4	10	11	1.8%	0.30 [0.01, 6.38]	
Subtotal (95% CI)		143		271	31.0%	1.38 [0.72, 2.63]	<b>•</b>
Total events	124		233				
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup>	= 5.03	df = 8 (F	= 0.75	5); $I^2 = 0\%$		
Test for overall effect:	Z = 0.98 (F	= 0.3	3)				
2.1.2 WON Akshintala 2013	29	41	29	40	11.1%	0.92 [0.35, 2.41]	
He 2016	29	11	29	13	4.7%	1.19 [0.20, 6.99]	
Jayanta S.2022	105	116	64	102	14.5%	5.67 [2.71, 11.87]	
Keane 2016	89	109	30	55	14.9%	3.71 [1.81, 7.61]	
Rana 2020	20	23	27	41	7.0%	3.46 [0.87, 13.66]	
Van 2020 Van 2020	53	62	51	67	12.0%	1.85 [0.75, 4.56]	<b></b>
Kie 2019	16	18	9	17	4.8%	7.11 [1.23, 40.98]	
Subtotal (95% CI)	10	380	9	335	69.0%	2.74 [1.56, 4.81]	•
Total events	320	200	219	200	001070		-
Heterogeneity: Tau <sup>2</sup> =		= 12.0		P = 0.0	$(6) \cdot l^2 = 50$	%	
Test for overall effect:				. 0.0	0,1 00		
	_ 0.00 (i	0.0	,				
Total (95% CI)		523		606	100.0%	2.23 [1.45, 3.41]	•
Fotal events	444		452				
Heterogeneity: Tau <sup>2</sup> =	0.18; Chi <sup>2</sup>	= 20.9	2, df = 15	(P = 0	.14); l² = 2	8%	0.01 0.1 1 10 10
Test for overall effect:	Z = 3.68 (F	<b>&gt;</b> = 0.0	002)				0.01 0.1 1 10 10 Favours [PD] Favours [ED]
Test for subaroup diffe	ranaaa Cl	ni2 - 2	15 df - 1	$(\mathbf{P} = 0)$	$12)  ^2 = 5$	9 2%	

Figure 2. (a) Forest plot of Technical success. (b) Forest plot of Clinical success.

# 3.3.4. Mortality

The mortality rate for the ED and PD groups was reported in seven studies. The OR for mortality was 0.24 (95% CI 0.09, 0.67)  $I^2$ =48%, p=0.006, indicating

that the mortality rate is considerably in favor of the ED group (Figure 4(b)). The number of deaths after the drainage was lower in the ED group than in the PD group. Only two POPFC studies reported an OR of

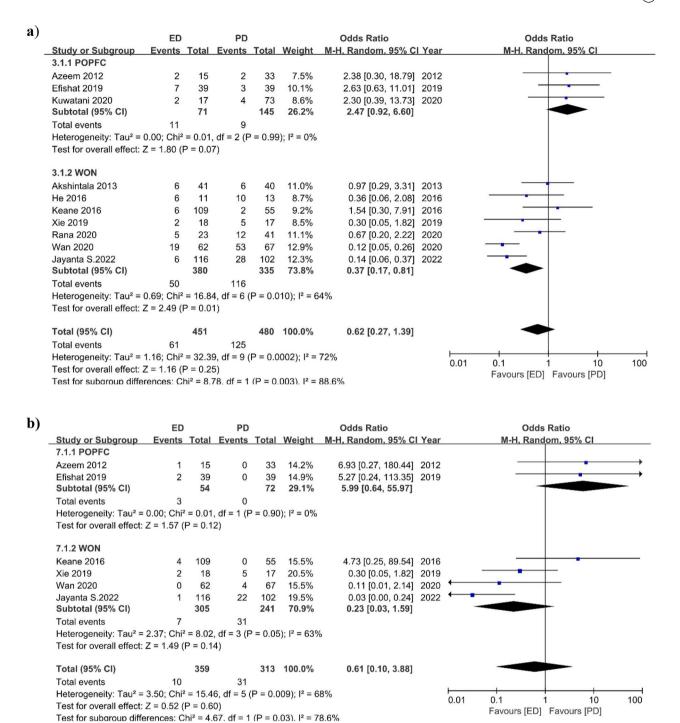


Figure 3. (a) Forest plot of adverse events. (b) Forest plot of Stent Migration.

0.12 (95% CI 0.02, 0.99)  $I^2 = 0\%$ , p = 0.05, and five WON studies produced an OR of 0.28 (95% CI 0.08, 1.00)  $I^2 = 64.0\%$ , p = 0.05. The subgroup analysis was also in favor of the ED technique.

#### 3.3.5. Re-interventions

Re-intervention occurrences were observed in eight studies, with an OR of 0.25 (95%Cl 0.16, 0.40)  $l^2=21\%$ , p=0.00001 (Figure 5). The re-intervention cases of the ED and PD groups varied significantly. POPFC studies had an OR of 0.51 (95% CI 0.24, 1.06)  $I^2 = 64.0\%$ , p = 0.05, while WON studies had an OR of 0.20 (95% CI 0.13, 0.32)  $I^2 = 0\%$ , p = 0.00001. The subgroup analysis also showed that ED was better than PD because the ED group needed fewer re-interventions than the PD group.

**3.3.5.1.** Publication bias and study effect. The risk of publication bias was found to be negligible in our metaanalysis. On the funnel plot, each outcome data displayed a)

,		PD		ED				Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV. Random, 95% Cl		
4.1.1 POPFC											
Futagawa2017	22.75	7.2	21	21	7.2	12	11.5%	1.75 [-3.36, 6.86]	-		
Kuwatani 2020	28.5	2.09	73	14.25	4.73	17	12.7%	14.25 [11.95, 16.55]			
Kwon 2013	90.75	56	11	44	28.53	9	1.6%	46.75 [8.77, 84.73]			
Onodera 2012	33	10.5	18	5.65	0.87	6	11.7%	27.35 [22.45, 32.25]	-		
Watanab 2019	73	36	4	39.8	17	11	1.7%	33.20 [-3.48, 69.88]			
Subtotal (95% CI)			127			55	39.2%	17.86 [6.91, 28.80]			
Heterogeneity: Tau <sup>2</sup> =	103.21;	Chi <sup>2</sup> =	54.16,	df = 4 (	P < 0.0	0001);	<sup>2</sup> = 93%				
Test for overall effect:	Z = 3.20	(P = 0	0.001)								
4.1.2 WON											
Akshintala 2013	14.8	6.7	40	6.5	6.7	41	12.5%	8.30 [5.38, 11.22]	-		
He 2016	66	37	13	40	25	11	3.2%	26.00 [1.04, 50.96]			
Jayanta S.2022	28	3.9	116	7.5	1.66	102	13.0%	20.50 [19.72, 21.28]			
Keane 2016	17	15.7	55	11	6	109	11.9%	6.00 [1.70, 10.30]	-		
Wan 2020	40.53	27.3	67	20.25	17.35	62	10.0%	20.28 [12.45, 28.11]			
Xie 2019	21	11.5	17	9	11.5	18	10.1%	12.00 [4.38, 19.62]	-		
Subtotal (95% CI)			308			343	60.8%	14.10 [6.75, 21.45]	•		
Heterogeneity: Tau <sup>2</sup> =	67.85; C	chi² = 1	104.26,	df = 5 (	P < 0.0	0001);	<sup>2</sup> = 95%				
Test for overall effect:	Z = 3.76	(P = (	0.0002)								
Total (95% CI)			435			398	100.0%	15.02 [9.86, 20.18]	•		
Heterogeneity: Tau <sup>2</sup> =	53.16; C	chi² = 1	177.59,	df = 10	(P < 0.0	00001)	<sup>2</sup> = 94%				
Test for overall effect:					,	,			-50 -25 0 25 50		
Test for subaroup diffe				'	- 0 -0	12 - 0	0/		Favours [PD] Favours [ED]		

#### b)

 ,	ED		PD			Odds Ratio			Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI Y	/ear		M-H, Rando	om, 95% Cl	
5.1.1 POPFC											
Futagawa2017	0	12	6	21	8.6%	0.10 [0.00, 1.86] 20	017	•			
Jurgenson 2018	0	39	4	59	8.7%	0.16 [0.01, 2.98] 20	018	•			
Subtotal (95% CI)		51		80	17.2%	0.12 [0.02, 0.99]					
Total events	0		10								
Heterogeneity: Tau <sup>2</sup> = 0	0.00; Chi <sup>2</sup>	= 0.05	, df = 1 (F	P = 0.82	2); l <sup>2</sup> = 0%						
Test for overall effect: Z	: = 1.97 (I	P = 0.0	5)								
5.1.2 WON											
He 2016	3	11	3	13	15.5%	1.25 [0.20, 7.96] 20	016			•	
Keane 2016	0	109	4	55	8.7%	0.05 [0.00, 0.99] 20	016	•	•		
Rana 2020	2	23	5	41	16.7%	0.69 [0.12, 3.85] 20	020				
Wan 2020	3	62	7	67	20.0%	0.44 [0.11, 1.77] 20	020			_	
Jayanta S.2022	3	116	30	102	21.9%	0.06 [0.02, 0.22] 20	022		-		
Subtotal (95% CI)		321		278	82.8%	0.28 [0.08, 1.00]					
Total events	11		49								
Heterogeneity: Tau <sup>2</sup> = 1	.27; Chi2	= 11.0	5, df = 4 (	P = 0.0	03); l <sup>2</sup> = 64	%					
Test for overall effect: Z	: = 1.97 (I	P = 0.0	5)								
Total (95% CI)		372		358	100.0%	0.24 [0.09, 0.67]					
Total events	11		59								
Heterogeneity: Tau <sup>2</sup> = 0	.83; Chi <sup>2</sup>	= 11.4	8, $df = 6$ (	P = 0.0	$(7);  ^2 = 48$	%				1	
Test for overall effect: Z					<i>,</i> .			0.01	0.1 1	10	100
Test for subaroup differ			,	(P = 0	.50). I <sup>2</sup> = 0	%			Favours [ED]	Favours [PD]	

Figure 4. (a) Forest plot of Hospital Stay. (b) Forest plot of Mortality.

the symmetric distribution of the data. While the effects of each study were evaluated by removing each study one by one, the findings indicated that none of the studies had a significant impact on the conclusion made.

# 4. Discussion

It is difficult to collect pancreatic fluids (PF) from patients, and this presents a significant obstacle to

their care. Surgical drainage for PF is a last choice due to the high risk of complications and the invasive nature of the procedure. In addition to endoscopy and percutaneous drainage, there are other alternatives. Several researchers have discovered an advantage of ED for PFCs. 17 studies reported on the PFC in this meta-analysis. OR was determined independently for POPFC and WON patients in subgroup analysis. According to our findings, the odds were strongly in

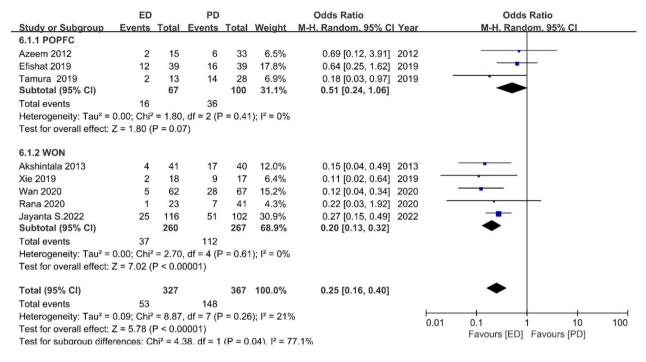


Figure 5. Forest plot of Re-intervention.

favor of ED. Subgroup analysis of the POPFC investigations found that in terms of technical success, clinical success, adverse events, recurrence of mortality, and stent migration, both ED and PD had the same results. However, the length of stay in the hospital and the rate of re-intervention in the ED group were much lower than in the PD group. Whereas for WON studies, OR showed that clinical success, hospital stay, recurrence, and mortality were significantly in favor of the ED group while technical success and stent migration were the same for the ED and the PD groups.

A meta-analysis of 13 studies by Mohan et al. [33] reported that ED and PD had similar adverse events and technical success. ED outperformed PD in clinical success (93.2% vs. 79.8%, *p*=0.002), disease recurrence, and PF management. This meta-analysis only included single-arm studies involving PFC patients. This meta-analysis did not compare ED and PD. Current meta-analysis solely compared ED and PD for PFCs. Khan et al. [34] reported that the pooled risk ratio (RR) for clinical success was 0.40 (95%CI 0.26, 0.61) in favour of ED in seven trials comparing the outcomes of ED versus PD. Meanwhile, both procedures had a virtually identical RR for adverse events of 0.77 (95%CI 0.46, 1.28). However, only seven papers were included in this analysis, and the results of the comparison between the two methods were different from those of the current study. Cai et al. [35] reported a data of 11 studies meta-analysis with OR for clinical success of 1.39 (95% CI 0.82, 2.37) that is in favour of ED and included studies with missing outcome data. But the current study included 17 studies all reporting our primary outcome clinical success. Studies not reporting clinical success were excluded from the meta-analysis.

Chen et al. [36] reported a meta-analysis of six studies about PFC after pancreatic surgery. According to the reported data, there is no difference in technical success, clinical success, recurrence, and adverse events between the two interventions. ED has comparable safety and efficacy to PD. In the subgroup analysis, the current study also analysed ten studies reporting ED and PD after pancreatic surgery and analysis also showed no significant difference in technical success, clinical success, mortality, recurrence, stent migration, and adverse events but hospital stay and re-intervention rate that were in the favour of ED. Reporting data from 25 studies' meta-analysis by Ramouz et al. [37] stated that compared to PD, ED produced higher clinical and technical success with fewer procedure-related complications and hospital stay time [38]. In this meta-analysis, single-arm studies and case reports describing the efficacy of only ED were included that did not describe the comparative data between the two interventions. The present study included up to-dated seventeen studies reporting the comparative data of ED and PD.

Endoscopic drainage will accrue an increasing number of benefits as time goes by, particularly when new stents and endoscopic procedures and abilities become available. In the meantime, ED can also

perform additional therapies for pancreatic duct strictures and pancreatic duct stones, as well as bile duct strictures and bile duct stones while the PD cannot conduct such additional therapies. ED also demonstrated an improvement in life guality and a reduced risk of infection, whereas PD patients required long-term care, which affected the patient's life quality and also carried the risk of developing an infection of the skin and an external pancreatic fistula [39]. Albers et al. [40] reported that during the follow-up period of 8.5 ± 5.9 months for the described treatment of IPN (infected pancreatic necrosis), 12 out of 13 patients obtained clinical success by utilizing ED through the utilization of stents and lumen debriment. Glucck et al. [41] reported that compared to only ED a combination of ED and PD can reduce hospital stay significantly (55 days vs. 26 days) for PFC. According to another study, the ED procedure was also used for abdominal abscesses and showed better results compared with the PD procedure [42]. Inamdar et al. [43] suggested ED should be the first line of treatment for malignant biliary strictures (MBS) patients because ED procedures showed fewer adverse events compared to PD. However, the current meta-analysis did not find any significant difference in adverse events between ED and PD. Metal stents can reduce bleeding risk as compared to plastic stents [44-48]. Chen et al. [49] reported that metal stent drainage is more effective with higher clinical success than plastic stents (92% vs. 84%). A recent meta-analysis of fifteen studies found that using metal stents for endoscopic drainage of WON resulted in better clinical outcomes and fewer adverse events compared to using plastic stents [50]. For the patients of necrotizing pancreatic collection, 'Step-up' treatment based on minimally invasive procedures is recommended [51,52]. WON patients need special care and multiple drainage secessions due to their aggressive nature. An RCT study of WON patients also demonstrates that there is no difference in technical and clinical success, adverse events between ED and laparoscopic internal drainage, and fewer hospital stays [53]. Hamada et al. reported an analysis of 5 studies of PFC for patients with disconnected pancreatic duct syndrome (DPDS). Results also supported the ED for the PFC [54]. Another meta-analysis of 30 studies of PFC with DPDS by Chong et al. reported that endoscopic transmural drainage is better than transpapillary drainage and endoscopic and surgical drainages interventions showed comparable success rates for the patients of DPDS [55].

ED procedure re-introduce pancreatic fluid (PF) into the GI tract preventing electrolytes and fluid loss compared to the PD procedure where PF is drained out of the body [19,56–58]. ED has only the disadvantage of inconvenient nasocystic drainage and repeated endoscopic procedures due to stent migration and incomplete drainage [59]. So this may be not suitable for all patients. While selecting the appropriate drainage procedure it is very important to take into account the patient's condition and the risk of the presence of solid debris from the necrotic tissues that cannot be drained out through PD. But ED will be useful in the detection of debris and necrosectomy that is not possible through PD.

Acute pancreatitis can result in different types of fluid collections, including ANCs and PFCs. While PFCs can often be managed with a passive drainage approach, APNCs may require a more aggressive approach and occasionally necessitate necrosectomy. However, the current literature lacks studies that specifically compare these two types of collections. Many studies report on both WON and pancreatic pseudocysts together, while it's also important to note that WON and some POPFCs may require a more aggressive drainage approach. While some studies have conducted separate meta-analyses for APNCs and POPFCs [37,38], our analysis combines both conditions. This is because there is a lack of comparative studies and it is important to understand the differences in management approaches between these types of collections. However, in our analysis, we conducted a subgroup analysis to compare the management of the two types separately. There are several limitations to this research. The primary concern with our analysis is the lack of randomized controlled trials. Our results show higher heterogeneity for some outcomes; thus, it is essential to keep this in mind when interpreting the results. Additionally, some studies included in our analysis had small sample sizes, and others reported incomplete data with different types of collections. Another limitation is that some studies presented data in different formats, which we standardized to ensure consistency, but this could have potentially influenced the results. Furthermore, the studies we included involved patients with different types, amounts, and locations of pancreatic fluid(PF) disorders. To draw more robust conclusions, future studies should focus on patients with identical PF characteristics and locations.

# 5. Conclusion

Based on the findings of this meta-analysis, the ED technique for pancreatic fluid(PF) draining is considered both safe and effective. The clinical success rate of this technique is better compared to other interventions, with a reduced rate of adverse events,

re-interventions, hospital stays, and mortality. Achieving gratifying results relies on selecting the appropriate patients and utilizing competent medical professionals. However, to fully evaluate the advantages of ED procedures in comparison to other interventions, randomized control trials involving large numbers of patients are necessary.

# Ethical Approval and consent to publish

All authors have approved this submission to your esteemed journal. Its publication is also approved tacitly by the responsible authorities where the work was carried out. The authors have no relevant financial or non-financial interests to disclose.

# **Author contributions**

Khizar Hayat: Wrote the original paper; Zhicheng Huang: Edit and correct the paper; Yanhua Wu: Literature search; Chenyu Le: Images Editing; Jianfeng Yang: Provided article ideas and article review.

#### **Disclosure statement**

No potential conflict of interest was reported by the author(s).

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#### Data availability statement

All data related to this study is available, please send mail to Yang Jianfeng for further information.

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