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Endoscopic and surgical drainage for pancreatic fluid collections are better than percutaneous drainage: Meta-analysis☆

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ABSTRACT

Background: Pancreatic pseudocyst (PP) and walled-off necrosis can be managed endoscopically, percutaneously or surgically, but with diverse efficacy.
Aims & methods: A comprehensive literature search was carried out from inception to December 2018, to identify articles which compared at least two of the three kinds of treatment modalities, regarding the mortality, clinical success, recurrence, complications, cost and length of hospitalisation (LOH).
Results: The outcomes of endoscopic (ED) and percutaneous drainage (PD) were comparable in six articles. The clinical success of endoscopic intervention was better considering any types of fluid collections (OR = 3.36; 95% confidence interval (CI) 1.48, 7.63; p = 0.004). ED was preferable regarding recurrence of PP (OR = 0.23; 95% CI 0.08, 0.66; p = 0.006). Fifteen articles compared surgical intervention with ED. Significant difference was found in postoperative LOH (WMD (days) = −4.61; 95%CI -7.89, −1.33; p = 0.006) and total LOH (WMD (days) = −3.67; 95%CI -5.00, −2.34; p < 0.001) which favored endoscopy, but ED had lower rate of clinical success (OR = 0.54; 95% CI 0.35, 0.85; p = 0.007) and higher rate of recurrence (OR = 1.80; 95% CI 1.16, 2.79; p = 0.009) in the treatment of PP. Eleven studies compared surgical and percutaneous intervention. PD resulted in higher rate of recurrence (OR = 4.91; 95% CI 1.82, 13.22; p = 0.002) and lower rate of clinical success (OR = 0.13; 95% CI 0.07, 0.22, p < 0.001).
Conclusion: Both endoscopy and surgery are preferable over percutaneous intervention, furthermore endoscopic treatment is associated with shorter hospitalisation than surgery.

Introduction

One of the most frequent gastrointestinal disorders are the different forms of pancreatitis [1,2]. The annual incidence of acute and chronic pancreatitis ranges from 13 to 100/100.000 persons and 5 to 25/100.000 persons, respectively [3]. Acute inflammation of the pancreas could affect the quality of life through its complications for long term [1,4,5]. Among these complications the management of peri- and/or intrapancreatic fluid collections is still a challenge.

Inflammatory fluid collections of the pancreas could be categorized according to the 2012 Revised Atlanta classification. Pancreatic pseudocysts (PP) are well circumscribed collections of fluid in the pancreas, they develop most often several weeks after an attack of acute pancreatitis. Walled-off necrosis (WON) originates from necrotizing pancreatitis; it needs four weeks to develop and contains necrotic tissue [6]. Up to 20% of the patients, suffering from acute pancreatitis, may develop PP, while it can occur up to 40% in the cases of chronic pancreatitis [7].

Both PP and WON need to be treated if they are symptomatic or there is a proven or strongly suspected infection. The appearance of

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minimal invasive techniques (percutaneous drainage (PD), endoscopic drainage (ED), minimal invasive surgery) provided a wider range of applicable methods. In some cases, the decision between these modalities is obvious, because of the location of the collection, while in other cases similar short-term outcomes can be expected from different modalities. The European Society of Gastrointestinal Endoscopy and the American Society of Gastrointestinal Endoscopy recommend ED or PD of infected WON as the first interventional method [8,9].

PD should be carried out through retroperitoneal access, with real-time imaging, where ultrasonography (US) is preferred over computed tomography (CT). ED incorporates many techniques (transpapillary or transmural endoscopic drainage usually with endoscopic ultrasound (EUS) guidance, transluminal endoscopic necrosectomy). The endoscopic intervention can be also applied as a step-up approach after percutaneous drainage [10]. The surgical approach contains traditional open necrosectomy or minimally invasive surgical necrosectomy. Hybrid interventions are also applicable in some cases [8].

The aim of this meta-analysis is to compare the three main modalities (ED vs. PD vs. surgical drainage (SD)) in the treatment of pancreatic fluid collections.

Methods

A meta-analysis was carried out using the population-intervention-control-outcomes (PICO) format. Those studies were selected where patients with PP or WON (P) were treated with surgical, percutaneous or endoscopic drainage (I and C) and at least two treatment modalities were compared. Mortality, clinical success, recurrence, complications, length of hospitalisation (LOH) were compared, as the outcomes of different treatment groups (O).

The meta-analysis was reported in accordance with the Preferred Reporting Items for Systematic Review (PRISMA) statement [11], and it was registered in advance in the PROSPERO database (registration number: CRD42018079200).

Search strategy

The electronic databases of PubMed and Embase were systematically searched for relevant studies from inception to December 2018. The search included the following keywords: (”pancreatic pseudocyst” OR “walled off necrosis”) AND (” drainage” OR “surgery” OR” percutaneous” OR” endoscopy”) AND (“drainage” OR “surgery” OR “percutaneous” OR “endoscopy”). The following filters were applied: language: English, date of publication: from 1990 to December 2018.

Inclusion and exclusion criteria

Articles were included if they provided data on at least two of the three treatment modalities on patients with either PP or WON or both reporting the outcomes mentioned above. PP and WON of common etiologies were included, articles focusing on post-surgical or traumatic fluid collections were excluded. Prospective and retrospective controlled observational studies, as well as randomized controlled trials were selected. Conference abstracts with sufficient data were also included. Non-English language studies, studies published before 1990, studies focusing on pediatric cases and studies with combined interventions were excluded.

Selection process

The publications were processed by the EndNote X7.4 software (Clarivate Analytics, Philadelphia, PA, USA). Duplications were removed, the remaining records were screened first by title, second by abstract, finally by full-text by two independent authors.

Data extraction

Numeric data were extracted into an Excel 2010 (Office 365, Microsoft, Redmond, WA, USA) sheet designed for this purpose. The investigators (LS and ÁV) extracted the number of subjects, methods of drainage, mortality, clinical success rate, recurrence, complications, postoperative and total LOH, and cost of the treatment from each publication independently, and then validated these data. Disagreements were discussed and resolved by consensus in plenum.

Statistical methods

Pairwise comparison between ED, PD and SD were carried out with the outcomes of recurrence, complications, mortality, clinical success and LOH. For binary and continuous outcomes, odds ratios (OR) and weighted mean differences (WMD) with 95% confidence intervals (CI) were calculated with the random effect model (DerSimonian and Laird estimation) and displayed on forest plots. Statistical heterogeneity was analysed using the I^2 statistic and the chi^2-test to gain probability-values; $p < 0.1$ was defined to indicate significant heterogeneity. Where mean with standard deviation was not reported for LOH, they were estimated from median, interquartiles and range by using the method of Xiang Wan (2014) [12].

Quality assessment of the studies included

The quality assessment of the articles was carried out by two authors independently (LS and ÁV), with the Newcastle-Ottawa Scale [13] for cohort and case-control studies and by using the Jadad score [14] in the cases of randomized controlled trials (RCTs).Supplemental Multimedia Component 1 and 2 presents the results of the quality assessment.

Subgroup analysis

One of our further goal was to carry out an analysis regarding only WON and PP. We also compared endoscopic intervention with minimal invasive surgery, hypothesizing that minimal invasive surgery provides better results, than open surgery.

Assessment of the grade of evidence

The GRADE system was used to assess the strength of recommendation and quality of evidence of our results. GRADE stands for Grades of Recommendation Assessment, Development, and Evaluation [15].

Results

Results of the selection process

We identified 1341 and 2863 articles in the Embase and PubMed databases, respectively. Finally, 25 relevant articles were included in the quantitative synthesis of this meta-analysis (Supplemental Figure 1).

Charasteristics of the studies included

Among the 24 articles, five records were available only in the form of conference abstracts. Two prospective observational studies, two randomized controlled trials and 20 retrospective observational studies were included in the quantitative synthesis. The characteristics of the studies, details of endoscopic

methodology, definition of clinical success and duration of follow-up are shown in Table 1, while the demographics of the patients and the details of fluid-collections are listed in Table 2.

Comparison of endoscopic drainage, percutaneous drainage and surgical drainage

Percutaneous drainage versus endoscopic drainage

Pseudocysts and walled-off necroses

Six studies compared ED and PD (including 688 and 286 patients, respectively) [16–21]. Among these, four compared the recurrence of the pseudocyst/WON [16–19], three the complications [16,18,20], two the mortality [16,17], four the clinical success [16,19–21] and two the postoperative LOH [16,20].

ED has significantly higher rate of clinical success (OR = 3.36; 95% CI 1.48, 7.63; p = 0.004, I^2 = 68.9%, p = 0.022) than PD (Fig. 1/A). Mortality (OR = 0.26; 95% CI 0.01, 4.55; p = 0.353, I^2 = 58.5%, p = 0.0121), occurrence of adverse events (OR = 1.36; 95% CI 0.52, 3.56; p = 0.531, I^2 = 18.6%, p = 0.293), recurrence (OR = 0.37; 95% CI 0.10, 1.38; p = 0.138, I^2 = 66.4%, p = 0.03) and LOH (weighted mean difference (WMD) (days) = −30.58; 95% CI -74.87, 13.71; p = 0.009, I^2 = 98%, p < 0.001) did not differ significantly between the two methods (Fig. 1/A, Supplemental Figure 2)

Pseudocysts

Five articles compared ED and PD regarding pseudocysts (in 579 and 231 patients, respectively) [17–21]. Among these, one article compared the mortality [17], three the recurrence [17–19], three the clinical success [19–21], two the complications [18,20] and one the LOH [20]. Rate of recurrence (OR = 0.23; 95% CI 0.08, 0.66; p = 0.006, I^2 = 35.1%, p = 0.214) showed a significant difference

Table 1
Description of the studies selected regarding the study-design and the number of patients. Conference abstracts are indicated with *. N/A: not applicable, NR: not relevant, Y: yes, N: no.

Study	Study design	Number of patients			Description of endoscopic methods	Endoscopic necrosectomy (Y/N)	Definition of clinical success	Follow-up
		ED	PD	SD				
Adams et al., 1992	retrospective	–	52	42	N/A	N/A	N/A	N/A
Akshintala et al 2014	retrospective	41	40	–	conventional transmural drainage [12] or EUS-assisted transmural drainage [29]	N	Reduction in size to 50% of initial size and resolution of symptoms	Endoscopic drainage: 909 days Percutaneous drainage: 671 days
Barthet et al 1993	retrospective	54	39	29	pancreatic sphincterotomy and dilatation of the pancreatic strictures	N	N/A	N/A
Bopanna et al 2017*	RCT	30	–	30	with or without EUS drainage, necrosectomy	Y	Complete resolution of the cyst	22 months
Heider et al 1999	retrospective	–	66	66	N/A	N/A	Rediographic resolution or resolution of the symptoms	N/A
Johnson et al 2009	retrospective	24	7	30	transmural drainage with or without transpapillary drainage	N	Complete resolution of the fluid collection	Endoscopy: 10 months Surgery: 15 months
Keane et al 2015	retrospective	109	55	–	EUS-guided transmural drainage, double pigtail stents	N	Complete resolution, or decrease in size to <2 cm	Endoscopy: 11 months (median) Percutaneous drainage: 17 months (median)
Khreiss et al 2015	retrospective	20	–	20	cystogastrostomy, double pigtail or SEMS	N	Lack of need for re-intervention	Endoscopy: 16 months Surgery: 6 months
Kumar et al 2014	prospective	12	12	–	not defined	Y	Resolution of symptoms	Endoscopy: 1.9 year Surgery 2.8 year
Melman et al 2008	retrospective	45	–	38	cystogastrostomy, double-pigtail stents	N	Symptom or cyst resolution	NR
Morton et al 2005	retrospective	–	8121	6409	N/A	N/A	N/A	N/A
Naoum et al 2003	retrospective	–	3	9	N/A	N/A	N/A	N/A
Nealon et al 2002	retrospective	–	50	148	N/A	N/A	N/A	N/A
Nq et al 1998	retrospective	–	17	13	N/A	N/A	Pseudocyst resolution	N/A
Pan et al 2015	retrospective	410	13	377	transmural drainage	N	Pseudocyst resolution	N/A
Rana et al 2015	retrospective	26	–	25	EUS-guided transmural drainage	Y	Pseudocyst resolution, and asymptomatic patient	Endoscopy: 22.3 months Surgery: 31 months
Redwan et al 2017	prospective	35	–	36	transmural or transpapillary drainage	N	Clinical or radiological resolution	At least 6 months
Saluja et al 2016*	retrospective	35	–	20	cystogastrostomy	N	N/A	N/A
Saul et al 2015	retrospective	21	–	43	EUS-guided drainage, double pigtail stents	N	Complete resolution or decrease of the size of the cyst to 2 cm or smaller	Endoscopy: 270 days (median) Surgery: 580 days (median)
Siddiqui et al 2017*	retrospective	42	–	39	EUS-guided cystogastrostomy	N	Absence of failure	N/A
Spofford et al 2011*	retrospective	12	–	15	not reported	Y	Resolution of symptoms	Endoscopy: 13.4 months Surgery: 38.5 months
Tan et al 2018*	retrospective	48	135	164	not reported	not reported	Pseudocyst resolution	At least 3 months
Varadarajulu et al 2013	RCT	20	–	20	cystogastrostomy	N	Clinical resolution of symptoms and radiological resolution	24 months
Varadarajulu et al 2008	retrospective	20	–	10	EUS-guided cystogastrostomy	N	Clinical resolution of symptoms and radiological resolution	At least 3 months
∑		**1004**	**8610**	**7583**				

Table 2
Description of the demographic characteristics of the patients and the fluid-collections. (ED: endoscopic drainage, PD: percutaneous drainage, SD: surgical drainage, M/F: male-female, L: laparoscopic subgroup, O: open surgery subgroup, H:head, B:body, T:tail, P: peripancreatic, E: entire gland, U: uncinate, EP: extrapancreatic, M: multiple, NR: not reported).

Study	Sex (M/F ratio)			Age (mean; years)			Size of the cyst (mean; cm)			Location of the cyst			Number of patients with WON		
	ED	PD	SD	ED	PD	SD	ED	PD	SD	ED	PD	SD	ED	PD	SD
Adams et al., 1992	–	44/8	29/13	–	43.2	45.5	–	NR	NR	–	H: 13 B:29 T:10	H:12 B:23 T:7	–	0	0
Akshintala et al 2014	28/13	26/14	–	47.1	52.7	–	9.5	9.4	–	H: 9 B: 14 T: 20 P: 14	H: 15 B: 15 T: 12 P: 19	–	0	0	–
Barthet et al 1993	125/18 (all pt)			NR	NR	NR	NR	NR	NR	H: 115 B: 33 T: 21 EP: 1			0	0	0
Heider et al 1999	–	41/25	45/21	41 (all pt)			–	8.2	7.4	–	NR	NR	–	0	0
Johnson et al 2009	NR	NR	NR	52	NR	49	9.5	NR	9.1	NR	NR	NR	0	0	0
Keane et al 2015	60/49	37/18	–	NR	NR	–	NR	NR	–	H: 41 B-T: 68	–	H: 20 B-T: 35	38	30	–
Khreiss et al 2015	9/11	–	16/4	NR	–	NR	11.2	–	15.2	H: 5 B: 11 T: 5 E: 2		H: 3 B: 15 T: 10 E: 4	20	–	20
Kumar et al 2014	8/4	9/3	–	58.9	53.3	–	1306 mL	1354 mL	–	NR	NR	–	12	12	–
Melman et al 2008	1.4	–	NR	51.8	–	NR	9.1	–	NR	NR	–	NR	0	–	0
Morton et al 2005	–	58%	59%	–	53	51	–	NR	NR	–	NR	NR	–	0	0
Naoum et al 2003	–	2/1	3/6	–	65	69	–	15	10	–	B: 1 T: 2	H: 2 B: 4 T: 3	–	0	0
Nealon et al 2002	187/66 (all patients)			46 (all patients)			–	NR	NR	–	NR	NR	–	0	0
Nq et al 1998	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0	0	0
Pan et al 2015	210/200	NR	197/180	57	NR	58	7.8	NR	6.7	H: 94 B: 176 T: 138 U: 2	NR	H: 76 B: 160 T: 97 U: 44	0	0	0
Rana et al 2015	21/5	–	20/5	35.4 (all patients)			10.8 (all patients)			NR	NR	NR	26	–	25
Redwan et al 2017	1.3/1	–	L: 1/1 O: 1.5/1	49.2	–	L: 51.8 O: 48.8	10.3	–	L: 10.1 O: 9.9	NR	–	NR	0	–	0
Saluja et al 2016 (abstract)	NR	NR	NR	NR	NR	NR	11	NR	14.2	NR	NR	NR	NR	NR	NR
Saul et al 2015	13/21	NR	29/43	44.4	NR	40	6.7	NR	10	H: 21 B: 43 T: 31			0	0	0
Siddiqui et al 2017 (abstract)	NR	–	NR	NR	–	NR	NR	–	NR	NR	NR	NR	42	–	39
Spofford et al 2011 (abstract)	5/7	–	11/4	50	–	52	NR	–	NR	B: 6 H–B: 1 T: 1 B-T: 1 E: 2 EP: 1		H: 1 B: 2 B-T: 1 E: 5 EP: 6	12	–	15
Tan et al 2018 (abstract)	193/154			46.85			NR			H: 129 B/T: 218			0	0	0
Varadarajulu et al 2013	12/8	–	16/4	48	–	51	NR	–	NR	NR	–	NR	0	–	0
Varadarajulu et al 2008	6/4	–	15/5	43.1	–	42.3	8.9	–	9.8	H: 2 B:1 T: 4 M: 3		H: 2 B: 3 T: 10 M: 5	0	–	0

which favored ED. Clinical success (OR = 2.84; 95% CI 0.90, 8.98; p = 0.076, I^2 = 74.8%, p = 0.019) and complications (OR = 0.87; 95% CI 0.31, 2.43; p = 0.787, I^2 = 0.0%, p = 0.737) did not differ significantly between the two interventional methods (Fig. 1/B).

Surgical versus endoscopic intervention

Pseudocysts and walled-of necroses

Fourteen articles compared ED and SD (including 842 and 896 patients, respectively) [17–19,21–32]. Among these articles, six reported data about mortality [17,21–25], thirteen about clinical

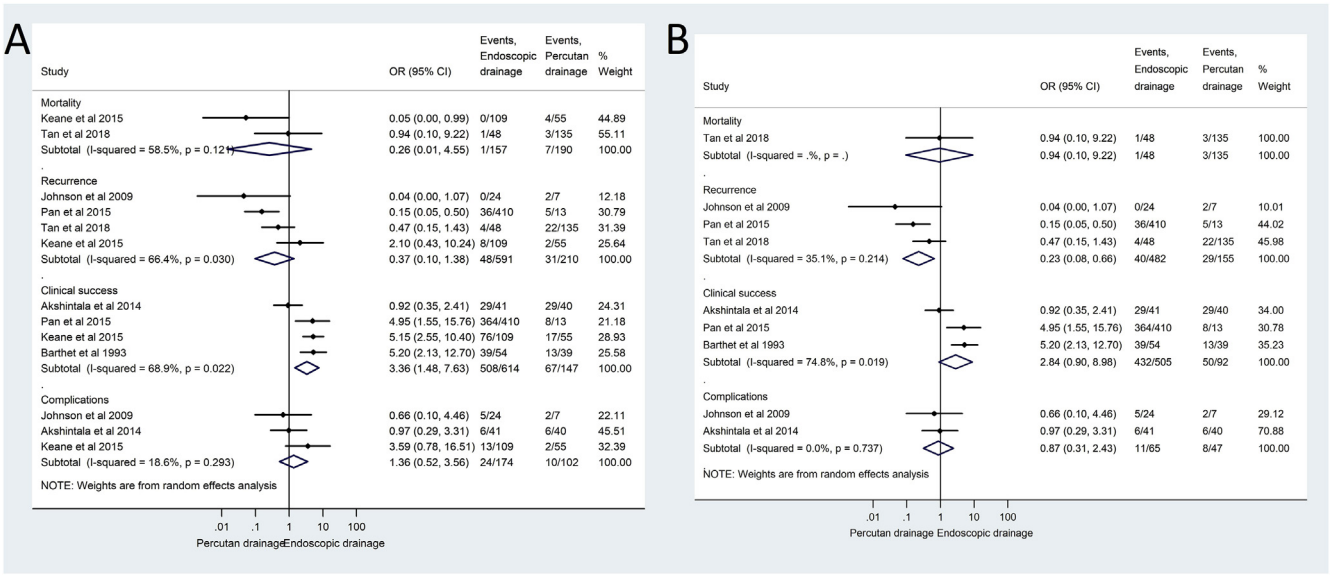

Fig. 1. A: Comparison of percutaneous and endoscopic drainage including both type of fluid collections, B: Comparison of the endoscopic and percutaneous drainage including only pseudocysts regarding mortality, recurrence, clinical success and complications.

success [18,19,21–25,27–32], ten about recurrence [17–19,21,22,24,26–29], ten about adverse events [18,22–25,27,28,30–32], five about postoperative [22,23,30–32], two about total LOH [23,27], and three about cost [22,23,27].

Significant difference was found in postoperative LOH (WMD (days) = −4.61; 95%CI -7.89, −1.33; p = 0.006, I^2 = 93.5%, p < 0.001) and at the total LOH (WMD (days) = −3.67; 95%CI -5.00, −2.34; p < 0.001, I^2 = 75.2%, p = 0.045), which favored endoscopic intervention (Fig. 2/A).

Clinical success of ED was lower than SD (OR = 0.59; 95% CI 0.37, 0.93; p = 0.022, I^2 = 19.2%, p = 0.250), but mortality (OR = 0.86; 95% CI 0.15, 5.06; p = 0.870, I^2 = 0.0%, p = 0.378), recurrence (OR = 1.79; 95% CI 0.93, 3.35; p = 0.068, I^2 = 27.2%, p = 0.211), complication rate (OR = 0.75; 95% CI 0.45, 1.25; p = 0.264, I^2 = 3.4%, p = 0.406), and cost (WMD (USD) = −3683.54; 95%CI -7723.38, −356.30; p = 0.074, I^2 = 98.7%, p < 0.001) were similar concerning the two methods (Supplemental Figure 3-4).

Pseudocysts

Eleven articles compared endoscopic drainage with surgery (including 739 and 797 patients respectively) including only pseudocysts [17–19,21,22,24,27,29–32]. Among them four studies compared mortality [17,21,22,24], eight recurrence [17–19,21,22,24,27,29], ten clinical success [18,19,21,22,24,27,29–32], seven complications [18,22,24,27,30–32], four the postoperative LOH [22,30–32]. Significant difference could be stated regarding clinical success (OR = 0.54; 95% CI) 0.35, 0.85; p = 0.007, I^2 = 13.1%, p = 0.322) and recurrence (OR = 1.80; 95% CI 1.16, 2.79; p = 0.009, I^2 = 0.0%, p = 0.456), both favored SD. Mortality (OR = 0.86; 95% CI 0.15, 5.06; p = 0.870, I^2 = 0.0%, p = 0.378), complications (OR = 0.82; 95% CI 0.44, 1.51; p = 0.523, I^2 = 10.6%, p = 0.248) and LOH (WMD (days) = −5.07; 95%CI -11.26, −1.12; p = 0.109, I^2 = 94.2%, p < 0.001) did not differ significantly (Fig. 2/B, Supplemental Figure 5).

Walled-off necroses

Four articles compared endoscopic drainage with surgery (including 100 and 99 patients respectively) regarding only walled-off necroses [23,25,26,28]. Among these, two compared mortality [23,25], two recurrence [26,28], three clinical success [23,25,28], three complications [23,25,28]. There was no significant difference between the two interventional methods regarding mortality (death did not occur in the two interventional methods), clinical success (OR = 1.01; 95%CI 0.23, 4.43; p = 0.990, I^2 = 40.1%, p = 0.188), recurrence (OR = 0.8; 95%CI 0.03, 18.72; p = 0.889, I^2 = 75.0%, p = 0.046), complications (OR = 0.56; 95%CI 0.19, 1.71; p = 0.311, I^2 = 14.6%, p = 0.310) (Supplemental Figure 6). There were not enough articles comparing the LOH and cost.

Minimal invasive surgery versus endoscopic drainage including both pseudocysts and walled-off necroses

Five articles compared the endoscopic drainage with minimal invasive surgery (including 172 and 103 patients respectively) [23,24,28,29,31]. Two articles compared the mortality [23,24], three the recurrence [24,28,29], five the clinical success [23,24,28,29,31], four the complications [23,24,28,31]. There was no difference between minimal invasive surgical or endoscopic drainage regarding mortality (no death occurred), clinical success (OR = 0.53; 95%CI 0.19, 1.49; p = 0.232, I^2 = 37.3%, p = 0.172), recurrence (OR = 2.7; 95%CI 0.44, 16.54; p = 0.281, I^2 = 0.00%, p = 0.559) or complications (OR = 0.68; 95%CI 0.28, 1.16; p = 0.377, I^2 = 0.00%, p = 0.831) (Supplemental Figure 7).

Minimal invasive surgery versus endoscopic drainage including only pseudocysts

Three articles compared endoscopic drainage with minimal invasive surgery including only patients with pseudocysts (110 and 44 patients respectively) [24,29,31]. Among these, one article was concerned mortality [24], two with recurrence [24,29], three with clinical success [24,29,31] and two with complications [24,31].

There was no significant difference regarding mortality, clinical success (OR = 0.48; 95%CI 0.11, 2.13; p = 0.332, I^2 = 53.8%, p = 0.115), recurrence (OR = 1.29; 95%CI 0.06, 28.09; p = 0.873) and complications (OR = 0.47; 95%CI 0.14, 1.61; p = 0.230, I^2 = 0.00%, p = 0.648) (Supplemental Figure 8).

Minimal invasive surgery versus endoscopic drainage including only walled-off necroses

Two articles compared endoscopic intervention with minimal invasive surgery including only patients with walled-off necroses

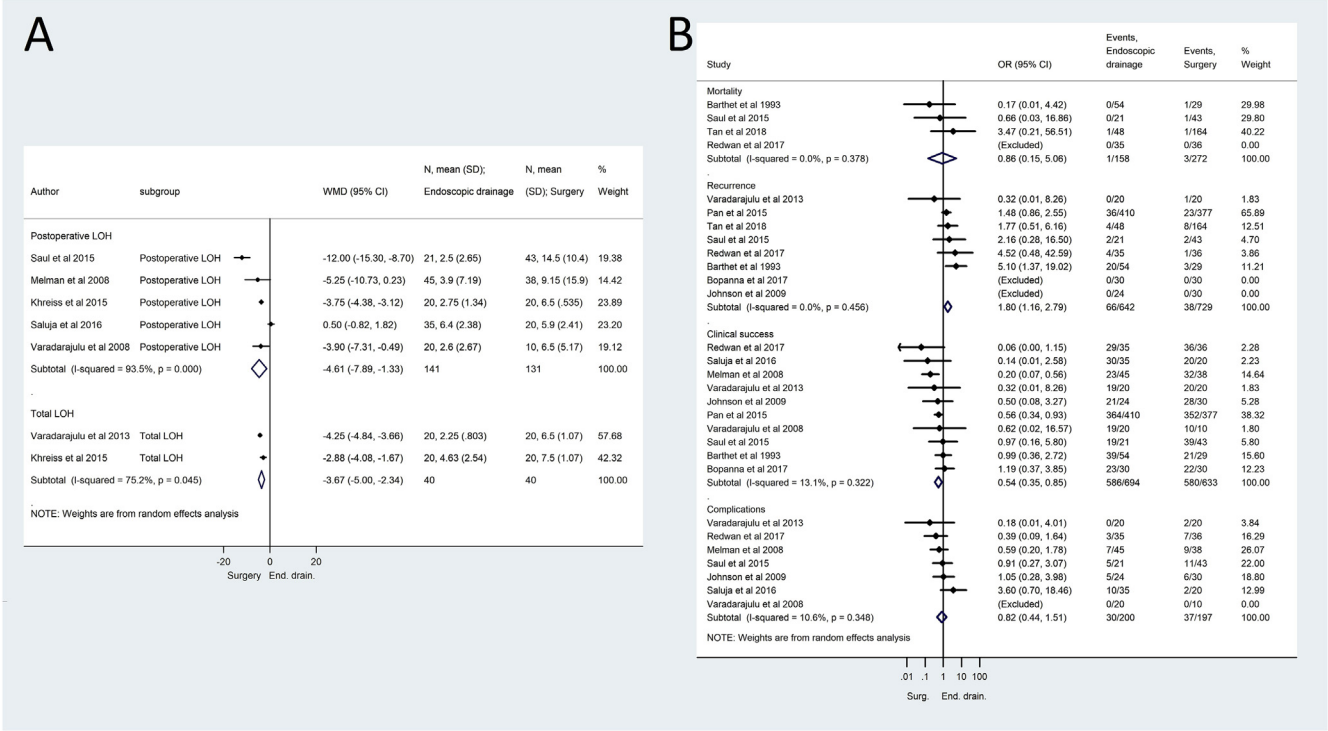

Fig. 2. A: Comparison of the endoscopic and surgical drainage regarding length of hospitalisation including both type of fluid collections, B: Comparison of the endoscopic and surgical drainage including only pseudocysts regarding mortality, recurrence, clinical success and complications.

(62 and 59 patients, respectively) [23,28]. Among these one was concerned with mortality [23], one with recurrence [28], two with clinical success [23,28], two with complications [23,28]. There was no significant difference regarding mortality (no death occurred), recurrence (OR = 4.00; 95%CI 0.43, 37.46; p = 0.225), clinical success (OR = 0.6.; 95%CI 0.08, 4.72; p = 0.625, $I^2 = 50.8\%$, p = 0.154) and complications (OR = 0.97; 95%CI 0.28, 3.31; p = 0.963, $I^2 = 0.00\%$, p = 0.952) (Supplemental Figure 9).

Surgical versus percutaneous drainage including both pseudocysts and walled-off necroses

Eleven articles compared the outcomes of PD and SD (including 8530 and 7300 patients, respectively) [17–19,21,33–39], among them seven reported data on mortality [33–38], six on clinical success [19,21,35–37,39], six on recurrence [17–19,35,36,38], five on adverse events [18,33,37–39] and two LOH [34,36].

Recurrence rate (OR = 4.91; 95% CI 1.82, 13.22; p = 0.002, $I^2 = 66.5\%$, p = 0.011), and clinical success rate (OR = 0.13; 95% CI 0.07, 0.22, p < 0.001, $I^2 = 0.0\%$, p = 0.774) was significantly better in SD compared to PD (Fig. 3). Mortality (OR = 2.23; 95%CI 0.81, 6.15 p = 0.120, $I^2 = 31.2\%$, p = 0.213), complications rate (OR = 1.27 95% CI 0.28, 5.82; p = 0.759, $I^2 = 79.8\%$, p = 0.001) and LOH (WMD (days) = 16.49 95% CI -4.09, 37.07; p = 0.074, I2 = 98.7, p < 0.001) did not differ in the two modalities (Fig. 3, Supplemental Figure 10).

The results are summarized in Table 3.

Discussion

Percutaneous drainage provided inferior outcomes compared to endoscopic intervention in our analysis. Clinical success was significantly higher in the ED group. Comparing pseudocysts only, significantly fewer recurrence occurred after ED. There were not enough articles comparing walled-off necroses only.

Surgery provides higher clinical success and lower recurrence rate than PD. Percutaneous fistulas were responsible for majority of the complications of the percutaneous treatment.

Finally, the shorter LOH makes endoscopic interventions favorable over surgery. Although SD had higher success rate and lower recurrence rate than ED in cases of pseudocysts, although there was a significant heterogeneity in both outcomes. The two modalities seem to be equally efficient regarding other outcomes. Cost of intervention also did not differ significantly between the two methods, although independently both Varadarajulu et al in 2013 [27] and Saul et al in 2015 [22] reported, that endoscopic intervention is more cost effective. Khreiss et al in 2015 [23] reported equal amount of cost. The study of Varadarajulu et al. from 2008 [32] could not be included in our analysis, as it did not report standard deviation, but it also reported lower cost of the endoscopic intervention. Including walled-off necroses only, significant difference could not be found between surgery and endoscopy. Significant difference could neither be found comparing minimal invasive surgery with endoscopic drainage.

Two important RCT comparing surgical and endoscopic treatment of WON was not included in our analysis, because 40–80% of patients in the PENGUIN trial [40] and all patients randomized to the surgical group in the TENSION trial [41] had PD procedures as the first step in their treatment. Furthermore, these trials recruited critically ill patient with proven or highly suspected infected necrosis, which best treated probably by the step-up approach [41].

A meta-analysis comparing endoscopic drainage and surgery was carried out earlier, which included four randomized controlled trials [42]. Three of the included articles compared different endoscopic methods, therefore, we could not include in our analysis [43–45]. It also found, that endoscopic intervention was associated with shorter LOH, which was also shown by our analysis.

Another meta-analysis comparing endoscopic drainage with percutaneous drainage was also carried out [10], which concluded,

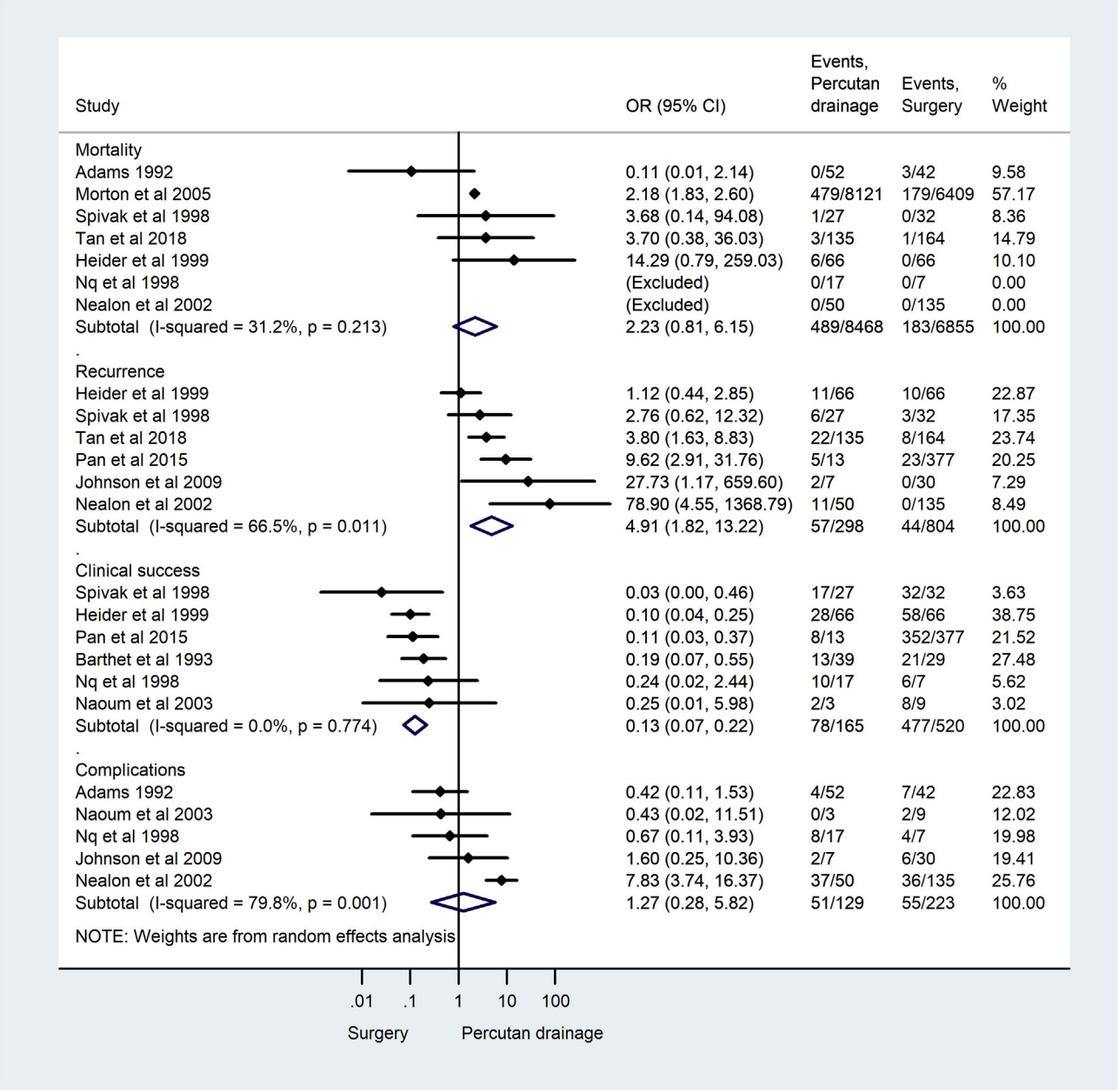

Fig. 3. Comparison of the surgical and percutaneous drainage including both type of fluid collections regarding mortality, recurrence, clinical success and complications.

Table 3
Summary of the results of the statistical analysis. NS = no significant difference. Comparison between ED and PD including only WON, and the comparison between PD and SD including only PC and only WON were not possible due to lack of studies.

		All fluid collection	only PC	only WON
ED versus PD	Recurrence	*NS*	**ED is better**	–
	Clinical success	**ED is better**	*NS*	
	NS in Mortality, Complications, Length of hospitalisation			
ED versus SD	Clinical success	**SD is better**	**SD is better**	*NS*
	Recurrence	*NS*	**SD is better**	*NS*
	Length of hospitalisation	**ED is better**	*NS*	*NS*
	NS in Mortality, Complications			
ED versus minimal invasive SD	*NS in Mortality, Recurrence, Clinical success, Complications and Length of hospitalisation*			
PD versus SD	Recurrence	**SD is better**	–	–
	Clinical success	**SD is better**		
	NS in Mortality, Complications and Length of hospitalisation			

that endoscopic intervention is favorable concerning clinical success, adverse events, and LOH. This meta-analysis included three additional articles, which were dealing with fluid collections after pancreatic surgery, therefore, we did not include them in our analysis [46–48].

A systematic review was also carried out comparing ED with minimal invasive, laparoscopic intervention [49]. According to this review, laparoscopic intervention is associated with higher clinical success and less adverse events compared to endoscopic drainage, although the authors emphasize that the heterogeneity is significant.

Another systematic review was carried out including non-comperative articles [50]. This review also concluded that endoscopic drainage is preferable over percutaneous drainage, although in certain group of patients one method might be more feasible over the others. The analysis also highlights, that direct comparison cannot be carried out sometimes due to the significant heterogeneities of the articles, which is also supported by our analysis.

Considering and summarizing our results and also incorporating the current scientific view of the treatment of pancreatic fluid collections, we propose a protocol for the treatment of pancreatic fluid collections (Fig. 4). The proper intervention for symptomatic pancreatic fluid collections can be chosen according to the location-based approach. If the location of the fluid collection allows different interventional modalities, the step-up approach can be applied. The endoscopic drainage seems to be the most effective and less invasive procedure in this treatment algorithm.

Limitations

The overall quality of evidence (GRADE) is very low (Supplemental, Multimedia Component 3). The heterogeneity is considerable in some of the outcomes. Our analysis included only 2 randomized clinical trials. Most of the studies had few numbers of patients. There was a difference between the number of patients comparing endoscopic and percutaneous drainage. Furthermore, we did not perform a subgroup analysis concerning the different types of endoscopic drainage. The six abstracts, which provided enough data to the analysis also carries a high risk of bias. Significant heterogeneity was found at multiple outcomes, which lowers the grade of evidence. The definition of clinical success differed between studies, but 13 out of the 24 studies defined it as radiological resolution. Six studies did not define clinical success. The length of follow-up period after intervention also varied, the shortest follow up was 3 month (in 2 studies), the longest follow up period was 38 months, while it was not specified in 11 studies. We included only English language studies.

Conclusion

The treatment of inflammatory pancreatic fluid collections is strongly influenced by local expertise and radiological findings, such as location and size of the collection. Surgery, percutaneous drainage and endoscopic intervention are all accepted treatment modalities and each method has a specific group of patients, where

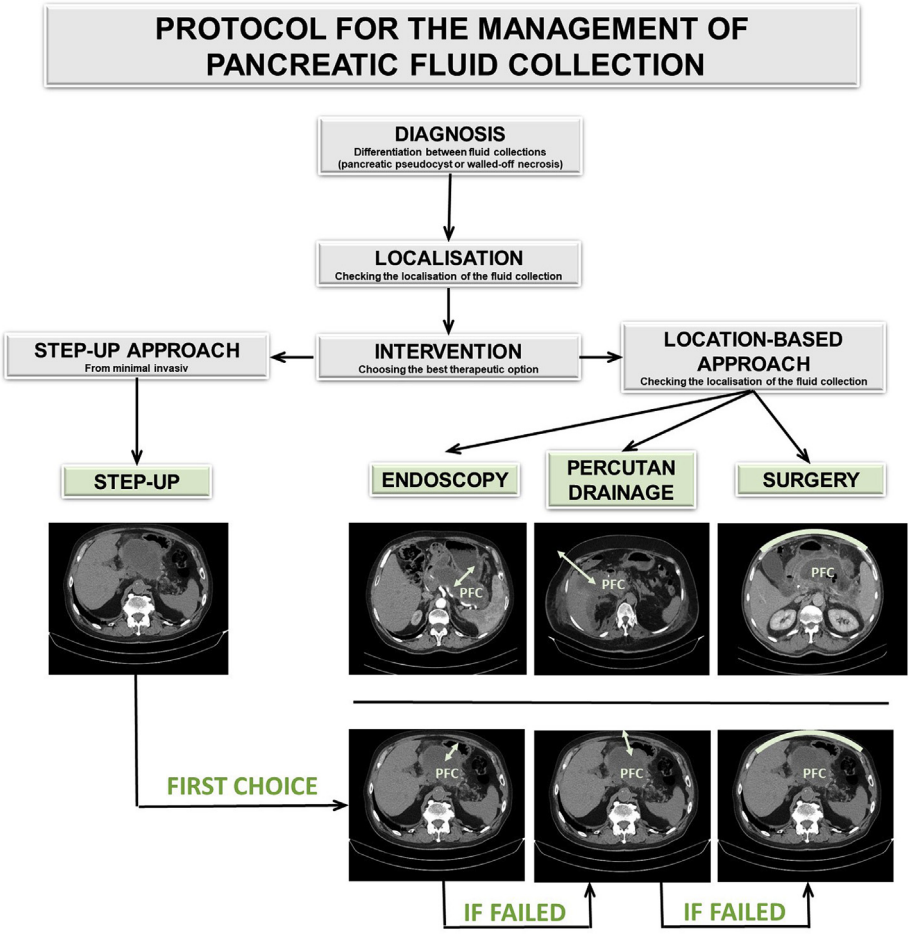

Fig. 4. Suggested protocol for the treatment of pancreatic fluid collections. (PFC = pancreatic fluid collection, white arrows indicate the suggested site of intervention).

it is more favorable over the other types of interventions.

According to our meta-analysis, endoscopic intervention and surgery seems to be equally efficient, although endoscopic modalities provide shorter LOH. Percutaneous drainage is less favorable than the other two modalities. This outcomes are also supported by a previous meta-analysis [10] and a systematic review [50]. To eliminate the significant heterogeneity and to provide a higher level of evidence, an objective reporting system and further prospective randomized multicenter studies are needed.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pan.2019.10.006.

Potential competing interests

None declared.

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