



Passive Versus Active Intra-Abdominal Drainage Following Pancreatic Resection: Does A Superior Drainage System Exist? A Systematic Review and Meta-Analysis

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Abstract Postoperative pancreatic fistula (POPF) is a major source of morbidity following pancreatic resection. Surgically placed drains under suction or gravity are routinely used to help mitigate the complications associated with POPF. Controversy exists as to whether one of these drain management strategies is superior. The objective was to identify and compare the incidence of POPF, adverse events, and resource utilization associated with passive gravity (PG) versus active suction (AS) drainage following pancreatic resection. MEDLINE, EMBASE, CINAHL, and Cochrane Library databases were searched from inception to May 18, 2020. Outcomes of interest included POPF, post-pancreatectomy hemorrhage (PPH), surgical site infection (SSI), other major morbidity, and resource utilization. Descriptive qualitative and pooled quantitative meta-analyses were performed. One randomized control trial and five cohort studies involving 10 663 patients were included. Meta-analysis found no difference in the odds of developing POPF between AS and PG ($p = 0.78$). There were no differences in other endpoints including PPH ($p = 0.58$), SSI (wound $p = 0.21$, organ space $p = 0.05$), major morbidity ($p = 0.71$), or resource utilization ($p = 0.72$). The risk of POPF or other adverse outcomes is not impacted by drain management following pancreatic resection. Based on current evidence, a suggestion cannot be made to support the use of one drain over another at this time. There is a trend toward increased intra-abdominal wound infections with AS drains ($p = 0.05$) that merits further investigation.

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Introduction

Pancreatic resection is commonly performed for diseases of the pancreas, duodenum, and distal bile duct [1, 2]. Despite advancements in surgical and perioperative management, morbidity following pancreatic surgery remains high, approaching 50% [2, 3]. The most common cause of major morbidity is the development of a postoperative pancreatic fistula (POPF), with reported incidence between 10 and 35% [3–5]. The resulting leakage of pancreatic effluent can lead to a cascade of complications including surgical site infections (SSI), hemorrhage, end organ failure, death and in the case of oncologic indications, a delay to adjuvant therapy [6–10].

The 2016 classification system for POPF by the International Study Group for Pancreatic Fistula (ISGPF) defines biochemical leak (Grade A) and clinically relevant POPF (Grade B,C). [4, 5] Patients developing POPF are

more likely to undergo additional procedures, have increased length of stay (LOS) and increased likelihood of hospital re-admissions [1, 5]. Furthermore, the healthcare costs of POPF are an estimated 1.5– 2.0 times that of patients without POPF [11–13]. Reducing the development and mitigating the severity of POPF are necessary given the associated clinical and economic burden.

Several strategies have been investigated to decrease POPF risk; however, incidence has remained relatively stable [5–7]. The effect of different intra-abdominal drainage systems on the development of POPF has yet to be robustly investigated. Intra-abdominal drains are commonly placed close to the pancreaticojejunal anastomosis following pancreaticoduodenectomy (PD) and the pancreatic transection line following distal pancreatectomy (DP). These drains can be managed with active suction (AS) or passive gravity (PG). The former is attached to a reservoir generating negative pressure while the latter is attached to a reservoir that acts as a vessel for effluent to flow by gravity. It has been postulated that an AS system promotes improved drainage and collapse of the surgical dead space, thereby potentially decreasing the severity of POPF, were it to occur [8, 14]. However, AS systems generate pressure measured at -150 mm Hg when the bulb is fully decompressed and up to -200 mm Hg when the drain is stripped [8, 14]. As such, it is also theorized that this pressure gradient could promote the development of a POPF. [8, 14] At this time, the utilization of one system over another largely depends on surgical dogma or institutional practice.

Considering both AS and PG are cost-effective, simple interventions, one would rapidly become standard of care over the other, should a true difference exist. Therefore, the objective of this systematic review and meta-analysis was to synthesize existing evidence comparing PG and AS drainage systems in patients undergoing pancreatic resection.

Materials and methods

This review was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) and Assessing the Methodological Quality of Systematic Reviews (AMSTAR) Guidelines (Appendix A) [15]. It was prospectively registered on Prospero on February 26, 2019, (CRD42019123647) and the protocol was published in BMJ Open [16].

Literature search strategy

A reference librarian (AD) developed database-specific search strategies (Appendix B). These were used to

conduct a systematic literature search of the following databases, from inception to May 18, 2020: MEDLINE (PubMed, PubMed in Process and Ovid), EMBASE, CINAHL, and Cochrane Central Registry of Controlled Trials. A manual search of references in primary studies, relevant reviews, and conference proceedings was conducted. Cited references were also searched using Web of Science.

Identified articles were exported to a citation manager (Covidence Systematic Review Software, Veritas Health Innovation, Melbourne, Australia [17]). Title and abstract screening were conducted independently and in duplicate. Three independent reviewers (LP, LB, HS) subsequently undertook a full-text review of eligible articles. Disagreements were resolved by consensus.

Eligibility criteria

Published studies comparing the incidence of postoperative adverse events in adult patients who had a drain placed to PG or AS at the time of an elective pancreatic resection were considered for inclusion. Pancreatic resections included patients undergoing PD, DP, central pancreatectomy, and pancreatic enucleation. A PG drainage system was defined as a drain that maintains a pathway for fluid to flow from the surgical site by gravity, connected to a reservoir maintained at atmospheric pressure. An AS surgical drainage system was defined as a drain connected to a collapsible reservoir, which generates a negative pressure relative to atmospheric pressure. Studies were excluded if they included patients who underwent pancreatic necrosectomy or total pancreatectomy. Studies involving external pancreatic stents, drains managed with continuous irrigation or open drains not connected to a reservoir were also excluded.

Outcomes of interest

The primary outcome of interest was development of POPF (Grade B and C), as defined by the 2016 ISGPF criteria [4, 5].

Secondary outcomes included incidence of biochemical pancreatic leak, postoperative adverse events, resource utilization, and quality of life (QOL). Postoperative adverse events of interest included overall and major morbidity (as defined by the Clavien–Dindo Grade 3 and above)[18], SSI (wound or intra-abdominal infections), delayed gastric emptying (DGE), postoperative pancreatitis, post-pancreatectomy hemorrhage (PPH), percutaneous drain insertion, re-operation, and death. Resource utilization was to be assessed by comparing: LOS, re-intervention, and re-admission to hospital. Surrogate QOL

measures were to be assessed by the number of days a drain was in situ and the presence of a drain at discharge.

Data extraction

Data extraction for included studies were conducted independently, in triplicate, by three reviewers (LP, LB, HS) using a standardized electronic data extraction form. Disagreements were resolved by the senior author (KB). The following data were extracted from each study: study identifiers, study design characteristics, patient characteristics (inclusion/exclusion criteria, baseline demographics, underlying pathology, fistula risk score (FRS) [19, 20]), intervention details, and primary and secondary outcomes of the present review, as previously described.

Study authors were contacted for missing information. In the event studies referring to the same patient population were identified, only the most comprehensive or recent study was included.

Risk of bias/quality assessment

The Cochrane Collaboration's tool for assessing risk of bias in randomized controlled trials (RCT) was used to assess randomized interventional trials. The Methodological Index for Non-Randomized Studies (MINORS) tool was used for non-randomized interventional studies. [21, 22]. A MINORS score ≥ 17 was considered high quality [22, 23]. Additionally the Risk of Bias in Non-Randomized Studies of Interventions tool (ROBINS-I) was used to supplement the evaluation of non-randomized studies. [24–29]

Data synthesis

Meta-analysis, where appropriate, was conducted using the RevMan 5.3 software (Copenhagen: The Nordic Cochrane Centre, 2014).

Using the Mantel–Haenszel method, odds ratio (OR) values were calculated for dichotomous variables. Inverse-variance weighting was used to calculate difference in means for continuous variables. All values were reported with 95% confidence intervals (CI), where possible, adjusted OR values were used. If the data were reported as a median and range, authors were contacted for mean and standard deviation (SD) values. If unsuccessful, an established method was used to translate the values into their mean and SD estimates [30]. Due to anticipated heterogeneity between studies, a random effects model was employed.

Clinical and methodological heterogeneity between studies was assessed by the I^2 statistic. The threshold for interpretation was defined in accordance with the Cochrane

Handbook for Systematic Reviews of Interventions [31]. When significant heterogeneity was identified, sensitivity analysis was performed to explore potential sources. Given that the complication profile of PD and DP are unique, all endpoints, besides POPF, were analyzed separately for PD and DP.

Results

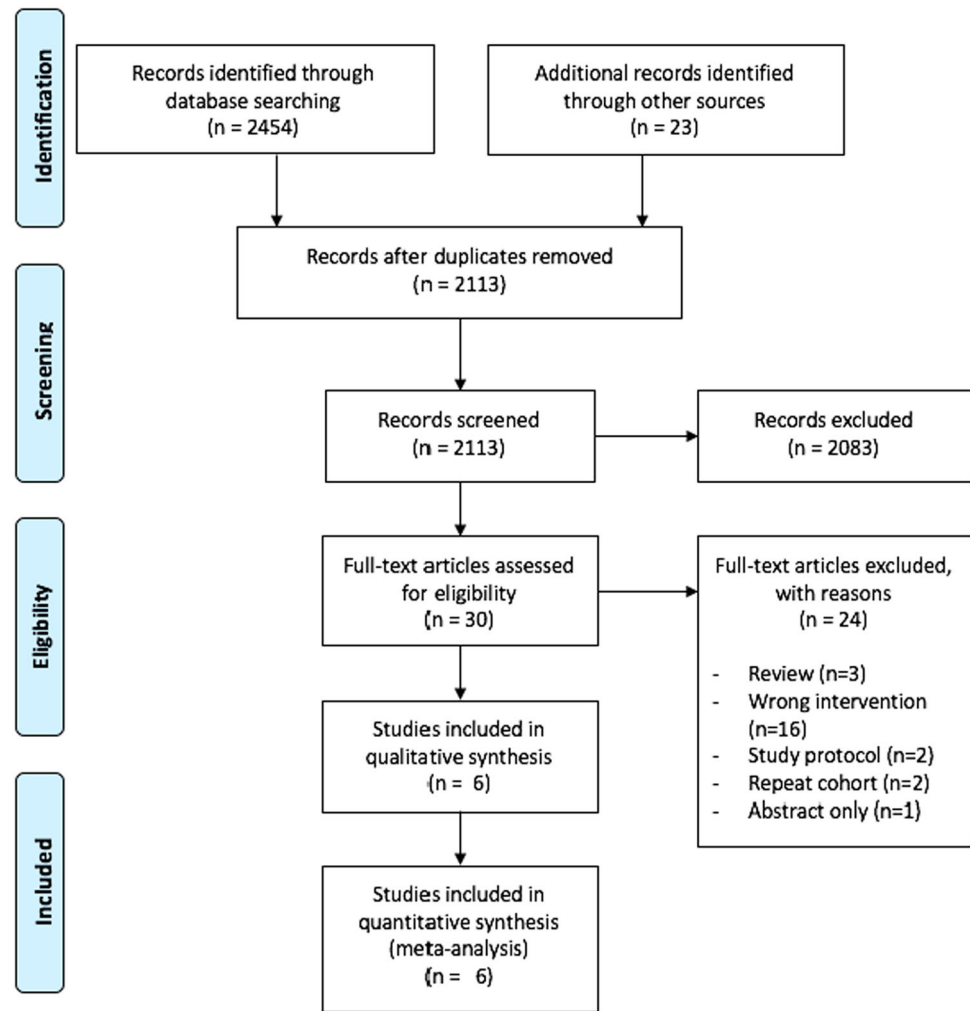
Literature search and study characteristics

The search strategy identified 2454 references (Fig. 1). After the duplicate references were removed, 2113 studies remained. Thirty articles were advanced to full-text review, of which 6 satisfied the eligibility criteria.

Table 1 outlines the characteristics of the included studies. One RCT [32] and five cohort studies (two prospective [25, 26], three retrospective [27–29]) were included in the review. One study utilized the 2016 American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) pancreas-specific procedure target participant use data file (PUF) [29]. Altogether, the selected studies included 10 663 patients. All studies were published in English between 2006 and 2020. Two studies included patients undergoing PD [27, 28], 1 study included patients who underwent laparoscopic DP [25], and the 3 remaining studies [26, 29, 32] included patients who underwent either DP or PD. Of note, the RCT by Cecka et al. [32] included patients undergoing both DP and PD, but the majority of outcomes were reported exclusively for the PD cohort. The authors were contacted for data pertaining to the DP cohort; however, additional data were only obtained for the outcome of POPF. Table 2 outlines variations in postoperative drain management strategies as well as the types of bulbs and drains that were used across institutions.

Risk of bias assessment

Table 3 outlines the risk of bias assessment for the included studies. One cohort study was determined to be low quality with a total MINORS score < 17 . [27] The remaining observational studies were considered high quality according to the MINORS criteria [22]. The ROBINS-I tool was applied, and all five non-randomized studies were considered to be of moderate risk of bias, which is interpreted to be sound for a non-randomized study, but not comparable to a rigorous randomized trial (Supplementary table 1). [24–26] For the single included RCT, high risk of bias was suspected in blinding and baseline imbalance [32]. Other factors, as outlined by the Cochrane risk of bias tool, were found to be at a low risk of bias [21].

Fig. 1 Study selection flowchart

Postoperative Pancreatic Fistula (POPF) development

All six studies reported on the incidence of POPF. While five of the studies followed the 2016 ISGPF definition of POPF [5], the study by Schmidt et al. included patient cohorts from 1980 to 2002, during which, different POPF definitions were used [27].

Aumont et al.[28] reported an association between AS and increased incidence of biochemical pancreatic leaks (21.5% vs. 8.3%, $p = 0.03$) [30], whereas Dokmak et al.[25] demonstrated an association between AS and decreased grade B POPF incidence (3% vs. 37%, $p < 0.001$). These findings were not replicated by the other studies, which did not find relations between drainage system and POPF.

Pooled analysis ($n = 5$ studies) demonstrated no difference in POPF between the AS and PG drainage groups (Fig. 2a). A sensitivity analysis was undertaken whereby the removal of the Dokmak et al.[25] study considerably

reduced heterogeneity without meaningful impacts on the effect size (OR 1.14 [0.79, 1.64], $p = 0.49$, $i^2 = 53\%$). This is likely explained by their unique population profile of solely laparoscopic DP [25]. Subgroup analysis by type of surgery also did not demonstrate significant differences in neither PD (Fig. 2b) nor DP (Fig. 2c) cohorts. The pooled analyses excluded the study by Schmidt et al.[27] because it did not follow the ISGPF definition of POPF.

Pooled analyses of biochemical leak (formerly grade A) and individual grades of POPF severity (B, C) [4] also did not demonstrate differences between the PG and AS groups.

Overall complications

Overall complications were reported by three studies [26, 28, 32] as a proportion of patients that experienced at least one of the following complications: wound infection, intra-abdominal infection, DGE, PPH, pneumonia, abdominal wound dehiscence, cardiac event, and

Table 1 Study characteristics

Author	Year	Country	Study period	Design/ single- or multicenter	PG (N)	CS (N)	Age (mean)	Sex (% male)	Reported outcomes of interest	Indication for surgery (%)	Surgery type (type of pancreatic anastomosis, if applicable)
Schmidt [32]	2006	USA	1980–2002	Retrospective cohort (SC)	241	269	58.0	56.0	POPF predictive factors (including type of drain used), effect of POPF on surgical outcomes	Periapillary cancer (57.6), pancreatitis (21.6), cystic neoplasms (11.4), islet cell neoplasms (3.7), trauma (1.6), other (4.1)	PD (PGY 251, 49.0%), (PJ 505, 99.0%), (pylorus preserving 259, 51.0%)
Aumont [30]	2017	France	2012–2015	Retrospective cohort (MC)	132	65	66.2±11.8	54.8	POPF, total complications, PPH, LOS	Pancreatic adenocarcinoma (68.0), cholangiocarcinoma (3.6), ampullary carcinoma (3.0) other (25.4)	PD (PGY 97, 49.2%), (PJ 98, 49.8%), (pylorus preserving 142, 72.1%)
Cecka [29]	2018	Czech Republic	2013–2016	RCT (MC)	111 (PD: 81)	112 (PD: 80)	DP: 62.2±12.9 PD: 64.6±10.9	DP: 32.8 PD: 55.3	POPF, DGE, total complications, mortality, PPH, SSI, LOS, re- operation, re- admission, time to drain removal	Pancreatic adenocarcinoma (72.7), ampullary carcinoma (9.3), cholangiocarcinoma (6.2), chronic pancreatitis (9.3), endocrine neoplasm (6.8), cystic tumor of pancreas (21.1), other (12.4)	PD (pylorus preserving 137, 85.1%) DP
Marchegiani [26]	2018	Italy	2016–2017	Prospective cohort (SC)	189 (PD: 115)	131 (PD: 81)	61.0	52.2	POPF, total complications, mortality, PPH, SSI, LOS, re- admission, time to drain removal	Pancreatic adenocarcinoma (52.5), cystic tumor of pancreas (16.2), endocrine neoplasm (15.0), other (16.2)	PD (PGY 3, 1.5%)(PJ 193, 98.5%) DP

Table 1 continued

Author	Year	Country	Study period	Design/ single- or multicenter	PG (N)	CS (N)	Age (mean)	Sex (% male)	Reported outcomes of interest	Indication for surgery (%)	Surgery type (type of pancreatic anastomosis, if applicable)
Dokmak [25]	2019	France	2008–2016	Prospective cohort (SC)	79	102	56.0 (IQR 18–87)	38.1	POPF, PPH, LOS, re-admission	Intraductal papillary mucinous neoplasia (27), adenocarcinoma (16), mucinous cystadenoma (11), neuroendocrine tumor > 2 cm; < 2 cm (11); (7) solid and cystic pseudopapillary tumor (6), chronic pancreatitis (5), Pan IN lesions and hereditary pancreatitis (4), degenerated intraductal papillary mucinous neoplasia (4), other benign or malignant diseases (9)	Laparoscopic DP
Kone [31]	2020	North America	2016–2017	Retrospective cohort (MC)	1345 (PD: 931)	7887 (PD: 5228)	67 (IQR 58–73)	52.0	POPF, SSI, drain amylase level, time to drain removal	Pancreatic adenocarcinoma (54.6), neuroendocrine (6.1), invasive IPMN (2.0), other cancer (7.7), benign (17.6)	PD (PGY 128, 2.1%), (PJ 5627, 91.4%) DP
Total					2097	8566					

PD = pancreaticoduodenectomy, DP = distal pancreatectomy, PGY = pancreaticogastrostomy, PJ = pancreaticojejunostomy, NR = not reported, SC = single-center, MC = multi-center

Table 2 Drain characteristics and management

Author	Description of drain		Decision for drainage selection	Drain management
	PG	AS		
Schmidt [32]	Gravity drain (Penrose, drainage collected via ostomy skin appliance)	Closed suction drain (bulb suction device, Jackson-Pratt style)	Surgeon's discretion	Drain amylase measured: POD 8 from 1980 to 1985, POD 11 from 1985 to 2002 Drain removal: Not reported
Aumont [30]	Passive drain (not further defined)	Closed suction drain (Shirley Drain™)	Surgeon's discretion	Drain amylase measured: POD 1, 3, 5 Drain removal: POD 5, unless there was POPF or biliary leak
Cecka [29]	Passive tube drains	Closed suction drain (BLAKE™ silicone drains)	Randomized	Drain amylase measured: daily after POD 3 Drain removal: POD 4–6, unless there was POPF
Marchegiani [26]	Open passive drains (Penrose)	Closed suction drain (Jackson-Pratt style drains)	Surgeon's discretion	Drain amylase measurement: POD 1, POD 5 Drain removal: POD 3 whenever fluid amylase activity on POD1 was < 5000U/L. Otherwise, fluid amylase re-measured on POD 5
Dokmak [25]	Multi-tubular drain (connected to stoma/ urinary collection bag)	Small suction drain (not further defined)	Temporal—used PG then institution started to use CS for all	Drain amylase measurement: not reported Drain removal: PG—on POD 10 in absence of POPF and until healing if presence of POPF; CS—on POD 7 if drain was nonproductive, otherwise drain remained until complete healing (healing defined as zero output during 2 consecutive days)
Kone [31]	Any closed drain system not placed on suction	Any closed drain system placed on suction	Surgeon's discretion	Not reported; multicenter review of ACS-NSQIP data

POD = Postoperative day

neurologic complication. The RCT [32] reported a unique trend between AS drainage and major morbidity ($p = 0.053$) after DP. However, pooled analyses for neither overall (OR 1.11, CI [0.77, 1.60], $p = 0.56$, $i^2 = 2\%$) nor major complications [18] (Fig. 2d) in patients undergoing PD demonstrated significant differences between the two drains. There were also no differences in 30-day mortality (OR 0.92, CI [0.31, 2.72], $p = 0.88$, $i^2 = 0\%$, $n = 2$ studies) [26, 32].

Post-pancreatectomy hemorrhage.

The incidence of PPH was reported by four studies. [25, 26, 28, 32] Individual and pooled analyses did not demonstrate statistically significant differences by drain type in neither PD (OR 1.18 [0.66, 2.09], $p = 0.58$, $i^2 = 0\%$) nor DP (OR 0.68 [0.04, 12.97], $p = 0.80$, $i^2 = 84\%$).

Surgical site infection

Three studies [26, 29, 32] reported on the incidence of wound infections and two [29, 32] on the incidence of intra-abdominal infections. The studies by Cecka et al.[32]

and Marchegiani et al.[26] did not demonstrate associations between SSI and either drainage groups. Kone et al.[31] reported an association between increased intra-abdominal SSI with AS drains in PD cohorts (12% vs. 16%, $p = 0.004$) on univariate and multivariate analysis, which was not maintained in propensity score matching ($p = 0.088$). There was no difference demonstrated in the patients undergoing DP.

Of note, the study by Marchegiani et al.[26] used open Penrose drains as their PG system, which theoretically holds a higher risk for ascending infection than a conventional closed PG system [26, 33, 34]. Therefore, this study was excluded from the meta-analyses for SSI as to avoid introduction of possible bias.

Thus, pooled analyses of two studies were undertaken for intra-abdominal and wound SSI among the PD cohort. These analyses did not demonstrate significant associations between drain type and wound infections (Fig. 2e) or intra-abdominal infections (Fig. 2f). There was a trend toward increased intra-abdominal infections with AS drains, but this did not reach statistical significance.

Resource utilization

To compare resource utilization, the following outcomes were assessed: LOS, re-admission, and re-intervention (including percutaneous drain insertion and re-operation).

Four studies [25, 26, 28, 32] reported data pertaining to LOS. Independent and pooled analyses for PD (− 0.22 days [− 1.42, 0.98], $p = 0.72$, $i^2 = 11%$) and DP (− 4.54 days [− 13.36, 4.28], $p = 0.31$, $i^2 = 94%$) did not demonstrate significant differences in LOS. The heterogeneity in the DP cohort is likely contributed by the Dokmak et al.[25] study, which reported range as opposed to SD, requiring estimation of the SD [30]. Of note, Dokmak et al. demonstrated that PG drains were significantly associated with a longer LOS in their cohort of

laparoscopic DP (11 days (5–44) vs. 20 days (7–73), $p < 0.001$) [25].

Incidence of re-operation was only reported by Cecka et al. [32] Greater re-operation rate with AS drains ($p = 0.053$) and greater re-admission rates with PG ($p = 0.053$) were reported in patients undergoing DP.

Percutaneous drainage (OR 0.91 [0.27, 3.10], $p = 0.88$, $i^2 = 34%$) and re-admission to hospital (OR 1.39 [0.57, 3.36], $p = 0.47$, $i^2 = 0%$) were meta-analyzed, including three [25, 26, 32] and two studies [25, 26], respectively. Pooled and individual analyses of both outcomes did not demonstrate differences between drainage systems.

Table 3 Risk of bias assessment for included studies

(a) Cochrane risk of bias for randomized controlled trials

Author	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete data outcome	Selective reporting	Other
Cecka[29]	L	L	H	H	L	L	H

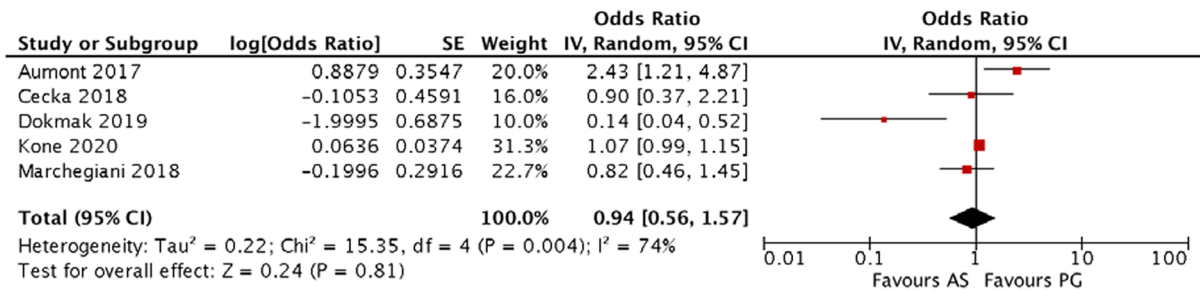
L	Low risk of bias
H	High risk of bias

(b) MINORS risk of bias for included observational studies

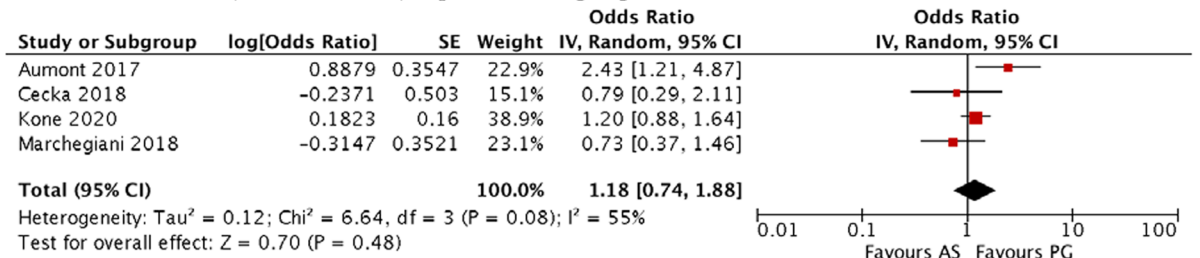
Author	Clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Appropriate endpoints	Blinded outcome assessors	Appropriate follow up period	<5% loss to follow-up	Study size calculation	Adequate control group	Contemporary groups	Baseline equivalence of groups	Adequate statistical analyses	MINORS score
Schmidt[32]	2	2	1	2	0	2	1	0	1	2	1	2	16
Aumont[30]	2	2	1	2	0	2	1	0	2	2	1	2	17
Marchegiani[26]	2	2	2	2	0	2	2	0	2	2	2	2	20
Dokmak[25]	2	2	2	2	0	2	2	0	1	1	1	2	17
Kone[31]	2	2	1	2	2	2	2	0	2	2	2	2	21

	Reported and adequate
	Reported but inadequate
	Not reported

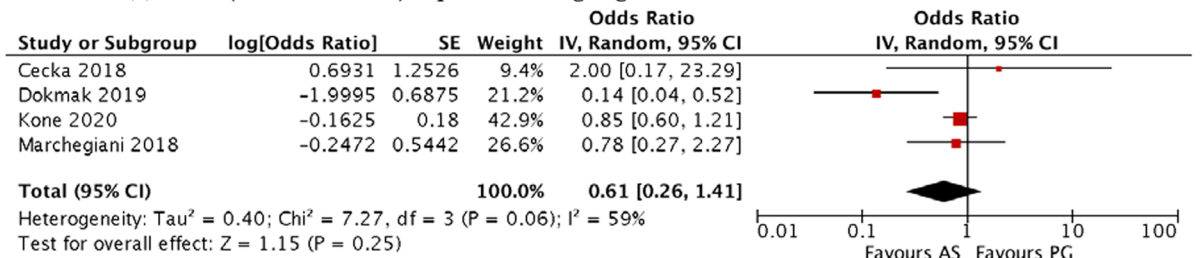
(a) All POPF in both PD and DP



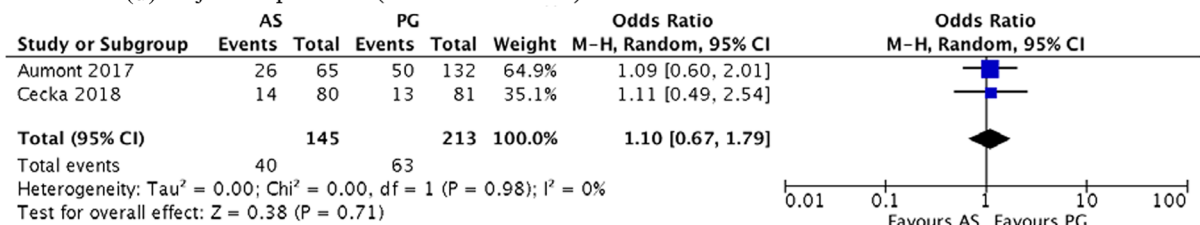
(b) POPF (ISGPF definition) in patients undergoing PD



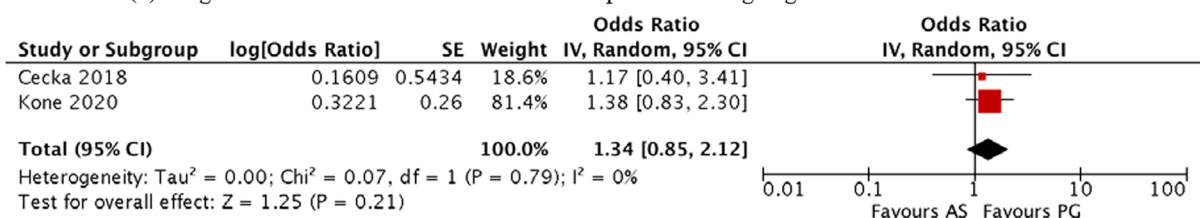
(c) POPF (ISGPF definition) in patients undergoing DP



(d) Major Complications (Clavien Dindo > III)



(e) Surgical site infections – wound infections in patients undergoing PD



(f) Surgical site infections – intra-abdominal infections in patients undergoing PD

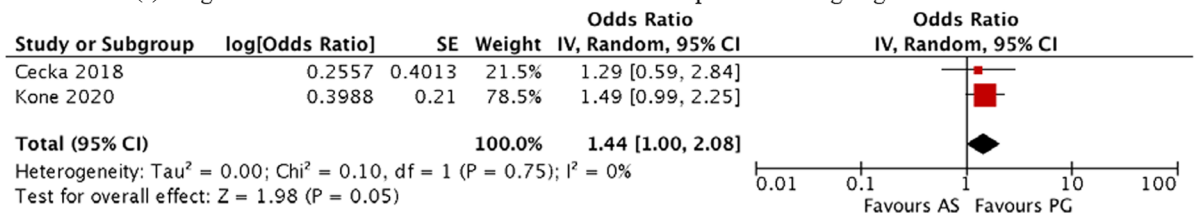


Fig. 2 **a** All POPF in both PD and DP **b** POPF (ISGPF definition) in patients undergoing PD **c** POPF (ISGPF definition) in patients undergoing DP **d** Major Complications (Clavien–Dindo > III) **e** Surgical site infections–wound infections in patients undergoing PD **f** Surgical site infections–intra-abdominal infections in patients undergoing PD

Quality of life

Effect on QOL was assessed by comparing surrogate outcomes including the length of time drains remained in situ and the presence of a drain at discharge.

Marchegiani et al.[26] demonstrated a statistically significant association between the PG drainage system and an increased incidence of hospital discharge with a drain (12.1% vs. 3.8%, $p = 0.009$). However, there was no difference between PG and AS in the number of days the drain remained in situ (8.1 ± 11.1 days vs. 6.8 ± 8.1 days, $p = 0.20$) or LOS (14.3 days vs. 9.5 days, $p = 0.20$). Conversely, Cecka et al.[32] demonstrated an association between AS and longer time to drain removal (median 6 days vs. 5 days, $p = 0.047$).

Discussion

The present review identified six studies comparing the incidence of adverse events following pancreatic resection with AS versus PG drainage systems. The type of drainage system was not found to influence the development of POPF. Furthermore, there were no associations between drainage systems and other outcomes of interest including SSI, mortality, morbidity, PPH, resource utilization, or QOL.

Interesting associations were reported independently by select studies. Dokmak et al.[25] reported increased Grade B POPF incidence with PG drain use, an association that was not demonstrated elsewhere. Whereas surgeon preference determined the selection of PG versus AS drains in other observational studies, the Dokmak study initially used PG drains and transitioned to using AS drains at the latter period of the 8-year project [25]. Additionally, the study solely included patients undergoing laparoscopic DP. Thus, the temporal switch in drainage systems in conjunction with a possible learning curve associated with laparoscopic DP may have contributed to reduced POPF with AS drains.

Kone et al. demonstrated increased intra-abdominal SSI with AS drains in univariate and multivariate analyses, which was not maintained in the propensity score matching [29]. This was the largest study included in the review and involved 9 232 patients. Therefore, this study strongly influenced the results when pooled with the study by Cecka

et al. [32]. Meta-analysis demonstrated a trend favoring PG, which did not reach statistical significance ($p = 0.05$). Theoretically, PG drains allow for pooling of fluids, more so than AS drains, and therefore would present higher risk of infections. Studies across various surgical disciplines that compared PG and AS drainage systems reported increased SSI risk with passive, albeit open, drains [35]. Nonetheless, the unique trend seen in a large sample population [32] merits further investigations.

The present study is the first systematic review and meta-analysis comparing the effect of intra-abdominal drainage selection on outcomes following all pancreatic resections. It is distinct from similar reviews primarily by its strict inclusion criteria limited to papers comparing operatively placed drains on suction versus drainage by gravity. Specifically, existing reviews by Zhang et al.[36] and Gachabayov et al.[37] included studies by Jiang et al.[38] and Lee et al.[39]. Although both these studies are RCTs, they were excluded from the present review as the drainage systems failed to meet the inclusion criteria. Jiang et al.[38] utilized an AS system that involved two drains, one that was kept on continuous suction and another that was primarily used for irrigation until POD 3. Lee et al.[39] described the use of an external pancreatic duct stent that was connected to negative suction or gravity drainage. This is entirely distinct from an intra-abdominal drain. Careful methodology screening with strict inclusion criteria for drain systems was done with intention to avoid inclusion of such studies. Furthermore, the present review compared AS versus PG drains in 10 663 DP and PD patients; this is a substantially greater sample population compared to the 1 519 and 160 PD patients included in the Gachabayov et al. and Zhang et al. studies, respectively. [36, 37]

While the present review includes the best available evidence on outcome differences between AS and PG drains following pancreatic surgery, some limitations remain. Although the included non-randomized studies were carefully screened for bias, observational studies cannot replace the level of evidence from a high-quality RCTs. Given that there is only one RCT on this subject, the strength of this review in answering whether drain management can alter outcomes is limited. Across the published literature, there are variations in postoperative management of drains as well as inconsistencies in the type of drain and bulb used across different institutions. Although this allows for the advantage of generalizability, these factors may have contributed heterogeneity to the analyses. Specifically, among AS drains, maximum negative suction occurs with an empty bulb and rapidly decreases as the bulb fills [8, 14, 40]. Thus, differences in how often and at what point the drain is emptied or stripped could impact the amount of time a drain is truly imparting a

negative pressure. Currently, available data on the topic of interest are largely observational, with the only included RCT having omitted most outcome data pertaining to the DP group. Two of the six included studies were also considered to be low-quality evidence according to the MINORS and Cochrane Risk of bias criteria. Finally, this review included patients undergoing either PD or DP. Understanding that differences between surgical procedures and complication profiles may introduce heterogeneity, all endpoints were analyzed separately by PD or DP. This was done at the cost of the sample size, thereby decreasing the power to detect differences, should they exist. This further highlights the need for larger trials to definitively answer the question of whether suction or gravity drainage is superior.

Conclusion

Pooled analyses of the best existing evidence on PG versus AS drains following pancreatic surgeries demonstrate that there are no differences between the two with regards to POPF development, mortality, PPH, wound infections,

intra-abdominal infections, severe morbidity, resource utilization, and QOL. Based on the existing literature, there lacks evidence to suggest the use of one drain over another at this time. The trend between AS and increased intra-abdominal infections as well as PG and increased Grade B POPF in laparoscopic DP merits further investigation. Greater numbers of well-designed, adequately powered RCTs may prove beneficial to draw robust conclusions as to whether a superior type of drainage system exists in the context of pancreatic surgery.

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Declarations

Conflict of interest The author(s) have no conflicts of interest to declare.

Appendix A: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4-5, 26-29
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4-6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7
Risk of bias across studies			
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7-8, 22
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7-8, 19-20
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	6,8,21
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	23
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	7-12,23
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	21
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	7-12
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	13-14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13-14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

Appendix B: Search Strategy

Database(s): **Ovid MEDLINE(R) ALL** 1946 to May 18, 2020, Search Strategy:

#	Searches	Results
1	Pancreatic diseases/su [Surgery]	2313
2	exp Pancreatic neoplasms/su [Surgery]	16,711
3	(pancrea* adj2 surg*).tw	5135
4	(pancrea* adj2 resection*).tw	5694
5	(pancrea* surg* or pancrea* resection*).kw	939
6	PANCREATECTOMY/ or PANCREATICOJEJUNOSTOMY/ or Pancreaticoduodenectomy/	20,311
7	(pancreatectom* or pancreaticojejunistom* or pancreaticoduodenectom*).tw,kw	16,222
8	whipple procedure*.tw,kw	840
9	or/1–8	38,595
10	drainage/ or drain*.tw,kw	145,869
11	9 and 10	3648
12	(Jackson pratt or jp drain*).tw,kw,kf	137
13	(closed or active or negative).tw,kw,kf	2,066,083
14	12 or 13	2,066,180
15	(open or passive or gravity).tw,kf	622,346
16	11 and 14 and 15	50
17	((active or closed or negative or jackson pratt or jp) adj4 drain*).tw	2498
18	((active or closed or negative or jackson pratt or jp) and drain*).kf	113
19	17 or 18	2546
20	((passive or open or gravity) adj4 drain*).tw	1914
21	((passive or open or gravity) and drain*).kf	63
22	20 or 21	1950
23	9 and (19 or 22)	130
24	16 or 23	142
25	*DRAINAGE/ or (drains or drainage).ti	28,790
26	DRAINAGE/is, mt [Instrumentation, Methods]	15,412
27	25 or 26	33,709
28	9 and 27	1120
29	24 or 28	1205
30	(child/ or infant/) not adult/	1,352,637
31	29 not 30	1180
32	animals/ not humans/	4,665,913
33	31 not 32	1153

Database(s): **Embase Classic + Embase** 1947 to May 18, 2020, Search Strategy:

#	Searches	Results
1	pancreas surgery/ or pancreas resection/	25,635
2	pancreaticoduodenectomy/	21,721
3	pancreatectomy/	3260
4	pancreaticojejunistomy/	3133
5	(pancrea* adj2 surg*).tw	9313
6	(pancrea* adj2 resection*).tw	9524
7	(pancreatectom* or pancreaticojejunistom* or pancreaticoduodenectom*).tw	26,569
8	whipple procedure.tw	1350
9	or/1–8	55,941
10	abdominal drainage/ or abdominal drain/	3498
11	drain*.tw	197,062
12	suction drainage/ or surgical drainage/ or suction drain/	19,950
13	or/10–12	205,973
14	9 and 13	5695
15	(Jackson pratt or jp drain*).tw	372
16	(closed or active or negative).tw	2,835,747
17	15 or 16	2,835,998
18	(open or passive or gravity).tw	820,661
19	14 and 17 and 18	88
20	((active or closed or negative or jackson pratt or jp) adj4 drain*).tw	3915
21	((passive or open or gravity) adj4 drain*).tw	2868
22	9 and (20 or 21)	212
23	19 or 22	256
24	9 and 10	381
25	(drainage or drains).ti	28,765
26	*abdominal drainage/ or *abdominal drain/	717
27	*suction drainage/ or *surgical drainage/	2649
28	or/25–27	29,619
29	9 and 28	988
30	24 or 29	1251
31	case report/	2,577,349
32	30 not 31	1024
33	(child/ or infant/) not adult/	1,669,345
34	32 not 33	1016

Database(s): **EBM Reviews—Cochrane Central Register of Controlled Trials** April 2020 Search Strategy:

#	Searches	Results
1	Pancreatic diseases/su [Surgery]	10
2	exp Pancreatic neoplasms/su [Surgery]	23
3	(pancrea* adj2 surg*).tw	820
4	(pancrea* adj2 resection*).tw	543
5	(pancrea* surg* or pancrea* resection*).kw	165

#	Searches	Results
6	PANCREATECTOMY/ or PANCREATICOJEJUNOSTOMY/ or Pancreaticoduodenectomy/	404
7	(pancreatectom* or pancreaticojejunostom* or pancreaticoduodenectom*).tw,kw	1371
8	whipple procedure*.tw,kw	59
9	or/1–8	2257
10	drainage/ or (drainage or drain*).tw	10,978
11	9 and 10	335

#	Query	Results
S5	TI (pancrea* N2 resection*) OR AB (pancrea* N2 resection*)	853
S4	TI (pancrea* N2 surg*) OR AB (pancrea* N2 surg*)	1,162
S3	(MH “Pancreatic Diseases + /SU”)	3,703
S2	(MH “Pancreas + /SU”)	711
S1	(MH “Pancreatic Neoplasms + /SU”)	2,277

Cinahl.

#	Query	Results
S28	S19 OR S23 OR S27	328
S27	S10 AND S26	315
S26	S24 OR S25	6,726
S25	TI (drains or drainage)	3,814
S24	(MH “Drainage + ”) OR (MH “Closed Drainage”)	4,830
S23	S10 AND S22	27
S22	S20 OR S21	762
S21	TI (((passive or open or gravity) N4 drain*) OR AB (((passive or open or gravity) N4 drain*))	312
S20	TI (((active or closed or negative or jackson pratt or jp) N4 drain*) OR AB (((active or closed or negative or jackson pratt or jp) N4 drain*))	481
S19	S14 AND S17 AND S18	8
S18	TI ((open or passive or gravity)) OR AB ((open or passive or gravity))	122,862
S17	S15 OR S16	332,486
S16	TI ((closed or active or negative)) OR AB ((closed or active or negative))	332,457
S15	TI ((Jackson pratt or jp drain*)) OR AB ((Jackson pratt or jp drain*))	40
S14	S10 AND S13	738
S13	S11 OR S12	23,692
S12	TI drain* OR AB drain*	18,008
S11	(MH “Drainage + ”) OR (MH “Closed Drainage”)	10,128
S10	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9	6,631
S9	TI whipple procedure OR AB whipple procedure	169
S8	TI ((pancreatectom* or pancreaticojejunostom* or pancreaticoduodenectom*)) OR AB ((pancreatectom* or pancreaticojejunostom* or pancreaticoduodenectom*))	2,298
S7	(MH “Pancreaticoduodenectomy”)	1,076
S6	(MH “Pancreatectomy”) OR (MH “Pancreaticojejunostomy”)	1,602

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