

Drain and nasogastric tube use following pancreatoduodenectomy: a narrative review

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Background and Objective: Patients with cancer affecting the head of the pancreas have a dismal prognosis. Around one fifth present early enough to be considered candidates for surgical resection. Pancreatoduodenectomy (PD) offers the potential of cure but remains high-risk. Traditionally, patients would leave theatre with at least one intraperitoneal drain and a nasogastric tube *in situ*. However, some authors argue that this is not necessary and practice is highly variable. We aimed to consolidate the recent evidence on the impact of routine drain and nasogastric tube use on PD perioperative outcomes.

Methods: A comprehensive search of the English literature (PubMed database) was undertaken. Articles from May 2011 to May 2021 reporting on intraperitoneal drain and nasogastric tube use and their impact on PD outcomes were included.

Key Content and Findings: Prophylactic drainage appears to correlate with increased overall morbidity and decreased perioperative mortality. This is mostly based on the findings of retrospective, non-randomised studies. The increased morbidity risk is likely due to a combination of drain-related complications, increased "pick-up" and surgeons electing not to place drains in low-risk patients. The decreased mortality rate may reflect the fact that drains facilitate the early diagnosis of procedure-specific major morbidity which requires timely intervention e.g., postpancreatectomy haemorrhage. Most authors conclude that the lack of a drain does not affect reintervention rates. Whilst most support early drain removal, the timing and criteria for this remain debated. A prospective, randomised study with strict protocol adherence would help address the highlighted issues. Nasogastric tubes are uncomfortable for patients and their routine placement does not improve outcomes. Hence, they should only be used when clinically indicated.

Conclusions: Placement of a drain is recommended following PD although the details surrounding this remain controversial. Nasogastric tubes should not be used routinely.

Keywords: Drain; morbidity; nasogastric tube; pancreatic cancer; pancreatic ductal adenocarcinoma (PDAC)

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Table 1 Summary of search strategy

| Items | Specification |
|---|---|
| Date of Search | 1 st May 2021 |
| Databases and other sources searched | PubMed only |
| Search terms used (including MeSH and free text search terms | 1. "drain" AND "pancreatoduodenectomy" |
| and filters) | 2. "nasogastric tube" AND "pancreatoduodenectomy" |
| Timeframe | 1 st May 2011 – 30th April 2021 |
| Inclusion and exclusion criteria (study type, language restrictions | 1. English language |
| etc.) | 2. Human studies |
| | 3. Studies with at least 100 pancreatoduodenectomies |
| | 4. Studies with statistically significant findings (P<0.05) |
| Selection process (who conducted the selection, whether it was conducted independently, how consensus was obtained, etc.) | Literature search carried out independently by TR. Efforts were made to include the most relevant studies |
| Any additional considerations, if applicable | Included were clinical studies, systematic reviews and meta-analyses reporting on intraperitoneal drain and nasogastric tube use and their impact on pancreatoduodenectomy outcomes |

Introduction

By 2030, it is predicted that pancreatic ductal adenocarcinoma (PDAC) will be a leading cause of cancerrelated death in the developed world (1). Prognosis is extremely poor with five-year survival being around 9% (1). For fit patients with early disease affecting the head of the pancreas, curative-intent pancreatoduodenectomy (PD) is recommended. This operation remains high-risk and is associated with considerable morbidity. Whilst patients traditionally left theatre with at least one intraperitoneal drain and a nasogastric (NG) tube in situ, some authors advise against this and practice is highly variable. This review aims to consolidate the findings of notable recent studies which have reported on these controversial topics. We present the following article in accordance with the Narrative Review reporting checklist (available at https:// apc.amegroups.com/article/view/10.21037/apc-21-18/rc).

Methods

A comprehensive online search of the PubMed database was carried out on 1st May 2021 (*Table 1*). One search was conducted using the terms ["drain" AND "pancreatoduodenectomy"] and an additional search was carried out using the terms ["nasogastric tube" AND "pancreatoduodenectomy"]. Articles from May 2011

through to May 2021 were included. Included were clinical studies, systematic reviews (SR), and meta-analyses (MA) reporting on intraperitoneal drain and NG tube use and their impact on PD outcomes. The following criteria were used: (I) English language; (II) human studies; (III) studies with at least 100 PDs; (IV) in terms of risk factors/ associations, only statistically significant results were considered (P<0.05). Where available, exact figures have been provided for direct comparison. Otherwise, odds ratio (OR), relative risk (RR), or mean/median difference (MD) has been provided.

Results

Drains

Surgical drains have been used in abdominal operations since the nineteenth century; they serve multiple purposes (2). Firstly, since drain contents can be inspected, measured and sent for laboratory analysis, they facilitate the diagnosis and monitoring of anastomotic leakage and postoperative bleeding. This is especially important following PD since the early diagnosis of postoperative pancreatic fistula (POPF) and post-pancreatectomy haemorrhage (PPH) can improve outcomes (3). Drains can also help prevent fluid accumulation and reduce the incidence of intra-abdominal abscesses (2). However, as

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an indwelling foreign body, they are an infection risk. Furthermore, the presence of a drain, and the resulting adjacent inflammation, may contribute to postoperative bleeding and has the potential to disrupt an anastomosis (4). Finally, drains can limit patient mobilisation which is associated with further morbidity such as pulmonary embolism and atelectasis (2). Whilst it is difficult to quantify these associations, drains should only be used when there is a clear indication. Recent authors have challenged their routine use in PD (2,4,5).

Drain placement

In a recent MA, Wang et al. [one randomized controlled trial (RCT), four non-randomised comparative studies, n=1,728, 45.3% in the drain group] concluded that prophylactic drainage correlated with decreased perioperative mortality (OR 2.32, P=0.02) (6). However, this also correlated with increased overall morbidity (OR 0.62, P<0.01), major morbidity (OR 0.75, P=0.01) and readmission (OR 0.77, P=0.04) (6). Rates of POPF (including biochemical leak), intra-abdominal abscess, PPH, bile leak, delayed gastric emptying (DGE) and re-intervention, including radiologicguided drainage, were unaffected (6). Three studies used the International Study Group of Pancreatic Fistula (ISGPF) definition of POPF and the remaining two used their own definitions. Due to the small number of studies available for analysis, the authors could not safely recommend or advise against drain use and suggested that future RCTs should compare routine versus selective drainage (6). Results from this MA are compared to other similar studies in Table 2. In another recent MA, Hüttner et al. (three RCTs, n=711, 50.5% in the drain group) found routine drainage did not affect rates of perioperative mortality, overall morbidity, reoperation, intra-abdominal abscess or surgical site infection (SSI) (7). POPF was more common in the drain group (15.9% vs. 7.1%, P=0.03) but this was not significant when biochemical leaks (formerly grade A POPF) were excluded (11.5% vs. 9.5%, P=0.67) (7). The authors concluded that the current evidence does not support routine drainage and advised that future research should focus on the identification of the sub-set of patients in whom a drain would be beneficial (7). As in the Wang et al. MA, only a limited number of studies were included.

In a retrospective, multi-centre study, Zaghal *et al.* (n=6,858, 87.4% in the drain group) found routine drainage correlated with reduced perioperative mortality (1.7% *vs.* 2.9%, P=0.003) but higher rates of overall morbidity (49.5% *vs.* 41.2%, P=0.0008), DGE (18.1% *vs.* 13.7%,

P=0.004), and POPF (19.4% vs. 9.9%, P<0.0001), and longer length of stay (3.1% vs. 1.6% >10 days, P=0.02) (4). This study employed a non-randomised design and only considered follow-up to 30-days postoperatively. In a similar retrospective, multi-centre study, Addison et al. (n=7,583, 87.9% in the drain group) reached contrasting conclusions. Drainage was associated with reduced risk of major morbidity (RR 0.73, P<0.0001), overall morbidity (RR 0.79, P<0.0001), and intra-abdominal collection (RR 0.72, P<0.0001) (8). Routine drainage did not affect incidence of clinically relevant (CR) POPF and, in those who had a drain placed, length of drainage was independently associated with major morbidity (HR 3.06, P<0.0001), overall morbidity (HR 2.48, P<0.0001) and intra-abdominal collection (HR 1.47, P<0.0001) (8). As such, the authors advise prophylactic drain placement and suggest early removal should be considered. Since this study was also retrospective and did not consider key confounding variables, the authors argue a prospective RCT with strict protocol adherence is required.

Finally, a more recent MA by Liu et al. (five RCTs and ten retrospective studies, n=16,648) also showed that routine drainage correlated with reduced perioperative mortality (OR 0.62, P<0.01) but overall morbidity rates were unaffected (9). Routine drainage was associated with increased incidence of CR-POPF (OR 1.98, P=0.002) but did not affect rates of bile leak, DGE, PPH, intra-abdominal abscess, SSI, reoperation, or unplanned readmission (9). As in the Wang et al. MA, definitions of POPF were not consistent between the included studies. This MA contained mostly non-randomised studies, important confounding variables were not considered (e.g., pancreatic texture, main pancreatic duct diameter etc.), and the use of drains was not standardised. Due to the heterogeneity of the included studies, the authors could not arrive at clinically relevant conclusions.

Drain fluid amylase

A key advantage of drain placement is that drain fluid can be inspected, measured and send for laboratory analysis. A high drain fluid amylase (DFA) may indicate POPF which is associated with prolonged length of stay, delayed adjuvant therapy, poor quality of life, and mortality (10). Conversely, a normal DFA is reassuring and suggests drain removal is appropriate. The timing of fluid analysis, as well as the threshold for diagnosing POPF, remain a source of debate. The International Study Group of Pancreatic Surgery (ISGPS) suggest POPF should be diagnosed when DFA is greater than three times the upper normal serum value,

| Table 2 Resu | ults from selv | Table 2 Results from selected recent studies which have investigated the impact of prophylactic drain placement on pancreatoduodenectomy outcomes | which have i | nvestigated | the impact c | of prof | hylactic dr | ain plac | ement on p | ancreatodu | odenectomy ou | itcomes | | |
|---|------------------|---|----------------------------|--|------------------------------|--------------|----------------|----------------------|------------------------------------|----------------------------|---|-----------------------------------|-------------------|----------------------------------|
| Study | Study type | Percentage of patients who received a prophylactic drain | Mortality | Overall morbidity | Overall morbidity CR-POPF | Bile leak | DGE | ННА | Intra- PPH abdominal abscess | SS | Radiologi Reoperation guided drainage | Radiologic- guided drainage | LoS | Readmission |
| Wang MA <i>et al.</i> (2015) (n=1,728) | MA (n=1,728) | 45.3% | ↓ (OR 0.43) | ↓ ↑ (OR 0.43) (OR 1.61) | I | I | I | I | I | NS | I | I | NS | ↑ (OR 1.30) |
| Hüttner MA <i>et al.</i> (2017) (n=711) | MA (n=711) | 50.4% | I | I | I | SN | SN | SN | I | I | I | I | NS | NS |
| Addison MCR <i>et al.</i> (2019) (n=7,583) | MCR (n=7,583) | 87.9% | I | ↓ (RR 0.79) | I | SN | I | SN | NS | ↓ (RR 0.72) | I | SN | ↑ (MD 1.0 day) | I |
| Zaghal MCR <i>et al.</i> (2020) (n=6,858) | MCR (n=6,858) | 87.4% | ↓ (OR 0.58) | ↓ ↑ ↑ ↑ 100 CR 0.58) (OR 1.40) (OR 2.19) | ↑ (OR 2.19) | SN | ↑ (OR 1.39) | SN | NS | NS | I | I | ↑ (1.97)* | I |
| Liu <i>et al.</i> (2021) | MA (n=16,648) | Not stated | ↓ (OR 0.62) | I | ↑ (OR 1.98) | I | I | I | I | I | I | I | NS | I |
| References not significal | within the a | References within the article text. *, length of stay >10 days. ↑, increased risk (compared to no drain placement); ↓, decreased risk (compared to no drain placement); -, risk not significantly affected by drain placement. CR-POPF, clinically relevant postoperative pancreatic fistula; DGE, delayed gastric emptying; LoS, length of stay; MA, meta- | of stay >10 int. CR-POF | days. ↑, inc F, clinically | creased risk relevant pc | (com | pared to n | o drain creatic | placement fistula; DG |); ↓, decrea E, delayed | >10 days. ↑, increased risk (compared to no drain placement); ↓, decreased risk (compared to no drain placement); -, risk POPF, clinically relevant postoperative pancreatic fistula; DGE, delayed gastric emptying; LoS, length of stay; MA, meta- | bared to no o ing; LoS, ler | drain plac | ement); -, risk ay; MA, meta- |

analysis; MCR, multi-centre retrospective; MD, median difference; NS, not studied; OR, odds ratio; PPH, post-pancreatectomy haemorrhage; RR, relative risk; SSI, surgical site infection.

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Table 3 Results from selected recent studies which have investigated the role of DFA as a tool for diagnosing POPF

| | | U | 6 6 |
|---------------------------------|--------------|----------------------------|--|
| Study | Study type | Suggested timing of DFA | Suggested cut-off DFA for keeping drain in situ (IU) |
| Yang et al. (2015) | MA (n=2,886) | POD 1 | 1,300 |
| Hasselgren <i>et al.</i> (2016) | SCR (n=170) | POD 1 | 3× serum reference range |
| Davidson et al. (2017) | SR (n=868) | Unable to comment | Unable to comment |
| Vutukuru <i>et al.</i> (2017) | SCP (n=110) | POD 5 (if raised on POD 3) | 3× serum reference range |
| Lee et al. (2019) | SCR (n=117) | POD 3 | 1,004 |

DFA, drain fluid amylase; POPF, postoperative pancreatic fistula; MA, meta-analysis; POD, postoperative day; SCP, single centre prospective; SCR, single centre retrospective; SR, systematic review.

starting from postoperative day (POD) three (11). Whilst numerous studies have demonstrated that DFA is useful for the early diagnosis of POPF, the addition of drain fluid lipase has not been shown to improve sensitivity or specificity (12).

Following a MA, Yang et al. (eight prospective and two retrospective studies, n=2,886) concluded that DFA on POD one may be more useful than DFA on POD three as a criterion for the early identification of POPF and suggested a threshold value of 1,300 IU (13). The pooled sensitivity and specificity of DFA on POD one was 81% and 87%, respectively (13). Figures of 56% and 79% were obtained for POD three DFA (13). However, this analysis also included biochemical leaks. The authors argue that DFA should be performed on POD one since this can assist with the early diagnosis of POPF and facilitate early drain removal. Most of the included studies were single centre, the sample size in each was relatively small and most did not consider important operation and drain factors. Hence, the authors argue a large, multi-centre study is required to validate their conclusions. Results from this MA and other similar studies are displayed in Table 3. In a retrospective, single centre study, Hasselgren et al. (n=170) also investigated the usefulness of POD one DFA. A DFA three times the upper limit of the serum reference range was used as the threshold. Patients with a raised DFA had a higher major morbidity rate but this was not significant (14). Two patients who developed a CR-POPF did not have a raised DFA on POD one, whereas 29 did (2.0% vs. 45%) (14). The authors concluded that raised DFA on POD one correlates with CR-POPF but did not suggest how this should affect management and argue a prospective, randomised trial is required to validate their findings (14).

In a recent SR, Davidson *et al.* investigated the diagnostic accuracy of DFA on or after POD two for the diagnosis of CR-POPF (two prospective and three retrospective studies,

n=868). Threshold amylase values and the timing of analysis was highly variable between the studies. Sensitivities ranged from 72-100%, and specificities from 73-99% (15). Posttest probability for POPF ranged from 35.9-94.5% for a positive DFA, and from 0-5.5% for a negative DFA (15). The authors acknowledged that not all grade B POPF are secondary to pancreatic leaks and this may have affected diagnostic accuracy calculations. Secondly, three of the included studies did not pre-specify the DFA threshold. Finally, the sample sizes were small and MA could not be performed due to the high degree of heterogeneity between the included studies. The authors concluded that there is no clear evidence which suggests DFA should be used for diagnosing CR-POPF and that the optimal cut-off for DFA is also unclear (15). They advised further diagnostic test accuracy studies with pre-specified DFA thresholds with appropriate follow-up and clearly defined reference standards.

In a single centre, prospective study by Vutukuru et al. (n=110), DFA was performed on POD three and this was repeated on POD five in patients who met the criteria for POPF (as per the ISGPS definition). Forty-four patients (40%) developed POPF (16). Of these, 36 (82%) had a normalised DFA on POD five, and eight (18%) had a persistently raised DFA. No patients in the former group developed CR-POPF, but six (75%) in the latter did (P<0.0001) (16). The authors concluded that DFA performed on POD five is more clinically relevant than DFA performed on POD three (16). Whilst only a small, single centre study, these results highlight that patients with a raised DFA on POD three are likely to have a normalising DFA by POD five and are unlikely to develop CR-POPF. Hence, the authors argue DFA should be repeated on POD five if it is raised on POD three (16).

In a retrospective series of all pancreatic resections,

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| Study | Study type | Timing for drain removal | Criteria | Proposed benefit |
|--------------------------------|---------------|-----------------------------|--|--|
| Ven Fong et al. (2015) | SCR (n=495) | POD 1 | POD 1 DFA <611 IU | N/A |
| Zorbas <i>et al.</i> (2018) | MCR (n=1,066) | On or before | POD 1 DFA <5,000 IU | \downarrow Major morbidity (OR 2.03) |
| | | POD 3 | | \downarrow Overall morbidity (OR 2.13) |
| | | | | ↓ POPF (OR 6.76) |
| | | | | ↓ Mean LoS |
| Beane <i>et al.</i> (2020) | MCR (n=2,698) | On or before | POD 1 DFA <5,000 IU | ↓ Mortality (RR 0.67) |
| | | POD 3 | | ↓ POPF (RR 0.11) |
| | | | | ↓LoS (MD 2.0 days) |
| Dai e <i>t al.</i> (2020) | SCP (n=144) | POD 3 | POD 1 and POD 3 DFA <5,000 IU | \downarrow Major morbidity (OR 0.31) |
| Taniguchi <i>et al.</i> (2020) | SCP (n=198) | POD 4 | Absence of soft pancreas intra-operatively | N/A |
| | | | Negative drain fluid cultures | |
| | | | POD 4 CRP <130 mg/L | |
| Iwasaki <i>et al.</i> (2021) | SCP (n=300) | POD 3 | POD 3 DFA<350 IU | N/A |
| | | | POD 3 CRP <140 mg/L | |

Table 4 Results from selected recent studies which have reported on timing of, and criteria for, drain removal following pancreatoduodenectomy

↓, decreased risk. CRP, C-reactive protein; DFA, drain fluid amylase; LoS, length of stay; MCR, multicentre retrospective; MD, mean difference; OR, odds ratio; POD, postoperative day; POPF, postoperative pancreatic fistula; RR, relative risk; SCP, single centre prospective.

Lee *et al.* (n=117) evaluated the clinical applicability of DFA to obtain appropriate baseline values. DFA on PODs one, three and five were all significantly higher in patients who developed CR-POPF. In contrast to the findings of Vutukuru *et al.*, POD three DFA was the only significant predictor of CR-POPF following multivariate analysis (P<0.001) (10). A cut-off value of 1,004 IU had the highest sensitivity (92%) and specificity (82%) for diagnosing POPF (10). This study also included distal pancreatectomies, where the risk of CR-POPF is higher, and so the findings should be interpreted with caution. Although the authors argue that if POD three DFA <1,004 IU it is safe to remove a drain, these findings require validation by prospective, multi-institutional studies.

Drain removal

Enhanced recovery after surgery (ERAS) protocols advise on minimising drain use and early removal where possible (17). The optimal timing for drain removal, as well as the criteria for this, remain a source of debate (*Table 4*). Some authors have suggested that drain removal can be considered as early as POD one. For example, in a single centre, prospective evaluation, ven Fong et al. (n=495) found POD one DFA of >611 IU was an accurate predictor of POPF (sensitivity 93%, sensitivity 79%) and concluded that a DFA <600 IU resulted in a <1% risk of POPF, and that drains should be removed on POD one in this subgroup (18). Others have suggested optimum outcomes are achieved if the drain is removed on or before POD three. In a multicentre retrospective study, Zorbas et al. (n=1,066) found this was associated with reduced major morbidity (OR 2.03, P<0.001), POPF (OR 6.76, P<0.001), overall morbidity (OR 2.13, P<0.001) and organ space infection (OR 2.46, P=0.001) (19). Mortality rates were unaffected (19). Those with POD one DFA \geq 5,000 IU were excluded. In another large, retrospective study, Beane et al. (n=2,698) matched patients with a POD one DFA of <5,000 IU who underwent drain removal by (and including) POD three (n=580) to patients whose drain was removed after POD three. The former had reduced overall morbidity (35.3% vs. 52.3%, P<0.05), POPF (0.9% vs. 7.9%, P<0.05), and length of stay (6 vs. 8 days, P<0.05) (20). The authors concluded that clinical outcomes were best when POD one DFA was <5,000 IU and drains were removed on or before POD

three (20). It is worth noting that just 21.5% of the included patients had a POD one DFA recorded. However, this was associated with shorter time to drain removal (P<0.01). In a single centre RCT, Dai *et al.* randomly assigned patients to either early drain removal (POD three) or standard removal (POD five), providing DFA was <5,000 IU on PODs one and three, and daily drain output was <300 mL. The former had reduced major morbidity (OR 0.31, P=0.039), and POPF rates was similar (21). This study also included distal pancreatectomy cases. The authors concluded that a further multicentre study with a larger sample size which only considers PD would be desirable to obtain higher powered results (21).

Other authors have suggested that serum C-reactive protein (CRP) level should be considered prior to drain removal. In a single centre, prospective study, Iwasaki et al. (n=300) concluded that drain removal on POD three was safe provided DFA was <350 IU and CRP was <140 mg/L (22). Fifty-percent of the patients included met these criteria (22). In another single centre, prospective trial, Taniguchi et al. (n=198) found a soft pancreas intraoperatively (OR 6.3, P<0.001), positive drain fluid culture on POD one (OR 2.7, P=0.026), and CRP \geq 130 mg/L on POD four (OR 3.6, P=0.019) were all independent predictors of CR-POPF (P<0.05) (23). The authors concluded that drain removal on POD four can be considered in the absence of these factors. Ninety-two percent of patients in the validation cohort met these criteria in whom incidence of CR-POPF was 5.6% (23).

Nasogastric tube

Traditionally, PD patients would leave theatre with a NG tube in place. This was thought to reduce rates of patient discomfort, wound dehiscence, anastomotic leakage, and respiratory morbidity (24). However, there is no strong evidence to support this and some authors argue this could be detrimental. Although mainly based on the findings of colorectal studies, there is evidence to suggest that patients who undergo abdominal surgery should not routinely have a NG tube placed (25). A MA from 1995 by Cheatham et al. (26 studies, n=3,964) suggested elective laparotomy patients managed with selective (rather than routine) NG tube placement had reduced rates of atelectasis (RR 0.46, 0.001) and pneumonia (RR 0.49, P<0.0001) (26). The authors concluded that, although these patients may be more likely to develop abdominal distention or vomiting, this is not associated with additional morbidity or increased length

of stay (26). A SR from 2005 by Nelson *et al.* (28 studies, n=4,194) found routine NG tube placement was associated with increased interval to first flatus (MD 0.5 days, P<0.001) and increased incidence of respiratory morbidity (RR 1.35, P=0.07), although the latter was not quite significant (27). The authors concluded that selective NG placement in high-risk patients is more appropriate (27). These findings have been validated by a more recent MA from 2011 (seven studies, n=1,416) (28).

Specific to pancreatic resection, there is no strong evidence to suggest that routine gastric decompression is indicated. In a single centre prospective trial, Kunstman et al. (n=250) studied the outcomes of two consecutive series, the first routinely had a NG tube placed intraoperatively which was maintained until clinically indicated. The second did not routinely have a tube placed and only received a NG tube if they required prolonged endotracheal intubation or if they developed a clinical indication for a tube. The latter tolerated a liquid (3.7 vs. 7.4 days, P<0.001) and solid diet (MD 4.9 vs. 9.2 days, P<0.001) sooner, had lower rates of DGE (8.0% vs. 18.4%, P=0.02) and shorter length of stay (6 vs. 7 days, P<0.001) (29). No difference was observed in terms of respiratory morbidity (29). Other recent studies have reached similar conclusions (24,30,31). Following a recent MA, Gao et al. (six studies, n=940), also concluded that routine gastric decompression did not improve clinical outcomes (32). Routine decompression was associated with higher incidence of DGE (OR 5.45, P<0.001), longer length of stay (MD 5.4 days, P=0.04) and higher perioperative mortality (OR 1.53, P=0.03) (32). Rates of overall morbidity, major morbidity, NG tube reinsertion and POPF were all unaffected. Whilst all six included studies employed a nonrandomised design, the results failed to show any benefit of routine gastric decompression. The authors argue a welldesigned RCT is indicated (32).

Discussion

The use of prophylactic intraperitoneal drainage following PD is a complex issue and one that remains controversial. Drains can assist with the early diagnosis of anastomotic leakage and postoperative bleeding, and may reduce the incidence of intra-abdominal collections. However, they are an infection risk, are uncomfortable for patients and can hinder mobility in the early postoperative period. Some authors have suggested that drains may contribute towards postoperative bleeding or disrupt newly formed anastomoses in rare circumstances. Concerning routine

versus selective drainage, three of the five included studies concluded that prophylactic drainage correlated with reduced perioperative mortality whilst two did not observe this. This is likely as early diagnosis of anastomotic leakage or postoperative bleeding results in timely intervention; however, this is assumed. Since the included studies were mostly non-randomised, this effect may be explained by surgeons electing not to place drains in low-risk patients. Two of the three included MA looked at five or fewer studies and the remaining MA considered data from mostly retrospective, non-randomised studies. The two large, multicentre studies included were retrospective and neither considered important confounding variables (e.g., patient comorbidities) or complications occurring after 30 days. A prospective, randomised study would potentially allow the identification of the sub-set of low-risk patients in whom a drain may not be necessary and the sub-set of high-risk patients in whom a drain would be beneficial.

Whether prophylactic drainage is a cause of additional morbidity or merely an association is unknown. Two of the five included studies suggest routine drainage is associated with increased overall morbidity whereas two did not observe this. One suggested this resulted in decreased overall morbidity. A prospective, randomised study would shed light on this. Whether prophylactic drainage is associated with CR-POPF is also controversial. Two of five included studies observed this effect whereas three found no association. Crucially, none of the included studies found prophylactic drainage decreased the incidence of CR-POPF.

None of the included studies suggested that patients who did not receive a drain had a higher rate of radiologicguided drainage or unplanned return to theatre. Hence, one might argue that on-demand drainage should be performed in those who develop a collection. We would argue against this as one of the key benefits of prophylactic drainage is the early diagnosis of anastomotic failure and PPH. Prophylactic drainage requires no additional procedure and is of minimal detriment to the patient, particularly if the drain is removed in a timely manner. Whilst this likely results in a proportion of patients who receive an unnecessary drain, this seems a reasonable approach.

Whilst most authors advise prophylactic drain placement, the timing of, and conditions for, drain removal is another complex issue. Whilst DFA is a useful tool for diagnosing POPF, drain fluid lipase is unlikely to be of any additional benefit. Although DFA is both sensitive and specific, when it should be performed, and what the cut-off for diagnosing POPF should be, remain debated. The Yang *et al.* MA included mostly prospective studies but these were of small sample size. The authors suggested POD one DFA was more clinically relevant than POD three DFA and suggested a cut-off value of 1,300 IU for diagnosing POPF. However, this included biochemical leaks. The SR by Davidson *et al.* contained mostly small, retrospective studies. Due to the high degree of heterogeneity between the included studies, the authors could not confidently suggest when DFA should be performed or what the threshold for diagnosing POPF should be. The other topical studies mentioned are all retrospective and single centre. They all arrive at contrasting conclusions. Further diagnostic test accuracy studies with pre-specified DFA thresholds and clearly defined reference standards are required as practice is not currently evidence-based.

Whilst most authors support early drain removal and argue this improves outcomes, what constitutes "early" drain removal remains debated. Some authors have suggested it is reasonable to remove drains on POD one providing certain criteria are met, whereas others might not consider this until POD four. Most of the large studies performed suggest drain removal on or before POD three is reasonable providing POD one DFA is <5,000 IU. However, these studies are all retrospective in nature. The prospective studies which have been carried out are all single centre and have small sample sizes. Threshold values for DFA anywhere between 600-5,000 IU have been suggested. Whereas most criteria for drain removal involve DFA only, some authors have suggested that threshold values for CRP and drain output should also be used. A further, multi-centre, prospective, randomised trial comparing outcomes of patients who have their drains removed on PODs one, three or five (providing they met pre-specified criteria) would address this.

PD patients would traditionally leave theatre with a NG tube *in situ*. These are uncomfortable and may affect patient mobilisation. The recent literature suggests routine NG tube placement is not beneficial to patients who undergo elective laparotomy (all types of resection) or PD. Whilst patients without a tube may be more likely to experience abdominal distention or vomiting, this doesn't corelate with additional morbidity and so they should only be used when clinically indicated. This results in reduced time to patients achieving adequate oral diet and reduced length of stay. Although most of the included studies employed a non-randomised design, none suggested that routine gastric decompression was of benefit. A well-designed, multi-centre RCT would validate these findings.

This review has limitations. It is a narrative review rather

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than a formal systematic review so not all the available evidence has been considered. We have attempted to include the most relevant recent studies as outlined in the method section. This article has not aimed to answer a specific research question but aims to provide the reader with a broad overview of the recent evidence on several important topics. We have not considered different types or sizes of drain, or the site of drain placement (we have assumed that most surgeons aim to place a drain adjacent to the pancreatic anastomosis and may elect to place an additional drain next to the hepato-jejunostomy). We have also not considered different sizes of NG tubes.

Conclusions

Prophylactic intraperitoneal drain placement following PD correlates with reduced perioperative mortality and increased overall morbidity. This is mostly based on the findings of retrospective, non-randomised studies. Some authors have argued routine drainage in low-risk patients is unnecessary but this is controversial. Early drain removal should be considered in those with a normal DFA and a low drain output. However, the exact criteria and timing for this remains debated. A randomised trial would address these issues. Routine NG tube placement does not improve outcomes so this should be performed selectively.

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Footnote

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appropriately investigated and resolved.

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