



Is peritoneal drainage essential after pancreatic surgery?

A meta-analysis and systematic review

Lu Huan, MD, Qilin Fei, MD, Huapeng Lin, MD, Lun Wan, MD, Yue Li, MD, PhD*

Abstract

Aim: Our objective is to assess the function of peritoneal drainage, which is placed after pancreatic surgery.

Background: With the medical advancement some study put forward that peritoneal drainage is not the necessary after pancreatic surgery; it cannot improve the complications of postoperation even leading to more infection and so on. However, there is no one study can clear and definite whether omitting the drainage after surgery or not.

Method: Searching databases consist of all kinds of searching tools, such as Medline, The Cochrane Library, Embase, PubMed, etc. All the included studies should meet our demand of this meta-analysis. In the all interest outcomes blow we take the full advantage of RevMan5 to assess, the main measure is odds ratio (OR) with 95% confidence, the publication bias are assessed by Egger test and Begg test.

Result: The rate of postoperative pancreatic fistula (POPF) in no drainage group is much lower than that in routine drainage group (OR=0.47, l^2 =43%, P<.00001). The result of the 2 randomized controlled trials (RCTs) in this pool are almost accord with the former (OR=0.57, l^2 =0%, P=.05). In subgroup the result suggest that the peritoneal drainage can increase the morbidity (OR=0.71, l^2 =15%, P=.0002) after pancreaticoduodenectomy (PD), but reduce the mortality (OR=1.92, l^2 =8%, P=.03) after PD. In distal pancreatectomy (DP) the rate of POPF and clinically relevant pancreatic fistula (CR-PF) is lower without drainage; there is no significant difference in the CR-PF, hospital stay, intra-abdominal abscess, radiologic invention, and the reoperation.

Conclusion: In the current meta-analysis, we cannot make a clear conclusion whether to abandon the routine drainage or not, but from the subgroup we can see something is safer than nothing to routine peritoneal drainage. And the patients who underwent DP can attempt to omit the drainage. But it still needs more RCTs to assess the necessity of drainage.

Abbreviations: CI = confidence interval, CR-PF = clinically relevant pancreatic fistula, DP = distal pancreatectomy, ISGPF = International Study Group on Pancreatic Fistula, MD = mean difference, NRCT = nonrandomized controlled trial, OR = odd ratio, PD = pancreaticoduodenectomy, PF = pancreatic fistula, POPF = postoperative pancreatic fistula, RCT = randomized controlled trial.

Keywords: distal pancreatectomy, meta-analysis, pancreatic surgery, pancreaticoduodenectomy, peritoneal drainage

1. Introduction

Although the pancreatic operation and postoperative management advanced, the rate of postoperative complication in pancreatic surgery still remains high. The lowest rate is 2%, but the highest is 40%.^[1–3] Owing to the distinctiveness of the pancreatic surgery the abdominal drainage is regarded as a customary way, as the drainage can find the early pancreatic

Editor: Shefali Agrawal.

The authors declare that they have no conflict of interest.

Department of Hepatobiliary Surgery, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China.

* Correspondence: Yue Li, Department of Hepatobiliary Surgery, The Second Affiliated Hospital of Chongqing Medical University, 74 Linjiang Road, Yuzhong District, Chongiqng 400010, People's Republic of China (e-mail: Teacher_huan@163.com).

Copyright © 2017 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution-NoDerivatives License 4.0, which allows for redistribution, commercial and non-commercial, as long as it is passed along unchanged and in whole, with credit to the author.

Medicine (2017) 96:51(e9245)

Received: 10 September 2017 / Received in final form: 28 October 2017 / Accepted: 21 November 2017

Acceptea: 21 November 2017

http://dx.doi.org/10.1097/MD.00000000000009245

fistula (PF), hemorrhage, biliary fistula, peritoneal fluid collection, and so on after Whipple. On the contrary, the abdominal drainage can generate the slowly healing of the wound, leading to abdominal infection and postoperative pancreatic fistula (POPF) because of the closed suction system.^[4,5]

Dating back to 1992, Jeekel^[6] reported that there was no significant difference comparing routine drainage group with or without abdominal drainage in the patients who underwent pancreaticoduodenectomy (PD). In 1998 Heslin et al^[7] take the advantage of observational cohort study to consider routine use of the drain is not indispensable. Until a decade later Conlon et al^[8] who completed the first randomized controlled trial (RCT) considered there is no obvious significant difference in the morbidity, mortality, PF, and so forth. Then the surgeons attempted to abandon the abdominal drain in some surgeries. For example Brown et al^[9] considered that the postoperative complications were almost similar in both no drain and routine drain.

Up to now Vanburn, [10] Metthew, [11] Helmut, [12] and Van Buren et al [13] compare the differences between routine drain and without drain successively whose study designs are RCTs. They all aim at assessing the patients who underwent pancreatic surgery with and without routine intraperitoneal drainage. Vanburn [10] considered omission of intraperitoneal drainage made the rate of mortality increase from 3% to 12%, the

proximate RCT Helmut^[12] find in the group of no drain the rate of clinical relevant PF and fistula associated is lower (no drain and with drain PF B/C:11/193, 24/202, P=.030; fistula-associated complications: 25/193, 53/202, P=.0008), the other results are no significant difference. Helmut and his colleagues deem there was no significant difference in the comparison. But whether the omission of abdominal drainage is safe is still unclear. Thus, in this meta-analysis we include all the relevant studies to analyze and assess if prophylactic drainage is indispensable in mortality, morbidity, PF, clinical relevant PF, hospital stay, reoperation, and radiologic intervention (Table 1).

2. Materials and methods

Ethical approval or patient consent was not required because the present study was a review of previous published literatures.

2.1. Searching strategy

We used the following way to search all the literature. We use medical subject headings (MeSH) and keywords, such as drainage (title/abstract), Whipple (title/abstract), pancreaticoduodenectomy (title/abstract), pancreaticoduodenectomy (mesh). In addition we used similar words about drainage such as suction that belongs to the same meaning with different description type. By this way we search from the PubMed, EMBASE, and Cochrane library to confirm the related articles. The words are contacted by AND or OR. What's more we search the relevant literature to assess whether is available to this study (Fig. 1).

2.2. Study selection

Two people (QF and LW) screen the searching studies again and again, if they have divergences other person (LH) reassesses the study. All the eligible studies should meet the following limitations: studies are comparison between abdominal drainage and no drainage after pancreatic surgery; the result include PF at least or more; the definition of PF after 2005 should use International Study Group on Pancreatic Fistula (ISGPF);

(Table 1); maybe in some literature they do not use the drainage but the meaning is as same as drainage, we also adopt them.

2.3. Data extraction

The data extraction which is based on a standardized collection is reviewed by 2 authors (LH and HL) and crosschecks. If the study compares early omission of drainage with late omission of drainage, we should exclude. The following data are my collection: the 6 trials characteristics, which mainly contain the year of publication, the authors, the design of research, the number of patients in each control, study country, the characteristics of operation consist of the number of operators, the characteristics of patients (men or women, age), the interest outcomes (dichotomous outcomes: POPF, CR-PF, morbidity, mortality; continuous outcomes: the length of hospital stay) (Table 2).

2.4. Evaluation of quality

The current meta-analysis include 5 RCTs^[8,10-13] and 8 nonrandomized controlled trials (NRCTs),^[7,16-22] their evaluation of quality are judged by 2 methods, RCT is according to the Cochrane Handbook, NRCT is on the basis of the Newcastle-Ottawa Scale. In the Cochrane Handbook we use low, high, or unclear to assess the quality in 7 fields which consist of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other sources of bias. In the NRCT we grade quality in 3 superior fields which include the selection of research group, group's comparability, and metrical results or exposure (Table 3, Figs. 2 and 3).

2.5. Data synthesis and statistical analysis

We use the Review Manager 5 software to complete data synthesis. In the outcomes of interest only the hospital stay is continuous variable, which is described as mean difference (MD) with 95% confidence interval (CI), the others belong to Dichotomous variables which is described as odd ratios (ORs)

|--|

Author	Mortality	Morbidity	POPF
Conlon	Deaths within 30 days of surgery	NA	Drain output on postoperative day 5 or >30 mL and amylase level >150 IU/L and/or 3 times greater than the serum value
Vanburn	Deaths within 90 days of surgery	Clavien classification[14]	ISGPF
Matthew	NA	NA	ISGPF
Helmut	Deaths within 30 days of surgery	NA	ISGPF
Hesllin	NA	NA	Drain output at a rate of ≥30 mL/days or more and lasting for >7 days
Fisher	Deaths within 30 days of surgery.	Common Terminology Criteria for Adverse Events (CTCAE)	ISGPF
Paulus	NA	NA	ISGPF
Correa-Gallego	Deaths within 90 days of surgery	CTCAE	Clinical signs and symptoms with amylase-rich drainage
			>50 mL/days beyond postoperative day 10
Adham	Deaths within 90 days of surgery	Clavien classification ^[14]	ISGPF
Lim	Clavien classification ^[15]	Clavien classification ^[14]	ISGPF
Mehta	Deaths within 30 days of surgery	Clavien classification ^[14]	ISGPF
Kunstman	NA	Clavien classification ^[14]	ISGPF
George Van Buren	Deaths within 60 days of surgery	CTCAE	ISGPF

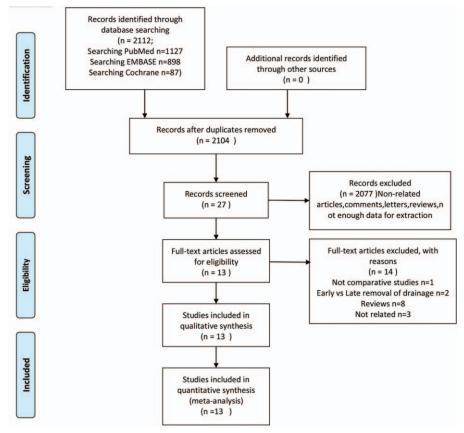


Figure 1. Flow diagram showing the selection of randomized controlled trials.

with 95% CI. To test the heterogeneity 2 researchers (LW and LH) independently affiliate the data into RevMan, when the value I^2 is beyond 50%, it means a high heterogeneity. [23] What's more we exclude the including literature in sequence to test the stability of the results. We use Egger test and Begg test to assess the publication bias (Fig. 4.1–4.3). That we take the literature into subgroup is based on the definition of International Study Group On Pancreatic Fistula (ISGPF) to analyze POPF and compare the PD with distal pancreatectomy (DP). [24] Owning to the number of including studies is <10, there is no funnel plot in the subgroup.

2.6. Outcomes of interest

In the current meta-analysis we include all the relevant literature and contain almost 3776 participants. The primary outcomes are morbidity, mortality, PF, and CR-PF. The secondary outcomes are hospital stay, reoperation, radiologic intervention, and abdominal abscess (Fig. 5). The forest plot of outcomes are presented in the Figure 1, and there are 2 subgroups, 1 is comparing the PF where the definition is defined by ISGPS as shown in Figure 4, the other is comparing all the results between PD and DP as given in Figures 6 and 7.

2.7. Morbidity

The 12 studies that contain 3639 participants all report the morbidity. The study Correa-Gallego (1) belongs to a part of Correa-Gallego et al^[18] whose operation is DP. The result suggests the no drainage is more superior than with abdominal

drainage group (OR = 0.71, I^2 = 54%, P < .00001) (Fig. 1). After removing every study the result does not change at all, indicating the steady of result is fine. Four RCTs in this pool suggest there is no significant difference (OR = 0.94, I^2 = 0%, P = .62) (Fig. 5.1).

2.8. Mortality

In this pool 9 studies are eligible. There is no significant difference between the 2 groups (OR=1.01, I^2 =43%, P=.93). The 4 pooled result of RCTs are in sympathy with the former (OR=1.92, I^2 =9%, P=.09). There is no obvious difference in heterogeneity and the result is stable (Fig. 5.2).

2.9. Postoperative pancreatic fistula

In the 8 studies the result suggest the rate of POPF in no drainage group is much lower than with routine drainage group (OR = 0.47, $I^2 = 43\%$, P < .00001). The result of the 2 RCTs in this pool are almost accord with the former (OR = 0.57, $I^2 = 0\%$, P = .05). There is no heterogeneity and the result is stable (Fig. 5.3).

2.10. Clinically relevant pancreatic fistula

This definition is based on the ISGPF; therefore, there are 10 studies in this pool. The rate of CR-PF in routine drainage is higher than that in the no drainage group (OR=0.64, I^2 =59%, P=.0007). Four RCTs in this pool suggest that there is no valuable difference (OR=0.82, I^2 =69%, P=.30). The sensitive test present there is no significant difference after eliminating the study Mehta^[21] (Fig. 5.4).

Table 2

The characteristics of including studies.

Author	Year	Country	Design	Number of patient	Group	Age	Male vs female	Number of operative method
Conlon	2001	United States	RCT	179	No drainage	69 (33–87)	43:48	PD:66,DP:26
					Drainage	66 (22-81)	46:42	PD:73,DP:15
Vanburn	2013	United States	RCT	137	No drainage	64.3 ± 12.6	38:31	PD:69
					Drainage	62.1 ± 11.7	37:31	PD:68
Matthew	2014	United States	RCT	137	No drainage	NA	NA	PD:69
					Drainage	NA	NA	PD:68
Helmut	2016	Germany	RCT		No drainage	62.5	126:67	PD:193
					Drainage	64.3	130:72	PD:193
Hesllin	1998	United States	OCS	89	No drainage	65 ± 2	32:19	PD:38
					Drainage	65 ± 2	18:20	PD:51
Fisher	2011	United States	OCS	228	No drainage	59 (51-57)	19:40	PD:30, DP:17
					Drainage	63 (53-72)	78:101	PD:123, DP:56
Paulus	2012	United States	OCS	59	No drainage	58 (52-68)	NA	DP:30
					Drainage	52 (44-66)	NA	DP:39
Correa-Gallego	2013	United States	OCS	PD:739	No drainage	NA	NA	PD:353
					Drainage	NA	NA	DP:386
				DP:350	No drainage	NA	NA	DP:196
					Drainage	NA	NA	DP:154
Adham	2013	France	OCS	242	No drainage	66.5 (19-85)	61:51	PD:69, DP:37
					Drainage	61.5 (20-85)	66:64	PD:79, DP:29
Lim	2013	France	OCS	54	No drainage	62 (38-78)	8:19	PD:27
					Drainage	62 (40-76)	8:19	PD:27
Mehta	2013	United States	OCS	709	No drainage	62.5	232:236	PD:458
					Drainage	60	130:121	PD:251
Kunstman	2017	United States	OCS	106	No drainage	62.2 ± 12.4	33:20	PD:53
					Drainage	63.3 ± 10	31:22	PD:53
George Van Buren	2017	United States	RCT	344	No drainage	60 (47-73)	67:103	DP:170
					Drainage	61 (49–73)	72:102	DP:174

DP = distal pancreaticoduodenectomy, NA = not available, OCS = observational cohort study, PD = pancreaticoduodenectomy, RCT = randomized controlled trial.

Table 3

Assessable quality of including studies.

Author	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Comparability between the 2 cohorts	Assessment of outcome	Length of follow-up
Heslin	Potential selection bias	Same patient base	Surgical record	No restriction/matching	Independent assessment	not mention
Paulus	Representative	Same patient base	Surgical record	No restriction/matching	Surgical record	not mention
Fisher	Representative	Different patient base	Surgical record	No restriction/matching	Surgical record	30 days
Adham	Representative	Same patient base	Surgical record	No restriction/matching	Surgical record	90 days
Correa-Gallego	Representative	Same patient base	Surgical record	No restriction/matching	Surgical record	90 days
Metha	Representative	Same patient base	Surgical record	No restriction/matching	Surgical record	90 days
Kunstman	Representative	Same patient base	Surgical record	No restriction/matching	Surgical record	Not mention
Case-control study	Representativeness of the exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Comparability between the two cohorts	Assessment of outcome	Definition of controls and cases
Lim	Potential selection bias	Hospital control	Surgical record	One to one matching	Surgical record	Surgical record

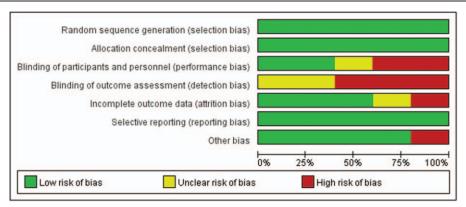


Figure 2. Risk bias of graph. Each risk of bias item presented as percentages across all of the included trials, which indicated the proportion of different level risk of bias for each item.

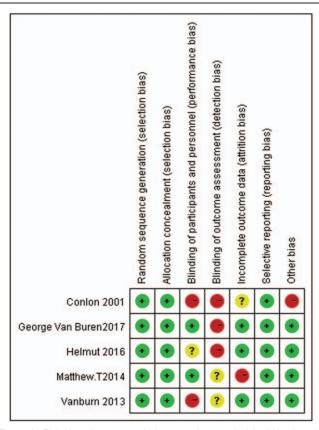


Figure 3. Risk bias of summary. Judgments about each risk of bias item for each included trials. Green indicates low risk of bias. Yellow indicates unclear risk of bias. Red indicates high risk of bias.

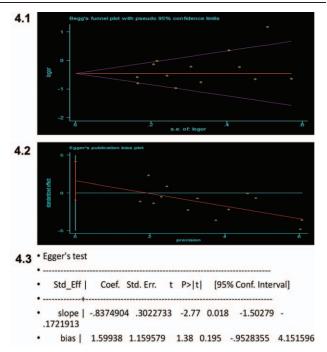


Figure 4. Begg test and Egger test. Considering the $P\!>$.05 the results suggest there is no publication bias.

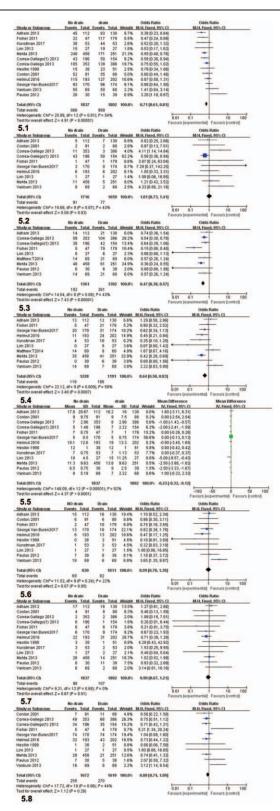


Figure 5. Forest plots of clinical outcomes in patients with peritoneal drainage vs those without drainage after pancreatic resection. The effect of prophylactic abdominal drainage on 5.1: mortality; 5.2: morbidity; 5.3: postoperative pancreatic fistula (POPF); 5.4: clinically relevant pancreatic fistula (CR-PF); 5.5: length of hospital stay; 5.6: abdominal abscess; 5.7: interventional radiology drainage; 5.8: reoperation.

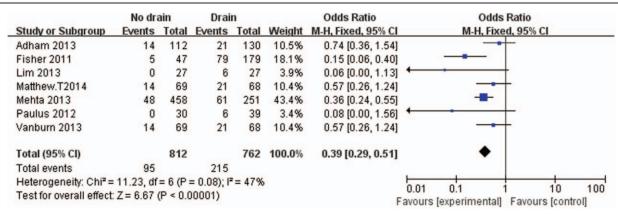


Figure 6. Forest plots of clinical outcomes in patients with peritoneal drainage vs those without drainage after pancreatic resection applying the definition of International Study Group on Pancreatic Fistula (ISGPF).

2.11. Hospital stay

In this pool there are 12 studies. The result suggests that the hospital stays of no drainage group is much shorter than that of with routine drainage (MD=-0.23, $I^2=92\%$, P<0.00001). Four RCTs in this pool suggest that there is no significant difference in both the groups (MD=0.01, $I^2=0\%$, P=.91). After eliminating the Correa-Gallego and Correa-Gallego (1) the result is accord with the RCTs. The test of the result is stable (Fig. 5.5).

2.12. Abdominal abscess

Ten studies are included in this pool. The result suggests that there is no significant difference between the 2 groups (OR = 0.99, $I^2 = 22\%$, P = .95). After limitation of RCTs the result is the same as the former (OR = 1.06, $I^2 = 67\%$, P = .78). The result is stable and there is no obvious heterogeneity (Fig. 5.6).

2.13. Reoperation

Twelve studies are included in this pool. The result suggest there is no significant difference between the 2 groups (OR = 0.90, I^2 = 0%, P = .51). After limitation of RCTs the result is the identical to the former (OR = 0.76, I^2 = 17%, P = .22). The result is stable and there is no obvious heterogeneity (Fig. 5.7).

2.14. Radiologic intervention

There is no significant difference in the rate of radiologic intervention (OR=0.89, I^2 =44%, P=.26). Four RCTs in this pool suggest there is no valuable difference (OR=0.98, I^2 =60%, P=.88). The result is stable and there is no obvious heterogeneity (Fig. 5.8).

2.15. Subgroup

(a). In 1 subgroup we only include the definition of PF by ISGPF to assess whether the definition will make an influence on the POPF. Seven studies are included. We found that no drainage group is superior to the routine drainage group (OR = 0.39, I^2 = 47%, P < 0.00001) (Fig. 6).

(b). In the other subgroup we compare all the interest results of different surgical method which are between PD and DP.

2.16. (b.1) The patients who underwent pancreaticoduodenectomy

We consider that routine abdominal drainage increase the morbidity (OR=0.71, I^2 =15%, P=.0002), POPF (OR=0.47, I^2 =10%, P<.00001), and CR-PF (OR=0.51, I^2 =65%, P=.0001), but it reduces the mortality (OR=1.92, I^2 =8%, P=.03. There is no significant difference in hospital stay (MD=-0.53, I^2 =81%, P=.12), intra-abdominal abscess (OR=1.04, I^2 =64%, I^2 =90), radiologic intervention (OR=0.84, I^2 =31%, I^2 =18), reoperation (OR=0.99, I^2 =0%, I^2 =94) (Fig. 7.1–7.8).

2.17. (b.2)The patients who underwent distal pancreatectomy

The result suggest that the peritoneal drainage can reduce the POPF (OR = 0.57, I^2 = 46%, P = .02) and CR-PF (OR = 0.52, I^2 = 43%, P = .03), and there is no significant difference in morbidity (OR = 0.90, I^2 = 79%, P = .47), mortality (OR = 0.66, I^2 = 64%, P = .08), hospital stay (MD = -1.47, I^2 = 98%, P = .09), intraabdominal abscess (OR = 0.91, I^2 = 0%, P = .78), radiologic intervention (OR = 0.95, I^2 = 28%, P = .74), and reoperation (OR = 0.73, I^2 = 0%, P = .40) (Fig. 8.1–8.8).

2.18. Publication bias

Owing to the data in which the value P is beyond .05 we consider there is no publication bias (Fig. 4.1–4.3)

3. Discussion

In the current meta-analysis although the rate of POPF in no drainage group is much lower than that in group with routine drainage (OR=0.47, I^2 =43%, P<.00001). And in subgroup the result suggest that the peritoneal drainage can increase the morbidity (OR=0.71, I^2 =15%, P=.0002) after PD. However, the abdominal drainage can reduce the mortality (OR=1.92, I^2 =8%, P=.03) after PD. There is no significant difference in the morbidity, mortality, CR-PF, hospital stay, intra-abdominal abscess, radiologic invention, and the reoperation. Therefore it's necessary to place a peritoneal drainage after PD; there is not a compelling evidence which imply we can omit peritoneal drainage after pancreatic surgery.

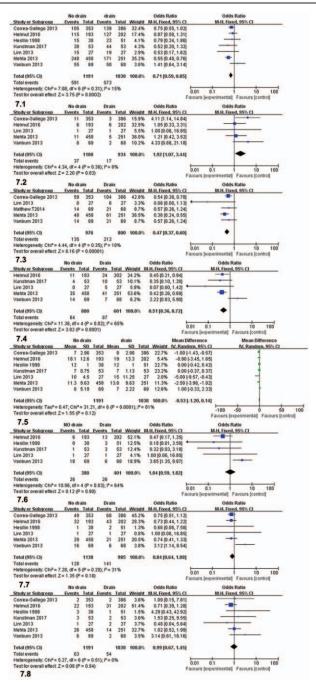


Figure 7. Forest plots of subgroup analysis of patients who underwent PD. For patients who underwentn the effect of prophylactic abdominal drainage on 7.1, mortality; 7.2, morbidity; 7.3, postoperative pancreatic fistula (POPF); 7.4, clinically relevant pancreatic fistula (CR-PF); 7.5, length of hospital stay; 7.6, abdominal abscess; 7.7, interventional radiology drainage; 7.8, reoperation.

As early as 1991 Monson et al^[25] found the drainage may be connect to the wound infections and subhepatic collections after cholecystectomy. Then Jeekel^[6] reported there was no significant difference comparing routine drainage group with without abdominal drainage in the patients who were underwent PD. One decade later Conlon et al^[8] complete the first randomize clinical trial after PF the suggested the routine drainage may lead to more intra-abdominal abscess and fistulas. Considering the RCTs were small number, some studies included some NRCTs, for example the Wang et al^[26] deemed the routine abdominal

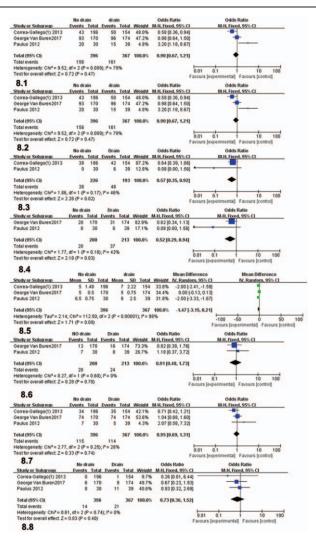


Figure 8. Forest plots of subgroup analysis of patients who underwent DP. For patients who underwent DP, the effect of prophylactic abdominal drainage on 8.1, mortality; 8.2, morbidity; 8.3, postoperative pancreatic fistula (POPF); 8.4, clinically relevant pancreatic fistula (CR-PF); 8.5 length of hospital stay; 8.6, abdominal abscess; 8.7, interventional radiology drainage; 8.8, reoperation.

drainage was still necessary although the intra-abdominal drainage could reduce the complication rates instead of increasing the mortality, Dou et al^[27] support the point of Wang. In the latest Helmut^[12] accomplished a relatively large number of randomize clinical trials and considered the routine abdominal drainage was not necessary, comparing the routine drainage group without drainage group is much better in PF after PD. And Cheng et al^[28] included 3 RCTs to analyze whether the abdominal drainage is necessary after pancreatic surgery or not, but they did not make a clear decision. Therefore, the RCTs are still a small number and cannot provide a high evidence. Up to now Van Buren^[13] complete another RCT with a high quality, considering it's feasible to abandon the peritoneal drainage after DP. Proximate studies almost consider omission of drainage is seemed feasible. However, in this current meta-analysis we consider that drainage cannot be omitted in some respects.

Up to now only 5 RCTs have reported the comparison between routine abdominal drainage and without drainage after pancreatic surgery. Meanwhile, almost 8 NRCTs have been reported this comparison today. Considering prospective observational

studies which use the identical characteristics are receivable, ^[29] in the present meta-analysis we include 2 different designed studies which are consist of RCTs and NRCTs, what's more, we perform another subgroup to compare the PD with DP.

In morbidity we find without drainage group seems much safer than the routine drainage group. Although the result is stable, restricting only RCTs there is no significant difference. The study design is not the most important factor, even the NRCTs which should be seemed as a supplement for RCTs can provide a same significance of RCTs. [30,31] The reason why the result is presented like this may be the RCTs which have a too small number, the NRCTs can provide a low evidence in our opinion. But whether the rate of morbidity in no drainage group is lower than the routine drainage group is still debated and it needs more high-quality RCTs, which compare the without drainage with routine drainage in the future.

In mortality there is no significant difference between the group without drainage and the routine drainage group. We note that in the PD subgroup the peritoneal drainage increase the morbidity, POPF, and CR-PF, but reduce the mortality. Almost postoperative complications result in delaying the time of postoperative recovery, even increasing the rate of mortality especially for POPF. We have no origin to clear whether some high risk factors (such as pancreatic gland texture, pancreatic duct diameter, etc) make a significant difference on the mortality. Furthermore, different studies follow the patients for the mortality to 30 or 60 or 90 days, on account of the duration some studies cannot definite the true mortality after PD. This point is the same as Vanburn. In the prospective studies the risk factors should be concerned to analyze necessity of peritoneal drainage after PD.

In the pool of POPF we find the without drainage group is more advanced than the routine drainage group, and the RCTs group shows the same result. However, there is no significant difference in the pool of CR-PF. Considering the definition of POPF has many different methods we set a subgroup in which the definition of POPF is defined by ISGPF to assess the result specially. And there is no heterogeneity and the result is stable. We consider there are several factors as below. Closed-suction drainage may have a high negative pressure and make the tissue injured, resulting in the POPF; there is no obvious clinical manifestation in the grade A POPF when there is no abdominal drainage, and it's unnecessary for patients to make a radioactive examine, it's hard to perceive, leading to some studies did not include the grade A POPF. There are some anastomosis in PD, PF almost is affected by some independent factors, such as body mass index, pancreatic duct diameter, pancreatic gland texture, intraoperative blood loss, and pathology. [11,32] In the current meta-analysis only 1 RCT Matthew refer to the above and grade that which is based on Callery et al. [33] Matthew considered that the drain can reduce the rate of CR-PF, but far too many risk factors will affect the rate of POPF, it still needs more RCTs which utilize the risk score or analyze these independent risk factors.

Intra-abdominal drainage seems as a common practice after pancreatic surgery, it can perceive the fistula and hemorrhage which has an great influence on the mortality and abscess, what's more, the drainage can preclude the POPF from getting much worse complication which can increase the mortality. [1] But Allen et al [34] did not consider the abdominal drainage would increase the POPF and selectively using abdominal drainage is feasible. In addition Bassi et al [15] suggested that the patients whose score of PF were low should remove the drainage early, because protracted removing drainage would increase the rate of

postoperative complication. The number of comparing drainage with no drainage is still small, it needs numerous RCTs.

With the development of medicine and postoperative management the complication will reduce, the more RCTs which assess the advantages and disadvantages of abdominal drainage will be proceeding. And more qualitative studies which utilize risk score of PF determine whether abdominal drainage after pancreatic surgery is placed or not.

4. Limitations

Several limitations are presented in this meta-analysis. First, most of the including studies are NRCTs, on earth RCT is seemed as criterion standard, the major difference between RCTs and NRCTs is the study design, the groups of NRCTs which are based on the results sometimes contain much subjective factors, so in this meta-analysis we specially probe into the result restrictive RCT group, finding the majority of the results are identified with general results and there is no obvious heterogeneity and publication bias. Second, several different definitions of POPF are in current meta-analysis; in addition, we set a subgroup to definite the different definitions do not make an influence on the results. Third, POPF which are grade A is not recorded in detail because of imperceptible symptom in no drainage group and the researchers have no reason to radioactive examination. Fourth, we have no data of long-term benefit or disadvantage of drainage so far (e.g., effect of long-term survival after cancer surgery). Moreover in this present meta-analysis surgical method can perform in different ways, for example, in PD the method of pancreaticojejunostomy includes end-to-end, end-to-side, invaginate, duct-to-mucosa, binding, etc. Fifth, only RCT^[11] applied the Fistula Risk Score for the prediction of clinically relevant fistula, we are unable to analyze the data. In the future it needs more integrated information.

5. Conclusion

Increase of morbidity in PD group and no significant change in DP group comparing less mortality in PD group and no significant change in DP group if one left a drain behind after pancreas surgery. Namely we consider omission of peritoneal drainage remains high risk in PD, in DP it seems to abandon the peritoneal drainage. However, we still need more advanced RCTs (e.g., applying the Fistula Risk Score Calculations to studies).

References

- Yamashita S, Ishizawa T, Ichida A, et al. Advantages and disadvantages of prophylactic abdominal drainage in distal pancreatectomy. World J Surg 2016;40:1226–35.
- [2] De Carlis L, Ferla F, Di Sandro S, et al. Pancreatico-duodenectomy and postoperative pancreatic fistula: risk factors and technical considerations in a specialized HPB center. Updates Surg 2014;66:145–50.
- [3] Zhang T, Xu J, Wang T, et al. Enucleation of pancreatic lesions: indications, outcomes, and risk factors for clinical pancreatic fistula. J Gastrointest Surg 2013;17:2099–104.
- [4] Grobmyer SR, Graham D, Brennan MF, et al. High-pressure gradients generated by closed-suction surgical drainage systems. Surg Infect (Larchmt) 2002;3:245–9.
- [5] Berliner SD, Burson LC, Lear PE. Intraperitoneal drains in surgery of the colon. Clinical evaluation of 454 cases. Am J Surg 1967;113:646–7.
- [6] Jeekel J. No abdominal drainage after Whipple's procedure. Br J Surg 1992;79:182.
- [7] Heslin MJ, Harrison LE, Brooks AD, et al. Is intra-abdominal drainage necessary after pancreaticoduodenectomy? J Gastrointest Surg V 2 1998;373–8.

- [8] Conlon KC, Labow D, Leung D, et al. Prospective randomized clinical trial of the value of intraperitoneal drainage after pancreatic resection. Ann Surg 2001;234:487–93.
- [9] Brown SR, Seow-Choen F, Eu KW, et al. A prospective randomised study of drains in infra-peritoneal rectal anastomoses. Techn Coloproctol 2001;5:89–92.
- [10] Van Buren G 2nd, Bloomston M, Hughes SJ, et al. A randomized prospective multicenter trial of pancreaticoduodenectomy with and without routine intraperitoneal drainage. Ann Surg 2014;259:605–12.
- [11] McMillan MT, Fisher WE, Van Buren G, et al. The value of drains as a fistula mitigation strategy for pancreatoduodenectomy: something for everyone? Results of a randomized prospective multi-institutional study. J Gastrointest Surg 2015;19:21–30.
- [12] Witzigmann H, Diener MK, Kienkotter S, et al. No need for routine drainage after pancreatic head resection: the dual-center, randomized, controlled PANDRA trial (ISRCTN04937707). Ann Surg 2016;264: 528–37.
- [13] Van Buren G 2nd, Bloomston M, Schmidt CR, et al. A prospective randomized multicenter trial of distal pancreatectomy with and without routine intraperitoneal drainage. Ann SurgV 266 2017;421–31.
- [14] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13.
- [15] Bassi C, Molinari E, Malleo G, et al. Early versus late drain removal after standard pancreatic resections: results of a prospective randomized trial. Ann Surg 2010;252:207–14.
- [16] Fisher WE, Hodges SE, Silberfein EJ, et al. Pancreatic resection without routine intraperitoneal drainage. HPB (Oxford) 2011;13:503–10.
- [17] Paulus EM, Zarzaur BL, Behrman SW. Routine peritoneal drainage of the surgical bed after elective distal pancreatectomy: is it necessary? Am J Surg 2012;204:422–7.
- [18] Correa-Gallego C, Brennan MF, D'Angelica M, et al. Operative drainage following pancreatic resection: analysis of 1122 patients resected over 5 years at a single institution. Ann Surg 2013;258:1051–8.
- [19] Adham M, Chopin-Laly X, Lepilliez V, et al. Pancreatic resection: drain or no drain? Surgery 2013;154:1069–77.
- [20] Lim C, Dokmak S, Cauchy F, et al. Selective policy of no drain after pancreaticoduodenectomy is a valid option in patients at low risk of pancreatic fistula: a case-control analysis. World J Surg 2013;37:1021–7.

- [21] Mehta VV, Fisher SB, Maithel SK, et al. Is it time to abandon routine operative drain use? A single institution assessment of 709 consecutive pancreaticoduodenectomies. J Am Coll Surg 2013;216:635–42.
- [22] Kunstman JW, Starker LF, Healy JM, et al. Pancreaticoduodenectomy can be performed safely with rare employment of surgical drains. Am Surg 2017;83:265–73.
- [23] Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60.
- [24] Bassi C, Dervenis C, Butturini G, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 2005;138:8–13.
- [25] Monson JR, Guillou PJ, Keane FB, et al. Cholecystectomy is safer without drainage: the results of a prospective, randomized clinical trial. Surgery 1991;109:740–6.
- [26] Wang YC, Szatmary P, Zhu JQ, et al. Prophylactic intra-peritoneal drain placement following pancreaticoduodenectomy: a systematic review and meta-analysis. World J Gastroenterol 2015;21:2510–21.
- [27] Dou CW, Liu ZK, Jia YL, et al. Systematic review and meta-analysis of prophylactic abdominal drainage after pancreatic resection. World J Gastroenterol 2015;21:5719–34.
- [28] Cheng Y, Xia J, Lai M, et al. Prophylactic abdominal drainage for pancreatic surgery. Cochrane Database Syst Rev 2016;10:CD010583.
- [29] Jee YM, Bak JS, Weinlander E, et al. Comparing nonrandomized observational studies with randomized controlled trials in cervical disc arthroplasty: a meta-analysis. Spine (Phila Pa 1976) 2016;41:419–28.
- [30] Furlan AD, Tomlinson G, Jadad AA, et al. Examining heterogeneity in meta-analysis: comparing results of randomized trials and nonrandomized studies of interventions for low back pain. Spine (Phila Pa 1976) 2008;33:339–48.
- [31] Naudet F, Maria AS, Falissard B. Antidepressant response in major depressive disorder: a meta-regression comparison of randomized controlled trials and observational studies. PLoS One 2011;6:e20811.
- [32] Hu BY, Wan T, Zhang WZ, et al. Risk factors for postoperative pancreatic fistula: analysis of 539 successive cases of pancreaticoduodenectomy. World J Gastroenterol 2016;22:7797–805.
- [33] Callery MP, Pratt WB, Kent TS, et al. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. J Am Coll Surg 2013;216:1–4.
- [34] Allen PJ, Gonen M, Brennan MF, et al. Pasireotide for postoperative pancreatic fistula. N Engl J Med 2014;370:2014–22.