Systematic Review and Meta-Analysis: Role of Negative Pressure Wound Therapy in Preventing Surgical Site Infections after Pancreaticoduodenectomy

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Abstract

Background Surgical site infection (SSI) after pancreaticoduodenectomy is associated with significant morbidity, increased hospital stays, delay in adjuvant treatment, and overburden on hospital resources. There is no consensus in the management of these wounds.

Methods We performed a systematic review. We searched the PubMed, Embase, and Scopus on March 23, 2022 for studies reporting on negative pressure wound therapy (NPWT) in patients operated on with pancreaticoduodenectomy. We included all studies that reported the comparative outcomes of NPWT in patients undergoing pancreaticoduodenectomy. All data were extracted by two reviewers separately. The pooled odds risk of SSI was calculated using the metabin command and Mantel–Haenszel approach.

We assessed the risk of bias using Joanna Briggs Institute's critical appraisal tool for cohort studies.

Results Four studies with 878 participants were included. The pooled odds ratio for SSI was lower in the NPWT group as compared with standard care (0.36; 95% confidence interval [CI]: 0.24–0.54; $I^2 = 0$). The pooled odds ratio of organ space infection was 0.40 (95% CI: 0.24–0.67; $I^2 = 0$) on the basis of three studies (484 participants). We did not perform any subgroup analyses because of lack of heterogeneity in the reported results and limited number of studies.

Conclusion Pancreaticoduodenectomy is associated with high risk of SSI. The use of prophylactic NPWT after pancreaticoduodenectomy is associated with decreased risk of SSI. The cost–benefit ratio of NPWT over standard care requires further comparative study.

Keywords
- wound infection
- SSI
- negative pressure wound therapy
- pancreaticoduodenectomy
- surgery

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Introduction

Pancreaticoduodenectomy (PD) is a commonly performed surgery for periampullary and pancreatic head tumors. In the last few decades, with improvements in the perioperative care and surgical techniques, a significant improvement in surgical outcomes has been noted.[1] However, surgical site infection (SSI) following PD is a major morbidity and associated with increased cost of treatment, hospital stay, delay in adjuvant treatment, and overburden on health resources.[2,3]

The reported incidence of SSI after PD is 26 to 60%.[3–5] The various factors including high body mass index (BMI), poor nutrition, prolonged surgery, blood loss, bactibilia, and biliary stenting have been implicated in the occurrence of SSI after PD.[6,7] Various attempts, like use of bile culture-based antibiotics, bile duct clamping after transection (to prevent uncontrolled spillage of infected bile), wound protectors during surgery, and use of negative pressure wound therapy (NPWT), have been made to decrease the risk of SSI.[5,8,9] NPWT may decrease the risk of SSI by decreasing the accumulation of infected fluid at the wound site. There is abundant literature on the use of NPWT on various surgical wounds after laparotomy with promising results.[10,11]

However, there is limited and largely unclear literature on the use of NPWT after PD. Considering the aforementioned controversies, we planned a systematic review to determine the impact of the use of NPWT on SSIs after PD.

Methods

We performed the present systematic review in accordance with the guidance provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement 2020 (33782057).

Search and Screening

Electronic databases were searched for relevant studies on March 23, 2022. We searched the PubMed, Embase, and Scopus databases using the keywords "pancreaticoduodenectomy" OR "Whipple operation" and combined with the operator AND with the keywords "vacuum closure" OR "negative pressure therapy." The detailed strategy is shown in ►**Supplementary Table S1** (available in the online version). The results were combined and duplicates were removed. The remaining articles were screened for the title and abstract by two reviewers independently (HS and KG). The eligible titles then underwent a full text screening by both the reviewers and those with relevant data were selected.

Study Selection

We included all studies that reported the comparative outcomes of NPWT in patients undergoing PD. We included studies irrespective of the study type (randomized trials, prospective, or retrospective observational studies), publication type, intervention type (NPWT type and duration), language of publication, and geographic location of the work. The studies should have reported an SSI in patients undergoing NPWT or standard care after PD. The other relevant outcome includes organ space infection (OSI), hospital stay, reoperation, and mortality. However, we excluded single arm studies, studies that did not have relevant outcomes, or studies that did not provide original data (reviews, comments, etc.).

Data Extraction

We extracted data regarding the study type, geographic location, number of patients, details of surgery, mean age and gender of the study population, and relevant outcomes (SSI and OSIs, duration of hospitalization, reoperation, or mortality). All data were extracted by two reviewers separately.

Analysis

The analysis was performed using R version 4.2.1. The base package was used with the additional "meta" and "metafor" packages. The pooled odds risk of SSI was calculated using the metabin command and Mantel–Haenszel approach. The heterogeneity was considered to be high if the I^2 values were greater than 50. We planned to address any heterogeneity using subgroup analysis (type of study and type or duration of NPWT) if sufficient studies were available.

Risk of Bias

We assessed the risk of bias using the Joanna Briggs Institute (JBI) critical appraisal tool for cohort studies.

We planned to assess the publication bias using the funnel plot and Egger's test if more than 10 studies were available.

Results

Screening and Selection

After the database search, we identified 775 titles, of which 63 were duplicates. Of the remaining 712 titles that underwent a title and abstract screening, 703 were excluded. Of the remaining nine articles that underwent full text screening, five were excluded for various reasons (►**Supplementary Table S2**, available in the online version). The process of study screening is shown in the PRISMA flowchart (►**Fig. 1**). ►**Table 1** shows the included studies with the characteristics of the included population.

Outcomes after NPWT versus Standard Care

Four studies with 878 participants reported the rates of SSI after PD. The pooled odds ratio for SSI was lower in the NPWT group as compared with the standard care group (0.36; 95% confidence interval [CI]: 0.24–0.54; $I^2 = 0$; ►**Fig. 2**). The pooled odds ratio of OSI was 0.40 (95% CI: 0.24–0.67; $I^2 = 0$) on the basis of three studies (484 participants; ►**Fig. 3**).

Analysis for length of hospital stay (2 studies; ►**Supplementary Table S3**, available in the online version) and mortality was not performed because of the absence of data from adequate numbers of studies.

Risk of Bias and Heterogeneity

The risk of bias as assessed by JBI critical appraisal tool (►**Supplementary Table S4**, available in the online version). No scores were provided as suggested by the JBI. No analysis for publication bias was performed as only four studies were available. We did not perform any subgroup analyses because

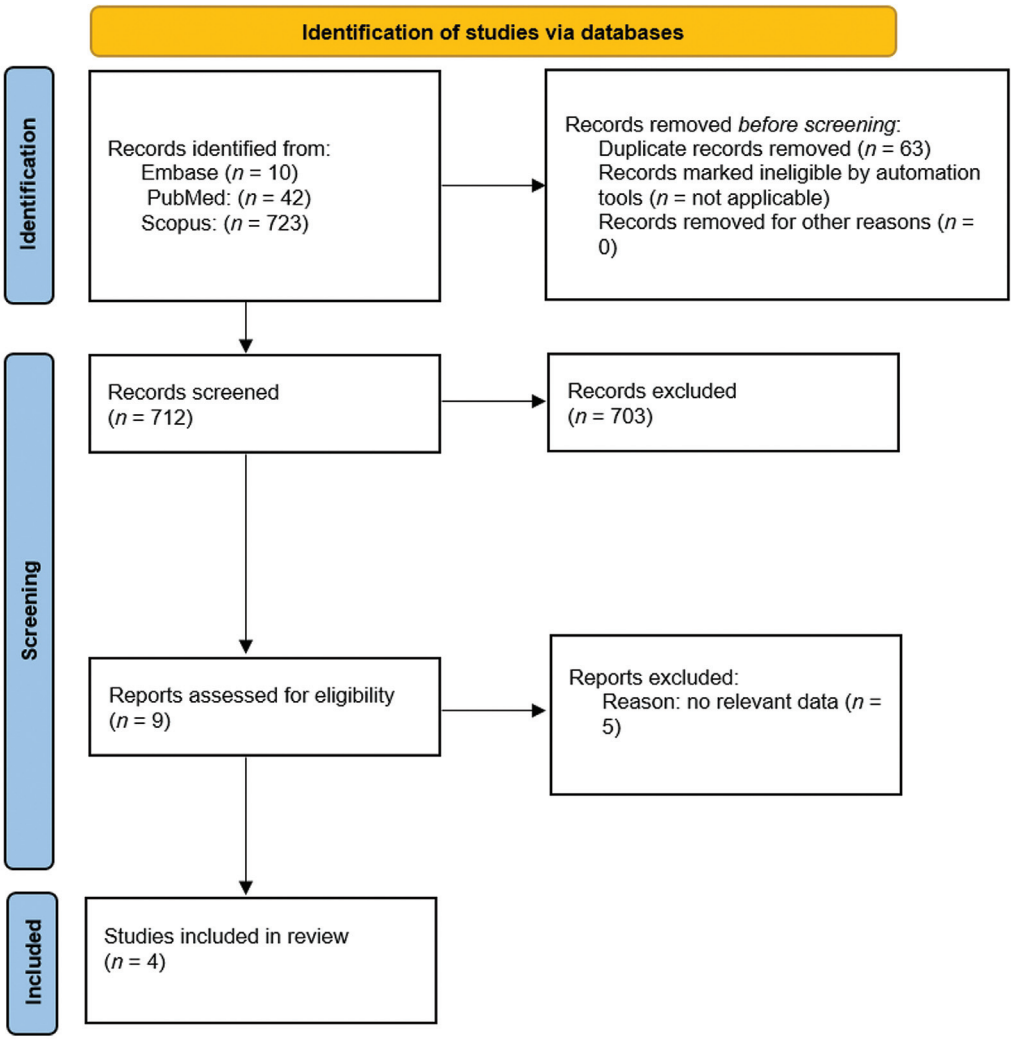

Fig. 1 The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart showing the process of screening and selection of eligible studies.

of lack of heterogeneity in the reported results and limited number of studies.

Discussion

The present meta-analysis shows that the use of NPWT after PD is associated with significant decrease in the incidence of SSI. Similarly, the organ space collections were also lower in the NPWT group as compared with the standard care group. The length of hospital stays and mortality were not compared due to lack of adequate comparative study.

The NPWT decreases the SSI by different mechanisms. Due to bile contamination, the wounds after PD are potentially contaminated. The NPWT helps in decreasing the stagnation of the infected fluid in the wound, which is important for growth of bacteria. It also improves the local perfusion at the wound site and decreases inflammatory mediators, which further helps in wound healing.[12] It also promotes wound healing by improving biomechanism and decreasing the tensile forces on the wound.[13]

There are various nonmodifiable factors that are responsible of SSI after PD. These factors include biliary stenting, neoadjuvant treatment, obesity, diabetes mellites, and operative time.[5–7] There is a significant scope of decreasing SSI by doing intervention on surgical incisions. These includes bundle of intervention like appropriate skin preparation, wound protectors, effective wound hemostasis, and specialized dressing like NPWT. The reduction of SSI with the use of NPWT showed consistent results in various studies.[10,11,14,15]

The routine use of NPWT is not in practice after PD due to limited evidence in PD. O'Neill et al[16] evaluated the role of NPWT in pancreatic resection surgery, but they did not find any significant benefit in the reduction of SSI. However, this study is limited by a heterogenous population of hepatic and pancreatic resection surgery. A randomized study showed significant reduction of SSI (9.7 vs. 31.1%) with the use of NPWT dressings.[9] Similarly, Gupta et al[17] in their retrospective analysis of PD surgery demonstrated significant reduction in the incidence of SSI with the use of NPWT (12 vs. 41%, $p = 0.01$). The benefit of the reduction in SSI after PD has been shown in few other studies as well. The studies by Burkhart et al[18] and Lawrence et al[19] also

Table 1 Characteristics of the studies included in the systematic review reporting comparative outcomes with and without negative pressure wound therapy (NPWT)

Study and location	Study design	Population and numbers	Age Gender	Intervention	Outcomes
Gupta et al[17] United States	Retrospective study January 2014–July 2016	Undergoing pancreaticoduodenectomy (N = 61) Standard care: 36 NPWT: 25	Standard care: 64.1 y NPWT: 61.1 y	NPWT for 7–10 d after full primary skin closure	SSI NPWT: 12% Standard care: 41% OSI NPWT:12% Standard care: 36%
Burkhart et al[18] United States	Retrospective analysis of prospectively maintained database October 2014–May 2016	Undergoing pancreaticoduodenectomy NPWT: 120 Standard care: 274	Male: 54.6% Age (>65 y): 51.3%	NPWT: 4 d, pressure of NPWT: 125 mm Hg	SSI within 30 d of surgery NPWT: 11.7% Standard care: 23.1%
Javed et al[9] United States	Randomized clinical trial January 2017–February 2018	Undergoing pancreaticoduodenectomy Standard care: 61 NPWT: 62	Age Standard care: 66.1 NPWT: 66.4 Males Standard care: 55.7% NPWT: 50.0%	NPWT: 4 d	SSI within 30 d of surgery NPWT: 9.7% Standard care: 31.1% OSI NPWT: 11.2% Standard care: 21.3%
Lawrence et al[19] United States	Observational study September 2016–June 2018	300 patients in two cohorts Cohort 1: no NPWT (150 patients) Cohort 2: NPWT (150 patients)	Age Standard care: 68 y NPWT: 69 y Males standard care: 51% NPWT: 55.0%	Cohort 2: NPWT for 7 d or till discharge and a bundle of additional interventions (wound protector, irrigation with antibiotic, change of gown and gloves prior to fascial closure)	SSI within 30 d of surgery NPWT: 11% Standard care: 22% OSI NPWT: 10.6% Standard care: 22%

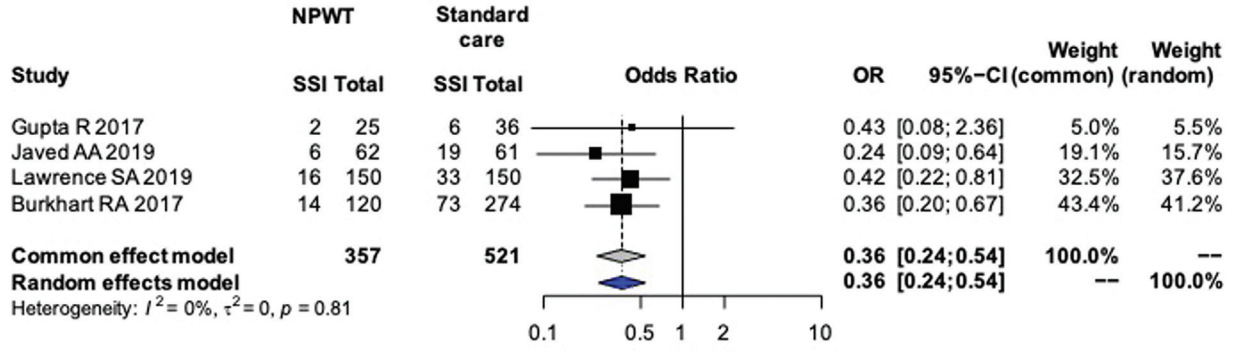

Fig. 2 Forest plot showing the pooled odds ratio (OR) of surgical site infection (SSI) in patients with the negative pressure wound therapy (NPWT) group as compared to the standard care group. CI, confidence interval.

reported significant decrease in the incidence of SSI with the use NPWT as compared with the standard care. The occurrence of SSI after PD is associated with significant morbidity to the patient, which further increases hospital stay, delays adjuvant treatment, and increases the risk of incisional hernia.[9,20] SSI not only increases patient-related morbidities but is also associated with a huge hidden financial burden on the health care system. The prophylactic use of NPWT for SSI prevention in PD may potentially be cost-effective and improve patient outcome.[19]

Various risk factors for SSI including preoperative biliary stenting, diabetes mellites, and use of neoadjuvant treatment were also compared between the two groups in the included studies.[9,17–19] These risk factors were comparable between the two groups.

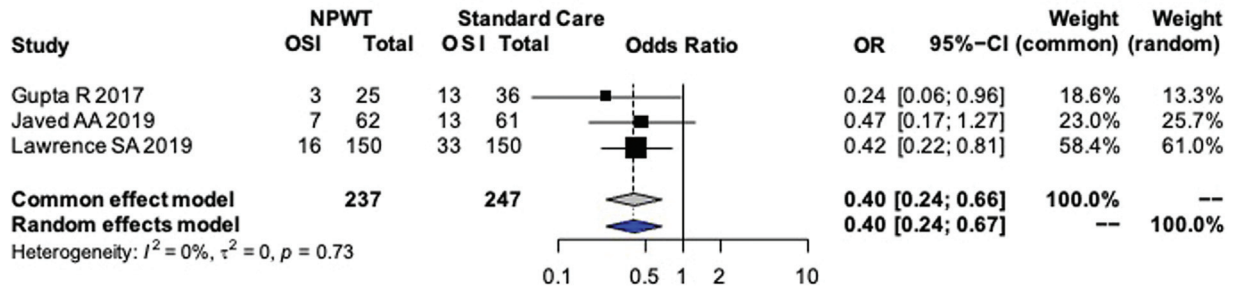

Fig. 3 Forest plot showing the pooled odds ratio (OR) of organ space infection (OSI) in patients with the negative pressure wound therapy (NPWT) group as compared to the standard care group. CI, confidence interval.

This study has some limitations. First, this study included only four studies, out which two were retrospective studies. Second, due to lack of data, cost analysis, hospital stay, and morality were not compared between the two groups. However, in general, the direction of effect was similar in all studies, which increases our confidence in the results.

In conclusion, PD is associated with high risk of SSI. The use of prophylactic NPWT after PD is associated with decreased risk of SSI. The cost–benefit ratio of NPWT and standard care requires further comparative studies.

Ethical Statement
Not applicable.

Data Availability Statement
Data from this study are available from the corresponding author upon reasonable request.

Authors' Contribution
All authors contributed equally to the article.

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Conflict of Interest
None declared.

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