Meta-analysis of preoperative placement of pancreatic stents to prevent postoperative leaks after distal pancreatectomy

Barham K. Abu Dayyeh, Samer Alkaade, Todd H. Baron

Abstract

Background: Pancreatic leaks and fistulae are common after distal pancreatectomy. The aim of this study was to determine effectiveness of prophylactic pancreatic duct (PD) stents on leak rate following distal pancreatectomy.

Methods: A meta-analysis of five studies including 218 patients. PD stents were placed endoscopically in two studies and intraoperatively in three studies. Octreotide was given postoperatively in one study.

Results: No significant difference in leak rates was seen with PD stents; however, when the study that also used Octreotide was removed, PD stents were favorable.

Conclusion: Placement of PD stents for prevention of PD leaks and fistulae following distal pancreatectomy cannot be routinely recommended.

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Keywords: Leaks, Meta-analysis, Pancreas, Stents
patients who underwent distal pancreatectomy without prophylactic PD stent placement.

Abstracts, letters, editorials, expert opinions, reviews without original data, case reports, and studies lacking a control group were excluded from the meta-analysis. All prospective randomized trials included met the majority of the criteria set forth by the Evidence-Based Gastroenterology Steering Group for methodologic quality indicating reasonable quality.

Data extraction

Two independent reviewers performed data extraction from each selected study. When ambiguity on outcome determination was present, a third reviewer was consulted and the outcome was determined by consensus. The primary outcome measured was the development of postoperative pancreatic fistula formation as defined by the International Study Group on Pancreatic Fistula (i.e., the presence of amylase-rich fluid greater than three times the upper limit of normal in the serum of any measurable volume on or after Day 3). Secondary outcomes were inconsistently reported and included postoperative morbidities, intra-abdominal fluid collections, hospital stay, duration to drain removal, operative time, gastric emptying, death, and PD stent-related adverse events.

Statistical analysis

To best summarize the available evidence, we conducted direct meta-analyses comparing the rates of pancreatic fistula formation after distal pancreatectomy with PD stenting (whether placed endoscopically or intraoperatively) versus no stenting. We calculated the pooled odds ratio with 95% confidence intervals (CI) using fixed and random-effects models. Statistical heterogeneity was evaluated by means of I2 statistics; an I2 value of more than 50% was considered to indicate high statistical heterogeneity. A funnel plot and Egger regression asymmetry were used to assess for potential publication bias. Analyses were performed using the comprehensive Meta-analysis software version 2 (Biostat, Englewood, NJ, USA).

Results

The literature search revealed a total of 2805 references. There were 2614 references that were excluded based on review of the title or duplication of the citation; subsequently, 191 abstracts were reviewed, which resulted in 178 abstract being excluded because they did not meet the inclusion criteria. The remaining 13 articles were fully reviewed and eight of these articles were excluded because they did not meet inclusion criteria. The remaining five articles were included in the study (Fig. 1). These five studies were published between 2008 and 2012 (Table 1). In two studies, patients had endoscopic PD stents placed preoperatively, and in three studies the stents were placed intraoperatively. Two studies were retrospective, two were prospective, and one was prospective with a retrospective control group. The prospective studies were not blinded, and only one was randomized.

Table 1 Studies Included in the Meta-analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>PD stent/leaks (%)</th>
<th>Control/leaks (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frozanpor et al 2012</td>
<td>26/13 (50)</td>
<td>27/10 (37)</td>
</tr>
<tr>
<td>Oida et al 2011</td>
<td>15/1 (6.7)</td>
<td>15/8 (32)</td>
</tr>
<tr>
<td>Rieder et al 2010</td>
<td>25/0 (0)</td>
<td>23/5 (22)</td>
</tr>
<tr>
<td>Fischer et al 2008</td>
<td>16/1 (6.3)</td>
<td>43/14 (33)</td>
</tr>
<tr>
<td>Okamoto et al 2008</td>
<td>7/3 (42)</td>
<td>11/3 (27)</td>
</tr>
<tr>
<td>Total</td>
<td>89/18 (20)</td>
<td>129/40 (31)</td>
</tr>
</tbody>
</table>

PD, pancreatic duct.
Only one of the studies (retrospective) showed a significant difference \((P < 0.05)\) in the rate of pancreatic fistula formation, and it favored PD stent placement.\(^7\)

Statistics of meta-analysis were performed with removal of each study separately. In four studies, the results were insignificantly changed from that of the entire meta-analysis.\(^7,9-11\) However, when removing the study by Frozanpor et al.,\(^8\) in which octreotide was used and pancreatic stents were placed intraoperatively, PD stent placement strategy was favored with an OR of 0.26 (CI 0.07–0.89, \(P = 0.03\); Fig. 4).

### Table 2  Detailed Information on Grades B and C Fistulae in the PD Stent Group vs. Controls

<table>
<thead>
<tr>
<th>Study</th>
<th>PD stent group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total no. of fistulae</td>
<td>Grades B &amp; C fistulae</td>
</tr>
<tr>
<td>Frozanpor et al 2012(^8)</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Oida et al 2011(^9)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Rieder et al 2010(^11)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fischer et al 2008(^7)</td>
<td>1</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Okamoto et al 2008(^10)</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

PD, pancreatic duct.

**Secondary outcomes**

PD stent placement-related adverse events were mentioned in four studies and summarized in Table 3.\(^7-11\) In the study by Frozanpor et al.,\(^8\) three of 26 patients in the PD stent group had PD stent-related pancreatitis without any further details, and the PD could not be cannulated in two patients. In the study by Okamoto et al.,\(^10\) two of seven patients in the PD stent group had mild pancreatitis. In the study by Rieder et al.,\(^11\) one of 25 patients in the PD stent group had mild pancreatitis and PD stent placement was successful in 23 patients (92%). Postoperative intra-abdominal abscess formation was reported in two studies with conflicting results. In the study by Frozanpor et al.,\(^8\) there was increased incidence of intra-abdominal abscess formation in the PD stent group, 11 (42%) versus five (18.5%) with \(P = 0.0658\). In the study by Fischer et al.,\(^7\) there was no significant decrease in the incidence of intra-abdominal abscess formation in the PD stent group compared to control, two (12.5%) versus three (6.9%) with a nonsignificant \(P\) value. Length of hospital stay was reported in three studies. A longer stay in the PD stent group was shown in one study,\(^8\) a shorter stay in the PD stent group in a second study,\(^7\) and no difference in length of stay in the third study (Table 3).\(^11\)
Discussion

Endoscopic stent placement for the treatment of bile leaks has become an accepted non-surgical therapy as biliary endoprostheses divert flow away from the leak site and abolish the high pressure gradient at the level of the biliary sphincter. Similarly, placement of PD stents has become an established therapy for PD leaks and fistulae from both surgical and nonsurgical causes. The concept of prevention of leaks following resective pancreatic surgery, particularly pancreaticoduodenectomy (Whipple procedure) has been attempted for many years, though recent data have not shown them to be of definitive benefit.

Using meta-analytic methods, we examined the effect of perioperative (2 studies) or intraoperative transpapillary placement of PD stents (3 studies) on postoperative leak rates following distal pancreatectomy. Meta-analysis of the five studies failed to show a significant difference in the rate of postoperative fistula formation between patients with prophylactic PD stents versus patients with no PD stents.

How does one reconcile that postoperative placement of PD stents effectively closes leaks yet a preoperative stent placement does not prevent leaks? Perhaps stents diameters are not large enough compared to the size of the leak. The main PD in most patients undergoing distal pancreatectomy is small in diameter and often does not permit placement of stents larger than 5 French in diameter. Indeed, 5-French stents were placed in the majority of patients.

The other way to explain why prophylactic PD stent placement did not show a benefit is to examine the results of this meta-analysis after excluding the single study in which octreotide was used. Although separately excluding the four studies in which octreotide was not used did not change the outcomes of the meta-analysis, excluding the study by Frozanpor et al., in which octreotide was used, showed a statistically significant difference in the rate of postoperative fistula formation favoring PD stent placement.

Table 3 Secondary Outcomes Including PD Stent Related Complications

<table>
<thead>
<tr>
<th>Study name</th>
<th>Pancreatitis in PD stent group (n/total)</th>
<th>Length of hospital stay</th>
<th>Abdominal abscess formation (PD stent vs. control)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n(%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p-value</td>
</tr>
<tr>
<td>Frozanpor 2012</td>
<td>3/26</td>
<td>Longer in the PD stent group (18.5)</td>
<td></td>
</tr>
<tr>
<td>Okda 2011</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Rieder 2010</td>
<td>1/25 (mild)</td>
<td>Similar stay in both groups</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Fischer 2008</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Okamoto 2008</td>
<td>2/7 (mild)</td>
<td>Shorter in the PD stent group (6.9)</td>
<td>Not mentioned</td>
</tr>
</tbody>
</table>

PD, pancreatic duct.

These findings suggest that octreotide use may somehow confound the results of the meta-analysis, and prophylactic PD stent placement alone helps to reduce the rate of postoperative pancreatic fistula formation after distal pancreatectomy.

Octreotide is a synthetic analog of endogenous somatostatin with more potency and longer half-life. Octreotids exerts its effects by inhibiting pancreatic exocrine secretion, and this mechanism has been proposed to reduce the rate of pancreatic fistula after pancreatic resection. Several clinical trials and reviews have evaluated the use of octreotide to prevent the development of pancreatic fistula after pancreatic surgery. The prophylactic use of perioperative somatostatin and its analogs to prevent postoperative pancreatic fistula remains controversial and does not result in a reduction of surgical mortality. In a meta-analysis by Alghamdi and colleagues that included seven studies, there was no significant reduction in the rate of pancreatic fistula formation or postoperative mortality in the group that received octreotide. The authors of this meta-analysis noted contradictory results between European and American studies included in the meta-analysis with higher incidence of fistula formation in the placebo group of European studies compared to American ones. In another study, prophylactic octreotide after pancreatic surgery did not affect the severity of postoperative pancreatic fistula.

Our study represents the first meta-analysis in the literature specifically assessing the value of prophylactic PD stent placement prior to distal pancreatectomy. We found similar meta-analysis in the literature, but they included patients with pancreaticoduodenectomy and pancreaticojejunostomy.

Limitations of this meta-analysis included the small number of patients in each study, the inconsistent reporting of adverse events associated with distal pancreatectomy, and PD stent placement.

In conclusion, the results of this meta-analysis did not show a significant difference in the rate of postoperative fistula formation after distal pancreatectomy when prophylactic PD stents were placed, but exclusion of patients who received octreotide showed significant findings favoring prophylactic PD stent placement. More evidence from randomized studies is needed including an investigation of the effect of perioperative octreotide on fistula formation in the presence or absence of prophylactic PD stents.

Conflicts of interest

No financial support was received. All contributing authors declare no conflicts of interest.

References


