Analysis of closure of the pancreatic remnant after distal pancreatic resection

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Abstract

Background. The appropriate management of the pancreatic remnant following distal pancreatic resection remains a clinically relevant problem. We carried out a retrospective analysis which focused on this issue and compared the two favored techniques of suture and staple closure.

Patients and methods. Forty-six patients underwent distal pancreatectomy between October 1999 and January 2006. The patients were retrospectively analysed based on the management of the remaining pancreatic gland. Thirty-seven patients had suture and nine patients had staple closure. The morbidity, mortality, incidence of pancreatic fistula, necessity of secondary surgical intervention, and the duration of hospital stay for the two groups were compared. Pancreatic fistula was considered according to the novel international standard definition (ISGPF). In addition, subgroup analysis of patients receiving octreotide was carried out.

Results. Overall, postoperative morbidity due to pancreatic fistula occurred in seven patients (19%) after suture and in one patient (11%) after staple closure (p = 0.54), with no deaths. The number of patients with surgical revision related to pancreatic leakage was two (5%) after suture closure vs no revision after staple closure (p = 0.65). The median number of total hospital days for the suture group was 19 (range 7–78 days) vs 21 (range 12–96 days) for the stapler group (p = 0.21). No significant benefit for the octreotide application could be determined.

Conclusion. According to the data, no significant difference for either suture or stapler closure was observed, with the tendency for staple closure to be superior.

Key Words: pancreatic resection, suture closure, staple closure

Introduction

Distal pancreatectomy is a relevant procedure for chronic pancreatitis, other benign diseases, malignant diseases, cysts of the pancreas, and pancreatic parenchyma damage after abdominal trauma, with overall increasing frequency and decreasing mortality below 5% in high volume centers [1–3]. Despite the experience gained since the technique for distal pancreas resection was outlined by Mayo in 1913 [4], the management of the remaining pancreatic tissue is still a considerable clinical problem [5,6]. In particular, pancreatic leak following distal pancreatic resection has been the foremost complication in terms of frequency and associated morbidity [7–9]. It is believed that patients with a non-dilated Wirsung’s duct and a soft friable pancreatic gland are especially susceptible to this complication [10–13].

From a very early stage, surgeons tried to minimize the complication rate with suitable techniques including end-to-side pancreaticojejunostomy [14]. Nevertheless, staple closure and suture closure of the pancreatic remnant have been the standard techniques referred to most [1,15–17]. Several other strategies, such as fibrin glue sealing of the stump or anastomosis, sealing of the parenchyma of the pancreatic stump with a radiofrequency device, patching the pancreatic stump with an omental plug or a patch taken from the falciform ligament, and the use of an ultrasonic or harmonic scalpel for tissue dissection, have been advocated as successful [9,18–21]. Furthermore, the development of techniques does not stand still and a novel method covering the pancreatic stump with the serosal surface of the first jejunal loop has been introduced recently [22]. However, no technique has proven to be satisfactory for all patients.

At the Department of General Surgery of the University of Würzburg, the techniques of suture and staple closure of the pancreatic remnant after
distal pancreatic resection have been performed exclusively. The aim of the present retrospective analysis of patients was an attempt to provide additional data as to which technique may be superior in terms of mortality, morbidity, and incidence of pancreatic fistula.

**Patients and methods**

**Patients**

A retrospective analysis of 46 patients (18 men, 28 women) receiving open left-sided or distal pancreatectomy between October 1999 and January 2006 was carried out. The patients’ characteristics are summarized in Table I. The patients were divided into two groups according to the management of the pancreatic remnant. Thirty-seven patients (14 men, 23 women) with an age range of 28–79 years underwent suture closure and 9 patients (4 men, 5 women) with an age range of 17–86 years had staple closure.

**Surgical technique**

All pancreatic resections were performed in accordance with the standardized procedure described elsewhere [23]. The common part of the distal pancreatectomy includes the transection of the pancreas to the left of the hepatic portal vein/superior mesenteric vein. At the Department of General Surgery of the University of Würzburg, two techniques of pancreatic stump closure after distal pancreatectomy have been used in parallel. The attending surgeons made the decision as to which technique was preferred intraoperatively for each individual patient. In the suture method, the Wirsung’s duct was first identified and afterwards ligated with non-absorbable sutures. After sewing the main pancreatic gland, the cut surface of the pancreatic gland was closed with interrupted, non-absorbable sutures that joined ventral and dorsal edges of the gland according to the fish mouth technique. In 20 patients (54%), the transected pancreatic gland was additionally sealed with TachoComb, a biodegradable hemostyptic (Nycomed Pharmaceutical Co. Ltd, Denmark). The intended benefit of the topical fibrin sealant application was to support sealing of the bleeding pancreatic surface. In the stapler group, a linear stapler GIA 50 or 90 mm (Tyco, Gosport, UK) was used in six patients and an ILA 75 stapler (Tyco) in three patients. In this group, the TachoComb hemostyptic was applied in four cases (44%).

Overall, a concomitant splenectomy was carried out in 26 patients (55%). All patients had at least an intrabdominal open drain (easy-flow) with their tips placed on the pancreatic remnant.

**Octreotide prophylaxis**

Octreotide (Novartis Pharma, Nürnberg, Germany) is the octapeptide analog of somatostatin, which is a powerful inhibitor of pancreatic secretion. Twenty-nine patients (78%) with suture and five patients (56%) with staple closure received octreotide (2 × 100 or 3 × 100 or 3 × 200 μg/day s.c.) before surgery (within 2 h of the start of surgery) and after surgery for 8 days.

**Perioperative management**

The intra-abdominal easy-flow drains were removed as soon as the amount of serosanguinous drainage fluid was <20 ml per 24 h. The diagnosis of pancreatic fistula was suspected on the basis of conspicuous macroscopic appearance of drain fluid that looked like pancreatic juice. Concomitant clinical findings could be inconstantly observed and ranged from abdominal pain and impaired bowel function to fever (≥38°C), serum leukocyte count >10 000 cells/mm³, and increased C-reactive protein. The pancreatic enzymes amylase and lipase were initially measured in the easy-flow drain fluid after suspicion of pancreatic fistula. In the case of a pancreatic fistula, further management depended on the individual patient; nevertheless, negative pancreatic enzyme secretion in the drain fluid was confirmed before removal of the drainage.

**Definition of pancreatic fistula**

In accordance with the novel international consensus agreement [24], pancreatic fistula was defined as a drainage fluid beyond the third postoperative day with at least threefold elevation of normal serum amylase (<110 IU/ml). The grading system (grades A, B, and C) of severity of pancreatic fistula was applied after complete follow-up (Table II).

**Statistics**

Statistical analysis for the data was done using the Fisher’s exact or Mann–Whitney U test. Statistical significance was taken as p < 0.05.
Results

Indications for distal pancreatectomy were pancreatic tumors in 30 patients, chronic pancreatitis in 8 patients, stomach tumors in 4 patients, abdominal trauma in 2 patients, and other reasons in 2 additional patients (Table I). In the suture group, operation was done for malignancy in 9 of 37 cases (24%) and in 3 of 9 cases (33%) in the stapler group. Splenectomy was additionally performed in 26 patients. Distal pancreatectomy was extended in nine patients (gastrectomy or partial gastrectomy in four, partial colon resection in four and partial hepatectomy in one).

A summary of postoperative data of patients is presented in Table III. There was no hospital mortality in either the suture or the stapler group. Nineteen patients (51%) in the suture group and five patients (56%) in the stapler group had no postoperative complications. Seven patients (19%) in the suture group and one patient (11%) in the stapler group developed a pancreatic fistula. The difference is not statistically significant. The patients with pancreatic fistula were subdivided according to the severity grading system. In the suture group, prolonged pancreatic drainage of >21 days combined with partial signs of infection occurred in four patients (severity grade B). Two of those required additional CT-guided drainage of pancreatic leakage formation. Re-operation due to pancreatic leakage was necessary for two patients with suture closure of the pancreatic remnant (severity grade C). One patient had no serious sequel following pancreatic fistula and drainage was suspended without further treatment (severity grade A). In the stapler group, the one patient with pancreatic fistula required CT-guided drainage (severity grade B). No re-operation was performed. Bowel dysfunction or delayed gastric emptying was noted for seven patients (18%) in the suture group vs no patients in the stapler group. The difference is not statistically significant.

Overall, for the eight patients with postoperative pancreatic fistula, the median (range) time to resolution of fistula was 29 (13–68) days.

A subgroup analysis was carried out to exclude bias towards sutured closure for extended or complicated resections. Extended distal resection was performed in the suture group in seven cases (19%) vs three cases (33%) in the stapler group. Postoperative pancreatic fistula occurred in two of those patients (28%) in the suture group. No pancreatic fistula was evident for patients with extended resection and staple closure. In summary, the rate of pancreatic fistula for suture closure and extended resection (28%) compared to the rate for suture closure and simple resection (17%) was not statistically different. Likewise, no statistical difference could be determined in the stapler group.

Furthermore, there was no statistically significant difference in the development of pancreatic fistula between benign versus malignant resection. Pancreatic fistula occurred in 5 of 34 (15%) patients in whom resection was done for benign disease, and in 2 of 12 (17%) patients with malignant disease.

In addition, subset analysis was performed for octreotide application (Table III). Overall, 33 patients (70%) received octreotide treatment regardless of the method of pancreatic stump closure. The incidence of pancreatic fistula was similar in the octreotide group (18%, 6/33) and the non-octreotide group (15%, 2/13).

The median length of hospital stay was 19 days (range 7–78 days) for patients in the suture group, compared to a median of 21 days (range 12–96 days) for the patients who underwent staple closure. The difference between groups is not statistically significant.

Discussion

The comparison of different studies with regard to pancreatic fistula formation after distal pancreatectomy remains problematic due to the lack of a standard definition of what constitutes a pancreatic fistula. Specifically, more than 20 fistula definitions have been reported [25]. As an attempt to solve the problem, an international standard definition for pancreatic fistula has recently been proposed [24].

Table II. Grading system of pancreatic fistula.

<table>
<thead>
<tr>
<th>Grade</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical conditions</td>
<td>Well</td>
<td>Often well</td>
<td>Ill appearance/bad</td>
</tr>
<tr>
<td>Specific treatment*</td>
<td>No</td>
<td>Yes/no</td>
<td>Yes</td>
</tr>
<tr>
<td>US/CT (if obtained)</td>
<td>Negative</td>
<td>Negative/positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Persistent drainage (after 3 weeks)†</td>
<td>No</td>
<td>Usually yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Re-operation</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Death related to pancreatic fistula</td>
<td>No</td>
<td>No</td>
<td>Possibly yes</td>
</tr>
<tr>
<td>Signs of infections</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Sepsis</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Re-admission</td>
<td>No</td>
<td>Yes/no</td>
<td>Yes/no</td>
</tr>
</tbody>
</table>

US, ultrasonography; CT, computed tomographic scan.

*Partial (peripheral) or total parenteral nutrition, antibiotics, enteral nutrition, somatostatin analog, and/or minimal invasive drainage.

†With or without a drain in situ.
In the present analysis, considerable attention has been focused on the novel definition. Therefore, this dataset will be more comparable to others and thus of direct clinical value.

The safety of distal pancreas resection has increased in recent years, mainly due to the improvement of the mortality rates, with $<5\%$, reported in high volume centers [1,2]. This is in accordance with the non-mortality rate reported in our retrospective analysis. On the other hand, morbidity remains high and can be up to $64\%$ [17]. Fistula formation related to the operative management of pancreatic remnant is the most commonly occurring complication after distal pancreatectomy and almost exclusively the cause of the high morbidity. Furthermore, pancreatic fistula is combined with numerous other complications, such as abscess formation, sepsis, enteric dysfunction, and hemorrhage, and influences healthcare expenditure for the patient [26]. Besides other techniques, stapler closure and suture closure of the pancreatic stump after resection are the most favored surgical procedures to avoid pancreatic fistula formation [5].

In the present study, occurrence of pancreatic fistula (which was considered as drainage fluid beyond the third postoperative day with at least threefold elevation of amylase) was not significantly different for stapler and suture closure, with $19\%$ vs $11\%$, respectively. Nevertheless, this result tends to favor the stapler closure over hand-sewn closure, in agreement with a meta-analysis published in 2005 [5]. This assumption is supported by the fact that no patient with staple closure has required further operative intervention related to pancreatic leakage. Moreover, bowel dysfunction was not noted after staple closure. It is supposed that the staple method resulted in less extravasation of pancreatic fluid from the cut surface of the residual pancreatic surface compared with the suture method [17].

A standard technique for preventing drainage of juice from the pancreatic resection surface including the ligation of Wirsung’s duct has been proposed for suture closure [8]. In this series, the main pancreatic duct was always ligated in the context of suture closure. In addition, small branches on the transected pancreatic surface were closed using the fish mouth technique, since the branches tend to be critical as a source of pancreatic leak [9,17]. Despite this technique, a rate of occurrence of a pancreatic leak of $9.6\%$, as reported recently [27], could not be observed in this study.

However, besides the surgical technique the surgeon is also considered a relevant risk factor for fistula formation [23]. In this regard, within the observation period of this systematic analysis, several surgeons carried out the procedures at the University Hospital of Wurzburg and this might explain the inferior rate of

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Suture closure ($n=37$)</th>
<th>Staple closure ($n=9$)</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>19 (51%)</td>
<td>5 (56%)</td>
<td>NS</td>
</tr>
<tr>
<td>Yes</td>
<td>18 (49%)</td>
<td>4 (44%)</td>
<td></td>
</tr>
<tr>
<td>Pancreatic fistula*</td>
<td>7 (19%)</td>
<td>1 (11%)</td>
<td>NS</td>
</tr>
<tr>
<td>Grade A</td>
<td>1 (3%)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Grade B</td>
<td>4 (11%)</td>
<td>1 (11%)</td>
<td>NS</td>
</tr>
<tr>
<td>Grade C</td>
<td>2 (5%)</td>
<td>0</td>
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<tr>
<td>Intra-abdominal abscess†</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bowel dysfunction</td>
<td>7</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Pulmonary complication</td>
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<td></td>
</tr>
<tr>
<td>Renal complication</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hepatic complication</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Others‡</td>
<td>4</td>
<td>3</td>
<td>NS</td>
</tr>
<tr>
<td>CT-guided drainage†</td>
<td>2 (5%)</td>
<td>1 (11%)</td>
<td>NS</td>
</tr>
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<td>Re-operation†</td>
<td>2 (5%)</td>
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Time to resolution of pancreatic fistula (days)
- Range: 13–63
- Median: 29

OCTreotide application
- Yes/no: 33/13
- Pancreatic fistula: 6 (18%)/2 (15%)

Duration of hospital stay (days)
- Range: 7–78
- Median: 19
- Range: 12–96
- Median: 21

NS, not significant.
*According to the international consensus agreement [24].
†With respect to pancreatic fistula.
‡Not related to pancreatic resection.

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<td>0</td>
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NS, not significant.
*According to the international consensus agreement [24].
†With respect to pancreatic fistula.
‡Not related to pancreatic resection.
pancreatic fistula in the group with suture closure compared with the rate in the quoted report. On the other hand, the staple technique seems to be simpler to apply and this might explain the inferior rate of pancreatic fistula besides the fact that several surgeons performed the procedures.

The concept of perioperative inhibition of exocrine pancreatic secretion by i.v. application of octreotide (somatostatin) to reduce the postoperative morbidity after pancreatic resection was first introduced in 1979 [28]. Although some studies [29] have shown a significant advantage, the role of perioperative and postoperative octreotide in prevention of pancreatic fistula formation remains unclear. In this study, no remarkable effect of octreotide for the rate of pancreatic fistula could be observed after subset analysis of patients in the suture and the stapler groups.

According to the data, no significant benefit could be shown for the suture group or the stapler group for the duration of hospital stay. The most frequent surgical complications were gastric emptying delay and postoperative pancreatic fistula. In this series, those complications were recorded in approximately 33% of the patients. Gastric emptying delay and pancreatic fistula have clinical relevance, as the affected patients remained in the hospital for more than a week longer [30]. That fact, besides comorbidities in some individuals, may explain the rather long median length of hospital stay in the suture and stapler groups. However, the length of hospital stay is of inferior quality among clinical parameters when discussing the impact of pancreatic fistula [24].

Finally, no significant difference could be shown for either suture or stapler closure of the pancreatic remnant after distal pancreatectomy. The suggested advantage for staple closure needs to be interpreted cautiously with respect to the number of evaluated patients. The second conclusion is that further clarification of the role of suture and stapler closure is still required through large, high quality, randomized trials, since the differences between stapler and suture closure are rather small and unlikely to be detected in single series. It is tempting to speculate that the perfection of a technique in each individual institution is just as important as the actual technique applied.

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References


