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ORIGINAL ARTICLE

The effect of mesh reinforcement of a stapled transection line on the rate of pancreatic occlusion failure after distal pancreatectomy: review of a single institution's experience

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Abstract

Background: Pancreatic occlusion failure (POF) after distal pancreatectomy remains a common source of morbidity. Here, we review our experience with distal pancreatectomy and attempt to identify factors which influence POF rates.

Patients and Methods: One hundred sixty-nine distal pancreatectomies were performed between 2002 and 2007. Review of the computerized medical records and physician office records was performed for all patients. Univariate and multivariate analyses were performed to determine factors which might influence the incidence of POF. The data set was analysed for factors which might influence the pancreatic occlusion rate. Analysis included patient and disease characteristics including: age, gender, body mass index (BMI), diagnosis, consistency of the pancreas and history of pancreatitis, as well as intra-operative variables including: surgeon, absorbable mesh reinforcement and operative approach.

Results: POF was the most common peri-operative complication. POF was identified in 32 out of 169 patients (19%). Transection technique (hand sewn, stapled, stapled with mesh) and procedure complexity were factors associated with differences in POF rates by both univariate and multivariate analyses. POF was identified in 7 out of 70 patients (10%) when an absorbable mesh was utilized, and 25 of 99 patients (25%) when mesh was not utilized ($P < 0.02$).

Discussion: These data suggest that a randomized controlled trial will be required to determine if mesh reinforcement reduces the rate and severity of POF after distal pancreatectomy.

Keywords

distal pancreatectomy, mesh reinforcement, pancreatic leak, pancreatic fistula

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Introduction

There have been dramatic improvements in the care of patients undergoing pancreatic resection. This is best exemplified by several large case series of pancreaticoduodenectomy from multiple centres demonstrating mortality rates of less then 2%.[1–8] Unfortunately, the improvements in operative technique, peri-operative care, surgical materials and instrumentation have not lead to a dramatic reduction in pancreatic occlusion failure (POF) after distal pancreatectomy. This is evidenced by recent studies reporting the persistence of the problem with many centres describing fistula rates of approximately 20–30%.[1,2,9] POF is one of the more extensively investigated issues facing pancreatic surgeons and a variety of operative techniques, drainage regimens and adjunctive hormonal analogues have been studied.[3,4,7,10–22] Although often promising in small case series, none have had a

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dramatic impact on the occlusion failure rate when subjected to a randomized controlled trial.[5,17,23–26]

The severity and subsequent sequelae of POF after distal pancreatectomy varies considerably.[27,28] The majority of patients' leaks will be identified early and many leaks are controlled with an intra-operatively placed drain. In other patients, occlusion failure may require hospital readmission, emergency department visits, percutaneous or open drainage, prolonged antibiotic therapy and radiological surveillance. While there is no clear consensus on the definition of a POF or its severity, most experts agree that the prevention of POF after distal pancreatectomy is critical in achieving an uneventful post-operative course and will significantly reduce costs.

A definition and severity grading system for POF has recently been proposed.[29] In this system, the severity of the intervention required and the overall outcome define the severity grading into 5 grades. Grade 1 is any deviation from normal post-operative course without the need for intervention. Grade 2 requires pharmacological treatment and grade 3 requires intervention. Grade 3 is further divided in Grade 3a and 3b depending on the need for general anaesthesia. Grade 4 results in permanent disability and grade 5 results in death.[29]

Here we review our experience with distal pancreatectomy over a 5-year period (2002–2007). During this same time period we introduced the use of an absorbable mesh. The rational for utilizing the mesh was based on the success with reduction in leaks in other areas of surgery including lung reduction[30,31] and gastric bypass.[32,33] All operative techniques were included in this analysis. This analysis sought to determine if the utilization of mesh or any other variables were associated with a change in POF rates after a distal pancreatectomy.

Methods

A retrospective review (March 2002–May 2007) of all distal pancreatectomies performed within the section of HPB/GI surgery at Washington University Medical Center/ Barnes-Jewish Hospital was performed. One hundred and sixty-nine patients underwent distal pancreatectomies from 22 March 2002 to 30 May 2007. All operative indications and both open and laparoscopic approaches were included in the analysis. All procedures were performed by one of six surgeons in the group. The choice of closure was at the discretion of the surgeon and there was no standard method applied to hand closure, mesh type or stapler utilized.

The main outcome measure was failure of occlusion of the pancreatic stump leading to leakage within the first 30 days of the post-operative period. POF included both fistulas and fluid collections (sterile or infected) except for ascites, unless it was shown to be amylase rich. POF was defined as a clinically relevant pancreatic fistula, fluid collection or other complication arising from leakage of pancreatic juice from the pancreatic stump. The term clinically relevant means that the event resulted in interventions that are not part of the normal post-operative course (e.g. antibiotics, drainage).[29] To be considered a POF which was clinically relevant there had to be amylase-rich fluid obtained from an intra-operatively placed drain at or beyond post-operative day 10 of at least 30 ml with a concentration three or more times greater than normal serum levels.[24,34] Fluid collections were detected by post-operative CT scan. Any fluid collection or abscess requiring a drainage procedure was considered a fistula without regard to the amylase level. CT scans were obtained when clinically indicated [i.e. elevated white blood cells (WBC), persistent fevers, haemodynamic instability, unrelenting nausea and vomiting, abdominal pain, etc).

Information was obtained from hospital and physician records and supplemented with information from the primary surgeons' records as needed and available. Groups were analysed for POF, morbidity and length of stay (LOS). Potential confounding variables were assessed to include: age, gender, operative approach, operative surgeon and extent of procedure. Extensive procedures were defined as partial or complete resection of a contiguous organ including: stomach, colon, liver and kidney. Splenectomy, adrenalectomy and/or extended lymphadenectomy were excluded from the grouping of extended procedure. Secondary outcome measures were assessed including: re-operations, other non-surgical therapeutic interventions (i.e. drainage via interventional radiology or CT), hospital readmissions and mortality.

Means were compared using the Student's *t*-test and proportions using the χ^2 or Fisher's exact tests. Time-to-event data were analysed using Cox proportional hazard models. For all analyses, a *P*-value of <0.05 was set as the threshold for statistical significance. Software used for statistical analysis was GraphPad Prism (GraphPad Software Inc., La Jolla, CA, USA) SAS 9.1.3 (SAS Institute Inc., Cary, NC, USA). This retrospective review was approved by the Human Studies Committee at Washington University.

Results

One hundred and sixty-nine patients (73 males and 96 females) underwent a distal pancreatectomy between March 2002 and May 2007 (Table 1). The median age of the patients at resection was 59 years (mean 57, range 23–84). Malignant or pre-malignant neoplasia (IPMN or MCN) accounted for the majority of lesions resected (73%). Of the primary pancreatic tumours, the final pathological diagnosis included 36 with pancreatic adenocarcinoma (21%). There were 23 neuroendocrine neoplasms (14%), 62 cystic neoplasms (37%, 7 of these were cystic adenocarcinomas) and 3 solid/pseudo-papillary neoplasms (2%). There were 27 patients who underwent distal pancreatectomies for non-pancreatic primaries. This included 20 patients with direct extension of cancer from a contiguous organ and 5 with an isolated pancreas metastasis. Non-pancreatic pathology included renal cell carcinoma (6), sarcoma (5), adrenocortical carcinoma (4), gastric carcinoma and lymphoma (12). Complex or extensive operations, as defined by removal of one or more contiguous organs, were performed on 63 out of the 169 patients (37%) including 24

partial or complete gastrectomies, 18 partial colectomies, 12 nephrectomies and 9 partial hepatectomies.

Patient demographics, pathology and procedures were analysed in order to identify significant changes, if any, in surgical indications, patient population or operative technique over the study period. Table 2 highlights some findings of this analysis. The patient population did not appear to differ between years. For example, the average patient age ranged from 51–63 with no significant change over time. Surgical indications and percentage of patients with a final diagnosis of cancer remained fairly constant.

Table 1 Clinicopathologic descriptors

Demographics	
Number	169
Age mean (median)	57 (59)
Gender (male : female)	73:96
Pathologic Diagnosis	
Adenocarcinoma	42 (25%)
Chronic pancreatitis	20 (12%)
Benign cystic neoplasms[a]	55 (33%)
Neuroendocrine neoplasm	24 (14%)
Non-pancreatic pathology	25 (15%)
Solid and pseudo papillary neoplasm	3 (2%)
Operative variables	
Laparoscopic approach	36 (21%)
Complex or extensive procedure	63 (37%)
Outcomes	
Pancreatic occlusion failure	32 (19%)
Intra-operative drain retained	15
Radiologically placed drain	15
Re-operation	3
Peri-operative mortality	0
Median length of stay (days)	9.4

[a]Cystic neoplasms included serous cystadenomas, mucinous cystic neoplasms and intraductal papillary mucinous tumours.

The number of distal pancreatectomies has increased in each study year. Laparoscopic resections have increased over the study period in both absolute number and as a percentage of all distal pancreatectomies ($P = 0.0002$, Table 2). Use of absorbable mesh to reinforce the pancreatic transection line has increased over the study period ($P < 0.0001$). The POF rate has varied over time ranging from a maximum of 29% in 2003 and a minimum of 13% in 2005. There was not a statistically significant trend towards a reduction in the POF rate or total LOS for the entire population of patients over the study period.

Univariate and multivariate analyses were carried out to identify factors which may be associated with POF after distal pancreatectomy (Table 3). In univariate analysis, complex or extended resections were significantly associated with an increased POF rate, when compared with those undergoing routine surgery ($P = 0.016$). Utilization of mesh was associated with a reduction in the POF rate, when compared with patients whose pancreatic stumps were closed with other techniques ($P = 0.003$). Although it is true that POF was identified in 7 out of 70 patients (10%) when an absorbable mesh was utilized and 25 out of 99 patients (25%) when mesh was not utilized ($P < 0.02$ χ^2, two groups), a closer look at the primary data demonstrates that the outlier in the analysis is the hand sewn technique and that the difference between stapled and stapled with mesh reinforcement is more modest and not statistically different. Analysis of all other factors including laparoscopic surgical approach, patient characteristics (age, gender), diagnosis and operative surgeon were not statistically significant.

Multivariate analysis for POF indicated that closure type and complexity of procedure both raised the probability of occlusion failure. Suturing had a probability about 4.4 times higher than mesh or stapling without mesh. Extended or complex resections had a probability of POF about 3.3 times higher then routine procedure, after adjusting for the effect of closure type. The effect of closure type and complexity of surgery are independent, with little interaction effect on the outcome of POF (Table 4).

Peri-operative morbidity and mortality are displayed in Table 5. There was no mortality in any group. A thorough chart review indicated that the majority of peri-operative morbidity was

Table 2 Patient characteristics' trends over time

	2007 1st Q (1st)	2006	2005	2004	2003	2002
N	15	38	31	32	28	25
Age	53	61	53	59	57	63
Gender (male : female)	10:5	18:20	13:18	14:18	7:21	10:15
Neoplastic lesion	11	27	21	27	20	16
Laparoscopic approach[a]	7 (47)	16 (42)	7 (23)	3 (9)	1 (4)	2 (8)
Buttressed material used[a]	15 (100)	28 (74)	21 (68)	7 (22)	0 (0)	0 (0)
POF	3 (20)	6 (16)	4 (13)	6 (19)	8 (29)	4 (16)
Median length of stay	6.1	9.9	10	9	9	11
Mortality	0	0	0	0	0	0

[a]Indicates statistically significant change over time.

Table 3 Univariate logistic regression analysis for pancreatic occlusion failure

Variables	N	Events	OR	95%CI	*P*-values
Ages					0.12
23–50	47	6	1.0		
50–65	64	16	2.28	(0.82,6.36)	
>65	58	10	1.42	(0.48,4.25)	
Gender					0.10
Female	73	14	1.00		
Male	96	18	1.92	(0.88,4.17)	
Diagnosis					
Adenocarcinoma	36	7	1.04	(0.41,2.65)	0.93
Neuroendocrine	23	5	1.22	(0.42,3.59)	0.71
Cystic	62	11	0.88	(0.39,1.98)	0.76
Chronic pancreatitis	18	3	0.84	(0.23,3.10)	0.80
Pseudopapillary	3	1	2.18	(0.19,24.78)	0.53
Non-pancreatic	27	5	0.97	(0.34,2.79)	0.95
Extent of resection					0.016
Routine	106	14	1.00		
Extended	63	18	2.63	(1.20,5.76)	
Operative approach					0.18
Open	133	24	1.00		
Laparoscopic	36	8	0.47	(0.15,1.44)	
Closure					0.003
Suture	55	18	1.00		
Stapler	44	7	0.39	(0.14,1.04)	
Mesh	70	7	0.23	(0.09,0.60)	

Table 4 Multivariate logistic regression for pancreatic occlusion failure

Variables	N	OR	95% CI	*P*-values
Closure				
Suture	18	4.57	(1.74,11.98)	0.002
Staple	7	1.73	(0.56,5.32)	0.34
Mesh	7	1.00		
Operative approach				
Extended	18	3.26	(1.37,7.75)	0.007
Routine	14	1.00		

OR, odds ratio; CI, confidence interval.

related to the presence or absence of POF. Table 5 shows the total length of stay (mean and median) for each group. Total length of stay includes the initial length of stay (peri-operative) added to any readmission or outpatient procedure days divided by the number of patients in that group. This formula is an attempt to capture the potential cost or benefit experienced by the patient as a result of a difference in POF rates. With this we saw no difference in length of stay between all three groups. While not statistically significant, it may be clinically significant to point out that patients who received buttress material or underwent staple closure of the pancreatic stump required less treatment for POF (drain maintenance, radiological intervention, re-operation) then patients whose stumps were closed with suture.

Two staplers accounted for the majority of stapled pancreas transections. These were the Echelon™ 60 (Ethicon Endo-Surgery Inc., Cincinnati, OH, USA) or Autosuture™ Endo GIA (Covidien, Mansfield, MA, USA). In the large majority of patients a thick tissue staple load (green) was utilized. There was no difference in leak rates when the data were stratified by stapler, or staple size (data not shown). In 63 patients the Seamguard® product (Gore Inc., Flagstaff, AZ, USA) was utilized to reinforce the staple line and in 7 patients the Peristrip Dry® (Synovis Surgical, St. Paul, MN, USA) was utilized to reinforce the staple line. There was no difference in leak rate by reinforcement type (data not shown). When performing a hand-sewn closure, surgeons generally performed a separate ligation of the pancreatic duct followed by reinforcement of the pancreas parenchyma. The technique varied slightly by surgeon (choice of suture, fish mouthing of the pancreas parenchyma) but was consistent for each surgeon. There was no difference in leak rates for the individual surgeons when analysis of the hand-sewn technique was performed (data not shown).

It is our routine to leave a drain with all distal pancreatectomies. The intra-operatively placed drain was maintained for POF in 15

Table 5 Peri-operative morbidity

	Mesh (n = 70)	Stapler (n = 44)	Suture (n = 55)	P-values
Mean age (years)	49 (29–82)	55 (23–82)	59 (24–84)	0.17
Gender distribution	38 F : 32 M	25 F : 19 M	32F : 23M	0.84
Neoplastic lesion	53/70 (76%)	29/44 (66%)	43/55 (78%)	0.50
Laparoscopic approach	24/70 (34%)	4/44 (10%)	4/55 (7%)	<0.0001
Complex/extensive operation	18/70 (26%)	24/44 (55%)	19/55 (35%)	0.013
POF	7/70 (10%)	7/44 (16%)	18/55 (33%)	0.006
Mean LOS (median days)	10.1 (8)	10.7 (8)	12.3 (9)	0.36
60-day mortality	0	0	0	
Treatment of POF				
Surgical drain retained	3	4	8	0.76
IR/CT drain	3	3	9	0.13
Re-operation	0	1	2	0.62

POF, pancreas occlusion failure; LOS, length of stay; IR/CT drain, international radiology/CAT Scan guided drain.

Table 6 Classification of pancreatic occlusion failure

	Non-Mesh group (n = 99)	Mesh group (n = 70)	P-values
Grade 1	6	1	NS
Grade 2	5	2	NS
Grade 3	16	3	0.02
3a	13	3	0.02
3b	3	0	NS
Grade 4/5	0	0	NS

out of 169 patients (9%). Additional drains were required in 15 patients. These data suggest that routine intra-operatively placed drains capture about one-half of clinically significant POF.

Stratifying our POF-related complications based on use of mesh reinforcement (Table 6), we found that mesh reinforcement was associated with fewer grade 3a complications ($P = 0.02$). Mesh placement demonstrated no difference for complications which required pharmacological treatment alone, although the capture rate for less severe complications is more than likely incomplete. Over this study period there were no life-threatening complications requiring ICU management (Grade 4) and no deaths (Grade 5) were observed.

Discussion

While survival after pancreatic surgery has improved dramatically, the morbidity remains unacceptably high. This review focused on POF which remains the most common cause of morbidity after distal pancreatectomy. In modern prospective series, the overall morbidity after distal pancreatectomy may be as high as 47%[2] and POF is the basis for more than half of this morbidity.[1,2,9] Uniform definition and severity grading of pancreatic stump closure remain controversial.[29,35,36] In this study, we found that the severity and outcome-based complication scale best met our needs.[29] While there is an obvious clinical and psychological benefit to an uneventful recovery from surgery, it is also important to note that there are significant societal benefits in reducing the rate of POF. For example, the average patient with POF will utilize significantly more health care resources and will incur a cost approximately twice that of a patient without POF.[37]

We began using mesh to reinforce a linear stapler in a sporadic fashion in 2004. We were encouraged by our initial experience and performed a prospective study over approximately a 1-year period.[38] In the prospective series of 29 mesh reinforced resections, there was a single instance of POF for a rate of 3.5%. While the data was encouraging, there were several limitations and confounding factors. For example, although we planned to utilize the mesh in all patients during the study period alternative closures were utilized in 11 patients and 4 of those developed POF (36%). We postulated that we may have unwittingly selected patients at less risk for POF or that the mesh was not applicable for patients at the highest risk for POF. We suggested that a randomized clinical trial would be required to truly elucidate the effectiveness of the mesh.

One of the driving factors for conducting this analysis was to convince ourselves that this issue was worthy of a randomized controlled trial and attempt to determine the power required for such a trial. As far as we know this case series represents the largest experience with mesh reinforcement[38,39] and doubles the total published experience.

In our present series, mesh reinforcement of a stapled transection was associated with a reduced POF rate by both the univariate and multivariate analyses. These data suggest that the utilization of mesh was associated with a 60% reduction in POF rate (25% without mesh, 10% with mesh, $P < 0.02$). However, when one breaks down closure technique we find no significant difference between mesh reinforcement and staple closure effect on POF. There also appeared to be no reduction in the mean/median total length of stay for patients who received mesh reinforcement when compared with those who did not.

Concurrently, it is important to point out that we used a larger percentage of mesh reinforcement in each successive year and yet the POF rate for the entire population of patients was not significantly reduced over the course of the study period.

We found a significant reduction in the leak rate when staplers are utilized (with or without mesh) when compared with the hand-sewn technique. As our group preferentially utilizes a stapler whenever technically feasible we can not utilize these data to comment on the issue of hand sewn versus the stapled closure of the distal pancreas. Following our prospective series on the potential benefit of utilizing the stapler with mesh we have attempted to utilize a mesh-covered stapler whenever technically possible. In doing so we have identified situations in which we have discovered that a stapler (with our without mesh) is not an ideal approach to closure. In our opinion it is in pushing the limitations of the mesh-covered stapler which is partly responsible for the reduction in apparent benefit between our initial experience and this series. As we continue to gain experience with the stapler we have found that the triangular pancreas, the very thick pancreas (>1.5 cm), the very firm or non-compressible pancreas and a transection plain to the right of the gastro-duodenal artery are suboptimal situations for a stapled closure. Future studies should aim to collect more details regarding the relevant pancreatic anatomy and consistency. Precise measures of these variables will enhance our ability to determine the ideal scenario for stapler transection and mesh reinforcement.

There was an absolute percentage difference in POF rate of 10% versus 16% in favour of mesh reinforcement of the stapler. Review of the literature suggests that the leak rate for mesh reinforcement may be less than 5% and that the leak rate for stapled transection without mesh may be as high as 20%. Utilizing these numbers and our current series as a best and worst case scenario a trial would require as many as 76–486 patients per group to attain a power of 80% at a 0.05 significance level. In our opinion this trial will best be achieved with a multiple-center randomized control design. After carefully reviewing our experience and the literature, our group believes that there is equipoise on this issue and are in the process of attempting to organize a multi-centre prospective randomized trial.

There were several unintended conclusions which arose from analysing these data. First, extended resections were associated with an increased POF rate. While it would be expected that more extensive surgery might result in increased mortality, or length of the stay, the reason for the increase in the POF rate is unknown. It might be speculated that extensive resections in our group included cases in which the pancreas was peripherally involved (i.e. sarcoma, gastric carcinoma). In patients where the pancreas is expected to be relatively soft,[5] more POF might be expected. It is also possible that the blood supply to the distal pancreas may be reduced as a result of the extent of resections.[8,40] Patients requiring such large resections might also be malnourished and fail to seal appropriately. The data are insufficient to clearly identify the cause but it is clear that larger resections were associated with an increased risk for POF.

We also found that laparoscopic resection appeared safe and did not differ in POF rates from open surgery. In fact the absolute number and percentage of POF were less in the laparoscopic group. This seemed counter intuitive because we found that laparoscopy was more often performed for patients with cystic neoplasms where the pancreatic tissue is soft and therefore more prone to POF. The equivalence of outcome in this setting is encouraging for the continued expansion of minimally invasive techniques in hepatobiliary surgery.

Lastly, we found that routinely placed drains were capable of capturing POF and preventing the need for additional procedures in 9% of the patients undergoing a distal pancreatectomy. In 169 patients there were 32 instances of POF (19%). In 15 out of the 32 POF (47%), the surgically placed drain was maintained as the only required treatment. We are not aware that any group has prospectively studied the question of routine drain placement in patients undergoing a distal pancreatic resection. In one study, when patients were randomized to receive a drain after pancreaticoduodenectomy, there was an increase in complications.[24] One could argue for or against routine drainage after distal pancreatectomy based on our data. In our opinion routine drains are currently indicated and will be required in our randomized clinical trial. If the leak rate can be reduced routine drainage may eventually become unnecessary.

Conclusions

Absorbable mesh reinforcement of a pancreatic transection line may reduce the POF rate associated with distal pancreatectomy. Although there was increased utilization of mesh over the duration of the study period, there was not a significant reduction in the POF rate for the entire population. Our group believes that the incorporation of mesh shows promise as a method to reduce the POF rate. The present work, while the largest review of the topic, inadequately addresses the differences between mesh utilization and stapler alone. A multi-institution randomized prospective trial is needed to conclusively address this issue.

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Conflicts of interest

None declared.

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