Combination of fibrin glue protection with microsurgical technique for duct-to-mucosa pancreatico-jejunostomy reduces the incidence of leakages after pancreaticoduodenectomy

Gaetano La Greca*, Stefano Primo*, Maria Sofia*, Rosario Lombardo*, Stefano Puleo**, Domenico Russello*, Antonio Di Cataldo**

*Dipartimento Scienze Chirurgiche, Trapianti d'organo e Tecnologie Avanzate, Az. Ospedaliera Cannizzaro, Catania, Italy
**Dipartimento Scienze Chirurgiche, Trapianti d'organo e Tecnologie Avanzate, Az. Universitaria Policlinico OVE, Catania, Italy

Combination of fibrin glue protection with microsurgical technique for duct-to-mucosa pancreatico-jejunostomy reduces the incidence of leakages after pancreaticoduodenectomy

The Achilles' heel of pancreatic surgery is the management of the pancreatic stump. Leakage from pancreatic anastomosis with subsequent fistula, abscess formation, sepsis, or bleeding is one of the most common causes of morbidity and mortality, and it also contributes significantly to prolonged hospitalization and increased hospital expenses. Many surgical methods have been developed aimed at reducing the incidence of post-operative pancreatic fistula. However, the best technique for pancreatico-enteric reconstruction continues to be disputed. Herein, we describe an interim analysis of 35 consecutive pancreatico-duodenectomies, all with the same standardized technique that combines microsurgical technique for duct-to-mucosa anastomosis, combined with routine sealing of the pancreatic anastomosis are key factors to efficiently manage the pancreatic stump. The good results obtained and especially the minimal rate of fistula suggests that this technical solution is a safe, feasible and reliable approach for pancreatic reconstruction after pancreatico-duodenectomy.

KEY WORDS: Duodenopancresectomy, Duct-to-mucosa anastomosis, Fibrin glue, Pancreatico-jejunostomy

Introduction

Since it was first introduced, and until the late 1970s, the mortality rate after pancreatico-duodenectomy was >20% 1,2, but advances in surgical technique and perioperative management have dramatically reduced postoperative mortality to less than 5%, and now this procedure is considered the “gold standard” for malignant and benign pancreatic and peripancreatic diseases. However, the morbidity rate remains quite high even in large series 3-7. Several clinical trials have focused on decreasing the incidence of pancreatic fistula through numerous variations of pancreatic anastomosis, accompanied by thirty years of testing drugs such as somatostatin analogues or gabesatemesilate 8-9, and the use of glue and sealants 10. However, the management of the pancreatic stump remains a significant surgical challenge and no technique for the prevention of pancreatic fistula has yet become standard. Herein, we describe our preliminary data using a combination of microsurgical duct-to-mucosa pancreatico-jejunostomy with the routine use of fibrin glue to seal the anastomosis.
Patients and Methods

35 consecutive patients who all underwent pancreaticoduodenectomy with microsurgical duct-to-mucosa pancreatico-jejunostomy and perianastomotic pancreatic sealing with fibrin glue were evaluated. The pancreaticoduodenectomy was performed according to the Whipple procedure including, for malignancies, a standard lymphadenectomy. The reconstruction after pancreatic resection was performed by using two separate jejunal loops for the anastomoses. The pancreatico-jejunal anastomosis was performed first, the hepatico-jejunal anastomosis was second and the gastro-jejunal third. The jejunal loop for both pancreatic and biliary anastomosis was usually passed in an anatomic retro-mesenteric position, or if not compliant, via a trans-mesocolonic incision on the right of the middle colic artery. The second jejunal loop for the gastro-jejunal anastomosis was also passed transmesocolonically on the left of the middle colic artery. The hepatico-jejunal anastomosis was performed end-to-side with interrupted 4/0 PDS sutures. Finally, the gastro-jejunal anastomosis was performed in a partial, aboral, end-to-side position with interrupted Vycril® 3/0 sutures. The pancreatico-jejunal anastomosis was performed as follows: the preparation of the pancreas stump was always the same but particular care was taken. The transection of the pancreas was exclusively performed with one or two clear cuts with the scalpel previously posteriorly protecting the mesenteric vein; after parenchymal transection the hemostase of the bleeding vessels on the cut surface of the pancreas was obtained only with a few 6/0 PDS® X stitches or low energy bipolar coagulation, and a few minutes of compression with Tabotamp®. The circular border of the pancreatic stump was prepared for the anastomosis but only for 10-12 mm, to avoid excessive devascularization. The jejunal loop was closed with a stapler and the stapler line was covered with an inverting running 3/0 suture. The technique of duct-to-mucosa anastomosis that we performed can be summarized in three main steps: a posterior layer between the pancreatic capsule and the serous-muscular layer of the jejunum realized by a 3-0 Vycryl® suture; a duct-to-mucosa anastomosis was realized by at least 8 interrupted stitches (5-0/6-0 absorbable suture Maxon®) with magnification by microsurgical loop at 2 or 4 X, with or without a temporary duct stent, removed prior to knotting the last two anterior sutures; the completion of the anastomosis was obtained with an anterior layer between the pancreatic capsule and the serous-muscular layer of the jejunum. The end to side hepatico-jejunalostomy was performed more distally on the same jejunal loop by an interrupted PDS 4/0 suture. Once these two anastomoses were completed the fibrin glue Tisseal® was applied all around the pancreatico-jejunalostomy beginning with the posterior part, first injecting in the space between the pancreas and the mesenteric vein, and then anteriorly and laterally covering the anastomosis (Fig. 1). Two closed system vacuum drains were positioned, the right one passing behind the jejunal loop and the biliary anastomosis with the tip posterior to the pancreatic anastomosis and the left-sided one behind the gastro-jejunal anastomosis and near the pancreatico-jejunal anastomosis. Gender and age of the patients, diagnosis and operative time were considered. Amylase and lipase levels were investigated in the two drains on postoperative day 3, and then every day until drainage removal, (normally on the 7th PO day). The amylase levels were recorded and the leakages were classified according to Clavien classification ISGPF. Rates of post-operative leakage and morbidity were registered and provided as a brief description of the technique adopted.

Results

35 patients underwent pancreatico-duodenectomy using the technique described above and the pancreatico-jejunalostomy was always performed the same, by a microsurgical duct-to-mucosa anastomosis. The male/female ratio was 3/1.5 and the mean age of the patients was 66 years (range 55-78). 26 patients were affected with pancreatic adenocarcinoma, in two cases malignant NET (Neuroendocrine tumor) was associated with the adenocarcinoma, 3 with a adenocarcinoma of the duodenum/papilla, in 4 cases with biliary carcinoma, and 2 with chronic pancreatitis. The mean overall operative time was 245-430 minutes while the duct-to-mucosa anastomosis required a mean time of 12 minutes (8-19 min). Postoperative amylase and lipase levels in the
drainage liquid were investigated daily. In only 2 patients (5.7%) did the amylase levels from the drains increase. In one patient amylase increased on day 4 but returned to normal within 3 days. Another patient developed a grade A fistula, which was treated conservatively and healed within 10 days with complete normalization of amylase levels. No biliary or other post-anastomotic fistulas occurred. The mortality rate was 2.8% to one patient who was rated as an ASA IV class with post-hepatitis Child-Pugh B cirrhotic liver, leading to death five days after surgery due to acute heart failure. One patient developed a delayed gastric emptying due to a stenosis of the gastrojejunal anastomosis that had to be treated with a second surgery 4 weeks after discharge, for the reconstruction of this anastomosis.

Discussion

The Achilles’ heel of pancreatic surgery is the management of the pancreatic stump. Leakage from pancreatic anastomosis, with subsequent pancreatic fistula (PF), abscess formation, sepsis or bleeding, is one of the most common causes of morbidity, and also contributes significantly to prolonged hospitalization and increased hospital expenses. In an attempt to prevent pancreatic anastomosis leakage, some factors have been identified as being related to the leakage. These factors include: the pancreas factor, (pancreatic texture, blood supply to the cut end, original pathology, pancreatic duct size, pancreatic juice output), the patient factor, (age, gender, level of jaundice, comorbid illness), and the operation factor, (total operation time, blood loss, type of anastomosis, stenting of anastomosis) 3-11. It is generally accepted that a fibrotic pancreatic remnant facilitates the pancreatico-enteric anastomosis, whereas a soft and fragile pancreatic remnant frequently results in a high pancreatico-enteric anastomosis leakage rate. A recent review estimated the incidence of PF complications to be 10 to 28.5% 3. A postoperative PF is currently defined by the International Study Group on Pancreatic Fistulas (ISGPF) as “output via an operatively placed drain (or a subsequently placed, percutaneous drain) of any measurable volume of drained fluid on or after postoperative day 3, with an amylase content greater than 3 times the upper normal serum value.” 3. The ISGPF has also recommended grading PFs by severity (A, B, and C), with grade A being least severe and grade C being most severe. The rate of postoperative pancreatic fistula is therefore the main parameter for measuring the success of the pancreatic anastomosis so that each new method to reduce the rate of leakages is a welcome solution to improve the overall results in this field. This is why a large variety of techniques have been developed and evaluated over the years. Pancreatico-jejunoanostomy has been the most commonly used method, but the best technique for pancreatico-enteric reconstruction continues to be disputed. A direct anastomosis between the Wirsung duct and the mucosa of the jejenum has shown an incidence of post-operative pancreatic fistula between 6.25-11% 14. Within the variations of pancreatico-jejunoanostomy the most commonly used is the duct-to mucosa pancreatico-jejunoanostomy which is normally performed in a standard manner without magnification. In recent years, the surgeon has been shown to be one of the most, if not the most, important factor in the prevention of pancreatic anastomosis leakage through level of experience and meticulous technique 15,17. Therefore, in aiming to minimize leakages and improve outcome, we decided to change our technique for the pancreatic anastomosis. While still utilizing the most commonly used technique, we also employed the best possible technical options. We chose to perform the end-to-side pancreatico-jejunoanostomy, implementing the precision of microsurgical duct-to-mucosa suturing while also deciding to add the routine use of fibrin sealant all around the anastomosis. For the duct to mucosa anastomosis we adopted interrupted suturing, considering it safer than a continuous suture as suggested 18. We adopted a microsurgical technique, strongly believing in the advantages of magnification and the ‘precision’ of microsurgery supported by extensive experience with clinical and experimental microsurgical technique 18,20, but also considering the clearly positive results reported using microsurgical technique in the duct to mucosa pancreatico-jejunal anastomosis 21. The technique most normally used employs only 4 sutures at the edges of the duct-to mucosa, also using microsurgical technique 21. We however applied at least 8 sutures, sometimes 10, this is because with only four sutures the mucosa of the jejunum will directly adapt at only four points, (as a square within the non-adaptable pancreatic duct, which is barely fixed to the parenchyma). Our technique helps avoid gaps between the sutures. Moreover, magnification and therefore precision is especially useful in small ducts that are related to a higher rate of leakage. The rationale behind the use of magnification is also related to the size of the Wirsung ducts, which in a recent series of 709 consecutive duodeno-pancreatectomies 22 with duct-to mucosa anastomosis, showed a mean size of 2.6 mm 22,3,8. This shows that precision and magnification can certainly be a relevant and useful aid in improving the anastomosis in the majority of such thin ducts. In comparison, it is clear that a standard “non-magnified” anastomosis for pancreatico ducts of this size is a “gross” technique with a high risk of leakage. In this very large series of duct-to mucosa pancreatico-jejunal anastomosis without the use of fibrin glue, the overall fistula rate was 15.4% with grade B/C fistulas 10,7 % higher than our 5.7%, of only grade A. We decided to add the fibrin sealant because there has been varying positive data and experiences with sealant and fibrin glue, despite none being statistically significant 10,23,25. It is also logical to conclude that sealing the pancreas from the outside, includ-
ing the surrounding peripancreatic structures, could be helpful in covering surgically cut or damaged, but anastomized, structures. This will aid in preventing the minimal lateral leakages, especially in the first days following surgery, and also prevent the chemical damage of amylase/lipase on surrounding pancreatic and peripancreatic tissues for the first post-operative days. The reinforcement of the site of pancreato-enteric anastomosis with a bio-compatible substitute has been reported to provide good support for the prevention of leakage in both pancreatico-jejunal anastomosis and other gastrointestinal anastomosis. In the only prospective randomized trial, the authors registered a 3.8% reduction of pancreatic leakage in the fibrin glue group, (40% glue group vs 43.8% non-glue group) that despite not being statistically significant was positive, even more when considering the “gross” invagination technique used for the anastomosis. The concept of the circular sealing of the pancreatico-jejunal anastomosis with glue, to also prevent minimal leaks and minimal early post-operative chemical damage of amylase/lipase on the surrounding tissues.

Our study is unique in its methodology as it combines microsurgical duct-to-mucosa pancreatico-jejunal anastomosis and the use of fibrin glue applied to all the reconstructive PD; resulting in only a 5.7% incidence of grade A pancreatic fistulas, and 0% grade B, or C fistulae. These are clearly positive results in a simple comparison with the data in the literature on the rate of fistula.

Potential criticism of this study could be the small sample size, but otherwise the strict standardization of technique and the indisputable and surprisingly positive results suggest that we publish it, with the aim of encouraging others to attempt the use this combination. Despite being limited by our preliminary results, this technique may be a safe and effective combination for preventing pancreatic fistula development after duodenopancreatectomy when performed by experienced surgeons, skilled in microsurgical technique. Further randomized clinical trials comparing this method with standard procedures are required to confirm its actual efficacy.

Riassunto

L’insorgenza della fistola pancreatica a seguito di anastomosi pancreatica rappresenta la causa più comune di morbilità e mortalità. Nel corso degli anni sono state sviluppate numerose tecniche di anastomosi pancreatica e sono stati usati diversi materiali e dispositivi (colle, stents) con l’intento di ridurre l’incidenza della fistola pancreatica post-operatoria. In questo lavoro presentiamo l’analisi di 35 consecutive duodenocefalopancreatectomie, tutte con la stessa tecnica standardizzata che combina la tecnica microchirurgica con l’uso di colla di fibrina per l’esecuzione dell’anastomosi pancreatico digiunale dottomucosa. I risultati ottenuti con questa combinazione sono promettenti in particolare se comparati ai risultati presentati in letteratura dove viene usata la stessa tecnica chirurgica ma senza l’utilizzo della microchirurgia e/o di colle di fibrina.

La precisione grazie alla magnificazione ottica degli strumenti microchirurgici combinata all’uso della colla di fibrina sono fattori chiave per l’anastomosi pancreatica. I risultati ottenuti e soprattutto il basso tasso di fistola pancreatica mostrano che questa tecnica è sicura ed efficace per la ricostruzione del moncone pancreatico.

References


