
Prospective Trial of a Blood Supply-Based Technique of Pancreaticojejunostomy: Effect on Anastomotic Failure in the Whipple Procedure

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- BACKGROUND:** Anastomotic failure at the pancreaticojejunostomy after a Whipple procedure, manifested either as a pancreatic fistula or intraabdominal abscess, is still an unacceptably common postoperative complication.
- STUDY DESIGN:** A prospectively collected series of 123 patients underwent a Whipple procedure. During the pancreaticojejunostomy, the blood supply at the cut surface of the pancreas was evaluated, and if deemed inadequate, the pancreas was cut back 1.5 to 2.0 cm to improve the blood supply. The anastomosis was performed under magnification with meticulous technique.
- RESULTS:** There were 123 Whipple procedures performed. In 47 (38%), the blood supply was considered inadequate and the pancreas was cut back. Postoperatively, there were 2 pancreatic fistulas (1.6%) and 2 intraabdominal abscesses (1.6%). There was 1 (0.8%) postoperative death from aspiration pneumonia.
- CONCLUSIONS:** Pancreatic fistula, the most serious complication of the Whipple procedure, can be almost entirely eliminated by a technique that combines meticulous attention to placement and tying of sutures under magnification with optimization of blood supply to the anastomosis. (*J Am Coll Surg* 2002;194:746–760. © 2002 by the American College of Surgeons)
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Fistula formation at the pancreaticojejunostomy is the “Achilles heel” of the Whipple procedure. Fistula rates of 10% are still common, even at tertiary care hepatobiliary centers.^{1–5} Anastomotic failure at the pancreaticojejunostomy, defined as either a pancreatic fistula or a postoperative intraabdominal abscess resulting from a leak at the pancreaticojejunostomy,⁶ is still one of the main causes of serious morbidity after pancreaticoduodenectomy. Although morbidity after a Whipple operation is increasingly uncommon, when it does occur, it is often associated with fistula at the pancreaticojejunostomy or an abscess secondary to a pancreatic leak.

Three years ago we presented preliminary information in this journal suggesting that the incidence of fis-

tula could be greatly reduced by using a method that combined precise anastomotic technique with consideration of the state of blood supply of the stump of the pancreas.⁶ This was the first mention in the literature that inadequate blood supply might contribute to anastomotic failure. We have continued to collect cases prospectively using this technique, with small modifications, and now are able to report the lowest fistula rate recorded in a large series of patients. But the main purpose of this article is to describe our technique in detail because we now consider it likely that the use of a precise technique is of equal importance to optimizing blood supply. Although we make no claim that it is the only technique that might achieve such results, we do believe that it is a method that can be readily performed by surgeons with an interest in this area, and if widely adopted would virtually eliminate this problem.

METHODS

Patient population

In a 4-year period, from 1996 to 2000, 123 patients having Whipple procedures on the hepatobiliary-pancreatic service of our institution had pancreaticoje-

No competing interests declared.

Presented at American College of Surgeons 87th Annual Clinical Congress, New Orleans, LA, October 2001.

Received November 1, 2001; Revised January 2, 2002; Accepted January 9, 2002.

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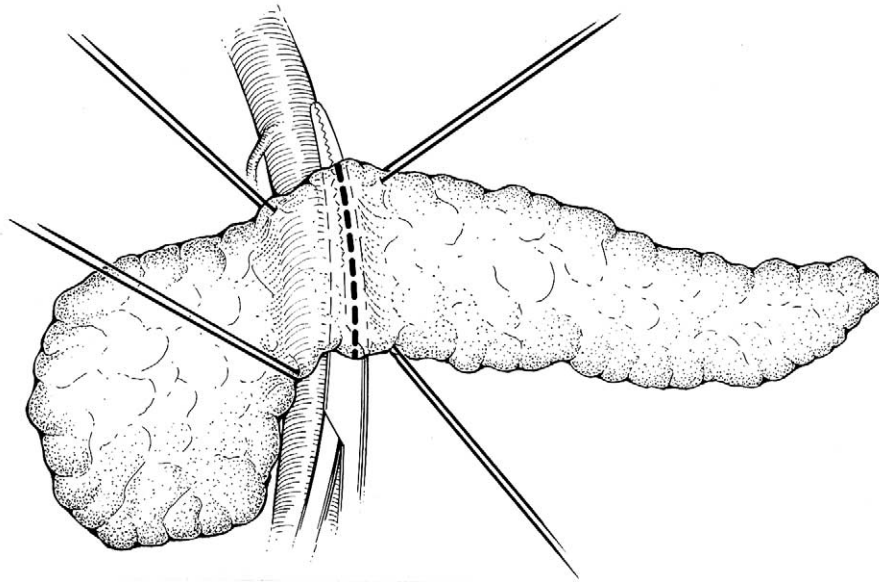


Figure 1. Transection of the neck of the pancreas. Note four silk stay sutures used to lift the pancreatic neck and a large clamp placed beneath the neck of the pancreas to protect the superior mesenteric and portal veins. Line of transection (dotted line) is close to left-sided stay sutures to increase chances of having an adequate blood supply.

junostomy performed in the manner to be described. There were 59 men and 64 women, and median age was 66 years (range 32 to 88 years).

Detailed description of method

Equipment

1. 2.5–3.5 \times power ocular loupes. Magnification is an absolute necessity to consistently perform this anastomosis with success on pancreatic ducts less than 3 mm in diameter. This is the median diameter of pancreatic ducts in our series. The anastomosis cannot be performed at all using this technique without magnification when the pancreatic duct is 1.5 mm or less.
2. 5-0 and 6-0 double-armed monofilament absorbable sutures.
3. 5-0 and 6-0 monofilament nonabsorbable sutures.
4. 2-0 silk sutures.
5. 3.5 Fr and 5 Fr pediatric feeding catheters.

Technique

Pancreas transection. The pancreatic neck is stabilized with four stay sutures of 2-0 silk suture (Fig. 1). The transverse (right to left) distance between the two sets of stays on the superior and inferior borders of the pancreatic neck is 1.5 to 2.0 cm (Fig. 1). A large Kelly clamp is placed behind the neck of the pancreas, anterior to the axis of the superior mesenteric vein and portal vein to protect these structures during transection. The neck

is divided sharply with a No. 10 scalpel blade on a long handle in several successive long strokes. Initially, the line of transection used was along a line halfway between the stay sutures, immediately over the longitudinal axis of the mesenteric vein.⁶ For reasons that will become clear, the technique has evolved so that now the line of transection is immediately adjacent to the left stay sutures (Fig. 1), ie, the neck of the pancreas is not so much transected as removed flush with the body of the pancreas. Suction is used to control bleeding during transection when necessary. The pancreatic body is not mobilized beyond this line of transection, so blood supply will not be disturbed, ie, the pancreas is cut flush with surrounding tissue, much as one aims for when cutting the common hepatic duct for anastomosis.

Control of bleeding from the cut surface of the pancreas. Immediately after division of the pancreas, bleeding from the right side of the transected pancreatic neck is controlled with cautery. During this maneuver, the neck is lifted away from the superior mesenteric and portal veins to protect them. It is rarely necessary to use sutures for hemostasis on this particular cut surface. Attention is then turned to the cut surface on the body of the pancreas. The position of the pancreatic duct is noted. The presence and location of arterial bleeding from the cut surface are also noted. Pulsatile bleeding is

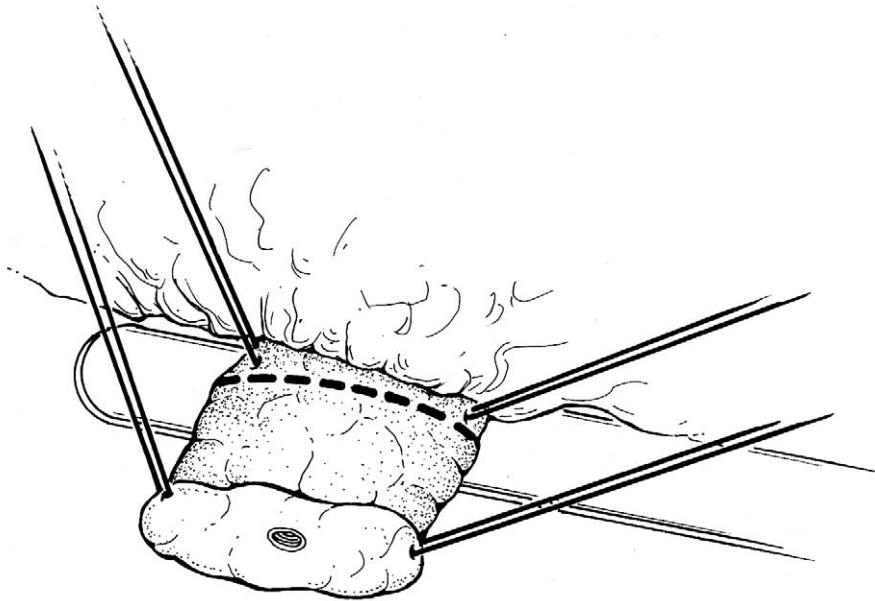


Figure 2. Cutting back the pancreas to a new resection margin. The pancreas has been mobilized for 1.5 to 2.0 cm. New stay sutures are placed at the left-most end of the dissected gland. A malleable retractor is placed behind the gland to protect the splenic vein. The pancreas is recut along a line (dotted line) adjacent to the new stay sutures. The pancreas is not mobilized beyond this point.

arrested with 5-0 or 6-0 monofilament nonabsorbable sutures. Minor bleeding may be controlled with needle-point cautery set at 15 W. During control of bleeding, great care is taken not to distort the pancreatic duct orifice by sutures or by the use of cautery in proximity to the ductal orifice.

Determination of adequacy of blood supply to the pancreatic neck. Blood supply is considered adequate when pulsatile arterial bleeding is present both superior and inferior to the pancreatic duct on the cut surface of the pancreas. The bleeding must be brisk, ie, of a level that requires sutures to stop the bleeding. If there is no bleeding, or if the bleeding points are of an oozing type that could be controlled without sutures, the blood supply is considered inadequate.

Cutting back the pancreas to a new resection line. Whether bleeding is adequate or not, the next step in the procedure is the uncinata dissection and removal of the specimen. After this is completed in patients in whom the cut margin of the pancreas is considered not to have adequate blood supply, the body of the pancreas is mobilized toward the left side by dissecting it off the splenic vein and surrounding structures for a distance of 1.5 to 2.0 cm. At the completion of this dissection, which usually takes 5 to 10 minutes, two stay sutures of 2-0 silk are

placed on the inferior and superior borders of the pancreas at the left-most point of the newly mobilized pancreas. A narrow malleable retractor is placed under the pancreas and the pancreas is recut just to the right of the newly placed stay sutures (Fig. 2) almost flush with the point to which the pancreas has been mobilized. The excised tissue contains the new resection margin and is sent for frozen section. Adequacy of blood supply is determined, and bleeding is arrested as noted. When the pancreas must be cut back because of a positive margin at the pancreatic neck, as opposed to vascular considerations, the same technique is used. The pancreas is cut back only once, unless there are oncologic reasons for additional resection.

Preparation of the jejunum for anastomosis (Fig. 3). The stapled end of the jejunum is turned in with a continuous 3-0 absorbable monofilament seromuscular suture. The two goals of jejunal preparation are to make an opening that corresponds in size with that of the pancreatic duct, and to evert the mucosa with sutures so that it will be included in all the jejunal stitches. Preparation of the jejunal opening is critical to the success of the technique. Without correct preparation, it is not possible to be certain that every suture has been correctly placed in a mucosa-to-mucosa fashion.

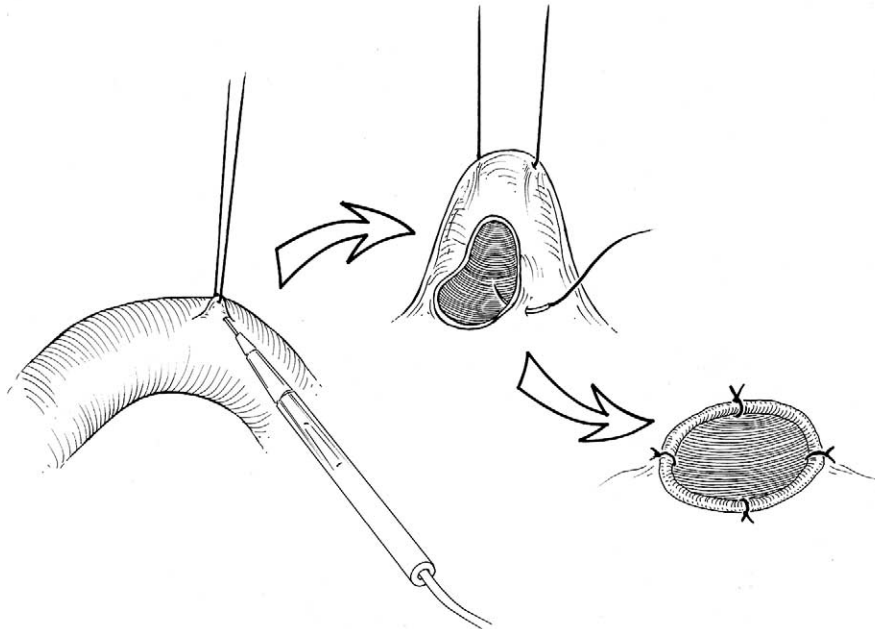


Figure 3. (Left) The bowel is picked up with a fine suture. The amount of tissue elevated depends on the size of the pancreatic duct, the goal being to make an equal-sized opening in the jejunum. The elevated tissue is cut away with blended cutting current. (Middle) After the bowel is picked up a second or third time, deepening the opening in the jejunum, a point is encountered at which the mucosa is incised. Sometimes opening the mucosa is facilitated by using fine tenotomy scissors. The incision is carried only half way across the mucosa until the initial 6-0 sutures are placed. (Right) The entire disc of the jejunum is excised and the mucosa everted with four 6-0 sutures. These are cut very short.

The jejunum is lifted up with a 5-0 suture on the antimesenteric border 3 to 4 cm from the occluded end. The tissue so elevated is excised using blended cutting current at 30 W with a standard cautery tongue blade or at 15 W with a needle point cautery tip (Fig. 3, left). The process is repeated until mucosa is incised and a full-thickness disc of bowel is removed. This disc can be as small as 1 mm in diameter or as large as 7 mm in diameter, depending on the size of the pancreatic duct. Then the mucosa is everted and fixed to the seromuscular layer with fine 6-0 absorbable monofilament sutures. Eversion assures that any needle entering or leaving the opening in the jejunum will pick up the mucosa. Four or more sutures are used to complete the eversion. Leaving a portion of the bowel disc attached until the first two or three sutures are placed facilitates this operation (Fig. 3, middle). It is essential that a full ring of mucosa is seen at the end of this stage (Fig. 3, right) or mucosa-to-mucosa anastomosis will not be assured.

Placement of anterior row of sutures in the pancreas. These sutures (5-0 absorbable monofilament) are used to pick up the wall of the pancreatic duct and 5 to 8 mm

of pancreatic tissue next to the duct. It is essential that good bites of tissue are obtained with each suture and great attention to detail is required in this regard when taking the first three sutures on the anterior wall, especially in a small duct. Sutures must be placed atraumatically or the duct will tear. The technique is designed not to pull or lift the duct. Once three sutures are taken, the pancreas becomes fixed, and the duct is splayed open, making placement of the remainder of the anterior row sutures easier.

Suture 1 (Fig. 4A). This is the inferior corner stitch (3 o'clock as one faces the pancreas). The surgeon stands on the right side of the patient. A Castroviejo-type needle driver is used. The needle is placed at a right angle to the length of the driver. The driver is placed in a vertical position (Fig. 4a), pointing directly posteriorly at a right angle to the transverse axis of the cut surface of the pancreas. The needle is pointed left toward the duct. It is inserted into the duct by moving the driver to the left. The needle is driven by spinning the driver clockwise around its long axis as seen from above. All movement of the needle is attained by rotation of the needle driver rather than caudal movement of the driver. This avoids

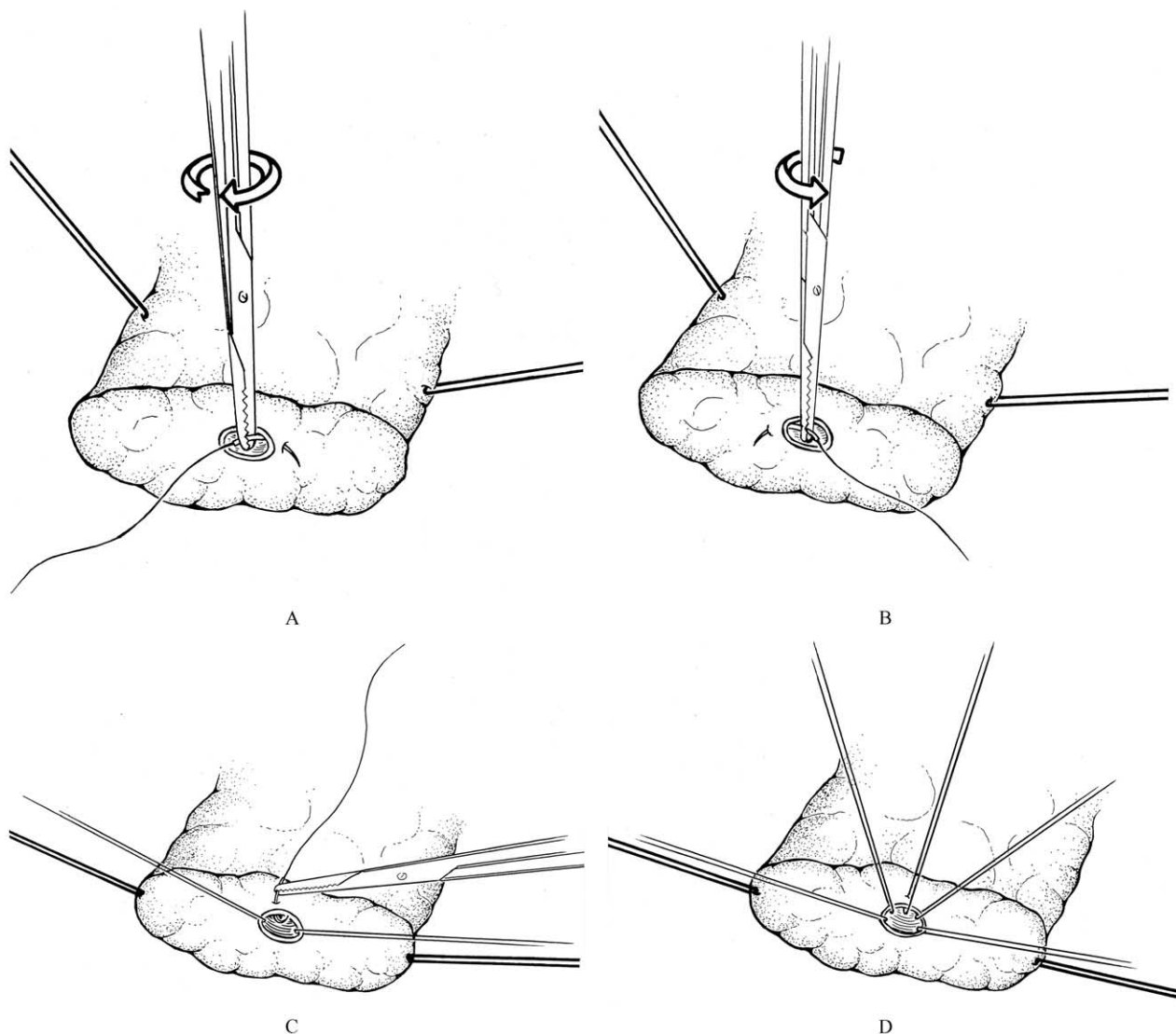


Figure 4. (A) First anterior row suture at the 3 o'clock position. The Castroviejo needle driver is placed at a right angle to the transverse axis of the cut surface of the pancreas. The needle is slipped into the lumen of the duct and the stitch taken entirely by a rotatory movement as shown. This places no lift on the pancreatic duct or pancreas. (B) Second anterior row suture at the 9 o'clock position. The suture is taken as the first, except backhanded. (C) The 12 o'clock suture is taken outside-in and the first two sutures stabilize the duct. (D) The other anterior row sutures are taken. The number of sutures depends on the size of the duct, but usually five or seven anterior wall sutures are placed.

placing a lifting force on the pancreatic duct that can result in injury to the duct, especially if it is small. In ducts smaller than 3 mm, it might be useful to add curvature to the needle manually. Neither the pancreas nor the pancreatic duct is handled with forceps. The needle will emerge from the cut surface of the pancreas 5 to 8 mm inferior to the duct.

Suture 2 (Fig. 4B). The needle is mounted “backhand” on the needle driver at a right angle to the long axis of the driver. It is driven superiorly in a “backhand”

motion (9 o'clock). Otherwise, this stitch is taken as the last, except that the rotation is counterclockwise.

Suture 3 (Fig. 4C). This suture is placed anteriorly at 12 o'clock. It can be taken from inside or outside the duct, but in our experience it is difficult to position the driver sufficiently horizontally to take the bite from the inside of the duct. To take the bite from outside the duct, the needle is positioned 5 mm anterior to the duct and driven into the lumen of the pancreatic duct, 3 to 5 mm from the cut end. When the duct is small, it can

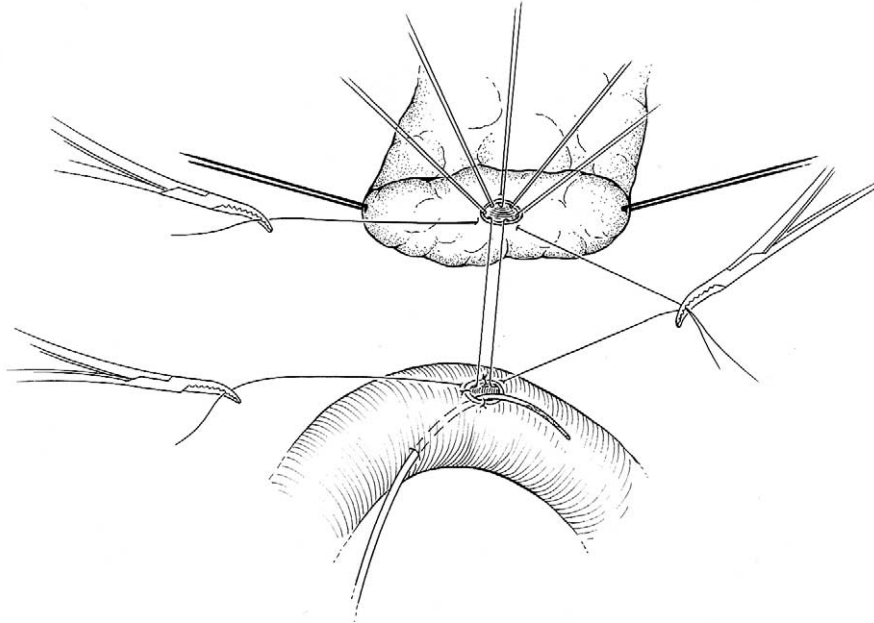


Figure 5. Posterior suture row. The sutures are placed so that they will be tied on the outside of the anastomosis. The ends are clamped separately, except for the first suture, to facilitate tying from the middle of the back row to the ends. The stent is shown for position only. A stent would not be used for a duct of the size shown, and it would be inserted into the jejunum only after all posterior row sutures had been placed. After those sutures are tied, it is inserted into the pancreatic duct.

be difficult to come through the anterior wall and exit through the cut end without picking up the posterior wall. This can be facilitated with the aid of a 5-F infant feeding catheter in the duct. The needle is purposely driven into the front wall of the tube, and then as the tube is extracted from the duct, the needle follows.

Subsequent anterior row sutures (Fig. 4D). The other anterior wall sutures in the pancreas are readily taken once the front wall has been triangulated. In most cases, either two (1.5- to 3-mm ducts) or four additional sutures (4- to 5-mm ducts) are placed. In the smallest ducts (1.0 to 1.5 mm), no additional sutures are placed. When ducts are larger than 5 mm in diameter, additional sutures are placed; but as duct size increases, sutures are placed somewhat deeper and farther apart so that the suture total does not exceed 9 or 10 even on the ducts as large as 8 mm. The anterior row of sutures is usually drawn to the left and covered so as not to tangle or be confused with the posterior row of sutures.

Placement of posterior row of sutures in the pancreas and the jejunum. The most posterior suture (6 o'clock) is placed first. Either the bowel or pancreas is taken first. The pancreatic suture is taken from the inside of the duct. If the bowel is picked up first, the stitch

can be taken outside-in, and then the same needle is used on the pancreas. If taken inside-out, the other needle is used for the pancreatic bite so that the suture will be tied on the outside of the anastomosis (Fig. 5). About 5 mm of full-thickness jejunum is taken. The two ends of the suture are placed in a shod mosquito clamp. Additional sutures are placed inferior and superior to the 6 o'clock stitch. Care is taken to space the sutures evenly. The number of sutures is usually two less than on the front row, because the front row has the superior and inferior corner stitches. As each subsequent stitch is placed, the ends are held in two separate clamps so that the posterior row can later be tied from the middle of the anastomosis to the corners (Fig. 5). The type of clamp can be varied for easier identification.

Placement of a stent. Stents are placed in all ducts less than 2 mm in diameter and in some ducts 2 to 3 mm in diameter, but not in larger ducts. Infant feeding catheters (3.5 F) are used in ducts less than 1.5 mm in diameter and 5-F feeding catheters are used in larger ducts. The stents are fed into the jejunum after the posterior row of sutures is placed, but before they are tied (Fig. 5). A thin-walled metal tube (a tonsil suction tip is usually used for this purpose) of slightly greater internal diame-

ter than the 5-F tube is inserted into the anastomotic opening in the jejunum. It is advanced toward the antimesenteric side of the bowel and down the bowel about 2 cm downstream from the anastomotic opening (Fig. 5). An incision in the jejunum is made at the point where the end of the metal tube is lifting the intestine and the metal tube is advanced out of the intestine. After inserting the end of the feeding catheter into the end of the metal tube, the metal tube is withdrawn through the anastomotic opening, bringing the infant feeding catheter with it. This method is preferable to using a clamp or other hinged instrument through the anastomotic opening, because passage of the metal tube does not dilate the opening, as might occur when a hinged clamp is opened to grasp the catheter.

The stent is inserted into the pancreatic duct after the posterior wall sutures are tied. It is advanced until resistance is met and then withdrawn 1 cm. The stent is fixed to the exit point on the bowel with a single 4-0 chromic suture. This suture is placed full thickness in the bowel and is used to close the opening around the stent and then used to tie the stent in place. An additional seromuscular suture of the same material is used to create a tunnel around the exit point of the stent. The main purpose of the stent is to provide extra visibility of the position of the lumen of the jejunum when placing the anterior row sutures in the jejunum.

Tying the posterior suture line. The jejunum is placed adjacent to the pancreas. The jejunum should be touching the pancreas and should lie loosely in this position so there is no tension when tying. If tension is placed on the sutures to draw the jejunum to the pancreas, there is a danger of the sutures cutting the pancreatic parenchyma or duct. Placement of small sponges behind the jejunum can facilitate achievement of the ideal position. The 6 o'clock suture is tied first with just enough tension to oppose the tissues. Holding slight tension between the first and second knot prevents loosening of the first knot. This seemingly minor point is to be emphasized because monofilament absorbable suture does not slip reliably. Sutures are cut as they are tied. The most superior and inferior sutures are tagged.

Placing and tying the anterior row of sutures in the bowel. The two corner sutures are placed in the bowel initially. The inferior corner suture is placed backhand or with the left hand. Subsequent sutures are taken working toward the middle to assure even spacing. The last suture taken is in the 12 o'clock position on the

anastomosis. With each suture, one must be certain to place the needle into the lumen of the intestine and pick up full thickness of the bowel. It is on the anterior row that the mucosal eversion is most helpful, especially on minute ducts, because one can see the knots of the previously placed 6-0 everting sutures, assuring that anterior wall mucosa is included in the suture. The sutures are tied and cut.

The second row of sutures. The anterior capsule of the pancreas and the pancreatic parenchyma anterior to the pancreatic duct are picked up with 2-0 silk suture and sewn to the seromuscular layer of the jejunum to cover the first layer (Fig. 6A). Only four or five sutures are used. When tying, the jejunum is brought to the pancreas. The sutures are cut. The silk stay suture on the inferior border of the pancreas that was placed before cutting the pancreas is passed posteriorly and the jejunum is raised, revealing the posterior aspect of the anastomosis. Mild traction on the stay suture helps to identify the most inferior portion of the pancreas. Retraction of the jejunum must be gentle while placing this posterior row so the posterior row of the first layer is not distracted. Retraction is best done by the individual who places the sutures from the right side of the patient, because only that person can see the area clearly. Four or five sutures are placed to complete the posterior row (Fig. 6B).

Great care is taken not to distract the anastomosis during the subsequent parts of the Whipple reconstruction. If the jejunum requires retraction during the hepaticojejunostomy, it is retracted toward the pancreaticojejunostomy. At the completion of the procedure, a 19-F Blake drain is placed near the anastomosis. Early in this series, as many as three drains were used, but because fistula rates have been very low, only one drain is placed currently in a position behind both the pancreaticojejunostomy and hepaticojejunostomy.

Postoperative management and evaluation

Octreotide was used early in this series as described in our initial report.⁶ Its use was discontinued as literature reports appeared that failed to support it,^{4,7} and less than one-half of the patients in this series received the drug.

Pancreatic fistula was defined as drainage of 50 mL or more of amylase-containing fluid of concentration greater than 500 IU/L (normal upper limit of serum levels 115 IU/L) for at least 3 consecutive days, one or more of those days being on or after the 10th postoperative

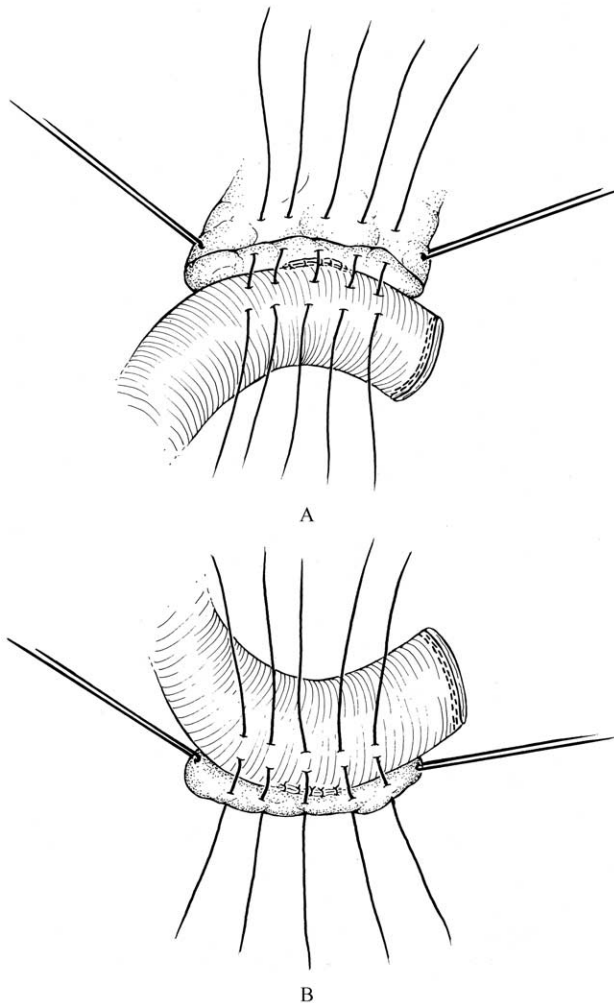


Figure 6. (A) Second layer, anterior row. Four or five sutures are placed through the pancreas as shown and the seromuscular layer of the bowel. Care is taken to stay anterior to the position of the pancreatic duct when in the vicinity of the duct. (B) Second layer, posterior row. The bowel is lifted to expose the underside of the anastomosis. Care is taken not to distract the first layer of sutures when placing the second.

day, or radiologic evidence of fistula. It is our routine to measure amylase levels from drains, but in some patients this was not done. The clinical circumstances in these cases were that the drainage volume was very low, and the patients were having uneventful recoveries. In these cases, drains were removed on resumption of reasonable oral intake, usually before the 10th postoperative day. In fact, many of these patients were discharged before that time. Any intraabdominal abscess was also considered to be from failure at the pancreatic anastomosis for reasons discussed below.

A postoperative mortality was defined as any death

Table 1. Pathologic Diagnoses

| Diagnosis | n |
|--------------------------------------|----|
| Neoplasms | |
| Pancreatic cancer | 48 |
| Ampullary cancer | 28 |
| Neuroendocrine tumors | 6 |
| Villous adenoma | 6 |
| Mucinous cystic neoplasm | 6 |
| Bile duct cancer | 5 |
| Duodenal adenocarcinoma | 3 |
| Serous cystadenoma | 3 |
| Intraductal papillary mucinous tumor | 1 |
| Gastrointestinal stromal tumor | 1 |
| Non-neoplastic conditions | |
| Chronic pancreatitis | 16 |

within 30 days of the procedure or any death occurring at any length of time after operation during the admission for the pancreaticoduodenectomy.

RESULTS

Procedures

The procedures constitute the consecutive experience of one surgeon over the entire period and the consecutive experience of a second surgeon over the final year of this time period. The most common diagnoses (Table 1) were pancreatic cancer in 48 of 123 patients (39%), ampullary cancer in 28 of 123 patients (23%), and chronic pancreatitis in 16 of 123 patients (13%). Another patient had pancreaticojejunostomy using our method. She was a 17-year-old woman, with a remote traumatic injury to the pancreas leading to pancreatic stricture. Pancreaticojejunostomy to the body of the pancreas was performed after excision of the neck of the pancreas and closure of the duct in the head of the pancreas. Her postoperative recovery was uneventful and her case is not discussed further. Forty of the patients in this series were included in our preliminary report.⁶

A standard pancreaticoduodenectomy was done in 88 patients (71%); in 35 patients (29%) the pylorus-sparing variant was used. Median pancreatic duct diameter was 3.0 mm, with a range of 1 to 8 mm. The anastomosis was carried out as indicated, except in three patients. In two patients with chronic pancreatitis, the anterior pancreas was also opened to deal with one or more strictures along the pancreatic duct. In another patient, early in our experience, an anastomosis to a very small duct (1 mm) was abandoned for technical reasons,

Table 2. Postoperative Complications

| Complication | n |
|--------------------------|----|
| Wound infection | 12 |
| Delayed gastric emptying | 11 |
| Biliary fistula | 3 |
| Intraabdominal abscess | 2 |
| Pancreatic fistula | 2 |
| Pulmonary embolus | 2 |
| Urinary retention | 2 |
| Fascial dehiscence | 1 |
| Line sepsis | 1 |
| ARDS | 1 |

and the pancreatic stump was invaginated into the bowel using the so-called “dunking” technique.

Portal vein excision and reconstruction were performed in 12 of 123 patients (10%), 10 of whom had pancreatic carcinoma, ie 10 of 48 patients (21%) with this diagnosis. In nine patients, the right lateral side of the vein was resected and repaired primarily with a vein patch. In three patients, a tubular segment of vein was resected and replaced with a vein graft. An intraoperative injury to the superior mesenteric artery occurred in one patient and was repaired without sequelae. Thirty-two patients (26%) received intraoperative blood transfusions, ranging from 1 to 5 units; eight received more than two units of blood.

Blood flow at the cut surface was considered adequate in 76 patients (62%). In the remaining 47 patients, the pancreas was mobilized and cut back. In 45 of 47 patients (96%), the new pancreatic cut surface bled briskly. In two patients it did not. As noted previously, the line of transection of the pancreatic neck at the beginning of this series was in the usual location, directly over the superior mesenteric/portal vein axis. But as the series progressed, the transection line was moved toward the left, adjacent to the left stay sutures on the neck of the pancreas. This was done to move away from the vascular watershed and toward the source of blood supply in the body of the pancreas.

Postoperative course

There was one postoperative mortality. An 85-year-old man died after readmission for gastric outlet obstruction that had resulted in vomiting and aspiration pneumonia. Postoperative complications occurred in 37 of 123 patients (31%), and these are listed in Table 2. The most common complications were wound infections and de-

layed gastric emptying. A pancreatic fistula developed in 2 of 123 patients (1.6%). These patients were the two described in whom resection of an additional portion of pancreas was not associated with an observable improvement of blood supply at the cut surface. Intraabdominal abscesses developed in 2 of 123 patients (1.6%), and both were drained percutaneously. In total, the incidence of anastomotic failure, defined as fistula or intraabdominal abscess, was 4 in 123 patients (3.2%).

One patient who developed a fistula has been previously described.⁶ The patient was asymptomatic, but his complication fit the definition of a fistula used in this study. In his case, amylase-rich fluid drainage of more than 50 mL was recorded on 3 days between postoperative days 10 and 14, at which time he was discharged on total parenteral nutrition (TPN). The fistula closed spontaneously between discharge and the first postoperative visit 2 weeks later. The second patient, a 72-year-old man, developed purulent drainage that persisted and was associated with a low-grade fever and leukocytosis. A fistula was demonstrated radiologically. The patient was managed with antibiotics and TPN. The fistula closed spontaneously. The patient was discharged after 30 days of hospitalization.

The median time to return to solid diet in the 123 patients was 8 days (range 5 to 34 days). The median length of stay was 11 days (range 7 to 83 days). Reoperation was needed in 1 of 123 patients (0.8%). The patient, a 53-year-old man, developed a deep wound infection with fascial dehiscence. He underwent debridement and resuturing of the abdominal wall under general anesthesia on day 7.

There were 16 readmissions in 15 of 123 patients (12%). One patient was admitted for treatment of a wound infection. All other admissions were from an inability to adequately aliment orally, usually caused by delayed gastric emptying or complications of treatment related to this condition (ie, line sepsis in two patients on TPN and Parkinson-like syndrome in another patient on a promotility agent). For the most part, the readmissions occurred in patients who were failing to thrive in the first 1 to 3 weeks after discharge. The readmissions were of 1 to 7 days duration, median 4 days, usually to rehydrate patients and institute home TPN. TPN was used in these patients and in patients who developed pancreatic and biliary fistulae.

DISCUSSION

The most important finding in this study is that pancreatic fistula after pancreaticojejunostomy can almost always be avoided by using a technique that combines meticulous apposition of the pancreatic duct mucosa to the jejunal mucosa, with preparation of the pancreatic anastomotic surface in such a way that blood supply is optimized. Both of the features of the method—precise, even painstaking—technique and attention to blood supply seem to be important to the method. But the study has not been performed in a way that would permit separation and delineation of the importance of each of these factors in a rigorous manner.

Problems of comparison of fistula and anastomotic failure rates among published case series

To gauge the impact of a new method, comparison with literature results is desirable. But, this is difficult because of variability in reporting methods. There are a large number of reports of fistula rates and intraabdominal abscess rates after the Whipple procedure available in the literature. A listing of 12 recent series, including the present one, is given in Table 3.^{1-5,8-13} Several pertinent observations can be made. The first is that comparison among series is, at best, crude because of variability of definitions. Four of the 12 series, including our own, have used the definition put forward by the Johns Hopkins group⁴ or one very close to it. This definition is both broad and precise in that it stipulates level of amylase, volume of drainage, and time after operation at which the definition applies. It also admits for the possibility of diagnosis by radiologic means. Other definitions are much looser and fail to define clearly one or any of these attributes^{2,3,13} (Table 3).

Some definitions are precise but much more restrictive as to what constitutes fistula.⁸ There is a very high probability that a patient group examined by criteria that stipulate 10 days of amylase-rich fluid drainage of > 5000 IU/L for diagnosis of fistula⁸ will have a much lower fistula rate than if examined by criteria that stipulate 3 days of amylase-rich fluid drainage of more than 500 IU/L for diagnosis of fistula.⁴ So variable definitions will make valid comparisons among series inaccurate.

Another problem in series comparisons is the makeup of the patient population, specifically the proportion of patients operated on for chronic pancreatitis. Pancreatic fistula is very rare in this condition because the scarred gland is very low in enzyme content; we have never seen

a fistula in these circumstances. The proportion of cases of chronic pancreatitis in the case series we have examined ranges from 5% to 40% (Table 3), and a lower fistula rate would be expected in those series with the higher proportion of patients with chronic pancreatitis. Of course, there is variability of pancreatic consistency among other diagnoses, but these would be expected to exhibit rather similar variability from center to center. We have not remarked on the consistency of the gland in our series, because it is the size and friability of the duct that is technically a consideration with our method and not the consistency of the gland. Both fistulas in our series occurred in “firm” glands. Finally, it should be noted that fistulas can be morbid, but today they are rarely fatal. Mortality rates from these hepatobiliary centers (Table 3) are uniformly low.

Importance of meticulous technique in the mucosa-to-mucosa method

Given all the considerations just described, it appears that centers using mucosa-to-mucosa techniques in which the duct is sewn to an opening in the jejunum have lower fistula rates than those that use the classical “dunking” technique in which the gland is invaginated into the bowel. There are three studies in the literature (including this one) that have emphasized the importance of meticulous technique to the success of the mucosa-to-mucosa method. These studies all report very low rates of anastomotic failure. Howard¹⁰ published a series of 56 patients having pancreaticoduodenectomy without a pancreatic fistula. He used a precise duct-to-mucosa technique, attributing his success solely to technical considerations. There were “three peripancreatic infections” in that series, which might have been from local leakage at the anastomosis. If these are considered anastomotic failures, then the failure rate in that series would be 3 in 56 patients (5.4%). Ohwada and associates¹¹ recently reported the results of a technique that uses a running suture for the pancreaticojejunostomy. Their technique first excises a disc of jejunum around the site of anastomosis, ie, the jejunal mucosa only is taken in the first layer. After placement of the running suture, the jejunum is parachuted down as the suture is pulled up. Fistula was defined as drainage of amylase-rich fluid greater than three times the serum levels or demonstration of a fistula on radiograms. Time of measurement of amylase, volume of fluid, or the days of flow of high amylase fluid were not included in their

Table 3. Rates of Pancreatic Fistulas, Intraabdominal Abscesses, and Anastomotic Failures after Pancreaticojejunostomy

| First author | Year | Data years | Site | Fistula definition | n | Chronic pancreatitis | | Fistulas | | Abscesses | | Anastomotic failure* | | Reoperations | | Mortalities | |
|----------------|------|------------------------|-------------------|--------------------|-----|----------------------|-----------------|----------|-----|-----------|-----|----------------------|----|--------------|-----|-------------|-----|
| | | | | | | n | % | n | % | n | % | n | % | n | % | n | % |
| Yeo | 2000 | 1998–2000 | Johns Hopkins | A | 211 | 21 | 10 | 21 | 10 | 14 | 7 | 25 | 17 | 13 | 6 | 1 | 0.5 |
| Buchler | 2000 | 1993–1999 | Bern, Switzerland | B | 331 | 133 | 40 | 7 | 2.1 | 4 | 1.2 | 11 | 3 | 13 | 4 | 7 | 2.1 |
| Gouma | 2000 | 1997–1999 [†] | Netherlands | C | 151 | NS | | 8 | 5 | 5 | 3 | 13 | 8 | 12 | 8 | 1 | 0.7 |
| Brooks | 2000 | 1993–1998 [†] | NYU | A | 111 | 6 | 5 | 15 | 14 | 2 | 2 | 17 | 16 | NS | | 0 | |
| Grobmeyer | 2000 | 1994–1998 | Cornell | (A) | 59 | 3 | 6 | 10 | 17 | 3 | 6 | 13 | 23 | 1 | 2 | 2 | 3.4 |
| Bottger | 1999 | 1985–1997 | Mainz, Germany | D | 221 | 18 | 8 | 18 | 8 | 12 | 5 | 30 | 13 | 19 | 9 | 7 | 3 |
| Rios | 1998 | 1983–1996 [†] | Charleston, SC | E | 98 | 27 | 28 | 13 | 13 | 1 | 1 | 14 | 14 | NS | | 1 | 1 |
| Sato | 1998 | 1992–1997 | Fukuoka, Japan | F | 62 | 7 | 11 | 9 | 15 | 2 | 3 | 11 | 18 | 2 | 3 | 1 | 2 |
| Castillo | 1995 | 1991–1994 | Mass Gen Hosp | E | 237 | 62 | 26 | 16 | 8 | 10 | 4 | 26 | 12 | 3 | 1 | 1 | 0.8 |
| Howard | 1997 | 1985–1997 | Toledo, OH | C | 56 | 13 | 23 [‡] | 0 | | 3 | 5 | 3 | 5 | 0 | 0 | 1 | 1.8 |
| Ohwada | 2001 | 1992–1999 | Maebashi, Japan | G | 100 | 8 | 8 | 4 | 4 | 1? | 1 | 5 | 5 | 3 | 3 | 2 | 2 |
| Present series | | 1996–2000 | Wash U/St Louis | A | 123 | 16 | 13 | 2 | 1.6 | 2 | 1.6 | 4 | 3 | 1 | 0.8 | 1 | 0.8 |

*Anastomotic failure = fistulas + intraabdominal abscesses.

[†]Latest reported period taken.

[‡]Thirteen with benign disease, chiefly chronic pancreatitis.

A, Johns Hopkins Group Definition: More than 50 mL amylase-rich fluid (more than threefold elevation above upper limit of normal in serum) per day through the surgically placed drains on or after postoperative day 10 or pancreatic anastomosis disruption demonstrated radiographically; (A), substantially the same definition with slight variation; B, secretion of 30 mL or more of amylase-rich drainage fluid (5000 units) per day for more than 10 days; C, not specifically defined; D, amylase concentration in drainage fluid of > 2000; E, “high” amylase drain output after day 7—“high” not defined; F, “high” amylase drainage or radiologic demonstration—“high” undefined; G, drainage of fluid with amylase concentration greater than 3 times normal or radiologic demonstration.

definition. Pancreatic fistula occurred in 4% of patients. No intraabdominal abscesses were reported. We have never attempted this method, but believe that most surgeons would find it easier to place interrupted sutures with accuracy in a very confined space rather than a running suture. Whatever the method, what characterizes these methods and our own is emphasis on precise and exacting placement of fine sutures and great care in apposition of tissues. It is our opinion, as stated earlier, that this cannot be achieved without magnification in a substantial proportion of patients.

The role of ischemia in anastomotic failure

We have not proved conclusively that ischemia at the cut surface of the pancreas is a factor in anastomotic failure. But we have provided the following compelling circumstantial evidence that this is so.

1. When we applied a precise technique only, without consideration of blood supply, our fistula rate was 10%.⁶ When precise technique was combined with optimization of blood supply, the fistula rate fell to 1.6% (anastomotic failure rate 3.2%).
2. The pancreatic neck contains a vascular watershed between the body of the pancreas, which is supplied by the splenic artery, and the head of the pancreas, supplied by the superior and inferior pancreaticoduodenal arteries.^{14,15} The dorsal pancreatic artery that supplies the left side of the neck and adjacent part of the body of the pancreas arises from the splenic artery. It is one of the most variable arteries in the upper abdomen¹⁶ and can be interrupted in the normal course of a pancreaticoduodenectomy. We have previously reviewed this pertinent vascular anatomy in detail.⁶ Because there is a watershed, there is an increased opportunity for ischemia on one side of the watershed when the watershed is divided (cf bile duct).
3. In 45 of 47 patients in this study whose pancreas was cut back, we observed a large increase in bleeding from the cut surface in keeping with the importance of the watershed concept.
4. The only two fistulae that we observed occurred in patients whose pancreas did not bleed when it was cut back.

All of these points support the argument first made in our preliminary report⁶ that ischemia contributes to the development of pancreatic fistulae in some cases. Nonetheless, we recognize that this claim has not been rigorously proved. To do so would require a randomized controlled trial. In that trial it would be necessary, in the control group, to perform an anastomosis to a pancreas, which in some cases would show no evidence of bleeding

from the cut surface. Whether such a trial could now be done is doubtful. But insistence of proof of the role of ischemia with scientific rigor is probably much less important than the empiric observation that use of a method that combines precise technique under magnification with attempts to optimize blood supply will result in the virtual elimination of pancreatic fistula as a clinical problem. That is the real point of this article.

Suggestions regarding terminology and definitions

The wide variability of definitions hampers comparison and progress. The Johns Hopkins definition⁴ has been widely, but not universally, adopted. It is a good definition because it is clinically relevant. It captures fistulae with even minimal clinical relevance, without including insignificant minimal biochemical abnormalities. In our opinion, it should be universally adopted until and unless an internationally recognized body of pancreatic experts arrives at another definition. We have included intraabdominal abscess as an indication of anastomotic failure. We believe this is advisable for the following reasons. Some surgeons do not drain pancreaticojejunostomies. When pancreatic leaks occur in these cases, they are more likely to be manifest as abscess than fistula. At other times, leaks can occur after removal of drains or in a location where drains cannot remove fluid because of the position of the fluid. Again, abscess rather than fistula will be more common in these situations. Some have argued that such abscesses should be considered to be pancreatic only if they contain amylase-rich fluid. But bacteria can digest human amylase, and otherwise amylase measurements might not be able to be performed on frank pus. So, it is our opinion that anastomotic failure should be considered the sum of pancreatic fistulae and intraabdominal abscesses, recognizing that some abscesses of other origin will be included.

In addition to reaching uniform definitions of fistula and anastomotic failure, it would also be useful to develop a classification of the degree of severity of a pancreatic fistula. None now exists, but obviously some fistulae are much more morbid than others. There is an obvious and important difference in outcomes between a patient who has an asymptomatic fistula and one who requires percutaneous procedures, or reoperation. The term "clinically relevant fistula" has been used to indicate conditions requiring prolonged TPN, or interventional procedures including reoperation.⁵ Pancreatic fistula would be readily graded on the basis of a schema that we

Table 4. Severity Grading of Anastomotic Failures of Pancreaticojejunostomy (Fistula or Intraabdominal Abscess)

| Grade | |
|-------|--|
| 1 | Requires bedside procedures only. Length of hospital stay does not exceed twice the median stay for the procedure. |
| 2a | Any anastomotic failure requiring one or more of: systemic antibiotics; total parenteral nutrition; hospital stay exceeding twice the median hospitalization for pancreaticoduodenectomy. |
| 2b | Any anastomotic failure requiring interventional procedure or reoperation. |
| 3 | Any anastomotic failure requiring reoperation with complete resection of the pancreas. Any anastomotic failure associated with permanent disability in an extrapancreatic site, such as stroke or myocardial infarction. |
| 4 | Death of a patient with anastomotic failure within 30 days of operation whether or not discharged, or within the same admission as the pancreatico-duodenectomy. |

introduced for grading complications of surgery¹⁶ some years ago (Table 4). Like a uniform definition, a uniform grading system might improve comparison among series.

In summary, a technique combining meticulous apposition under magnification coupled with attention to blood supply can result in a very low rate of anastomotic failure after pancreaticojejunostomy. Again, we make no claim that it is the only technique that might achieve such results, but we do believe that it is a method that can be readily performed by surgeons with an interest in this area, and if widely adopted would virtually eliminate this problem.

AUTHOR CONTRIBUTIONS

Study conception and design: Strasberg, Drebin, Linehan

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Analysis and interpretation of data: Strasberg, Drebin, Mokadam, Green, Jones, Ehlers, Linehan

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