

Multivariate analysis of technical variables in pancreaticoduodenectomy: the effect of pylorus preservation and retro-mesenteric jejunal position on early outcome

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Background: To evaluate the effect of technical modifications to pancreaticoduodenectomy (PD) on postoperative outcome, we established a register of all patients undergoing PD at Victoria General Hospital (Queen Elizabeth II Health Sciences Centre), a tertiary care, university-affiliated hospital. **Patients and method:** Data from 78 consecutive patients who underwent PD from January 1998 through November 2000 were collected for univariate and multivariate analyses of clinical and technical factors on early outcome after PD, including duration of gastric stasis, development of complications and length of hospital stay. **Results:** Two patients (2.6%) died; complications were recorded in 43 (55%). Upon univariate analysis, 3 factors (a diagnosis of chronic pancreatitis, pylorus preservation, and route of the jejunal limb) significantly affected duration of gastric stasis; but on multivariate analysis, only pylorus preservation and jejunal-limb route remained significant. Retromesenteric jejunal-limb placement was associated with longer periods of gastric stasis (mean 11.9 d, standard deviation [SD] 8.1 d) than the antemesenteric (retrocolic) route (mean 7.2, SD 3.6 d; $p < 0.05$); likewise pyloric preservation (mean gastric stasis 10.4 d, SD 5.9 d) compared with resection of the pylorus (mean 7.0 d, SD 3.2 d; $p < 0.05$). Pancreatic leaks occurred in 18% of retromesenteric and 8% of antemesenteric reconstructions ($p = 0.3$). Fewer patients with mucomucosal pancreaticojejunostomy suffered complications than those with invaginated anastomoses, but their hospital stays were similar in length. **Conclusion:** Route of the jejunal efferent limb and preservation of the pylorus are independent technical variables affecting early outcome after PD.

Contexte : Pour évaluer l'effet de modifications techniques de la pancréaticoduodénectomie (PD) sur le résultat postopératoire, nous avons dressé un registre de tous les patients qui ont subi une PD à l'Hôpital Victoria General (Centre des sciences de la santé Queen Elizabeth II), hôpital universitaire de soins tertiaires. **Patients et méthode :** On a recueilli des données sur 78 patients consécutifs qui ont subi une PD entre janvier 1998 et novembre 2000 pour procéder à des analyses à variable unique et à variables multiples de facteurs cliniques et techniques qui jouent sur les premiers résultats après une PD, y compris la durée de la stase gastrique, l'apparition de complications et la durée du séjour à l'hôpital. **Résultats :** Deux patients (2,6 %) sont morts; on a consigné des complications dans 43 cas (55 %). L'analyse à variable unique a révélé que trois facteurs (diagnostic de pancréatite chronique, conservation du pylore et position de l'embranchement jéjunal) ont eu un effet important sur la durée de la stase gastrique. L'analyse à variables multiples a toutefois révélé que seule la conservation du pylore et la position de l'embranchement jéjunal demeuraient importantes. On a établi un lien entre la situation rétromésentérique de l'embranchement jéjunal et une stase gastrique plus longue (moyenne de 11,9, \pm ET 8,1 j c. 7,2 \pm 3,6 j, $p < 0,05$) comparativement à la situation antémésentérique (rétrocolique). On a établi le même lien entre la conservation du pylore (10,4 \pm 5,9 j) comparativement à la résection (7,0 \pm 3,2 j, $p < 0,05$). Il y a eu des fuites pancréatiques dans 18 % des reconstructions rétromésentériques et 8 % des reconstructions antémésentériques ($p = 0,3$). Moins de patients qui ont subi une pancréaticojéjunostomie mucomuqueuse ont eu des complications que ceux qui ont subi une anastomose invaginée, mais la durée de leur séjour à l'hôpital se ressemblait. **Conclusion :** La voie de l'embranchement efférent du jéjunum et la conservation du pylore sont des variables techniques indépendantes qui ont des répercussions sur les premiers résultats à la suite d'une PD.

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From the beginning of pancreaticoduodenectomy (PD), various options for resection and reconstruction have been available to the surgeon. In 1935, Whipple and colleagues¹ began the first series of PDs, initially performing a cholecystogastrostomy and preserving the upper gastrointestinal tract to the proximal duodenum. Six years later, Whipple² modified the procedure, not only completing the operation in a single stage but also moving the proximal resection line up to include the distal stomach. Gastrointestinal continuity was restored with end-to-side gastroenterostomy.

Three years after this, Watson³ reported a single-stage procedure with preservation of both the pylorus and proximal duodenum and reconstruction by end-to-end duodenojejunostomy. A reduction in postoperative mortality seen in the 1980s was first ascribed to the reintroduction of the pylorus preservation technique,⁴ but later attributed to a restriction of PD to experienced surgeons.^{5,6} Morbidity in these and other series nevertheless remains a problem. Early complications occur in 46% of patients, with delayed gastric emptying (23%) and pancreatic fistula (17%) being the most common.⁷

Many surgeons prefer to use a single PD technique with which they have become familiar. We wished to develop our technique to improve outcomes after surgery. Reviewing the procedure, we realized that when the options available at each operative step are combined geometrically, the large number of resulting scenarios would make a randomized controlled trial difficult unless alternative techniques at a single step alone could be targeted. To choose such a target, we decided to establish a registry of patients undergoing PD at our large tertiary-care centre so that the effect of each technical element could be analyzed.

Before our study, there had been a patient at our centre requiring reoperation after PD. This person's biliary-pancreatic efferent jejunal limb

(BPL) was found to be engorged up to the point where it passed under the mesenteric vessels. Treatment by mobilizing the mesentery and straightening the jejunum was successful. We felt that obstruction of venous drainage of the BPL might have been avoided if it had been relocated in the antemesenteric position. Care was therefore taken in the registry to include details on routes of the efferent jejunum in the operative data.

Here we report a multivariate analysis of the operative techniques used during PD.

Patients and methods

From January 1998 through November 2000, PD was completed on 78 patients (32 men, 46 women), mean age 62.6 years (range 25–83 y). Surgery was performed by senior residents under the direct supervision of 2 of us (B.V. and V.M.), both experienced in PD. Data entered into a database (Microsoft Excel) included

patient demographics, indications for surgery, concomitant illnesses, preoperative care and operative data such as resection-reconstruction details, length of hospitalization (including time spent under intensive care), duration of gastric suction, reinsertion of a nasogastric (NG) tube and development of complications. Technical variations included:

1. resection of the pylorus, or not
 2. resection of the gallbladder (if present), or not
 3. retromesenteric (Fig. 1) or antemesenteric (retrocolic) route of BPL (Fig. 2)
 4. retromesenteric or antecolic route of the efferent jejunal limb from the stomach
 5. end-to-side, end-to-end or Roux-en-Y gastro- or duodenojejunostomy
 6. invagination or mucocomucosal pancreaticojejunal anastomosis
- Vagotomy was not performed. Prokinetic agents were not given prophylactically, but prescribed only after the 7th postoperative day (POD).

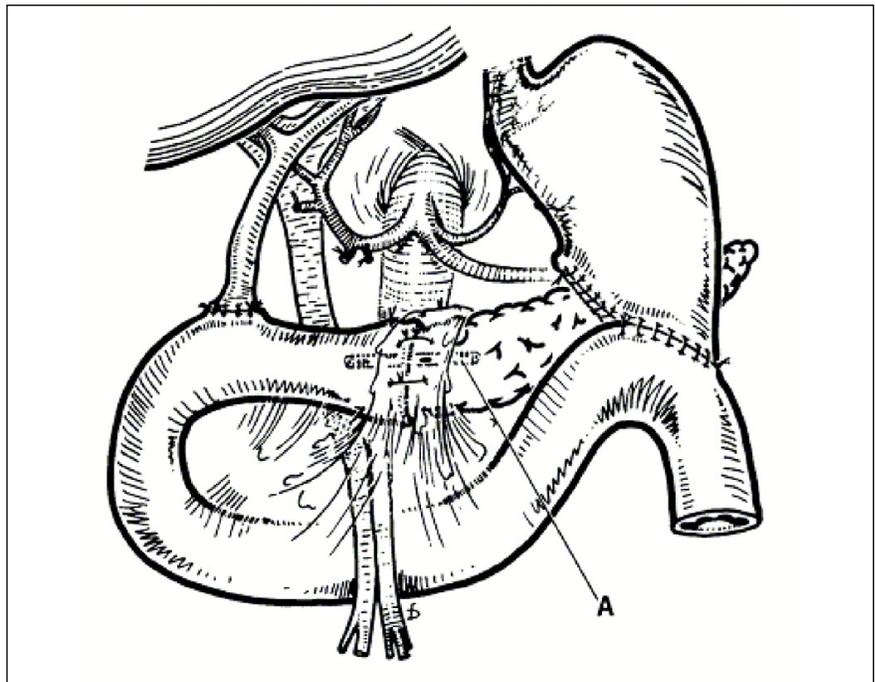


FIG. 1. The retromesenteric route of the biliary-pancreatic limb. (A indicates a stent in the pancreatic duct, but none was used in the current report.) Reprinted (with permission from Elsevier) from A.R. Moosa and M. Lavelle-Jones, "Whipple pancreaticoduodenectomy." Page 877 of *Surgery of the Liver and Biliary Tract*, edited by L.H. Blumgart (Edinburgh: Churchill Livingstone; 1988).

The senior resident decided when NG tubes would be removed and patients discharged from hospital according to standardized criteria: NG tubes were clamped on the first day of passing of flatus and removed if tolerated for 12 hours. In cases where an NG tube was reinserted, NG drainage duration was reckoned from the operation until the time of removal of the last NG tube. Patients were discharged from hospital as soon as they were mobile and had normal gastrointestinal function. Delayed gastric emptying was defined as dependence on NG suction after the 10th POD. Pancreatic anastomotic leaks were defined by the presence of amylase-rich fluid in abdominal drains after the 5th POD.

Statistical analysis

Results are expressed as means (and standard deviations [SD]). Univariate analysis was carried out using 2-tailed Student's *t* tests, χ^2 tests and 1-way analysis of variance. Multivariate analysis was calculated with multiple linear regression and logistic regression with forward selection (SAS, version 6.12).

Results

Two patients (2.6%) died, of pneumonia on POD 15 and liver failure on POD 3, respectively. Complications occurred in 43 patients (55%): 22 cases of delayed gastric emptying (28% of all 78 patients), 17 of pneu-

monia (22%), 10 of pancreatic anastomotic leak (13%), 4 of gastrointestinal hemorrhage (5%) and 3 of intra-abdominal abscess (4%). The resulting periods of hospitalization averaged 23.3 days (SD 14.2 d) for the entire group.

The complication rate was higher in patients with chronic pancreatitis (11/13) than those with cancer (32/65); this difference was significant according to univariate analysis ($p < 0.03$), but not multivariate analysis. The difference in the incidence of specific complications between these 2 groups was not statistically significant, and the durations of NG drainage (7.5 [5.3] d v. 9.2 [6.8] d) and hospitalization (18.8 [8.4] d v. 20.2 [14.2] d, respectively) were similar.

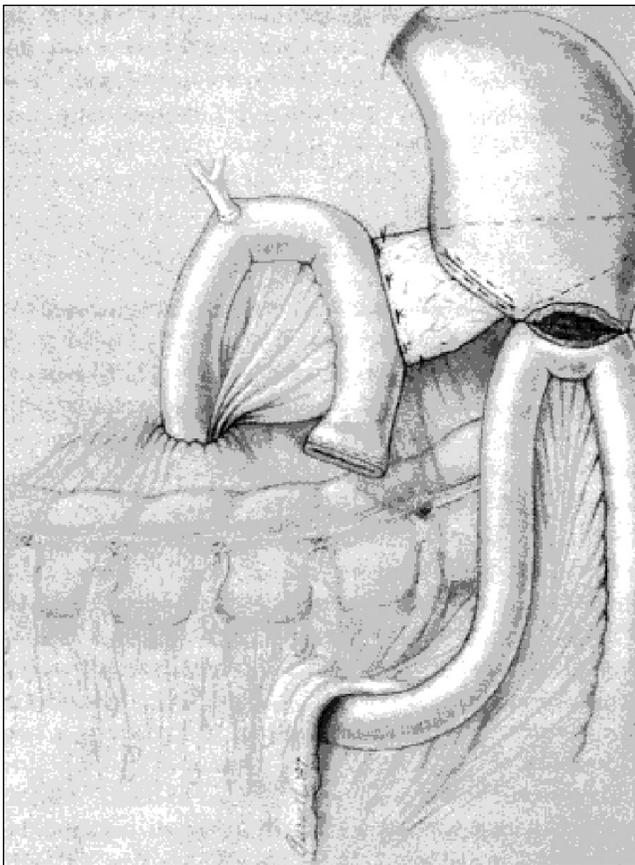


FIG. 2. Use of the mesocolic window for a antemesenteric/retrocolic route for the biliary-pancreatic efferent jejunal limb. Reprinted (with permission from Elsevier) from M.F. Brennan, "Pancreaticoduodenectomy." On page 1081 of *Surgery of the Liver and Biliary Tract*, edited by L.H. Blumgart and Y. Fong (London: W.B. Saunders Company Ltd.; 2000).

Table 1

Outcomes after pancreaticoduodenectomy (PD)

Surgical procedure & statistical analysis	n	Mean (and SD), d		Complications, pts (& %)
		Nasogastric drainage	Hospital stay	
Prior CC	23	8.6 (3.4)	18.6 (6.5)	10 (43)
CC & PD	20	10.2 (7.8)	23.8 (11.9)	12 (60)
PD without CC	35	7.2 (5.9)	17.9 (12.8)	21 (60)
Univariate		$p = 0.11$	$p = 0.12$	$p = 0.59$
Pylorus preserved	44	10.4 (5.9)	21.6 (11.9)	24 (55)
Pylorus resected	34	7.0 (3.1)	19.6 (11.9)	19 (56)
Univariate		$p < 0.02$	$p = 0.44$	$p = 0.93$
Multivariate		$p < 0.03$		
Pancreaticojejunostomy:				
Invaginated	30	9.9 (4.2)	21.5 (7.4)	21 (70)
Mucomucosal	48	8.9 (6.5)	20.3 (13.7)	22 (46)
Univariate		$p = 0.38$	$p = 0.99$	$p < 0.04$
Multivariate				$p < 0.04$
Gastrojejunostomy:				
Retromesenteric	36	10.9 (8.2)	23.3 (12.7)	21 (57)
Antecolic	42	7.7 (5.2)	19.7 (12.4)	22 (52)
Univariate		$p = 0.06$	$p = 0.23$	$p = 0.96$
Multivariate		$p = 0.08$		
End-to-end	6	3.8 (2.3)	11.8 (2.8)	3 (50)
End-to-side	62	9.8 (6.4)	22.6 (11.9)	34 (55)
Roux-en-Y	10	7.6 (3.9)	15.0 (5.6)	6 (60)
Univariate		$p = 0.14$	$p = 0.11$	$p = 0.94$
Biliary/pancreatic efferent jejunal limb:				
Retromesenteric	38	11.9 (8.1)	23.8 (10.2)	22 (56)
Antemesenteric	40	7.2 (3.6)	18.7 (11.4)	21 (56)
Univariate		$p < 0.03$	$p = 0.16$	$p = 0.62$
Multivariate		$p < 0.05$		

CC = cholecystectomy; pts = patients; SD = standard deviation

Table 1 summarizes outcomes associated with each technical variable. Patients who underwent cholecystectomy at PD tended to have longer periods of NG drainage and hospitalization than those who did not or who had prior cholecystectomy, but the differences did not reach significance. If the pylorus was preserved, the duration of NG requirement was significantly longer on multivariate analysis, whereas the complication rate and length of hospital stay did not differ significantly.

Biliary and pancreatic anastomoses were made on the same efferent jejunal limb in all patients. Complications were more common after invagination of the pancreatic remnant compared with reconstruction by mucomucosal anastomosis. This was because of higher rates of pneumonia (4/30 v. 3/48, respectively) and of anastomotic leakage (6/30 v. 4/48, respectively), but these specific differences were not statistically significant and did not result in longer postoperative hospitalization.

Use of gastro- or duodenojejuno-stomy technique (end-to-side, end-to-end or Roux-en-Y loop anastomosis) was unassociated with significantly different outcomes. Durations of NG drainage and hospitalization were shorter if the efferent jejunal limb from the stomach was in the antecolic position, but this difference did not reach statistical significance.

Upon multivariate analysis, NG drainage was significantly shorter if the BPL was repositioned through a window in the mesentery of the transverse colon rather than if it continued behind the mesenteric vessels like the duodenum before resection. This tended to reduce the hospital stay. Three pancreatic anastomotic leaks (7.5%) were observed in the antemesenteric group compared to 7 (18%, *p* not significant) in the retromesenteric group.

Discussion

This study demonstrates the usefulness

of multivariate analysis. Univariate analysis of the complication rate suggested a statistically significant difference between chronic pancreatitis and cancer, but on multivariate analysis this difference was found to depend on other factors. We did not find a difference in specific complications, gastric stasis or hospitalization between these diagnostic groups. On the other hand, prospective randomized controlled trials have previously shown pylorus preservation to be associated with prolonged gastric stasis.^{8,9} This retrospective multivariate analysis also found pylorus preservation to be an independent variable that affects recovery after PD.

The novel finding here is that a retromesenteric route of the BPL is also an independent variable associated with prolonged stasis. Poor emptying of the BPL would put the biliary and pancreatic anastomoses at risk of leakage. We found a higher pancreatic leak rate (18% v. 7.5%) in the group with the retromesenteric BPL, but to reach statistical significance this finding would have to be repeated in a series of 230 patients. Because surgical preference might confound this result, confirmation by randomized controlled trial is required.

The position of the BPL is an aspect of the surgical technique that has not been discussed in detail before. An informal poll of colleagues suggests that a large proportion of surgeons reposition the BPL so that it passes from the lower abdomen through a window in the colonic mesentery into the subhepatic space, whereas the rest bring the limb behind the mesenteric vessels in the gutter where the fourth part of the duodenum lies. Illustrations in textbooks are similarly divided.^{10,11}

The gastroenterostomy is most often constructed as an end-to-side anastomosis. It may be in the subhepatic space so that its efferent limb passes behind the mesentery, or placed in the antecolic position to avoid obstruction by recurrent cancer

in the posterior abdomen. In this study, the retromesenteric route for the gastroenterostomy drainage limb tended to be associated with 50% longer periods of NG drainage. This did not quite reach statistical significance, likely owing to inadequate sample size. There was considerable overlap in the groups, with the retromesenteric route being used for both the BPL and the efferent limb of the gastroenterostomy in many patients.

Luminal or vascular obstruction of the gastroenterostomy efferent limb as it passes behind the mesenteric root may have been the cause of prolonged gastric stasis. It is unclear why a retromesenteric route for the BPL should effect gastric emptying if the limb draining the gastroenterostomy does not also pass behind the mesentery. Venous obstruction of the BPL may inhibit peristalsis and thus delay emptying of the downstream gastroenterostomy, whether or not the efferent limb of the latter anastomosis passes behind the mesenteric root.

Imanaga¹² and Hishinuma and colleagues¹³ reintroduced Watson's 1944 technique³ of end-to-end anastomosis between the stomach or duodenal resection line and the proximal jejunum. Gastrointestinal continuity was restored in 6 of our patients by means of end-to-end duodenojejuno-stomy with an antemesenteric efferent-limb route. These patients all did well, but the differences were not significant on multivariate analysis, suggesting that the benefit was derived from the limb route rather than the method of gastroenterostomy. Hishinuma's group¹³ also used the antemesenteric window in the mesocolon for the efferent limb, but with scintigraphy still found evidence of some limb dysfunction. In a separate report,¹⁴ they found delayed gastric emptying (experienced by 45% of their patients) to be the most common complication.

We did not use prophylactic prokinetic drugs in this study. However, erythromycin, a motilin agonist, has been shown to improve gastric emp-

tying if given intravenously for 10 days, by replacing the motilin source lost by duodenectomy.¹⁵ Preservation of even longer segments of duodenum is associated with an increase up to 3-fold in motilin production and improved gastric emptying.¹⁶

The beneficial effect seen in this study of antemesenteric placement of the efferent loop should be verified by randomized controlled trial. It appears to be independent of other aspects of reconstruction. This suggests that it may be useful in conjunction with prophylactic motility promoters or with other technical modifications such as duodenal preservation.

Competing interests: None declared.

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