ABSTRACT
Objective: To assess the safety of the pancreatic anastomosis after pancreatico-duodenectomy (PD).
Design: Non-randomized prospective trial in consecutive patients.
Setting: University hospital.
Subjects: 171 consecutive patients with resectable periampullary cancer (80%) or intractable pain due to chronic pancreatitis (20%) undergoing PD.
Interventions: Pancreateicojejunostomy (PJ) and pancreaticogastrostomy (PG).
Main outcome measures: Mortality and morbidity rates due to anastomotic leak following PJ and PG.
Results: 91 PJ and 80 PG patients were comparable for age, gender, total bilirubin, ASA grading, indication for PD, operating time, pancreas texture, blood loss and replacement. The rate of pancreatic fistula was significantly higher in PJ patients (13%) than in PG patients (3.7%) (12 vs. 3, p = 0.029). Overall death rate was significantly higher after PJ (12%) than after PG (3.7%) (11 vs. 3, p = 0.047). Fatal outcome due to pancreatic leak (3 vs. 1, p = 0.83) and other death rates (8 vs. 2, p = 0.14) were not significantly different in PJ and PG groups, respectively.
Conclusion: PJ was associated with significantly higher pancreatic leak rate than PG. However, there was no statistically significant difference in mortality rates directly related to pancreatic leak.
Key words: pancreaticoduodenectomy, pancreaticejejunostomy, pancreaticogastrostomy.

INTRODUCTION
While an operative mortality of 20% after pancreaticoduodenectomy (PD) was not exceptional in the mid 1970’s, modern series have reduced it to the level of 5% (3) and indeed one series has done even better than that (19). Nevertheless, anastomosing the pancreatic remnant to a hollow viscus after PD is still the weak link of the operation and leakage of the pancreatic anastomosis remains a problem. This dreaded complication occurs in 10% to 14% of the patients and carries a 24% mortality rate when pancreaticejejunostomy (PJ) is the method of reconstruction (18).

There has been considerable recent interest in pancreaticogastrostomy (PG) as an alternative reconstruction. The advantages are said to be that there is a lower leak rate and a lower mortality (1, 5, 6, 14, 16). However, both of these points are open to debate for some authors have presented a very low leak rate with PJ (18), while others (4) have shown that 73% of leaks at PJ can be managed conservatively. In the latter study (4), the directly fistula-related fatal outcome was 1.3%.

The aim of this study was to compare PJ with PG with regard to safety of the pancreatic anastomosis.

PATIENTS AND METHODS
From January 1980 to June 1994, 171 consecutive patients with resectable periampullary cancer (79.5%) or chronic pancreatitis (20.4%) underwent PD. Patients with chronic pancreatitis (n = 35) were resected because of intractable pain. According to a non-randomized surgeons design (20), patients were assigned to one of two groups of surgeons who performed only one of two reconstruction procedures throughout the study: PJ or PG. All four surgeons had the same level of training and similar pretrial routines. Ninety-one patients (53.2%) underwent PJ, while PG was performed in 80 patients (46.8%). The PJ and the PG patient groups were not significantly different with regard to age, gender, preoperative total bilirubin, ASA grading, and indications for surgery (Table I).

The standard PD included resection of the gastric antrum. Truncal vagotomy was not performed, but H2-
Restoration of continuity entailed single-layer hand-sewn anastomoses with interrupted 3–0 polyglycolic acid sutures, no stent across anastomoses, no tube gastrostomy, no feeding jejunostomy, and two round silicone closed-suction drains placed in the vicinity of the pancreatic and biliary anastomoses. The PJ group underwent invaginated end-to-end PJ, hepaticojejunostomy and gastrojejunostomy on a single Roux loop brought through a rent in the transverse mesocolon. Similarly, the retained jejunum was used for reconstruction in the PG group, who underwent implantation of the pancreatic stump in the posterior gastric wall.

An anastomotic leak at PJ or PG was defined as the recovery of >50 mL fluid with an amylase content three times greater than upper limit of normal in serum from the drain placed in the vicinity of the pancreatic anastomosis or from the drain site after postoperative day 10, radiographically documented leakage, and/or anastomotic breakdown confirmed at reoperation. Mortality was defined as any death within 30 days postoperatively in or out of hospital. No patient underwent preoperative radiation.

Results are presented as the mean ± the standard error of the mean (SEM) where appropriate. Statistical comparative analysis including chi-square and Fisher’s exact tests was made with the aid of a Statview® II software (Abacus Concept, Berkely, CA, USA) with the level of significance (p value) being less than 0.05.

RESULTS

No significant differences between the PJ and the PG patient groups were observed on comparison of operating time, pancreas texture, blood loss and replacement (Table II). The overall mortality rate was 8.1% (14/171). Death rate was significantly higher in the PJ (11/91, 12%) than in the PG group (3/80, 3.7%) (11 vs. 3, p = 0.047). Fatal outcome due to pancreatic leak was not significantly different in the PJ (3/91, 3.2%) and in the PG group (1/80, 1.2%) (3 vs. 1, p = 0.83). The rate of other deaths was not significantly different in the PJ (8/91, 8.7%) and in the PG group (2/80, 2.5%) (8 vs. 2, p = 0.14) (Table III).

Morbidity is as shown in Table IV. The overall pancreatic leak rate was 8.7% (15/171). It was significantly higher in the PJ (13%) than in the PG group (3.75%) (12 vs. 3, p = 0.0295). Most leaks (11/15; 73.3%) were managed with intraoperatively placed drains, parenteral nutrition, intravenous antibiotics, but no somatostatin analogue and recovered eventually without further surgery. Four of these 15 patients (26.6%) underwent completion pancreatectomy deemed necessary because of necrosis prohibiting repair or reanastomosis. None of these four patients had additional leak at hepaticojejunostomy or gastrojejunostomy. These re-interventions were performed an average of 14 days (range 10–16 days) after PD. Three other patients were re-operated on due to intra-abdominal bleeding (n = 2) and biliary peritonitis (n = 1). The overall re-operation rate was 4% (7/171). Mortality in this group of patients (n = 7) was 100%.

The consistency of the pancreatic remnant was soft (normal histology) in 31/171 (18.1%) patients and hard (chronic pancreatitis) in 140/171 (81.8%) patients. The rate of pancreatic fistula was significantly higher in patients with soft (38.7%) than in patients with hard texture (2.1%) (12 vs. 3, p = 0.001). The length of stay

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pancreaticojejunostomy (n = 91)</th>
<th>Pancreaticogastrostomy (n = 80)</th>
</tr>
</thead>
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<tr>
<td>Median (range) age (years)</td>
<td>59 (36–75)</td>
<td>60.7 (41–74)</td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Male</td>
<td>64</td>
<td>49</td>
</tr>
<tr>
<td>– Female</td>
<td>27</td>
<td>31</td>
</tr>
<tr>
<td>Median (range) total bilirubin concentration (µmol/L)</td>
<td>223 (15–335)</td>
<td>231 (17–390)</td>
</tr>
<tr>
<td>American Society of Anesthesiologists grade:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– I</td>
<td>32</td>
<td>36</td>
</tr>
<tr>
<td>– II</td>
<td>31</td>
<td>22</td>
</tr>
<tr>
<td>– III</td>
<td>28</td>
<td>22</td>
</tr>
<tr>
<td>Indication for operation:</td>
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<td></td>
</tr>
<tr>
<td>– Pancreatic cancer</td>
<td>43</td>
<td>30</td>
</tr>
<tr>
<td>– Ampullary cancer</td>
<td>13</td>
<td>20</td>
</tr>
<tr>
<td>– Cancer of the bile ducts</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>– Cancer of the duodenum</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>– Chronic pancreatitis.</td>
<td>18</td>
<td>17</td>
</tr>
</tbody>
</table>

Data are expressed as number of patients unless otherwise stated.
was 18 days (range 10–35 days) in the PJ group and 16 days (range 8–30 days) in the PG group.

DISCUSSION

Attempts at comparison of PJ with PG have been performed in a prospective (12, 21) and retrospective (7, 8) fashion. PG was reported to be safer than PJ in a retrospective study (8) with historical controls and in a small prospective randomized trial (12), which was abandoned because of a 25% mortality rate directly related to anastomotic leakage after PJ. Although a review (7) of prior anecdotal reports on 277 patients having undergone PG showed a pancreatic leak rate of 2%, a large prospective randomized trial (21) found no benefit from PG when compared with PJ.

The present study was carried out as a non-randomized surgeons design, which entailed that no surgeon had to learn a new technique with possibly initial inferior outcome, while the patients were always offered the best treatment. Although some variability in outcome will always be surgeon-related (13), data drawn from the present study showed that PG was associated with a statistically significant lower pancreatic leak rate than PJ. The 8.7% (15/171) overall rate of pancreatic fistula in the whole series was somewhat lower than the 11.7% (17/145) rate reported in the prospective randomized trial of Yeo et al (21).

One of the main questions remains whether leak rate is indeed a variance of definition, observation or of technique. Criteria to define pancreatic fistula vary from the daily recovery of 10 mL drainage with high
amylase persisting throughout the fourth or the eighth postoperative day (10,11) to the more clinically relevant definitions of the Johns Hopkins (21) and the Mayo Clinic (4) groups. However, the absence of sphincters between the secreting organs after non-pylorus preserving PJ or PG accounts for the unreliability of the above mentioned definitions. In fact, amylase-rich fluid can be recovered at drain sites from a leak of any anastomosis. Technical issues as serosa-to-serosa or mucosa-to-mucosa anastomosis, and transanastomotic stent or not, seem to have a bearing on long-term patency rather than on postoperative leak rate.

Whilst leakage occurs, modern experience is that it rarely leads to the fatal outcome that it did in the past. A large retrospective study (4) involving 375 patients has shown that 73% (48/66) of leaks at PJ can be managed by maintenance of intraoperatively placed drains. Similarly, 75% (9/12) of our fistulae in the PJ group were treated conservatively. Additional therapy with octreotide recommended by some authors (10,11) has been reported as disappointing by others (4).

Furthermore, no convincing evidence is found in the literature in favour of the use of the somatostatin analogue as prophylaxis against the development of pancreatic leakage in patients with soft texture of the pancreatic remnant (2,9). Among the non-technical intraoperative parameters, pancreatic consistency after PD has been reported to correlate with the risk of pancreatic fistula (21). Our data are consistent with these findings (21) in supporting the hypothesis that pancreatic leak rate is significantly higher in patients with soft texture of the pancreatic remnant.

In spite of the ability to treat most anastomotic leaks non-operatively, re-operation may become necessary in critically ill patients with uncontrolled dehiscence of the pancreatic anastomosis (2,9). Among the non-technical intraoperative parameters, pancreatic consistency after PD has been reported to correlate with the risk of pancreatic fistula (21). Our data are consistent with these findings (21) in supporting the hypothesis that pancreatic leak rate is significantly higher in patients with soft texture of the pancreatic remnant. In 6% to 10% of patients undergoing re-laparotomy (4,15), necrosis of the pancreatic remnant makes unfeasable any anastomotic repair or reconstruction. Thus, completion pancreatectomy may be required as a last resort. Mortality in this group of patients varies from 21% to 71% when PJ is the method of reconstruction (4,17). Different timing for performing completion pancreatectomy might account for this variation in fatal outcome rate. A 21% mortality rate was reported in patients re-operated on at a mean of seven days following PD (17). Mortality was 64% in patients re-operated on at a mean of 18 days postoperatively (15). In our study, 4/171 patients (2.3%) underwent completion pancreatectomy an average of 14 days after PD and all died. A retrospective study (4) also carried out in the 1980s reported a similar completion pancreatectomy rate (7/375, 1.8%). While it seems that completion pancreatectomy is seldom performed nowadays (17,21), it is certainly better done in the early postoperative period (17). There are no reports of completion pancreatectomy following PG, but again this could be simply due to the limited number of PG procedures performed (7) and/or to technical difficulties in managing complications after PG.

Our study like several others (4,7,8,12,21) testifies to the ongoing effort towards the achievement of an uncomplicated pancreatic anastomosis with minimal mortality and morbidity. Our data confirm that PG is associated with lower leak rates than PJ and therefore deserves more widespread use.

ACKNOWLEDGEMENT

Helge E. Myrvold, M.D., Ph.D., Professor of Surgery, University Hospital of Trondheim, Norway is acknowledged for valuable advice.

REFERENCES


RESUMÉ
But: Etudier la fiabilité des anastomoses pancréatiques après duodéno pancréatérectomie céphalique (PD).

Type d’étude: Essai prospectif non randomisé chez des patients consécutifs.

Provenance: Hôpital universitaire, France.

Patients: Cent soixante et onze patients consécutifs ayant un cancer périmallulaire opérable n = 136, (80%) ou des douleurs de pancréatite chronique résistantes aux antalgiques n = 35 (20%).

Méthodes: Anastomose pancréatique-jéjunale (PJ) ou anastomose pancréatique-gastrique (PG).

Principaux critères de jugement: La mortalité et la morbidité en rapport avec une déviation anastomotique des anastomoses PJ ou PG.

Résultats: Il y avait 91 PJ et 80 PG et les patients étaient comparables en ce qui concerne l’âge, le sexe, les concentrations préopératoires de bilirubine totale, la classe ASA, l’indication de la PD, la durée opératoire, la texture du pancréas, les pertes sanguines et le nombre de culot globulaire transfusé. Le taux de fistule pancréatique était significativement plus élevé après PJ (13%) qu’après PG (4%) (12/91 contre 30/80, p = 0,03). La mortalité globale était significativement plus élevée après PJ (12%) qu’après PG (4%) (11/91 contre 3/80, p = 0,05). La mortalité en rapport avec une déviation de l’anastomose pancréatique était significativement plus élevée après PJ (3% contre 1/80, p = 0,8) et celles en rapport avec d’autres causes (8/91 contre 2/80, p = 0,1) n’était pas significativement différente entre les groupes.

Conclusions: Les PJ se compliquent significativement plus de fistule pancréatique que les PG. Cependant la mortalité directement liée à la fistule pancréatique n’était pas significativement différente.

Mots-clés: Duodéno pancréatérectomie céphalique, anastomose pancréatique-jéjunale, anastomose pancréatique-gastrique.

ZUSAMMENFASSUNG
Ziel: Sicherheit der Pancreasanastomose nach Duodenopancreatektomie.

Studienanordnung: Nicht randomisierte, prospektive Studie.

Patienten: 171 Patienten mit resektablen peripankreatären Karzinomen (n = 136, 80%) oder konservativ nicht beherrschbarer Schmerzsymptomatik auf dem Boden einer chronischen Pankreatitis (n = 35, 20%)


Ergebnisse: Bei 91 Pat. wurde eine PJ und bei 80 Pat. eine PG durchgeführt. Die Pat. wiesen keine Unterschiede hinsichtlich Alter, Geschlecht, Gesamtbilirubin, ASA Klassifikation, Operationsindikation, Operationszeit, Pancreasbeschaffenheit, Blutverlust und Substitutionsbedarf auf. Nach PJ war die Incidenz einer Anastomoseninsuffizienz mit Pancreasfistel signifikant häufiger als nach PG (11 von 91 Patienten (13%) vs. 3 von 80 Patienten (4%), p = 0,05). Die Mortalität nach Anastomoseninsuffizienz betrug 3 von 91 Patienten verglichen mit 1 von 80 Patienten (p = 0,8). Andere Todesursachen zeigten keinen signifikanten Unterschied zwischen den Gruppen.

Schlussfolgerung: Im Vergleich zur PJ kam es nach PJ signifikant häufiger zu einer Anastomoseninsuffizienz mit Pancreasfistel ohne signifikanten Unterschied hinsichtlich der Mortalität.

РЕЗЮМÉ
Цель: Изучить безопасность панкреатических анастомозов после панкреатодуоденэктомии (ПД).

Характер исследования: Нерандомизированное проспективное исследование консеквативных пациентов.

Клиника: Университетский госпиталь, Франция.

Пациенты: 171 консеквативный пациент с местными периферическими опухолями, n = 136 (80%) или пациенты с терминальной близостью к хроническому панкреатиту, n = 35 (20%).

Методы: Панкреато-jejunosomia (PJ) или панкреато-gastrostomia (PG).

Задачи исследования: Изучение послеоперационных осложнений и летальности, ассоциирующихся с недостаточностью анастомоза после PJ или PG.

Результаты: Был выполнен 91 PJ и 80 PG у пациентов сравнимых по возрасту, полу, концентрации билирубина в сыворотке крови, степени риска (American Society of Anesthesiology), показаний к
PD, времени операции, структуры поджелудочной железы, кровопотере, а также количеству анастомозов. Процент панкреатических свищей был статистически достоверно выше после PJ (12%) по сравнению с PG (4%) (12 из 91 по сравнению с 3 из 80). Летальность была статистически достоверно выше после PJ (12%) чем после PG (4%) (11 из 91 по сравнению с 3 из 80, $p=0.05$). Смерть в результате недостаточности панкреатического анастомоза была 3 из 91 пациента по сравнению с 1 из 80 пациентов, что не составило статистически достоверной разницы.

\textit{Выводы: PJ} ассоциируется с более высокими цифрами недостаточности панкреатического анастомоза по сравнению с PG, однако, не было отмечено статистически достоверной разницы в летальности, связанной с недостаточностью панкреатического анастомоза.

\textit{Ключевые слова:} Панкреато-дуоденоктомия, панкреато-энтеростомия, панкреато-гастроэнтеростомия.

Submitted February 28, 1998; accepted March 24, 1998

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