Inflammatory response in obstructive jaundice and peritonitis

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The effect of preoperative biliary drainage on postoperative complications after pancreaticoduodenectomy

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ABSTRACT

Background: The benefit of preoperative biliary drainage in jaundiced patients undergoing pancreaticoduodenectomy for a suspected malignancy of the periampullary region is still under debate. This study evaluated preoperative biliary drainage in relation to postoperative outcome.

Study Design: At the Academic Medical Center Amsterdam, the Netherlands, a cohort of 311 patients undergoing pancreaticoduodenectomy from June 1992 up to and including December 1999 was studied. Of this cohort, 21 patients with external and/or surgical biliary drainage were excluded and 232 patients who had received preoperative internal biliary drainage were divided in 3 groups corresponding with severity of jaundice, according to preoperative plasma bilirubin levels: <4 [M (n = 177), 40 - 100 [M (n = 32)] and >100 [M (n = 23)], respectively group 1, 2, and 3. These groups were compared with patients who underwent immediate surgery (n = 58) without preoperative drainage.

Results: The median number of stent tries placements was 2 (range 1-6), with a median drainage duration of 41 days (range 2 to 182 days), and a stent dysfunction rate of 33%. Although patients in group 1 were better drained than patients in groups 2 and 3 (median reduction of bilirubin levels respectively 82%, 57% and 37%) (p < 0.01), there was no difference in overall morbidity among the drained groups, respectively 50%, 50% and 52%. Finally, there was no significant difference in overall morbidity between patients with and without preoperative biliary drainage, respectively 50% and 55%.

Conclusions: Preoperative biliary drainage did not influence the incidence of postoperative complications and although it can be performed safely in jaundiced patients, it should not be used routinely.

INTRODUCTION

Operations on patients with obstructive jaundice carry an increased risk of postoperative complications. The concept of preoperative biliary drainage has been developed to reduce this morbidity and mortality. Drainage can be accomplished either externally, by inserting percutaneously a transhepatic catheter (PTD) into the biliary tract, or internally, by endoscopic retrograde cannulation of the bile duct with insertion of an endoprosthesis. Nowadays, both techniques are used safely, but the benefit of preoperative biliary drainage is still questioned for several reasons.

Early non-randomized studies reported encouraging results on reduction of mortality in jaundiced patients after preoperative biliary drainage. Several randomized clinical trials however on PTD failed to show an overall improvement in postoperative complications. These clinical and experimental studies showed that PTD did not improve the outcome of subsequent operations probably due to bile loss and subsequent endotoxemia. Although internal biliary drainage does have a beneficial effect based on experimental data by restoring the nutritional status, immune function, and by reducing endotoxemia, clinical benefit has not been proven yet. A recent randomized trial on preoperative biliary drainage, performed by Lai et al., revealed no difference in morbidity and mortality rates in patients.
who had either early elective surgery or first preoperative endoscopic biliary drainage. This lack of effect may in part be explained by the fact that recovery of metabolic and immune functions requires 4-6 weeks after biliary drainage. In a previous retrospective study on preoperative internal biliary drainage from our institution no significant difference in the incidence of postoperative complications was found between patients who had preoperative biliary drainage and those who did not. The drawbacks of internal biliary drainage have also become clear: biliary stents induce bacterial contamination and enhance the risk of cholangitis due to clogging. In addition, biliary stenting generates a severe inflammatory response in the wall of the bile duct, probably a factor increasing the risk of bile leakage of the biliodigestive anastomosis. Despite the negative outcome of the retrospective study from our department mentioned above, most patients with obstructive jaundice caused by periampullary tumors presented for surgery at the Academic Medical Center, Amsterdam, still undergo preoperative biliary drainage. Therefore the aim of this study was to evaluate prospectively the outcome of preoperative biliary drainage in a cohort of 290 patients undergoing pancreaticoduodenectomy for a suspected malignancy of the pancreatic head region. The benefit of preoperative biliary drainage was analyzed by comparing the postoperative outcome of subgroups stratified according severity of preoperative jaundice. Furthermore, a comparison was made of the incidence of postoperative complications between patients with and without preoperative biliary drainage, although we realize that the group of non-drained patients is not fully comparable with the subgroups that were drained.

PATIENTS AND METHODS

Patients and study design
A consecutive series of 311 patients undergoing pancreaticoduodenectomy for a suspected malignancy of the pancreatic head region at the Academic Medical Center, Amsterdam, were included from June 1992 up to and including December 2000. Of these, 290 patients were analyzed, since 21 patients were excluded because they underwent several forms of external and/or surgical biliary drainage (e.g., PTD alone, papillary resection, choledocho-duodenostomy or insertion of a T drain) instead of endoscopic (internal) biliary drainage. All clinical, operative, pathologic, and follow-up data were obtained from the prospectively collected database, in which the primary goal was to investigate the long term survival after pancreaticoduodenectomy. Retrospective review of hospital discharge records to insure completeness was not necessary.

The following patient characteristics were assessed: age, gender, risk factors (weight loss, diabetes mellitus), type of tumor, surgical staging (lymph node status and radical resection), and type of operation. Type and incidence of the preoperative biliary drainage procedure used, indications for recurrent biliary drainage procedures and the occurrence of biliary drainage procedure related complications, as well as morbidity and mortality of the operation were determined.
Biliary drainage before pancreaticoduodenectomy

Patients who had undergone preoperative internal biliary drainage were stratified into subgroups to evaluate the effect of preoperative biliary drainage in relation with severity of jaundice. The subgroups were defined according to their plasma bilirubin level after stenting but prior to the operation. Group 1 had preoperative bilirubin levels less than 40 μmol/L (twice the average reference value for adults) and was considered not jaundiced. Group 2 had bilirubin levels between 40-100 μmol/L and was moderately jaundiced. Finally, group 3 had bilirubin levels higher than 100 μmol/L and was considered severely jaundiced. For the sake of completeness, these preoperatively drained subgroups were compared with patients without preoperative biliary drainage (n=58).

Diagnostic work up, biliary drainage and operative procedure

Tumor staging was done by combinations of ultrasound, Doppler, CT scan, endoscopic ultrasound, endoscopic retrograde cholangiopancreatography (ERCP), and diagnostic laparoscopy as reported previously. Biliary drainage was done by ERCP and sphincterotomy with or without an endoprosthesis, or the combination of endoprosthesis with percutaneous biliary drainage (PTD).

Plastic stents were used in most patients and were selected by the endoscopist according to the length and characteristics of the obstruction. The types of stents used were straight Amsterdam type 10 French polyethylene stents (Wilson Cook Medical Inc., Winston Salem, North Carolina) usually 9 cm, sometimes 11 cm. When endoscopic biliary drainage was unsuccessful, PTD under ultrasonic guidance was done and followed as soon as possible by a "rendezvous procedure" to achieve internal biliary drainage.

Biliary drainage was not done in the absence of jaundice, if it was technically not feasible (e.g., previous gastric surgery (Billroth), failure of cannulation of the common bile duct, or inability to pass a guide wire or push a stent through the strictures) or when the operation was planned within three days after the decision had been made for surgical treatment.

The operation was planned within 4-6 weeks after assessment of resectability and insertion of the internal drainage catheter. All operations were covered by 24 hours prophylactic antibiotics (gentamicin and amoxycillin). The operation for resection of the tumor was a standard modified subtotal pylorus preserving pancreaticoduodenectomy as described before.

Complications of the drainage procedure and postoperative mortality and morbidity

Drainage procedure related complications are defined as early complications following ERCP and comprise perforation of the duodenal wall, bleeding, and pancreatitis. Stent dysfunction is defined as recurrent jaundice and/or cholangitis (due to, i.e., clogging or migration of the stent).

Mortality is defined as death occurring during the hospital admission or as a direct result of a postoperative complication.

Postoperative overall morbidity included all postoperative complications during hospitalization and was divided in surgery related complications and general complications. Surgery related complications were classified as hemorrhage, anastomotic leakage, intra abdominal abscess, delayed gastric emptying, wound infection, and complications requiring operative and non-operative intervention (ultrasound guided abscess drainage or biliary drainage). Delayed gastric emptying was defined as described previously as either the necessity of nasogastric intubation for 10 days or more or the inability to tolerate a regular (solid) diet on or before the 14th postoperative day. General complications included pulmonary and cardiac complications, and urinary tract infections.
Statistical methods
Data are summarized as numbers and percentages of patients, with median and ranges where indicated. The statistical methods included Chi-square tests, Fisher’s exact test and Mann-Whitney U statistics, where appropriate. When more than two groups were compared simultaneously, the Kruskal-Wallis H test was used. Following a significant result in the Kruskal-Wallis H test, post hoc multiple comparisons were carried out using Bonferroni’s correction. All comparisons were two-tailed. \( P < 0.05 \) was considered significant, if 3 groups were compared, \( P < 0.017 \), and if 4 groups were compared, \( P < 0.008 \) was considered significant. All statistical calculations were conducted with standard statistical programs (SPSS 8.01, SPSS Chicago, IL).

RESULTS

Patient characteristics
The clinical characteristics at initial presentation of patients undergoing pancreaticoduodenectomy with \( n = 232 \) or without \( n = 58 \) preoperative biliary drainage are summarized in table 1. No significant differences were found among the four groups in age, gender, risk factors, weight loss, pathology, and surgical staging. Patients in the biliary drainage group were more jaundiced at presentation as expressed by higher median plasma bilirubin levels predrainage compared with preoperative plasma bilirubin levels, respectively 126 (5-616) \( \mu \text{mol/L} \) and 17 (2-252) \( \mu \text{mol/L} \). There was no significant difference in preoperative levels of bilirubin, alkaline phosphatase and \( \gamma \)-glutamyl transpherase between patients with and without preoperative biliary drainage.

Complications during biliary drainage
Of the 232 patients that underwent preoperative internal biliary drainage, 192 patients (83%) had sphincterotomy followed by placement of a stent. 27 (12%) were decompressed by sphincterotomy only and 13 patients (6%) underwent PTD in combination with a stent (rendezvous procedure) (10) or sphincterotomy (3).

Of the 58 patients (20%) without preoperative biliary drainage, 25 patients underwent work up with diagnostic ERCP only (median bilirubin 95 (21-239) \( \mu \text{mol/L} \)). Twenty-four patients were clinically not jaundiced (median bilirubin ten (5-17) \( \mu \text{mol/L} \)) and nine patients had immediate operation planned after failure of the drainage procedure (median bilirubin 153 (113-239) \( \mu \text{mol/L} \)).

Of the 232 patients drained, 14 patients suffered from drainage procedure related complications. Four patients suffered from duodenal perforation, diagnosed after the stenting procedure, but this was managed conservatively. Four patients who underwent preoperative biliary drainage developed pancreatitis. In six patients, the ERCP was postponed because of bleeding. Also in the drainage group, 77 patients (33%) had recurrent jaundice due to stent dysfunction and 27 patients (12%) had one or more episodes of cholangitis within two weeks after the drainage procedure and were treated with antibiotics, and in this group 21 patients (9%) needed stent exchanges (1-6 times) probably because of clogging of the endoprosthesis.
Analysis according to severity of jaundice
Despite preoperative biliary drainage, 32 (14%) patients remained moderately jaundiced and 23 (10%) patients were still severely jaundiced at the time of surgery (Table 2). No significant differences were found among the three subgroups when age, gender, risk factors, weight loss, pathology, and surgical staging were compared.
Adequate biliary drainage was achieved in group 1 compared with groups 2 and 3 (median reduction of bilirubin levels respectively 82%, 57%, and 37% (p < 0.05) (Table 2). The median duration of 49 days for patients in group 1 was 2-fold longer than that for patients in groups 2 and 3; this was however not an intentional delay in order to allow for overall improvement in liver function but delays due to extensive work up, waiting lists, or other medical or non-medical reasons. Patients in groups 2 and 3 underwent significant more stent replacements than patients in group 1, respective medians two (range 1-4), two (range 1-6) and one (range 1-3) (p = 0.02). There were no significant differences among the three subgroups regarding operative time, blood loss, and intraoperative transfusions (Table 1). There were three in-hospital deaths (1.0%) in the study population (n = 290); all in group 1 (Table 3). Two patients died of multiple organ failure because of sepsis caused by intraabdominal abscesses, due to respectively an anastomotic dehiscence of the pancreaticojejunostomy and exacerbation of pre-existing pancreatitis, and the third patient died from severe intraabdominal hemorrhage.
Ammong the three groups, no difference in overall morbidity was found. The median lengths of postoperative hospital stay in group 1 did not differ significantly from groups 2 and 3, respectively 13 (6-167) days, 15 (12-39) days and 15 (10-70) days (p = 0.55). Nor was there a significant difference in number of relaparotomies in group 1 (12%) compared to groups 2 (13%) and 3 (17%) (p = 0.49). However, there was a difference in anastomotic leakage, increasing in incidence within the group of patients with preoperative stenting: 'no jaundice' = 12%, 'moderate jaundice' = 16%, and 'severely jaundiced' = 22%, although this difference did not reach a statistical significance (p =0.45).
Finally, a comparison was made between patients with stent related complications (n = 83), and patients with preoperative biliary drainage but without stent related complications (n = 149) and patients without preoperative biliary drainage (n = 58). No significant differences were found between these groups when postoperative overall morbidity, ICU admittance, postoperative hospital stay and number of relaparotomies were compared.

Surgical procedures in patients with and without biliary drainage
The four groups were well matched for operative technique and characteristics. In all, 269 pancreaticoduodenectomies were performed in patients with preoperative biliary drainage (n = 216) and in patients without drainage (n = 53). An end-to-side-pancreaticojejunostomy was performed in 224 patients undergoing preoperative biliary drainage and in 56 patients who were not drained preoperatively. Operative time, estimated blood loss, and intraoperative transfusion requirements were similar in all 4 groups (data not shown).
Mortality and morbidity of patients with and without biliary drainage

There was no difference in the incidence of complications in patients with and without preoperative biliary drainage. 117/232 (50%) compared to 32/58 (55%) respectively ($p = 0.69$). The median lengths of postoperative hospital stay was shorter in patients who underwent preoperative biliary drainage (groups 1, 2, and 3, respectively) compared with patients without (13, 15, and 15 days versus 16 days, respectively), but this difference was not significant ($p = 0.09$). Furthermore, although statistically not significant, there was a clinically important difference in incidence of anastomotic leakage: patients with preoperative biliary drainage (groups 1 + 2 + 3) suffered more from anastomotic leakage than patients with immediate surgery, 14% versus 7% respectively ($p = 0.19$). General complications including urinary tract infections, cardiac and pulmonary complications, occurred in respectively 6%, 7% and 10% in patients with preoperative biliary drainage and respectively 8%, 8% and 14% in patients without biliary drainage.

DISCUSSION

In the present series still 80% of the jaundiced patients underwent preoperative internal biliary drainage although the previous series from our institution (1983-May 1992) did not show a reduction of postoperative complications in patients after preoperative biliary drainage. Clearly, the indication to perform preoperative biliary drainage is not only to reduce the postoperative complications. For logistic reasons, preoperative biliary drainage is preferred as a temporary measure to avoid cholangitis, and to reduce jaundice because of an expected delay in surgery due to the need for preoperative assessment or a relatively long waiting time before surgery.

Although drainage procedure related complications were at an acceptable low rate (6%), still a significant percentage (33%) of the preoperatively biliary drained patients suffered from stent dysfunction (recurrent jaundice and/or cholangitis) and needed stent exchanges, not much different from previously reported (34%). In a report from Seitz and Soehendra these rates vary from 8 to even 52%. Nevertheless, one should bear in mind that the drain procedure related morbidity in the present study is biased and not the result of a single institute practice. In our institution, and in many other experienced/referral centers in Europe, patients are often seen for the first time by gastroenterologists of community hospitals, which many times lack alternatives as MRI/MRCP. By the time patients are presented for surgery, many of them already have had numerous stent (re) placements with the risks of concurrent morbidity. The role of preoperative biliary drainage has been an issue for debate for many years. In the United States most patients with malignant obstructive jaundice are operated upon without preoperative biliary drainage, whereas in many major centers in Europe, preoperative biliary drainage is still being done routinely. This difference in drainage policy however has so far not led to a different outcome concerning mortality and morbidity in both
Biliary drainage before pancreaticoduodenectomy

In the past decade, mortality associated with (pylorus preserving) pancreaticoduodenectomy has decreased to less than 6% in specialized centers and is in particular related to hospital volume. \(^{33,36}\) In the present series, mortality for (pylorus preserving) pancreaticoduodenectomy was 1.0%, which is similar to other published reports. \(^{33,36}\) It is unlikely that preoperative biliary drainage will significantly influence mortality after (pylorus preserving) pancreaticoduodenectomy.

Independent of the policy of preoperative biliary drainage, the morbidity of (pylorus preserving) pancreaticoduodenectomy remains high with rates between 25% - 68%. \(^{37-42}\) The postoperative overall morbidity in the present series (51%) tends to be in the high range, but all postoperative complications, e.g. surgery related and general complications are taken into account, including delayed gastric emptying and all minor complications (e.g. urinary tract infections). In the present study, the directly surgery related complication rate was 41%, this might seem acceptable, but still more efforts should be undertaken to further decrease pancreato-biliary surgery related complications.

Analyzing the subgroups 'no jaundice', 'moderate jaundice' and 'severe jaundice', according preoperative plasma bilirubin levels, showed that there was no difference in overall morbidity (respectively 49%, 50%, and 52%). One might expect that after reducing bilirubin levels and thus attenuating operative risks (the benefit of endoscopic drainage), a reduction should be found in the complication rate as expressed in this subgroup analysis. The only difference notable was the increased incidence of anastomotic leakage in 'severely' jaundiced patients compared with 'moderately-' and 'non-jaundiced' patients, and more often anastomotic leakage in patients with preoperative biliary drainage compared with non-drained patients. Sohn et al. \(^{32}\) also reported in a prospectively collected large series of stented patients an increased rate of pancreatic fistula formation and an increased rate of wound infection secondary to bactibilia, both related to preoperative biliary instrumentation and preoperative biliary drainage. In another prospective database cohort of stented patients, Povoski et al. \(^{31}\) also reported preoperative biliary drainage to be associated with an increased incidence of overall complications, infectious complications, intra abdominal abscess, and even death. As reported by Karsten et al. \(^{22,23}\) this is most likely a result of pancreatic and or bile duct wall inflammation. Preoperative biliary drainage, with a median duration of 42 days until surgery, was however also without any reduction of postoperative overall morbidity compared to patients without preoperative biliary drainage (52% versus 55%, respectively).

There was no significant difference in postoperative hospital stay within the stented group, comparing non-jaundiced, moderately and severely jaundiced patients, nor between stented-versus non-stented patients. Yet, the number of patients in groups 2 and 3 were relatively small compared with those in group 1 and the lack of a significant difference in outcome might be related to the insufficient sample size. Furthermore, one can imagine that many patients who underwent immediate surgery were in a relatively better preoperative condition as compared with the stented patients, but this is inherent with the poor methodological...
design of retrospective studies. Marcus et al., however, reported in a retrospective analysis an increased length of hospitalization (five days) in patients with preoperative stenting compared to patients with immediate surgery, but this was also based on a small retrospective series (30 patients versus 22 patients, respectively), treated from 1985 to 1996. Moreover, similar results as reported in the present study were also obtained from large prospectively collected databases by Povoski et al. and Sohn et al.

In previous series a bilirubin level of 170 μmol/L was clearly shown to be a risk factor for postoperative complications. Although two-third of the patients in group 3 had bilirubin levels above 200 μmol/L, one could argue that since one third of the patients in this group had bilirubin levels above 150 μmol/L, group 3 as a whole was not severely jaundiced. But also in the study of Lai et al., patients with preoperative stenting and bilirubin levels ranging from 106-195 μmol/L did not have less morbidity than patients with immediate surgery and bilirubin levels ranging from 221-306 μmol/L.

It could also be argued that the results showed that preoperative biliary drainage might be useful since the postoperative complication rate of the 177 patients in group 1 who had significant jaundice before preoperative biliary drainage were reduced to a level comparable to the 58 ‘good risk’ patients without significant jaundice that underwent immediate surgery. Still, taken into account the co-morbidity of the drainage procedure itself, and the extra time before surgery (4-6 weeks), there are also arguments in favor of performing immediate surgical resections of periampullary tumors as soon as possible after diagnosis and reserving preoperative biliary drainage only for patients with severe jaundice (bilirubin >150 μmol/L), cholangitis, malnutrition, or a suspected delay before surgery due to extensive preoperative diagnostic work up or a waiting list.

Arguments against internal biliary drainage by stents are the drainage procedure associated risks particularly that of infection. Under normal conditions, human bile is sterile. Infected bile due to biliary tract disease occurs in 8%-42% and factors related to bile colonization are advanced age, cholecystitis and obstructive jaundice. After drainage of the biliary tract, infection of bile is most likely to occur, particularly when endoprosthesis are used, resulting in an open passage to the duodenum. Furthermore, during long term stenting (> four weeks) an extensive inflammatory reaction occurs in the bile duct wall due to the presence of a stent. These factors, combined with the presence of a foreign body in the bile duct, provide ideal conditions for bacterial colonization of the biliary tree and clogging of the stent, and probably potentiating the risk of anastomotic leakage after surgery as mentioned before.

Although the quality of drainage (88% reduction of median plasma bilirubin levels), the length of drainage (49 days), and type of biliary drainage (internal endoscopic biliary drainage), was more adequate compared with previous series, no difference in postoperative complications was found. Remarkably internal biliary drainage has well known advantages as demonstrated in experimental studies leading to a reduction in endotoxemia, decrease in mortality, quicker normalization of T cell dysfunction, and restoration of mononuclear phagocytic capacity. Theoretically, internal biliary drainage should produce
better results by preventing external loss of fluid and electrolytes, and by avoidance of the disruption of the enterohepatic circulation. Because previous studies did not show a reduction in complications, it should be questioned why the treatment strategy did not change accordingly. A possible explanation could be found in the diagnostic work up of jaundiced patients with suspected malignant tumors. During the past decades ERCP has been used in a relatively early phase in the diagnostic work up before referral. Arguments for an early ERCP were not only the diagnostic aspects, differentiation between benign diseases (e.g. bile duct stones) and malignant tumors, but also the fact that an endoprosthesis could be inserted during the same diagnostic procedure. One should realize that endoscopic drainage is the treatment of choice in most patients (75-85%) because of advanced disease. Secondly, if an ERCP is performed and contrast is injected above a bile duct stricture, a stent should be inserted to prevent the risk of cholangitis, also in patients who are candidates for a curative resection.

Another argument for preoperative biliary drainage is that jaundiced patients presenting with a potential resectable lesion will undergo further diagnostic work up and be on a waiting list before surgery can be performed (2-4 weeks), which can be done safely since this study confirmed that preoperative drainage did not deteriorate postoperative outcome. Nevertheless, presently other non-invasive imaging techniques as spiral CT scan, and MRI/MRCP, have taken over from the diagnostic ERCP. Subsequently the ideal strategy should probably be a diagnostic work up without invasive technique and accurate non-invasive selection of patients for endoscopic palliative stenting and immediate surgery without preoperative biliary drainage, in particular in patients without severe jaundice and/or cholangitis.

The benefit of preoperative biliary drainage in terms of reducing postoperative complications, remains to be investigated in a large prospective randomized study. However, such a study is unlikely to ever be performed since often the biliary stent has already been placed by the time the surgeon becomes involved in the decision making process. In conclusion, this analysis shows that stented patients with ‘normal’ preoperative bilirubin values have equal postoperative morbidity compared with stented patients with a relatively ‘high’ preoperative bilirubin level. Nevertheless, biliary drainage should not be used routinely in patients presenting with a tumor in the periampullary region awaiting surgical resection, unless more time is required for other investigations or visiting referral centers because of centralization of high risk surgery. Therefore, despite the co-morbidity of the drainage procedure itself, preoperative biliary drainage can be performed safely in jaundiced patients.
REFERENCES


Biliary drainage before pancreaticoduodenectomy


49. Megison SM, Dunn CW, Hutton JW, Chao H. Effects of biliary obstruction on mononuclear...


**Table 1** Clinical and operative characteristics of 290 patients before (pylorus preserving) pancreaticoduodenectomy.

<table>
<thead>
<tr>
<th>Patient and operative characteristics</th>
<th>“&lt;40”, group 1 n = 177</th>
<th>“40-100”, group 2 n = 32</th>
<th>“&gt;100”, group 3 n = 23</th>
<th>No drainage, group 4 n = 58</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y), median [range]</td>
<td>66 [31-84]</td>
<td>64 [51-78]</td>
<td>67 [48-78]</td>
<td>65 [36-75]</td>
</tr>
<tr>
<td>Male/female (% male)</td>
<td>89/88 (50.3)</td>
<td>17/15 (53.1)</td>
<td>12/11 (52.2)</td>
<td>30/28 (51.7)</td>
</tr>
<tr>
<td>Risk factors. Diabetes Mellitus</td>
<td>11 (6.2)</td>
<td>2 (6.3)</td>
<td>2 (8.7)</td>
<td>5 (8.6)</td>
</tr>
<tr>
<td>Pathology. Malignant tumors</td>
<td>153 (86.4)</td>
<td>28 (87.5)</td>
<td>20 (87.0)</td>
<td>50 (86.2)</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>79 (44.6)</td>
<td>15 (46.9)</td>
<td>11 (47.8)</td>
<td>26 (44.8)</td>
</tr>
<tr>
<td>Ampullary cancer</td>
<td>49 (27.7)</td>
<td>8 (25.0)</td>
<td>5 (21.7)</td>
<td>13 (22.4)</td>
</tr>
<tr>
<td>Cancer of the common bile duct</td>
<td>20 (11.3)</td>
<td>3 (9.4)</td>
<td>3 (13.0)</td>
<td>8 (13.8)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (2.8)</td>
<td>2 (6.3)</td>
<td>1 (4.3)</td>
<td>3 (5.2)</td>
</tr>
<tr>
<td>Benign tumors</td>
<td>24 (13.6)</td>
<td>4 (12.5)</td>
<td>3 (13.0)</td>
<td>8 (13.8)</td>
</tr>
<tr>
<td>Staging.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive lymph node status</td>
<td>91 (51.4)</td>
<td>17 (53.1)</td>
<td>11 (47.8)</td>
<td>25 (43.1)</td>
</tr>
<tr>
<td>Radical surgical resection</td>
<td>103 (58.2)</td>
<td>20 (62.5)</td>
<td>15 (52.2)</td>
<td>35 (56.3)</td>
</tr>
<tr>
<td>Operating time (h), median [range]</td>
<td>4.9 [2.5-10.5]</td>
<td>5.2 [2.1-9.9]</td>
<td>4.2 [2.7-8.3]</td>
<td>4.3 [2.5-10.5]</td>
</tr>
<tr>
<td>Estimated blood loss (L), median [range]</td>
<td>1.5 [0.1-8.7]</td>
<td>1.3 [0.3-3.6]</td>
<td>1.1 [0.2-2.1]</td>
<td>1.4 [0.2-5.1]</td>
</tr>
<tr>
<td>Patients in need of transfusions</td>
<td>65 (36.7)</td>
<td>14 (43.8)</td>
<td>9 (39.1)</td>
<td>22 (37.9)</td>
</tr>
<tr>
<td>Operating time (h), median [range]</td>
<td>4.9 [2.5-10.5]</td>
<td>5.2 [2.1-9.9]</td>
<td>4.2 [2.7-8.3]</td>
<td>4.3 [2.5-10.5]</td>
</tr>
</tbody>
</table>

Figures are numbers (%) of patients, unless otherwise stated. Stented patients are subdivided according to bilirubin levels after stenting but prior to operation.
Table 2  Success of biliary drainage and related complications in 290 patients before (pylorus preserving) pancreaticoduodenectomy.  

<table>
<thead>
<tr>
<th>Biliary drainage characteristics</th>
<th>“&lt;40”, group 1</th>
<th>“40-100”, group 2</th>
<th>“&gt;100”, group 3</th>
<th>No drainage, group 4.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 177</td>
<td>n = 32</td>
<td>n = 23</td>
<td>n = 58</td>
</tr>
<tr>
<td>Bilirubin (μM) at presentation * †</td>
<td>120 [5-616]</td>
<td>143 [38-410]</td>
<td>212 [50-415]</td>
<td>24 [4-238]</td>
</tr>
<tr>
<td>Percentage reduction in bilirubin level after drainage * †</td>
<td>82 [74-93]</td>
<td>57 [51-64]</td>
<td>37 [29-45]</td>
<td></td>
</tr>
<tr>
<td>At least 50% reduction in bilirubin level after drainage, patient numbers (%)</td>
<td>154 (87.0)</td>
<td>26 (81.3)</td>
<td>18 (78.3)</td>
<td></td>
</tr>
</tbody>
</table>

Other liver chemistry at time of operation


Days of drainage


Number of drainage procedures

| Number of drainage procedures | 1 [1-3] | 2 [1-4] | 2 [1-6] |  |

Drainage procedure-related complications, patient numbers (%)

| Drainage procedure-related complications, patient numbers (%) | 11 (6.2) | 2 (6.3) | 1 (4.3) |  |

Stent dysfunction, patient numbers * †

| Stent dysfunction, patient numbers | 52 (29.4) | 12 (37.5) | 13 (56.5) |  |

Figures are median [range], unless otherwise stated. Stented patients are subdivided according to bilirubin levels after stenting but prior to operation.

* P < 0.05; Kruskal-Wallis H test; †, group 1 versus 3. P < 0.01 (significant following Bonferroni’s correction).
Table 3  Mortality and morbidity in 290 patients after (pylorus preserving) pancreaticoduodenectomy.

<table>
<thead>
<tr>
<th>Complications and postoperative hospital stay</th>
<th>Patients divided according preoperative plasma bilirubin or no preoperative drainage</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>“&lt;40”, group 1</td>
</tr>
<tr>
<td>Mortality</td>
<td>n = 177</td>
</tr>
<tr>
<td></td>
<td>3 (1.7)</td>
</tr>
<tr>
<td>Overall morbidity</td>
<td>89 (50.3)</td>
</tr>
<tr>
<td>Surgery related complications</td>
<td>71 (40.1)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>14 (7.9)</td>
</tr>
<tr>
<td>Anastomotic leakage</td>
<td>22 (12.4)</td>
</tr>
<tr>
<td>Intra-abdominal abscess</td>
<td>28 (15.8)</td>
</tr>
<tr>
<td>Delayed gastric emptying</td>
<td>36 (20.3)</td>
</tr>
<tr>
<td>Wound infection</td>
<td>12 (6.8)</td>
</tr>
<tr>
<td>General complications</td>
<td>32 (18.1)</td>
</tr>
<tr>
<td>ICU admittance</td>
<td>26 (14.7)</td>
</tr>
<tr>
<td>Relaparotomy</td>
<td>22 (12.4)</td>
</tr>
</tbody>
</table>

Figures are numbers (%) of patients, unless otherwise stated. Stented patients are subdivided according to bilirubin levels after stenting but prior to operation.