The optimal duration of preoperative biliary drainage for periampullary tumors that cause severe obstructive jaundice

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KEYWORDS:
Pancreas; Common bile duct; Ampulla of Vater; Jaundice; Obstructive; Drainage

Abstract

BACKGROUND: Despite routine preoperative biliary drainage (PBD) with periampullary cancer, its optimal duration has not been established. The objective of this study was to investigate PBD in severely jaundiced patients.

METHODS: A total of 120 patients with periampullary tumors who underwent surgery with intent to cure after PBD for severe obstructive jaundice were enrolled. According to the duration of PBD, 66 and 54 patients were classified into the long-term (≥ 2 weeks) and short-term (< 2 weeks) groups.

RESULTS: PBD-related complications occurred in 6 (9.1%) and 14 (25.9%) patients in the short-term and long-term groups, respectively (P = .014). Rates of surgery-related complications and mortalities were not significantly different between the 2 groups. The R0 resection rate tended to be lower (P = .054) and the mean length of hospital stay was significantly longer (P = .039) in the long-term group.

CONCLUSIONS: PBD duration < 2 weeks is more appropriate in severely jaundiced patients with periampullary cancer.

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progressive obstructive jaundice is associated with a proinflammatory state, resulting from portal and systemic endotoxemia and bacterial translocation.3–7 This proinflammatory state causes an uncontrolled induction of the inflammatory cascade, contributing to the development of complications.8,9 Obstructive jaundice is also associated with impaired cellular immunity.3,10,11 The degree of jaundice correlates with disturbances in coagulation, decreased hepatic function, and the development of cholangitis.12 Moreover, cholestasis has deleterious effects on the cardiovascular system and blood volume, leading to renal dysfunction.7,13,14

Because surgery in patients with jaundice carries an increased risk for postoperative complications, preoperative biliary drainage (PBD) has been introduced as a routine procedure.15,16 However the efficacy of PBD is controversial. In several previous experimental and retrospective studies, PBD reduced morbidity and mortality after surgery.17,18 On the contrary, several meta-analyses of randomized trials showed that routine PBD carried no benefit in reducing morbidity and mortality.19–21 In addition, a recent multicenter, prospective randomized trial comparing PBD followed by surgery versus early surgery in patients with obstructive jaundice (serum total bilirubin level, 2.3 to 14.6 mg/dL) due to pancreatic head cancer revealed that routine PBD increased the complication rate.22 Thereafter, PBD has not been accepted as the routine management in periampullary tumors, including pancreatic head cancer.

Patients with severe obstructive jaundice (serum total bilirubin >15 mg/dL [>258 μmol/L]) due to periampullary cancers usually undergo PBD in clinical practice, because previous studies have shown that severe jaundice is a risk factor for postoperative complications.23,24 Concerning the duration of PBD, it has been suggested that adequate recovery of hepatic function depends on the duration of biliary decompression and the duration of obstructive jaundice before decompression.23,25,26 A minimum of 4 to 6 weeks of PBD was advised, with even longer periods proposed for patients with prolonged biliary obstruction before decompression. A more recent study showed that preoperative decompression is necessary for ≥3 weeks before coagulation and hepatic and reticuloendothelial system function start improving.27 However, increased drainage duration has been known to increase the risk for drainage-related complications,20,22 and the optimal duration of PBD has not been established.

To investigate the optimal duration of PBD in severely jaundiced patients with periampullary cancers, we evaluated clinical outcomes according to the duration of PBD in this study.

Methods

Patients

A prospectively maintained database was queried for patients who were diagnosed with severe obstructive jaundice (serum total bilirubin >15 mg/dL [>258 μmol/L]) due to periampullary tumor and who underwent surgery with intent to cure with PBD between October 2003 and May 2011 at Seoul National University Hospital, Seoul National University Bundang Hospital, and the National Cancer Center in Korea. Patients who had evidence of distant metastasis or local vascular involvement on computed tomography were not included. Patients who had definite evidence of cirrhosis or other hepatic disease causing hepatic dysfunction or who had histories of alcohol abuse were also excluded. Therefore, a total of 120 patients were analyzed in this study.

This study protocol was approved by each institutional review board of the Human Clinical Research Center.

Patients were divided into 2 separate groups according to the duration of PBD. Patients who underwent PBD for ≥2 weeks were classified as the long-term drainage group, and those who underwent PBD for <2 weeks constituted the short-term drainage group. Biliary drainage was done by endoscopic retrograde cholangiopancreatography or percutaneous transhepatic cholangiography. The standard surgical procedure for resectable tumors was pancreaticoduodenectomy or pylorus-preserving pancreaticoduodenectomy. If resection was deferred because of metastasis or local spread, palliative bypass surgery, which was mostly hepaticojejunostomy with or without gastroenterostomy, was done. All clinical, operative, pathologic, and follow-up data were obtained by retrospective chart review. The following patient characteristics were assessed: age; sex; body mass index; weight loss; duration of symptoms; selected laboratory values, including initial serum total and direct bilirubin and preoperative serum total bilirubin; initial serum creatinine; type of PBD method; type of tumor; and type of operation.

The rates of PBD procedure-related complications, surgery-related complications, and mortality up to 90 days after PBD were evaluated as the primary outcomes. R0 resection rate and hospital stay (from the day of the biliary drainage procedure to discharge) were evaluated as the secondary outcomes.

Definition of events

Drainage procedure–related serious complications included cholangitis, bleeding, acute pancreatitis, acute cholecystitis, bowel perforation, and stent occlusion. Surgery-related serious complications included anastomotic leakage, delayed gastric emptying, intra-abdominal abscess, wound infection, cholangitis, bleeding, and portal vein thrombosis. Other general complications, such as pneumonia and any complications requiring laparotomy, were also evaluated. In-hospital mortality and the length of hospital stay were assessed. The definitions of complications have been used in previous studies that evaluated the management of complications on the basis of generally accepted criteria.18,23–30 Details on the definitions of complications are listed in Table 1. Immediate procedure-related complications were defined as complications such as
cholangitis, cholecystitis, pancreatitis, hemorrhage, and perforation <48 hours after drainage procedures.

Statistical analysis

Results are expressed as mean ± SD and ranges or as the number and percentage of the total number of patients. Descriptive statistics were calculated for all variables. Continuous variables were compared using Student’s t tests, whereas categorical variables were compared using chi-square or Fisher’s exact tests as appropriate. P values <.05 were considered statistically significant. All statistical analyses were performed using SPSS version 17.0 for Windows (SPSS, Inc, Chicago, IL).

Results

Overall characteristics of patients

The demographics and clinical characteristics of patients are summarized in Table 2. There were no significant differences in age, sex, body mass index, duration of symptoms, initial serum total and direct bilirubin levels, and creatinine level between the 2 groups. The most common type of tumor was distal common bile duct cancer in both groups, followed by pancreatic head and ampulla of Vater cancer. The proportions of types of tumors were not significantly different between the groups.

The number of patients who had cholangitis before the drainage procedure was not significantly different between
the 2 groups \(P = .575\). In addition, the rates of drainage-related immediate complications were not significantly different between the groups \(P = .684\). Within 2 weeks, biliary drainage procedure–related complications developed in 6 patients in the short-term drainage group (9.1%) and in 9 patients in the long-term drainage group (16.7%). These rates were not significantly different between the groups \(P = .212\).

All patients underwent PBD by means of endoscopic retrograde cholangiopancreatography or percutaneous transhepatic cholangiography. There was no significant difference in the drainage method between the 2 groups \(P = .131\).

**Clinical outcomes according to the duration of preoperative biliary drainage**

All patients underwent surgery with curative intent; however, palliative bypass surgery was performed if local spread or metastasis was detected at laparotomy. The percentage of patients undergoing resection did not differ significantly between the 2 groups: 61 patients in the short-term drainage group (92.4%) and 47 in the long-term drainage group (87.0%) \(P = .328\). Primary outcomes related to either PBD or surgery are outlined in Table 3.

Overall primary outcomes, including biliary drainage procedure–related complications, surgery-related complications, and mortality, according to the duration of PBD were not significantly different \(P = .912; \text{Fig. 1}\). However, complications that were associated with PBD occurred in 6 patients in the short-term drainage group (9.1%) and in 14 patients in the long-term drainage group (25.9%), with a significant difference \(P = .014\). The most common complication related to drainage was stent occlusion. Surgery-related complications occurred in 31 patients in the short-term drainage group (47.0%) and in 23 patients in the long-term drainage group (42.6%), without a significant difference \(P = .632\).

In the evaluation of secondary outcomes, the R0 resection rate tended to be higher in the short-term drainage group \(P = .054\), and the mean length of hospital stay was significantly longer in the long-term drainage group \(P = .039\) (Table 4).

**Comments**

In this study, we examined how long PBD should be performed in patients with severe obstructive jaundice caused by periamplullary tumors. We found that PBD for \(\geq 2\) weeks did not improve primary outcomes. Drainage-related complications were increased with long-term drainage. In addition, there was no significant beneficial effect with regard to surgery-related complications. Moreover, total hospital stays were lengthened significantly with long-term drainage. The rates of overall complications were similar in both the short-term and long-term drainage groups. The rates of R0 resection tended to be lower in the

**Table 2**  Demographic and clinical characteristics of the patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Short-term drainage (&lt;2 wk)</th>
<th>Long-term drainage ((\geq 2) wk)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>64.7 ± 8.8</td>
<td>64.8 ± 8.5</td>
<td>.988</td>
</tr>
<tr>
<td>Men</td>
<td>48 (72.7%)</td>
<td>39 (72.2%)</td>
<td>.951</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.2 ± 3.1</td>
<td>22.8 ± 2.8</td>
<td>.413</td>
</tr>
<tr>
<td>Duration of symptoms (wk)</td>
<td>2.7 ± 1.7</td>
<td>2.4 ± 1.2</td>
<td>.366</td>
</tr>
<tr>
<td>Weight loss (kg)</td>
<td>2.6 ± 3.4</td>
<td>2.8 ± 3.7</td>
<td>.716</td>
</tr>
<tr>
<td>Initial bilirubin level (mg/dL)</td>
<td>19.3 ± 3.8</td>
<td>20.0 ± 3.9</td>
<td>.321</td>
</tr>
<tr>
<td>Initial creatinine level (mg/dL)</td>
<td>0.94 ± 0.3</td>
<td>0.96 ± 0.2</td>
<td>.683</td>
</tr>
<tr>
<td>Type of tumor</td>
<td></td>
<td></td>
<td>.134</td>
</tr>
<tr>
<td>CBD</td>
<td>30 (45.5%)</td>
<td>36 (66.7%)</td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td>26 (39.4%)</td>
<td>12 (22.2%)</td>
<td></td>
</tr>
<tr>
<td>AoV</td>
<td>8 (12.1%)</td>
<td>5 (9.3%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>2 (3.0%)</td>
<td>1 (1.9%)</td>
<td></td>
</tr>
<tr>
<td>Type of biliary drainage</td>
<td></td>
<td></td>
<td>.131</td>
</tr>
<tr>
<td>ERCP</td>
<td>31 (47.0%)</td>
<td>18 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>PTC</td>
<td>35 (53.0%)</td>
<td>36 (66.7%)</td>
<td></td>
</tr>
<tr>
<td>Type of surgical treatment</td>
<td></td>
<td></td>
<td>.328</td>
</tr>
<tr>
<td>Resection</td>
<td>61 (92.4%)</td>
<td>47 (87.0%)</td>
<td></td>
</tr>
<tr>
<td>Palliative bypass procedure</td>
<td>5 (7.6%)</td>
<td>7 (13.0%)</td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD or as number (percentage).  
AoV = ampulla of Vater; CBD = common bile duct; ERCP = endoscopic retrograde cholangiopancreatography; PTC = percutaneous transhepatic cholangiography.
long-term drainage group compared with the short-term drainage group, without a significant difference.

The benefit of PBD is controversial. A recent prospective randomized trial revealed that PBD in patients with pancreatic head cancer increased the rates of overall complications. However, this study excluded severely jaundiced patients (serum total bilirubin >14.6 mg/dL [250 μmol/L]), which is a population that may have derived the greatest benefit from PBD, because the degree of jaundice correlates with disturbances in coagulation and decreased hepatic function.

In clinical practice, patients with severe obstructive jaundice due to periampullary tumors usually undergo PBD. And preoperative biliary decompression is the primary strategy for severely jaundiced patients in the institutions included in this study. However, the optimal duration of PBD remains undetermined. Though several experimental and clinical studies have advised 4 to 6 weeks of PBD, the evidence is lacking.

Increasing drainage time increases the risk for malfunction of the drainage. Long-term PBD with stents could cause an extensive inflammatory reaction in the bile duct wall. This provides conditions for bacterial colonization of the biliary tree, clogging of the stent, and probably potentiates the risk for anastomotic leakage after the operation. Also, there are reports that PBD has caused increased incidence of infectious complications. These drainage-related problems would result in a prolonged postponement of surgery, which would be unjustifiable for a potentially resectable tumor.

Using the antipyrine clearance method, McPherson et al reported that hepatic function does not consistently improve during drainage. The currently advised 4 to 6 weeks of PBD is based mostly on experimental studies.
conducted in the 1980s. Koyama et al.25 showed that it took >6 weeks to normalize hepatic mitochondrial function. However, even in this study, abnormalities of liver function tests decreased rapidly after biliary decompression and were mostly normalized within 3 weeks. There is a lack of clinical studies about the duration of PBD. Van der Gaag et al.22 reported that symptoms that were associated with obstructive jaundice resolved <10 days after successful biliary drainage. Accordingly, we hypothesized that 2 weeks of PBD would be appropriate. Therefore we analyzed our patients by dividing them into 2 groups according to the duration of biliary drainage, ≥2 or <2 weeks. We have shown that PBD for ≥2 weeks has no beneficial effect in reducing morbidity and mortality. On the contrary, significantly increased drainage-related complications and lengthened total hospital stays were found in the long-term drainage group.

In this study, the R0 resection rate tended to be lower with long-term drainage. In a previous study comparing PBD followed by surgery versus early surgery, the rate of R0 resection also tended to be lower in the PBD group.33 In addition, another study reported up to 6% of percutaneous transhepatic biliary drainage tract implantation metastasis with or without metastasis of other sites.34 Considering that all patients underwent curative intent surgery in this study, we think that the cause of a lower likelihood of an R0 resection was associated with the possibility of tumor seeding via long-term drainage tract.

There were several limitations to this study. First, the sample size was relatively small because of the rarity of cases meeting our inclusion criteria. Second, because patient data were retrospectively collected, the results need to be interpreted with caution. The longer duration of PBD might have caused the high rate of drainage-related complications and vice versa. However, because the percentage of patients who had cholangitis at initial presentation and the rates of immediate drainage-related complications were not different between the 2 groups, it is reasonable to conclude that the longer duration of drainage caused more drainage-related complications. Third, this study included heterogeneous disease entities. However, only patients with periampullary tumor were included, and obstructive jaundice, which needed biliary decompression, was the common feature.

In conclusion, this analysis showed that PBD for ≥2 weeks is not beneficial in reducing postoperative and overall complications. On the contrary, drainage-related complications increased with long-term drainage. Therefore, PBD duration <2 weeks would be more appropriate in severely jaundiced patients with periampullary cancer. A further prospective randomized trial is warranted to establish the optimal duration of PBD.

Acknowledgment

We would like to thank all the participating patients.

References


