Endoscopic biliary drainage
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Long-term results of endoscopic drainage of common bile duct strictures in chronic pancreatitis

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submitted for publication
ABSTRACT

Background: Endoscopic stent therapy is an established treatment modality to resolve postoperative biliary strictures. Results regarding long-term outcome of biliary stenting in chronic pancreatitis (CP) are scarce.

Methods: All CP patients who underwent endoscopic biliary drainage of a benign stricture in our hospital between 1987-2000, were included in this retrospective study.

Results: Fifty-eight CP patients underwent biliary stenting (median age 54, 44 male). Procedure related mortality rate was 2% and complication rate 4%. Median follow-up was 45 months (range 0-182). Endoscopic treatment was successful in 22 patients (38%). Multivariate analyses identified presence of concomitant acute pancreatitis as the only predictor of successful outcome. Sub-analysis of these 12 patients revealed a success rate of 92%, as opposed to 24% in cases without acute inflammation. In this latter group, continued stenting beyond a one year period almost never resulted in additional stricture resolution.

Conclusions: For fibrotic biliary strictures due to CP, without evidence of concomitant acute inflammation, long-term success rate of endoscopic therapy is poor and only one out of four strictures is resolved successfully. If stricture resolution has not occurred after a one year period, surgery should be considered.

INTRODUCTION

In chronic pancreatitis (CP), common bile duct (CBD) stenosis is a frequent complication, with a reported incidence of 10 to 30% (1-4). CBD obstruction can develop from two distinct features; compression due to peri-ductal inflammatory swelling or fibrotic structuring caused by chronic inflammation. A CBD stenosis may lead to cholestasis, jaundice, recurrent cholangitis and secondary biliary cirrhosis (2,5).

In the past, a surgical bilio-digestive anastomoses was the only treatment option for these patients, with considerable morbidity and mortality. For this reason, other treatment modalities were investigated as an alternative therapy. Endoscopic biliary stenting was first introduced as a palliative treatment for malignant stenosis (6). In addition it has become an established treatment to resolve benign postoperative biliary strictures (7-9). In analogy, biliary strictures due to CP are also treated by endoscopic stenting, but results regarding long-term outcome are scarce.

Although short-term results are excellent with immediate relieve of cholestasis in almost all cases, it remains unclear whether endoscopic stent placement can achieve definite stricture resolution in CP, especially in case of tight fibrotic strictures. No prospective studies have been carried out. A number of retrospective studies described results of a limited number of patients with long term success rates ranging from 10-95% (10-17).

In this study, we report on our experience in endoscopic treatment of biliary strictures complicating CP over the past 14 years. The aims of this study were to evaluate long-term results and to identify factors predictive of outcome.
**MATERIALS AND METHODS**

**Patients**

All consecutive CP patients who underwent biliary stenting in our hospital between 1987 and 2000 were retrieved from an endoscopic database. Patients with pancreatic malignancy were excluded, as were patients with a stenosis caused by concrements or pseudocysts. We evaluated technical success rate, complication rate and long-term success rate of the stent therapy.

**Technique**

Patients were examined with a side viewing therapeutic endoscope in the left lateral position under conscious sedation with midazolam. In all patients a diagnostic cholangiogram was obtained. The CBD stricture was identified as a significant stenosis with prestenotic dilatation and/or delayed run off of contrast. A flexible guide wire was passed through the stricture, followed by a guiding catheter. A polyethylene Amsterdam-type endoprosthesis (10 Fr) was inserted over the guiding catheter to bridge the stenosis. As a rule the shortest possible stent was used. The decision for sphincterotomy was at the discretion of the endoscopist. If sphincterotomy was performed, the patient was observed clinically for 24 hours. After three months, ERCP was repeated. The stent was removed and a cholangiogram was obtained to evaluate the stenosis. The stricture was considered sufficiently dilated if the stricture waist had disappeared, and/or a 6.5 Fr catheter could pass without resistance and rapid run off of contrast was evident. If a significant stricture was still present, a new stent was inserted. Stents were exchanged electively every 3 months or when signs of stent dysfunction were present.

**Follow-up**

After stent removal, all patients were seen in the outpatient clinic at regular intervals for clinical and laboratory examination. Follow-up information was obtained from hospital charts and prospectively completed by written questionnaires send to the patient as well as the attending physician.

**Definitions**

Treatment was considered 'Successful' if no signs of biliary obstruction developed after permanent stent removal. 'Treatment failure' was defined by any one or more of the following: 1. Severe procedure related complications resulting in death or need of surgery. 2. Failure of the stricture to resolve, resulting in the need of further therapy (continued endoscopic stenting, metal stent insertion or surgery). 3. Recurrence of the stenosis for which treatment was necessary. ‘End of follow-up’ was defined as the time of failure, death, or the end of the follow-up period in November 2002.
Statistics
Primary outcome parameters were success rate, complication rate and recurrence rate. Secondary outcome parameters were identification of prognostic factors predictive of a successful outcome. Quantitative data are expressed as medians with lower and upper values. Logistic regression was performed to identify prognostic factors of outcome. The level of statistical significance was set at $p < 0.05$. Multivariate analysis was performed using step-by-step logistic regression. All variables with a $p$ value $< 0.1$ were considered for multivariate analyses.

RESULTS
From our endoscopic database, we identified 58 patients with CP that underwent endoscopic stent therapy for a CBD stenosis; 44 male (76 %), with a median age of 54 years (range 19 - 83). Patient characteristics are summarised in Table 1. All patients suffered from chronic pancreatitis with median disease duration of 23 months. Alcohol abuse was the predominant cause of pancreatitis (64 %). Twelve CP patients (21 %) had concomitant acute pancreatitis at time of drainage (defined as swelling of the pancreatic head and peri-pancreatic infiltration on imaging studies). Cholestasis was present in all patients. Jaundice was the leading clinical symptom in 26 (45 %).

ERCP
Sphincterotomy was performed in 25 patients (43 %), 15 of which underwent pre-cut sphincterotomy. Fourteen patients had already undergone a sphincterotomy during a previous procedure. The pancreatic duct (PD) was canulated in 43 patients (74 %) and in 14 a PD stenosis was present (24 %), for which three received a prosthesis.

CBD drainage
After the cholangiogram revealed the distal CBD stenosis, a 10 Fr endoprosthesis was placed successfully in all cases (Technical success rate 100 %). Median duration of drainage was 274 days (range 3-2706 days). A median of two stent exchanges took place during this period (range 0-17). Although nowadays some centres insert multiple stents in a sequential fashion, in this population, 53 (91 %) received a single endoprosthesis. In the remainder five patients multiple stent insertion was applied, with a maximum of three stents.

Morbidity and mortality
One procedure related death was recorded (Mortality rate 2 %). This patient died of a cerebral infarction, a day after surgical intervention for a duodenal perforation caused by ERCP. In addition, procedure related complications occurred in two patients (Procedure related complication rate 4 %); a mild flare-up of pancreatitis which was treated conservatively, and a liver abscess which was surgically drained.
Stent related complications were observed in 28 patients (Stent related complication rate 50 %); stent occlusion occurred in 27 cases and in one case the stent dislocated. All of these cases were successfully treated by stent exchange.

**Long-term results**
Median follow-up was 45 months (range 0-182) after stent insertion. Overall, endoscopic treatment achieved stricture resolution in 22 patients (Overall success rate 38 %) (Table 2). In three of these cases the cholangiogram still showed some residual narrowing of the CBD after stent extraction, but no signs of functional obstruction (easy passage of a 6.5 Fr catheter and rapid runoff of contrast were present). During the follow-up period, five patients (9 %) died of unrelated causes with a stent still in situ. On average, stent insertion was continued for a three year period in these patients. Therefore, endoscopic treatment was not considered successful. Furthermore, 29 patients (50 %), underwent additional treatment modalities because endoscopic stenting failed to resolve the stricture. Seventeen of these patients (29 %) underwent bypass surgery (hepatojejunostomy in 4 and choledochojejunostomy in 13 patients). In 12 patients (21 %), surgery was contraindicated or refused by the patient. A metal stent was inserted in 11 and one patient is still treated with repeated plastic endoprosthesis exchanges. Of the 22 patients that were successfully dilated, 18 (31 %) are still alive and none developed a recurrent stenosis after a median follow-up of 85 months.
Besides presence of acute peri-pancreatic inflammation no other predictors of successful outcome were identified with multivariate analyses (table 3). A sub-analysis of these 12 patients revealed a success rate of 92 % in this group, as opposed to only 24 % in the group without concomitant acute pancreatitis (Table 2).
For the group as a whole, a longer stent duration was not associated with a more successful outcome. To shed more light on the required duration of stenting of fibrotic strictures, we further analysed this subset of patients without signs of acute pancreatitis. As shown graphically (Figure 1), when stenting successfully resolved the stricture, this was almost always accomplished after three stent exchanges. Because stents were changed electively every three months, this covers a one year stenting period. As seen in figure 2, continued stent insertion beyond this time, almost never lead to additional stricture resolution.

**DISCUSSION**
Approximately 10 to 30 % of patients with chronic pancreatitis will develop a common bile duct obstruction during the course of their disease(1-4). Accepted indications for drainage are cholestasis, jaundice, and cholangitis. Besides symptomatic relief, prevention of secondary biliary cirrhosis is an important goal of treatment. Endoscopic stenting is often chosen as the initial treatment for biliary strictures in CP, in analogy with therapy for postoperative benign biliary strictures. In the latter case, results of endoscopic stenting are favourable and treatment success is reported
in the range of 43 to 83% (7, 8, 11). This study evaluates whether these positive results can indeed be extrapolated to strictures caused by CP. It encompasses the experience of a large endoscopic unit and is one of the largest series to date, with a median follow-up of 45 months. Although this study is retrospective, all follow-up data were obtained prospectively from multiple sources.

The main finding of this study was that a differentiation should be made between CBD stenoses due to compression by an oedematous inflamed pancreas and fibrotic strictures. In the first case, endoscopic treatment is highly successful because the obstruction is only temporal and resolves spontaneously when the inflammation subsides. On the other hand, in true fibrotic strictures, endoscopic treatment resulted in permanent dilation of only one out of four strictures. Furthermore, extending the duration of stent therapy beyond a one-year period, has no additional benefit in this latter group.

The lack of differentiation between fibrotic and non-fibrotic stenosis is probably the major explanation for the wide range of success rates reported earlier (from 10 to 95%) (10-17). Inclusion of diverse aetiologies of the biliary stenosis is probably another explanation. Vitale et al. for instance, also included strictures caused by stone disease (18).

According to our results, morbidity and mortality of endoscopic treatment of CBD strictures due to chronic pancreatitis is acceptable. Procedure related mortality rate was 2% in this study, which is in accordance with previous literature (10-17). Importantly, this death seemed related to the patient's co-morbidity and not to the procedure itself.

Plastic stent dysfunction remained a frequent long-term complication and occurred in almost half of the patients despite elective three monthly stent exchanges. In some small series these complications are described less frequently (11-13). However, the present data are in accordance with our own previously published data and the largest reported series by Farnbacher et al. (10, 15). Although cumbersome for patients, stent associated complications can usually be controlled safely by removal or exchange of the plastic prosthesis. Preliminary reports indicate that in a selected group of patients in whom plastic stent therapy failed and surgery is contraindicated, metal expandable stents show favourable results (19).

A possible way to improve the outcome of endoscopic stenting might be sequential insertion of multiple plastic stents (e.g. insertion of as many stents possible at the first ERCP and increasing the number at subsequent procedures). This follows the assumption that aggressive stenting with multiple stents results in stronger radial dilation forces leading to improved stricture resolution. In a small series of nine patients this approach was successful in 44% of patients (20, 21). Use of multiple stents may also lower the incidence of stent obstruction.

Given the disappointing results of endoscopic stent therapy in fibrotic strictures, it is questionable whether it should be considered an appropriate first-line therapy in CP. On the one hand, one may argue that it does prevent surgery in one quarter of
patients. On the other hand, it requires multiple invasive procedures, which in the end will not result in stricture resolution in the majority of cases. When patients are treated endoscopically, results should be evaluated after a one-year period. If the stricture has not resolved by this time, surgery should be considered. Furthermore, if other pancreatitis related complications require intervention (i.e. pancreatic duct stenosis), surgery might be considered at an even earlier stage, as in these cases successful therapeutic endoscopy is even less likely.
Table 1. Patient and drainage characteristics.

<table>
<thead>
<tr>
<th>Patients</th>
<th>All n = 58</th>
<th>Success n = 22 (38%)</th>
<th>Failure n = 36 (62%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median, years)</td>
<td>54 (19 - 85)</td>
<td>54 (19 - 85)</td>
<td>54 (32 - 76)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>44 (76%)</td>
<td>16 (73%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>14 (24%)</td>
<td>6 (27%)</td>
</tr>
<tr>
<td>Cause of pancreatitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>37 (64%)</td>
<td>9 (41%)</td>
<td>28 (78%)</td>
</tr>
<tr>
<td>Stone disease</td>
<td>1 (2%)</td>
<td>1 (3%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Divided pancreas</td>
<td>1 (2%)</td>
<td>1 (3%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>13 (22%)</td>
<td>10 (46%)</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (3%)</td>
<td>1 (5%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (7%)</td>
<td>2 (9%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Duration disease (median, months)</td>
<td>23 (0 - 176)</td>
<td>3 (0 - 109)</td>
<td>59 (1 - 176)</td>
</tr>
<tr>
<td>Concomitant acute pancreatitis</td>
<td>12 (21%)</td>
<td>11 (50%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Cholestasis</td>
<td>58 (100%)</td>
<td>22 (100%)</td>
<td>36 (100%)</td>
</tr>
<tr>
<td>Jaundice</td>
<td>26 (45%)</td>
<td>7 (32%)</td>
<td>19 (53%)</td>
</tr>
<tr>
<td>Sphincterotomy</td>
<td>25 (43%)</td>
<td>10 (45%)</td>
<td>15 (42%)</td>
</tr>
<tr>
<td>Pancreatic duct stenosis</td>
<td>18 (31%)</td>
<td>7 (32%)</td>
<td>11 (31%)</td>
</tr>
<tr>
<td>Number ERCP's (median)</td>
<td>3 (1 - 18)</td>
<td>2 (2 - 8)</td>
<td>3 (1 - 18)</td>
</tr>
<tr>
<td>Duration drainage (median, days)</td>
<td>274 (3 - 2706)</td>
<td>160 (66 - 2706)</td>
<td>320 (3 - 2623)</td>
</tr>
<tr>
<td>Number stent exchanges (median)</td>
<td>2 (0 - 17)</td>
<td>0 (0 - 6)</td>
<td>2 (0 - 17)</td>
</tr>
<tr>
<td>Maximum nr stents</td>
<td>53 (91%)</td>
<td>20 (91%)</td>
<td>33 (92%)</td>
</tr>
<tr>
<td>&gt;1</td>
<td>5 (9%)</td>
<td>2 (9%)</td>
<td>3 (8%)</td>
</tr>
</tbody>
</table>
Table 2. Treatment failures; subdivided in fibrotic strictures and strictures caused by periductal swelling due to concomitant acute pancreatitis (AP).

<table>
<thead>
<tr>
<th>Cause of treatment failure</th>
<th>All strictures (n=36, 62%)</th>
<th>Fibrotic strictures (n=35, 76%)</th>
<th>Strictures due to AP (n=1, 8%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Morbidity requiring surgery</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Death with stent in situ</td>
<td>5 (9%)</td>
<td>5 (11%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Insufficient stricture resolution</td>
<td>29 (50%)</td>
<td>28 (61%)</td>
<td>1 (8%)</td>
</tr>
</tbody>
</table>

Table 3. Multivariate analyses: prognostic factors of successful endoscopic drainage.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate p value</th>
<th>Univariate Odds ratio (95% CI)</th>
<th>Multivariate p value</th>
<th>Multivariate Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>0.66</td>
<td>0.8 (0.2 - 2.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt; 54 yr.</td>
<td>0.74</td>
<td>1.3 (0.4 - 3.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute pancreatitis</td>
<td>0.001</td>
<td>33 (4.0 - 333)</td>
<td>0.005</td>
<td>33 (2.9 - 333)</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>0.006</td>
<td>0.18 (0.05 - 0.63)</td>
<td>0.28</td>
<td>0.21 (0.01 - 3.3)</td>
</tr>
<tr>
<td>Sphincterotomy</td>
<td>1.0</td>
<td>0.9 (0.3 - 2.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jaundice</td>
<td>0.12</td>
<td>0.4 (0.1 - 1.3)</td>
<td>0.30</td>
<td>3.1 (0.4 - 25)</td>
</tr>
<tr>
<td>Drainage &lt; 274 days</td>
<td>0.21</td>
<td>2.0 (0.7 - 5.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Figure 1.** Number of stent exchanges in patients in whom biliary stenting resulted in successful resolution of fibrotic CBD stricture; n=11 (24%).

Patients

![Bar chart showing number of stent exchanges](chart1)

Number of stent exchanges (exchanges unknown: n = 1)

**Figure 2.** Number of stent exchanges in patients in whom biliary stenting failed to resolve fibrotic CBD stricture; n = 35 (76%).

Patients

![Bar chart showing number of stent exchanges](chart2)

Number of stent exchanges
REFERENCES


