Endoscopic biliary drainage
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A prospective randomized trial of teflon versus polyethylene stents for distal malignant biliary obstruction

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ABSTRACT

Background and Study Aims: Clogging of biliary stents continues to be a major clinical problem. Different polymer materials may have different effects on clogging. In vitro studies have shown a direct relation between the frictional coefficient of a polymer and the amount of encrusted material. Teflon appeared to be the best polymer for biliary stents. Two different types of stents made of Teflon have been tested in clinical practice and showed favourable patency rates. However, a randomized trial has never been performed. We compared the patency of an Amsterdam type polyethylene stent with a Teflon stent in a prospective randomized trial.

Patients and Methods: Between September 1995 and November 1996, 42 patients received a Teflon stent and 42 patients a polyethylene stent. All patients had a distal malignant biliary stricture without a previous drainage procedure. Diagnoses included carcinoma of the pancreas (n=76), papilla (n=1), bile duct (n=5) and metastases (n=2). The internal and external diameter (10 Fr), length (9cm) and stent design (a straight stent with two side flaps and one side hole at each end) were similar for both stents.

Results: A reduction in bilirubin of more than 20% within one week was seen in 91% of the patients. Early complication rates were similar in both groups (10%). The median follow-up was 142 days. Stent dysfunction occurred in 28 Teflon and 29 of polyethylene stents. The thirty-day mortality was 14% in both groups. Patient survival did not differ significantly between the groups (median survival: Teflon 165 days, polyethylene 140 days). The median stent patency was 83 days for Teflon and 80 days for polyethylene stents, and was not significantly different either.

Conclusion: Teflon material did not improve patency in biliary stents with an Amsterdam-type design.

INTRODUCTION

Clogging of biliary stents continues to be a significant problem in the treatment of malignant obstructive jaundice. The conventional Amsterdam type polyethylene stent becomes occluded after 3-6 months (1-5). Since the introduction of this stent in 1980 (6), it remains the routine stent used for endoscopic biliary drainage. Efforts to prolong stent patency by changing size or design or by altering bile composition have been unsatisfactory (7-12). Only the development of the self-expanding metal stent has proved to be effective in prolonging stent patency (3,5). However, the high costs of these stents and the fact that it is impossible to remove them are restricting factors encouraging the further improvement of plastic stents. The mechanism of stent clogging is multifactorial and includes binding of biliary proteins and adherence of bacteria to the inner wall of the stent (13,14). Different materials may have an effect on stent patency because of different surface smoothness. In vitro studies have shown that stents constructed of Teflon have a lower coefficient of friction than other plastics and therefore should be more able to prevent
stent blockage (7). In vivo studies showed that straight polyethylene stents with side holes accumulated significantly more sludge than stents of the same material without side holes (7).

Soehendra took advantage of these findings by developing the so-called Tannenbaum stent: a Teflon stent without side holes. In a non-randomized trial these stents showed a favourable patency rate compared with Teflon pigtail stents (11,15). It is not known which of the two factors, Teflon material or the absence of side holes, contributed most to a longer patency. Sung et al. showed in a randomized trial that polyethylene stents with and without side holes performed equally well (12).

We conducted a prospective randomized trial to compare the patency rate of stents of identical size (10 Fr, 9 cm) and design (Amsterdam type) but constructed of either polyethylene or Teflon in patients with unresectable distal malignant bile duct strictures.

PATIENTS AND METHODS

Criteria for Eligibility

Patients were included in the trial if they had distal biliary obstruction due to an unresectable malignancy without a previous drainage procedure. The diagnosis was based on the presenting symptoms, radiographic examinations, and endoscopic retrograde cholangiopancreatography (ERCP).

Treatment

Patients were referred from various hospitals in the Netherlands. A diagnostic ERCP was performed to assess the biliopancreatic anatomy. When a distal common bile duct stricture was seen and cannulation was successful, patients were randomly assigned to receive a polyethylene or a Teflon stent. Randomization was performed by computer generated random numbers in sealed envelopes.

Both types of stents were straight, 10 Fr, with two side flaps to prevent dislocation and one side hole at each end, with a total length of 9 cm. The material used for stent construction was polyethylene (PBN Medicals, Denmark) or Teflon (PBN Medicals, Denmark). Stents were inserted by standard techniques (16).

Follow-up and Definition of End Points

All patients were interviewed by telephone at monthly intervals until death or until the end of the follow-up period in February 1997. If they developed jaundice, cholangitis, or a flu-like syndrome and cholestasis, an ERCP was performed to confirm obstruction of the stent. An occluded stent was removed and replaced by a polyethylene stent or a self-expandable metal stent.

The duration of stent patency was calculated from the interval between the time of stent insertion and of its replacement or the presence of both jaundice and fever at the time of death. Drainage was considered successful if stent placement resulted in
a decline of bilirubin concentration greater than 20% of the pre-procedure value within one week after stent insertion. Complications of ERCP and sphincterotomy were assessed according to the criteria of Cotton (17).

Processing the Endoprostheses
Clogged endoprostheses were removed endoscopically and stored at -20 °C. To measure the dry weight of the encrusted material, the stent was cut and rinsed with 1 ml distilled water per cm stent. To remove all encrusted material, the stent parts were sonicated at 50-60 Mhz for 60 minutes. The stent parts were then removed and the remaining fluid lyophilized in preweighted vials. The protein content of the dried material was estimated as described by Lowry (18).

Scanning Electron Microscopy
Stent segments were fixed in gluteraldehyde, washed twice in phosphate buffer, dehydrated in ascending concentrations of ethanol, critical-point dried and sputter coated with about 15 nm of gold. The samples were examined in an ISI SS 40 scanning electron microscope at an accelerating voltage of 25 kV.

Statistical Analysis
Patient survival and stent patency in the two groups were analysed using the Kaplan-Meier method and compared using the Wilcoxon test. The Mann-Whitney U test was used for comparison of quantitative variables.

RESULTS
Enrollment and Exclusion of Patients
From September 1995 to November 1996, 97 consecutive patients were included in the study. Thirteen patients were later found not to comply with the entry criteria, because of selection for duodenopancreatectomy (n=11), a percutaneous transhepatic choledochal drainage (n=1), and refusal of treatment (n=1). The remaining 84 patients were followed until February 1997. Patient characteristics were comparable between the two groups (Table 1). Presenting symptoms included jaundice (82), abdominal pain (33), pruritus (38), fever (6) and weight loss (58). The median duration of jaundice before endoscopic intervention was two weeks (range 0-24). Ultrasonography was done in 79 patients (94%) and CT scan in five patients (6%) showing a pancreatic mass in 65 (77%) and dilatation of both the intrahepatic and extrahepatic ducts in 81 (96%).

Previous attempts to cannulate the bile duct in the referring hospital had failed once in 28 patients and twice in seven patients. We achieved bile duct cannulation during the first attempt in 78 patients and during the second attempt in the remaining six. Overall 43% (n=36) of the patients had a previous ERCP. Sixteen had had a previous sphincterotomy.
Cannulation of the common bile duct was achieved with standard techniques in 41 patients and after a precut papillotomy in 40 patients. Three patients had a stent placed through an intact papilla. The pancreatic duct was cannulated in 54 patients (64%). A stricture of both the pancreatic duct and the distal common bile duct (double-duct sign) was found in 46 patients (55%). Brush cytology was performed in 12 patients and evidence of malignancy was found in three. Forty-two patients received a polyethylene stent (PE) and 42 patients a Teflon stent (TE). Stent placement was successful in all patients.

Drainage
Biliary drainage was equally effective in both groups: 90% in the TE group and 92% in the PE group. The remaining seven patients had no decline of serum bilirubin concentration >20% of the pre-procedure value within one week after stent insertion. One patient died two days after stent placement from cardiac failure (PE) and one patient died three days after the procedure from severe cholangitis and septicemia (PE). One patient had a repeat ERCP and stent exchange and pus came out (TE). In the remaining four patients jaundice subsided slowly without intervention (TE 2, PE 2).

Early Complications and 30-Day Mortality
Procedure-related complications occurred in eight of the 84 patients (10%), four in the TE group and four in the PE group. Five patients had cholangitis (TE group two and PE group three), treated by antibiotics in four patients. The fifth patient died three days after the procedure because of progressive jaundice and septicemia. One patient developed pancreatitis and was treated conservatively (TE). Another patient bled and was given blood transfusions (TE). One patient had fever which improved after antibiotic treatment (PE). The 30-day mortality was 14% for both treatment groups.

Survival and Late Complications
The median follow-up after stent insertion was 142 days (range 2-476) (Table 2). No patients were lost to follow-up. Median survival was 165 days in the TE group and 140 days in the PE group (Figure 1). There was no significant difference between the groups (P=0.60).

Stent dysfunction occurred in 57 patients (68%). An ERCP was performed in 49 patients; the remaining eight were unfit for further treatment. The indications for re-ERCP were cholangitis (25) jaundice (12) and a flu-like syndrome and cholestasis (12). Median stent patency was 83 days in the TE group and 80 days in the PE group (Figure 2). There was no significant difference in patency rate between groups (P=0.93).
The overall mean number of ERCPs per patient was 1.8; there was no difference between the groups. Patients whose stents blocked received a polyethylene (n=42) or a self-expandable metal stent (n=7). Eventually, 13 patients were treated by insertion of a self-expandable metal stent.

**Quantitative Sludge Analysis**
Sludge from 26 stents was examined and protein concentration measured (TE 14, PE 12). The mean weight gain per unit length was 4.5 (SD 2.8) mg/cm for TE stents and 3.4 (SD 2.6) mg/cm for PE stents. The difference between the two groups was not significant (P=0.19). Mean protein concentration was 34.5% (SD 25.1) for TE stents and 23.5% (SD 16.8) for PE stents and was also not significantly different (P=0.29).

**Scanning Electron Microscopy**
Two occluded Amsterdam type Teflon stents were examined by scanning electron microscopy. The inner surface of both stents showed multiple shallow pits and ridges along the longitudinal axis (Figure 3). Bacteria and deposits of sludge were often seen on the ridges.

**Factors Influencing Stent Patency**
Prognostic factors influencing stent patency were evaluated by univariate analysis. The following variables were assessed: sex, age above 75 years, duration of jaundice longer than 14 days, bilirubin above 300 μmol/l, and previous failure of cannulation. Patients from both study groups were combined for the analysis. The variable associated with reduced duration of stent patency was a previous failure of cannulation (n=36, P=0.03). We identified three subgroups of previous failure of cannulation: patients in whom the papilla was not found (n=7; TE 1, PE 6), patients in whom contrast was introduced into the common bile duct without papilotomy (n=13; TE 6, PE 7), and patients who had had a previous papilotomy (n=16; TE 8, PE 8). These subgroups were compared with the group of patients who had not had a previous ERCP. Stent patency in patients in whom the papilla was not found was comparable with patients with no previous ERCP (P=0.79). Stent patency was significantly reduced in patients in whom contrast had been introduced into the common bile duct without papilotomy (P=0.004). A previous papilotomy was marginally associated with reduced stent patency (P=0.08) (Figure 4).

**DISCUSSION**
In this prospective randomized study we compared Amsterdam type biliary stents of two different materials, Teflon and polyethylene, and showed no difference in patency rate. Furthermore, the dry weight of encrusted material was not different between Teflon and polyethylene stents. This is in contrast to our earlier *in vitro* studies,
which showed less accumulation of biliary sludge in Teflon tubing than in polyethylene tubing (7). However, the presence of side holes confounded the difference between the stent materials.

Our findings differ from Soehendra's experience of the Teflon Tannenbaum stent (11,15). In a non-randomized study, these stents showed superior patency rates. They differ from the conventional Amsterdam type polyethylene stent not only in material, but also in stent design. Our findings that Teflon material does not improve the patency rate may reflect the fact that the absence of side holes is the most important cause of the presumed longer patency of the Tannenbaum stent. The absence of side holes has been studied in vitro and has shown to play a part in improving patency rate (7,8). However, Sung et al showed in a randomized trial that polyethylene stents with and without side holes perform equally well (12). This last study may be criticised because it was conducted in a heterogeneous patient population with various types of malignant bile duct obstruction including bifurcation strictures.

If side holes do not play an important part in determining stent patency in vivo we must ask why we did not see a difference in patency rate between Teflon and polyethylene stents. To address this question we studied the surface of Teflon stents by scanning electron microscopy and found multiple surface irregularities. The low frictional coefficient of Teflon material may well be nullified by the roughness of the stent surface which may create niches on which sludge can accumulate. Analysis of factors influencing stent patency showed a decreased stent patency in patients in whom cannulation had previously failed. This has not previously been described as unfavourable for stent patency. The high rate of previous failures of cannulation in our patient population offered us the possibility to study this factor. A significantly reduced stent patency was found in patients in whom contrast was injected into the common bile duct and no papillotomy was performed. This might be explained by the fact that during cannulation of the common bile duct bacteria were introduced. The infected biliary tract could not drain because of the distal stenosis. This may have resulted in early sludge formation and high numbers of bacteria which colonized the newly inserted stent. Interestingly, in patients with a previous papillotomy the reduction in duration of stent patency was not significant. Although the number of patients in this subgroup is too small to draw a firm conclusion, it suggests that a papillotomy ameliorates the biliary obstruction to some extent. Relatively high stent dysfunction and low patency rates were found in our study. This might be due to the large number of patients with previous failure of cannulation, which seems to be unfavourable for stent patency.

Our study has added firm data on the clinical outcome of biliary drainage, but has also increased the confusion about plastic stents. We found no beneficial effect of Teflon material for stent construction. Teflon stents without side holes showed superior patency rates and the presence of side holes may have more effect than the mate-
rial chosen for stent construction. Scanning electron microscopic examination of the inner surface of Amsterdam type Teflon stents showed multiple surface irregularities and we cannot exclude the possibility that the superior flow characteristics of Teflon material are nullified by these imperfections.
### Table 1. Patient characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Teflon stent</th>
<th>Polyethylene stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligible</td>
<td>42</td>
<td>42</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>23/19</td>
<td>18/24</td>
</tr>
<tr>
<td>Age* (years)</td>
<td>77 (47-88)</td>
<td>77 (54-97)</td>
</tr>
<tr>
<td>Cholecystectomy</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Billroth II</td>
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<td>2</td>
</tr>
<tr>
<td>Diabetes (recent onset)</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Serum bilirubin* (μmol/l)</td>
<td>154 (26-500)</td>
<td>216 (43-469)</td>
</tr>
<tr>
<td>Alkaline Phosphatase* (U/l)</td>
<td>484 (187-1200)</td>
<td>470 (85-2051)</td>
</tr>
<tr>
<td>ERCP in referring hospital</td>
<td></td>
<td></td>
</tr>
<tr>
<td>One attempt</td>
<td>10</td>
<td>18</td>
</tr>
<tr>
<td>Two attempts</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>ERCP Amsterdam</td>
<td></td>
<td></td>
</tr>
<tr>
<td>One attempt</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>Two attempts</td>
<td>3</td>
<td>3</td>
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<tr>
<td>Diagnosis</td>
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<td></td>
</tr>
<tr>
<td>Pancreas carcinoma</td>
<td>38</td>
<td>38</td>
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<td>Papillary carcinoma</td>
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<tr>
<td>Cholangiocarcinoma</td>
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<td>2</td>
</tr>
<tr>
<td>Metastatic</td>
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<td>2</td>
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* Values are median (range).
Table 2. Survival and late complications.

<table>
<thead>
<tr>
<th></th>
<th>Teflon stent (n=42)</th>
<th>Polyethylene stent (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up, days*</td>
<td>148</td>
<td>134</td>
</tr>
<tr>
<td>Survival, days*</td>
<td>165 (2-476)</td>
<td>140 (3-373)</td>
</tr>
<tr>
<td></td>
<td>[93,208]</td>
<td>[87,191]</td>
</tr>
<tr>
<td>Stent dysfunction</td>
<td>28</td>
<td>29</td>
</tr>
<tr>
<td>ERCP performed</td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td>No ERCP performed</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Stent patency, days*</td>
<td>83 (4-223)</td>
<td>80 (3-257)</td>
</tr>
<tr>
<td></td>
<td>[37,144]</td>
<td>[54,121]</td>
</tr>
<tr>
<td>Number of ERCP’s</td>
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<tr>
<td>1</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>17</td>
<td>19</td>
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<td>5</td>
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<tr>
<td>Total number of ERCP’s</td>
<td>79</td>
<td>75</td>
</tr>
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</table>

* Values are median (range), [95% confidence interval].
**Figure 1.** Overall survival of patients (n=84), P=0.60.

**Figure 2.** Cumulative patency of stents (n=84), P=0.93.
Figure 3. Scanning electron micrograph of the inner surface of an Amsterdam type Teflon stent showing multiple shallow pits and ridges along the longitudinal axis (magnification 442 x).
Figure 4. Relationship between patency of stents and previous failure of cannulation.
REFERENCES