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Lack of complications following short-term stent therapy for extrahepatic bile duct strictures in primary sclerosing cholangitis

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Background: **In 10% to 20% of patients with primary sclerosing cholangitis, a dominant stricture of an extrahepatic bile duct is responsible for symptoms and an exacerbation of cholestasis. The complications of a dominant stricture can usually be relieved by endoscopic placement of a stent through the stricture. The conventional policy of leaving stents in situ for 2 to 3 months is associated with a high incidence (e.g., 50%) of clinical deterioration due to stent occlusion. We have attempted to overcome this problem by substantially reducing the duration of stent placement.**
Methods: **Sixteen patients with symptomatic primary sclerosing cholangitis and dominant extrahepatic bile duct strictures were treated by stent placement for a median interval of only 9 days.**
Results: **In all patients endoscopic stent therapy was technically successful with a 7% incidence of transient procedure-related complications. During median follow-up of 19 months (range 7 to 27 months) serum biochemical evidence of cholestasis decreased substantially and 13 (81%) of the 16 patients became asymptomatic. No patient had a recurrence or exacerbation of either symptoms or biochemical evidence of cholestasis that could be attributed to stent occlusion.**
Conclusions: **Short-term endoscopic stent therapy is a safe and effective treatment for symptomatic dominant extrahepatic bile duct strictures in patients with primary sclerosing cholangitis. (Gastrointest Endosc 1997;46: 344-7.)**

Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease of unknown cause characterized by patchy fibroproliferative inflammation of the intrahepatic and extrahepatic bile ducts. Disease progression leads to secondary biliary cirrhosis and sometimes cholangiocarcinoma.[1] In 10% to 20% of patients a dominant stricture of an extrahepatic bile duct develops and is responsible for the precipitation or an exacerbation of symptoms and an increase in cholestasis.[2, 3] Surgery for this complication is associated with substantial morbidity and mortality and may increase the technical difficulty and risk of possible future liver transplantation.[4] Percutaneous trans-hepatic dilation and stenting of dominant strictures have been reported in small numbers of patients with PSC.[2, 5] However, this approach carries a substantial risk of infection and is technically difficult because the intrahepatic bile ducts are usually not dilated.

Current endoscopic therapy consists of sphincterotomy, graduated catheter or balloon dilation, placement of endoprostheses, and/or nasobiliary catheter drainage.[6-8] These endoscopic treatment modalities are often used in combination and are all aimed at relieving the large bile duct obstruction.

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In a recent retrospective study we evaluated the results of endoscopic stent therapy for symptomatic dominant extrahepatic bile duct strictures in patients with PSC. The median period of stent therapy was 3 months and although our policy was to remove or exchange stents electively after 2 to 3 months, nonelective indications for this procedure were jaundice and/or cholangitis attributable to stent occlusion in 50% of instances.[8] The optimal time to leave stents in situ to achieve adequate stricture dilation with minimal complications due to stent occlusion is unknown. We have tested the hypothesis that short-term (1 week) stent intervention might not only be efficacious in relieving the consequences of dominant strictures but also avoid the complications of stent occlusion.

PATIENTS AND METHODS

From January 1994 until October 1995, 16 patients with PSC (8 men and 8 women) were selected for short-term stent therapy because of clinical and serum biochemical findings putatively related to dominant extrahepatic bile duct strictures. The patients studied had not previously been treated with endoscopic therapy. Their median age was 43 years (range 17 to 69 years). One patient had clinical signs compatible with cirrhosis at the time of stent therapy. Associated inflammatory bowel disease was present in 10 (63%) of the 16 patients for a median of 9 years (range 0 to 16 years). Twelve patients complained of fatigue, 10 complained of pruritus, 7 had right upper quadrant pain, 5 were jaundiced, and fever was present in 2 of the 16 patients.

The diagnosis of PSC was established by peroperative cholangiography after cholecystectomy in 2 patients and by ERCP in 3 patients, with a median interval of 37 months (range 5 to 108 months) before stenting. At that time a dominant extrahepatic bile duct stricture was already present in 4 of these patients. In the remaining 11 patients, the diagnosis of PSC was made by ERCP at presentation for stent therapy. Dominant extrahepatic bile duct strictures were defined as proximal, mid, or distal, when located in the main hepatic ducts, common hepatic duct, or common bile duct, respectively.

Six patients had been treated with ursodeoxycholic acid (UDCA) for a median interval of 36 months (range 5 to 60 months) before stenting, and in another 5 patients UDCA was started within 2 months of stent therapy. In these 11 patients UDCA was continued during follow-up after stenting.

Patients received antibiotics (intravenous gentamycin 2 mg/kg b.i.d. and amoxycillin 1 g q.i.d.) before and for 24 hours after each ERCP procedure. A brush cytology specimen (GCB-200-3-3.5, Wilson-Cook, Winston-Salem, N.C.) of the stricture was obtained before stent insertion.

Endoscopic treatment consisted of placement of a 10F endoprosthesis (straight polyethylene Amsterdam type) through the dominant stricture and leaving it in situ for 1 week. If necessary, pre-cut sphincterotomy was performed to achieve deep cannulation of the bile ducts or to facilitate stent placement. If a stricture was very tight, placement of a 10F stent was preceded by dilation with wire-guided dilator catheters (Soehendra) or balloons (Rigiflex), short-term placement of a nasobiliary drain, and/or placement of a 7F stent for 1 week. Stents (7F and/or 10F) were inserted over a guidewire using a video duodenoscope (Olympus TJF100, Olympus, Hamburg, Germany) with a 4.2 mm instrumentation channel. Adverse events occurring within 30 days of each ERCP were considered procedure-related complications and were graded according to established criteria.[9]

During follow-up, patients were seen every 2 months on an outpatient basis for assessment of clinical status and serum biochemical liver tests. Mean values for serum biochemical liver tests and prevalence of symptoms before stent placement and at the last clinic visit were compared using the Wilcoxon matched-pairs signed-ranks test and the Sign test, respectively. The mean improvements of serum biochemical liver tests after stent therapy were compared between patients either receiving or not receiving UDCA therapy using the two-tailed t test for independent samples. P values < 0.05 generated by the two-tailed test were considered significant. Statistical analysis was performed using the SPSS statistical software package (SPSS Inc., USA).

RESULTS

A total of 42 ERCPs were performed for short-term (median 9 days) stent therapy in 16 patients. All patients received antibiotics (intravenous gentamycin 2 mg/kg b.i.d. and amoxycillin 1 g q.i.d.) before and for 24 hours after each ERCP procedure and 6 patients also received antibiotics (oral ciprofloxacin 500 mg b.i.d.) for the total period of stent placement. Median follow-up after stent removal was 19 months (range 7 to 27 months). Stent occlusion did not occur.

Locations of dominant extrahepatic bile duct strictures were distal in 8, mid in 2, proximal in 1, and both proximal and distal in 5 patients. Brush cytology, performed in 14 of the 16 patients, did not reveal evidence of malignancy. Pre-cut sphincterotomy had to be performed to achieve deep cannulation of the bile ducts in 4 patients and to facilitate stent placement in 3 patients; all of these 7 patients had distal strictures. Furthermore, to facilitate stent placement, predilation of the stricture was performed with wire-guided dilator catheters in 5 patients (with balloon dilation in 1) and with placement of a nasobiliary drain for a median of 4 days (range 1 to 4 days) in 3 patients; in 5 patients placement of a 10F stent was preceded by placement of a 7F stent for a median of 7 days (range 3 to 15 days). Fourteen patients were treated with placement of a 10F stent through the dominant stricture(s) for a median interval of 7 days (range 6 to 9

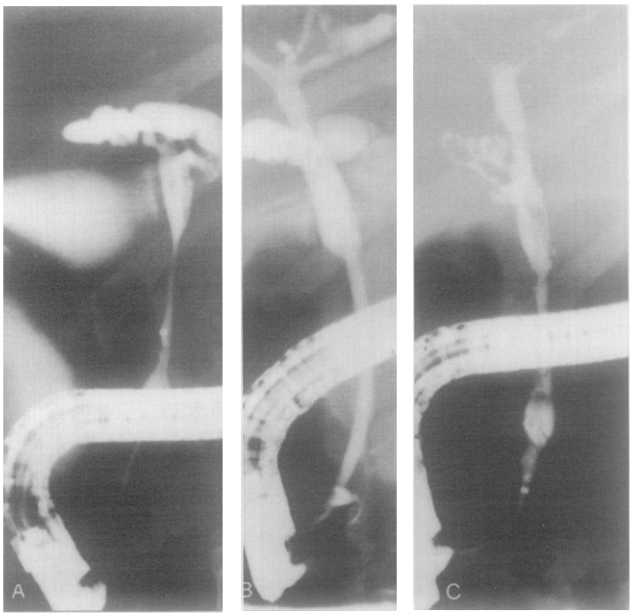

Figure 1. A, Cholangiogram of a patient with PSC showing a dominant stricture in the common bile duct. **B,** A 10F biliary endoprosthesis is inserted through the stricture. **C,** After removal of the endoprosthesis 1 week later a clear dilation of the stricture is apparent.

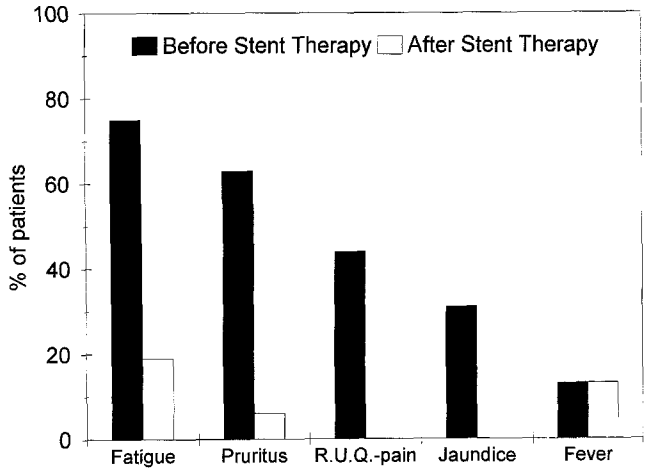

Figure 2. Comparison of the prevalence of fatigue (p = 0.0039), pruritus (p = 0.0039), right upper quadrant pain (p = 0.0156), jaundice (p = 0.0625), and fever (p =1) in 16 patients with PSC before and during follow-up after short-term endoscopic stent therapy.

days) (Fig. 1) and 2 patients were treated with a 7F stent only, 1 for 7 days and the other for 13 days. The median period of (7F and/or 10F) stent placement in all patients was 9 days (range 7 to 23 days). After stent therapy, 13 (81%) of the 16 patients became asymptomatic and remained so throughout follow-up (Fig. 2). Comparison of the mean serum

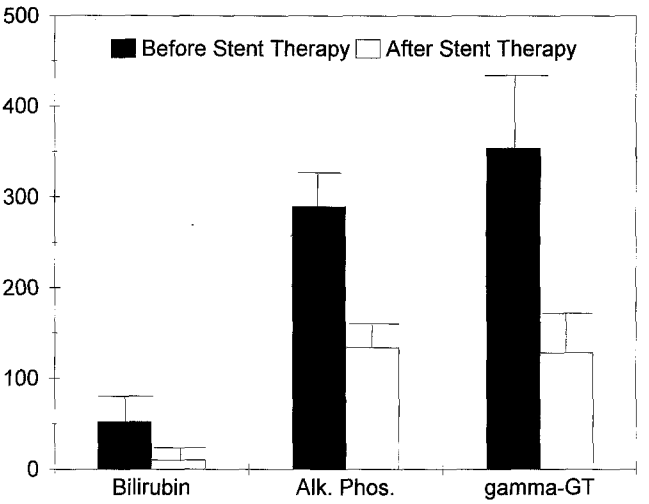

Figure 3. During follow-up after short-term endoscopic stent therapy in 16 patients with PSC, significant decreases in serum levels of total bilirubin (p = 0.0004) (μmol/L), alkaline phosphatase (p = 0.0005) (U/L), and gamma-glutamyltransferase (p = 0.0011) (U/L) occurred (serum biochemical liver tests are expressed as mean values; error bars represent standard error of the mean).

levels of total bilirubin, alkaline phosphatase, and gamma-glutamyltransferase before stenting to corresponding values at the last clinic visit showed significant decreases of these serum biochemical liver tests in all patients (Fig. 3). There were no significant differences in the mean improvement of serum biochemical liver tests after stent therapy between patients either receiving or not receiving UDCA therapy (Fig. 4). All 3 patients with recurrent or persisting symptoms after stent therapy were receiving UDCA treatment.

There were three (7%) procedure-related complications. Two patients had a small perforation at the stricture site (graded as a mild complication) and one patient developed moderately severe pancreatitis.[9] No sphincterotomy had been performed in these patients.

DISCUSSION

Because our prospective study was uncontrolled, it is not possible to conclude that short-term stent therapy is unequivocally beneficial for symptomatic dominant extrahepatic bile duct strictures in patients with PSC. However, the results obtained in this study are striking and gratifying. Endoscopic stent therapy for a median period of 9 days was technically successful in all patients. During median follow-up of 19 months (range 7 to 27 months) after stent removal, 13 (81%) of 16 patients became asymptomatic with substantial decreases of serum

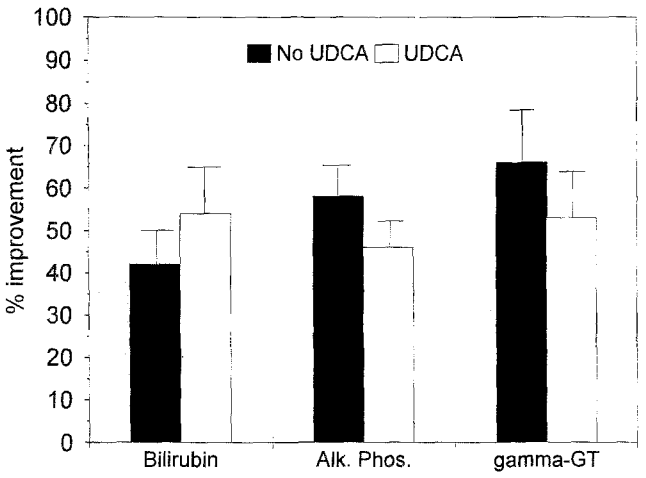

Figure 4. During follow-up after short-term endoscopic stent therapy, there were no significant differences in the percentage of improvement of serum levels of total bilirubin ($p = 0.5$) (μmol/L), alkaline phosphatase ($p = 0.2$) (U/L), and gamma-glutamyltransferase ($p = 0.4$) (U/L) between patients either receiving or not receiving UDCA treatment (percentages of improvement of serum biochemical liver tests are expressed as mean values; error bars represent standard error of the mean).

biochemical indexes of cholestasis. Stent occlusion did not occur. These results are clearly superior to those obtained in a recent retrospective study by our group on the efficacy of stent therapy for symptomatic dominant strictures in PSC.[8] That retrospective study found that stent therapy for a median duration of 3 months (range 0.5 to 34 months) was associated with complete resolution of symptoms and significant decreases of serum biochemical indexes of cholestasis in 12 (57%) of 21 patients; although stents were electively exchanged or removed after 2 to 3 months, complications due to stent occlusion were the indication for this procedure in 50% of instances. Comparison of the data obtained in the two studies suggests that superior clinical outcomes can be achieved by stenting for a median period of 9 days rather than 3 months. It appears that stent therapy of short duration can be efficacious in treating the consequences of dominant strictures while avoiding the complications of stent occlusion. Furthermore, the procedure-related complication rate (7%) in the current study was lower than that recorded in previous studies of endoscopic therapy in PSC (14% to 15%).[7, 8]

To avoid complications of stent occlusion, balloon dilation without subsequent stenting may be an alternative for short-term stent therapy. However, multiple sessions of endoscopic balloon dilation are often required to achieve sustained stricture dilation.[6, 10]

UDCA therapy has been reported to be associated with improvements in abnormal serum biochemical liver tests and periportal inflammation in the liver in patients with PSC.[11, 12] However, in our study there were no significant differences in the improvement of serum biochemical liver tests after stent therapy between patients either receiving or not receiving UDCA treatment. We conclude that short-term endoscopic stent therapy is a safe and effective treatment for symptomatic dominant extrahepatic bile duct strictures in patients with PSC. The short duration of stent placement appears to prevent complications due to stent occlusion that commonly occur when stents remain in place for longer periods.

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