Endoscopic management of post-laparoscopic cholecystectomy biliary strictures
Long-term outcome in a multicenter study

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SUMMARY
Objectives — The aim of this retrospective study was to assess the long term results of long-lasting endoscopic stenting for benign biliary strictures related to laparoscopic cholecystectomy. Additional biological and morphological data were collected from these patients during follow-up.

Methods — Patients undergoing ERCP for post-laparoscopic cholecystectomy biliary stricture in one of the three participating centers between 1990 and December 2001 were identified. Only patients with successful endoscopic stenting were subsequently included and analyzed. Follow-up data were obtained from referring centers, general practitioners and patients or relatives. Hepatic blood tests and abdominal ultrasound were proposed to all the patients who had not undergone further treatments after stent removal.

Results — Eight-eight patients had undergone ERCP for benign biliary stricture related to laparoscopic cholecystectomy. Stenting failed in 19 patients. Balloon dilatation alone was used in four patients. Strictures were successfully stented in 65 patients. The mean number of stents inserted at the same time was 1.6. The mean duration of stenting was 14 months (range 1-120 months). Eighteen patients (28%) developed biliary or pancreatic symptoms during stenting. ERCP was considered satisfactory at the end of stenting (i.e. no remaining stricture or minor remaining change on ERCP) in 45 patients (69%). Twenty-two patients were lost to follow-up. Twenty-nine out of forty-three patients (67%) remained symptom-free with normal updated blood tests and abdominal ultrasound during a mean follow-up of 28 months (range 12-117 months) after stent removal. None of the patients with a normal ERCP at the end of stenting developed stricture recurrence during follow-up. Eleven patients were operated (8 with persistence of stricture, 2 for stricture recurrence up to 63 months after stent removal, 1 for pancreatitis).

Conclusion — Based on clinical, morphological and biological criteria, a long-term success was obtained in 70% of patients with post-laparoscopic cholecystectomy benign biliary strictures, after several months of endoscopic stenting.

RÉSUMÉ
Traitement endoscopique des sténoses biliaires bénignes après cholecystectomie laparoscopique : résultats à long terme d’une étude multicentrique
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Objectifs — Le but de cette étude rétrospective était d’évaluer les résultats à long terme du calibrage de longue durée des sténoses biliaires post-cholecystectomie par prothèse mise en place par voie endoscopique. Nous avons de plus recherché des données biologiques et morphologiques actuelles de ces malades.

Méthodes — Les malades ayant eu une cholangiographie rétrograde pour strénose biliaire post-cholecystectomie dans l’un des 3 centres entre 1990 et décembre 2001 ont été identifiés. Seuls les malades traités avec succès par endoprothèse ont ensuite été analysés. Les données du suivi ont été obtenues auprès des correspondants, des médecins traitants et des familles. La réalisation d’une échographie abdominale et de tests hépatiques a été proposée à tous les malades qui n’avaient pas eu d’autre traitement au cours du suivi.

Résultats — Quatre-vingt-huit malades ont eu une cholangiographie rétrograde pour strénose biliaire post-cholecystectomie. L’insertion d’une prothèse a échoué chez dix-neuf malades ; quatre malades ont eu une dilatation endoscopique seule. Soixante-cinq malades ont été traités par la mise en place d’une prothèse. Le nombre moyen de prothèses par séance était de 1,6. La durée moyenne du traitement endoscopique était de quatorze mois (extrêmes : 1 à 120 mois). Dix-huit malades (28%) ont eu des manifestations biliariennes ou pancréatiques au cours du traitement. Le calibrage était jugé satisfaisant à la fin du traitement endoscopique (c’est-à-dire absence de sténose résiduelle ou anomalie résiduelle minime) chez quarante-cinq malades (69%). Vingt-deux malades ont été perdus de vue. Vingt-neuf malades sur quarante-trois (67%) sont restés asymptomatiques avec un bilan hépatique et une échographie normaux avec un suivi de 28 mois après l’ablation de prothèse (extrêmes : 12 à 117 mois). Aucun malade ayant une voie biliaire principale normale à la fin du traitement endoscopique n’a récidivé. Onze malades ont été opérés (8 sténoses persistantes, 2 récidives de sténose à 63 mois du traitement endoscopique et 1 pancréatite).

Conclusion — Un succès défini sur une base clinique, biologique et morphologique pouvait être obtenu après un calibrage de plusieurs mois dans près de 70% des cas de sténose biliaire bénigne post-cholecystectomie.

Introduction
Laparoscopic cholecystectomy has become the treatment of choice for symptomatic gallstones. Widely used for more than ten years, the most significant complication is operator-dependent injury to the biliary tree. The proportion of patients who develop cholecystectomy-related benign biliary stenosis has varied from 0.2 to 0.5% after open procedures to 0 to 2.7% after laparoscopic procedures. Direct injury is involved in 95% of the biliary strictures developing after surgical treatment [1-3]. The injury can involve partial or total section or clipping or ligation of the duct, generally the common duct. Strictures can also result from ischemia by devascularization or from thermal...
trauma [1, 2, 4]. Sometimes associated with loss of tissue from the extrahepatic ductal walls, these post-cholecystectomy strictures are prone to fistulization. The biliary injury may be recognized intraoperatively or become apparent postoperatively. The most frequent symptoms are jaundice, fever, and abdominal pain. Late symptoms include cholestasis, recurrent cholangitis, ductal stones, or secondary biliary cirrhosis.

Reconstructive surgery is usually undertaken for the treatment of postoperative biliary strictures, usually with a hepaticojejunostomy [6-8].

More recently, endoscopic management has been proposed for benign strictures. The endoscopic method consists in balloon dilatation associated or not with insertion of one or more stents to calibrate the zone of stricture [9-11]. Most of the published studies on endoscopic treatment have included small numbers of patients with short- or mid-term follow-up. The long-term efficacy of stenting remains to be described in detail although certain authors have reported very encouraging results obtained in referral centers. Certain authors recommend a one-year stenting protocol, changing stents every three months [11-21].

The purpose of this work was to evaluate the long-term effects of endoscopic stenting for post-laparoscopic cholecystectomy benign biliary stenosis in three referral centers in the Paris area. In addition to a retrospective analysis of outcome, we recorded biological and morphological data in patients whose biliary stricture was managed exclusively by endoscopic means.

Patients and methods

Inclusion criteria

Patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) for post-laparoscopic cholecystectomy benign biliary stricture were included in this retrospective analysis. The inclusion period ran from 1990 through December 2001 in order to have a follow-up period of at least twelve months after surgical treatment.

Exclusion criteria

Presence of malignant stricture, post-sphincterectomy stricture, simple biliary leakage without stenosis, Mirizzi syndrome, stenosis of a biliary digestive anastomosis, extrinsic compression secondary to calcifying pancreatitis, primary sclerosing cholangitis, bile duct stone, and post-transplantation stricture were exclusion criteria. Patients whose stent was inserted percutaneously were also excluded from the analysis.

Definitions of successful and unsuccessful treatment

Successful endoscopic treatment was defined as the absence of radiologically detectable stenosis in a symptom-free patient with normal or nearly normal liver tests (gamma-glutamyl-transpeptidase and/or alkaline phosphatase less than twice the upper limit of normal [ULN]). Persistence of an abnormal duct caliber on the ERCP was not considered a failure if normal drainage of the intrahepatic ducts was visualized.

Long-term success was defined as the absence of biliary symptoms in a patient with a normal abdominal ultrasound and normal or nearly normal liver tests (gamma-glutamyl-transpeptidase and/or alkaline phosphatase less than twice ULN) at last follow-up.

Therapeutic failure was defined as the presence of altered hepatic function (cholestasis > 2 ULN) or the presence of biliary symptoms requiring surgical revision.

Data collection

Data were collected in three phases:

1. at stent insertion
2. during long-standing stenting for duct dilatation
3. after stent removal.

Data on stent insertion, replacement and removal were collected from the ERCP reports in the patient’s medical files.

Follow-up data after stent removal were collected from several sources:

1. phone interview with the primary care physician to collect data on medical problems, especially biliary problems, occurring after stent removal,
2. questionnaires mailed to patients to collect data on biliary complications occurring late after treatment,
3. liver tests and abdominal scan, proposed (with consent of the primary care physician) with the questionnaire. Patients who did not respond were contacted by phone. In the event of death, phone contact was made with the family or the primary care physician to ascertain the cause of death and the medical history following stent removal. The operative report was requested for patients who had undergone a secondary surgical procedure.

Statistical analysis

Stata version 7 was used for the statistical analysis. Qualitative variables were compared with the chi-square test, percentages with the exact Fisher test. The non-parametric Kruskal-Wallis test was used for small sample sizes (N < 30). Cox logistic regression was used for multivariate analysis to search for factors predictive of success or failure of endoscopic management. P < 0.05 was considered statistically significant. The following variables were evaluated: age, gender, time between surgery and ERCP diagnosis of biliary stenosis, location of the stenosis, presence or not of fistulae, number of simultaneous stents.

Results

During the study period, 99 patients underwent ERCP in one of the three participating centers for possible post-operative benign biliary stricture. Post-liver transplantation stenosis was diagnosed in 11 patients who were excluded from the analysis. Laparoscopic cholecystectomy had been undertaken initially in all 88 patients retained for analysis (38 men and 50 women, mean age 64.1 ± 7 years, age range 27-97 years). The procedure was completed laparoscopically in 32 (36%), and converted to open surgery in 50 (57%) and hepatectomy in 6 (7%).

Repair by ductoductal anastomosis on a T-tube had been attempted in 37 of the 50 conversion patients (42% of study population) before referral for ERCP.

Signs of biliary stricture had appeared on average 101 weeks after the cholecystectomy (range 0-1768 weeks). Twenty-seven patients (31%) presented cholestasis without jaundice. Thirty-two patients (36%) had jaundice, 21 (24%) cholangitis, and 8 (9%) an external leakage. ERCP was performed on average 112 weeks (range 0-1768 weeks) after cholecystectomy. ERCP enabled identification of the stricture, its localization and the presence or not of a fistula or of tissue loss. The caliber of the stenotic zone was tested with the guidewire to determine whether a stent could be inserted. The stricture was total in 20 patients (23%) and partial in 68 (77%). Twenty-five patients had a fistula (28%). The localization of the stenotic zone is detailed in table I. Loss of biliary tissue was detected in five patients (6%); no unusual anatomic variant was detected.

Feasibility of endoscopic management (figure 1)

Endoscopic failure in 19 patients (22%). Surgical repair (hepaticojejunostomy or ileal Y-loop anastomosis) was performed in these patients who were removed from the analysis.

Endoscopic treatment was thus performed in 69 of the 88 patients: 78% feasibility. Balloon dilatation was performed alone in four patients (6%) who were excluded from the long-term outcome analysis (two had already been excluded due to ERCP failure).

Causes of ERCP failure were:

— ligation, clipping or total section of the common duct leading to complete obstruction (no upstream opacification), (N = 15 patients),
— erroneous guidewire trajectory, \( N = 1 \) patient,
— obstructive lithiasis associated with ductal stricture and failure of endoscopic extraction, \( N = 1 \) patient,
— exclusive passage of guidewire into a large fistula associated with the stricture, \( N = 1 \) patient,
— unsuccessful passage through a well defined stenotic zone, \( N = 1 \) patient.

**Modalities of endoscopic treatment** (table II)

A biliary stent was inserted in 65 patients (94%): treatment was exclusively endoscopic in 53 of them (82%) and associated with fluoroscopy-guided percutaneous treatment in 12 (18%). Stenting was performed with dilatation in 55 patients (85%) and without in 10 (15%). On average, 1.6 stents were inserted per ERCP session (range 1-4).

On average, stents were changed 3.4 ± 2.8 times during the endoscopic treatment (1-15 ERCP procedures per patient). Mean duration of the endoscopic treatment was 14 ± 12.5 months (range 1-120 months).

**Short-term outcome** (figure 1)

Early complications were observed in 18 patients (28%): stent migration in 8 patients, acute pancreatitis in 7, digestive perforation in one, bleeding in one, and cholangitis in one. All of these complications resolved with medical treatment with no mortality. Ten patients (15.5%) were lost to follow-up during the course of treatment. Short-term outcome was thus evaluated in 55 patients. At the end of the endoscopic treatment, the common bile duct was considered normal in 27 patients. A slightly abnormal morphology of the common duct persisted in 18 patients with no impact on bile drainage. Overt stricture persisted in 10 patients (15.5%). Thus, at the end of the endoscopic treatment, outcome was thus considered satisfactory in 45 patients.

**Long-term outcome** (figure 2)

Among the 10 patients with persistent stricture, eight underwent surgery, one was lost to follow-up, and one did not undergo surgery despite altered liver function.

Among the 45 patients with a partially or totally satisfactory ductal morphology at stent removal, five were lost to follow-up and six died from an unrelated cause: colonic cancer \( (N = 2) \), gastric cancer \( (N = 1) \), cardiovascular disease \( (N = 1) \), unknown cause \( (N = 2) \). Complementary explorations (abdominal ultrasound and liver tests) were performed in 31 patients who were followed on average 28 ± 15 months (range 12-117 months) after the end of the endoscopic treatment. The abdominal ultrasound and liver tests were normal in 29/31 patients. Thus among 49 patients followed on average 28 months or until death, the long-term outcome after endoscopic treatment was successful in 35 (72%) and unsuccessful in 14 (28%).

**Surgical revision** (table III)

Besides the eight patients who underwent surgery because of persistent stenosis, three other patients had revision surgery despite the partial success of the ERCP. These patients were the two with recurrent biliary stricture and a third one whose revision procedure was an empiric precautionary decision. The rate of recurrent stricture after successful ERCP was thus 4.5% \( (2/45 \text{ patients}) \). The revision procedure was performed on average 23 months after the end of stenting in 11/12 patients (immediately after ERCP in one). For the two patients who developed recurrent strictures, surgical treatment was performed on average 63 months after the end of stenting. The first patient only presented a minimal lateral defect on the left aspect of the common duct but developed cholangitis. The second pre-
sent ductal dilatation upstream from a zone of moderate stenosis.

Factors predictive of success

There was no significant difference in the success rate regarding the three participating centers, patient age or gender, localization of the stricture, presence or not of a fistula, and time between cholecystectomy and ERCP. The probability of success was not affected by the number of stents used or the duration of the stenting or follow-up. At multivariate analysis, the only factor significantly associated with long-term success was a normal morphological aspect of the common bile duct at the end of the endoscopic treatment.

Discussion

In this series, endoscopic management of post-operative biliary stricture was feasible in 78% of patients. Defined morphologically, successful treatment could be achieved in about 70% of patients after several months of stenting. The risk of recurrence later was low. The factor best predicting long-term success was a normal cholangiogram at the end of the endoscopic treatment.

Surgery has been the mainstay treatment for traumatic injury of the bile ducts. In experienced hands, surgery can provide good long-term outcome, but morbidity is about 25% and mortality 4-13% [4, 22-25]. Long-term success ranges from 70-91%. Nevertheless, 12-45% of patients develop recurrent stricture of the biliobiliary anastomosis leading to necessary revision in 18 to 35% of patients [22-26]. In one study, restenosis was observed in 18% of patients after primary repair of the biliary tree and in 26% after secondary repair [7].

Other options have been proposed. Besides interesting results obtained with percutaneous techniques [27], endoscopic management is preferred by many teams because it provides a non-invasive solution to an iatrogenic problem. There were 65 stented patients in the present series, one of the largest in the literature. The failure rate was 22%, comparable with the series reported by Bergmann et al. [17] but better than the series reported by Costamagna et al [15]. The complication rate during stenting was 28%. This information is rarely mentioned. Stent migration is the most frequent complication during treatment. Only one patient in our series developed cholangitis after stent obstruction. The initial success rate (normal cholangiography or minimal change in the morphology of the common duct) was 69% in our series. This is somewhat lower than in earlier reports [13, 15, 17] but ten patients were lost to follow-up at the end of the endoscopic treatment. The duration of stenting (14 months on average) and the failure rate (33%) were comparable with data in the literature [15, 17].

The prospective follow-up of our patients enabled collection of original data on liver function and biliary morphology. For 45 patients with a mean follow-up of 28 months, the long-term success rate was 67%. Only two patients (4%) developed secondary biliary stricture more than five years after treatment.
long-term success was the nearly normal morphology of the common biliary duct after endoscopic treatment. Larger series would be needed to demonstrate the impact of morphological criteria on prognosis and to search for factors related to the endoscopic technique.

In conclusion, successful endoscopic management of postlaparoscopic cholecystectomy biliary stricture, defined clinically, biologically and morphologically, can be achieved in nearly 70% of patients after several months of stenting. This success rate compares honorably with that obtained after surgical repair, warranting a first-intention attempt with ERCP before resorting to surgery. However, because of the lack of a factor predictive of long-term outcome which can be identified before making the therapeutic choice, and the uncertainty concerning the outcome of surgical repair after failure of endoscopic treatment, opting for one or other method should be a collegial decision.

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REFERENCES


