Title:
Usefulness of fully covered self-expandable biliary metal stents for the treatment of post-sphincterotomy ERCP bleeding

Authors:
Andres Conthe, Óscar Nogales, Carlos Martínez Flores, Javier García Lledó, Laura Rayón, Leticia Pérez Carazo, Seila García Mulas, María López Ibáñez, Javier Aranda Hernández, Beatriz Merino

DOI: 10.17235/reed.2019.6393/2019
Link: PubMed (Epub ahead of print)

Please cite this article as:

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.
OR 6393

Usefulness of fully covered self-expandable biliary metal stents for the treatment of post-sphincterotomy ERCP bleeding

Andrés Conthe, Óscar Nogales, Carlos Martínez-Flores, Javier García-Lledó, Laura Rayón, Leticia Pérez-Carazo, Seila García-Mulas, María López-Ibáñez, Javier Aranda-Hernández and Beatriz Merino

Department of Gastroenterology. Hospital General Universitario Gregorio Marañón. Madrid, Spain

Received: 31/5/2019
Accepted: 20/07/2019
Correspondence: Andrés Conthe. Department of Gastroenterology. Hospital General Universitario Gregorio Marañón. C/ Doctor Esquerdo, 46. 28007 Madrid, Spain
e-mail: andres.conthe@salud.madrid.org

ABSTRACT

Background: post-sphincterotomy endoscopic retrograde cholangiopancreatography (ERCP) bleeding is an adverse event with an estimated incidence rate of 1.34%. There is no established consensus about how to treat this particular type of gastrointestinal bleed. Placement of fully covered self-expandable biliary metal stents (FCSEBMS) has been evaluated as an alternative treatment with positive outcomes and a low complication rate.

Aim: to report the results of a cohort of patients with post-sphincterotomy bleeding treated in a tertiary care referral hospital with FCSEBMS.

Methods: a retrospective cases series study was performed including all post-ERCP bleeds treated with FCSEBMS (immediate or delayed) from January 2015 to June 2017. Clinical data, laboratory results and endoscopic reports were collected in order to evaluate the rebleeding rate after endoscopic treatment. Two different scenarios were considered: a) prophylactic stent placement after effective endoscopic treatment; and
b) stents placed for the treatment of an active postsphincterotomy bleed, refractory to standard endoscopic therapy.

**Results:** twenty-two patients (14 male, eight women) diagnosed with postsphincterotomy bleeding were treated with FCSEBMS placement. The stents were placed prophylactically in 15 patients, while the stents were placed as a treatment for a refractory bleed in seven patients. No differences were found between both groups except for a higher anticoagulation rate in the treatment group. Clinical success was achieved in all but one patient, with no complications in relation to stent placement. Distal migration was described in two of the 22 patients included in the study.

**Conclusions:** temporary placement of FCSEBMS seems to be a technically feasible treatment option for post-ERCP bleeding with a high clinical success rate. The complication rate was low, although randomized studies are needed.

**Key words:** Endoscopic retrograde cholangiopancreatography. ERCP. Post-ERCP bleeding. Biliary stent. FCSEBMS.

**INTRODUCTION**

Bleeding is a serious adverse event of endoscopic retrograde cholangiopancreatography (ERCP) and most commonly occurs as the result of endoscopic biliary and/or pancreatic sphincterotomy, with an estimated incidence rate of 1.34% (1.16-1.52%) (1). Other etiologies associated with post-ERCP bleeding include splenic or hepatic injury and vessel laceration or pseudoaneurysm. In addition, hemobilia may occur after ERCP, especially after stricture dilation, biopsy of the biliary tree and ablative biliary therapies. Risk factors for post-sphincterotomy bleeding such as coagulopathy, anticoagulation medication within three days of sphincterotomy, cholangitis before ERCP, bleeding during initial sphincterotomy and lower endoscopist ERCP case volume have been reported (2). Nowadays, there is no established consensus with regard to how to treat this particular type of gastrointestinal bleed in clinical guidelines (3). Techniques such as epinephrine injection, bipolar probe cautery, argon plasma coagulation at the site of bleeding or exposed vessels, hemoclip placement or even band ligation have been widely used (4-7). Since 2010 (8), the
placement of fully covered self-expandable biliary metal stents (FCSEBMS) has been evaluated as a valuable alternative, with positive outcomes and a low complication rate.

In this study, we report our experience in the treatment and prevention of post-sphincterotomy bleeding with FCSEBMS.

MATERIAL AND METHODS

Patients and procedures

All ERCPs were performed by four experienced endoscopists in an academic tertiary hospital using Olympus Q180V duodenoscopes. Procedures were performed under deep sedation controlled by anesthesiologists. The electrosurgical unit used in all procedures was an ERBE VIO® 200S (ERBE Elektromedizin GmbH) and the current mode for endoscopic sphincterotomy was the Endo Cut®. Autotome RX cannulating sphincterotomes and CRE™ balloon dilatation catheters (both from Boston Scientific, Massachusetts, USA) were used to perform sphincterotomy and sphinteroplasty, respectively. WallFlex™ fully covered biliary stent were used of 10 x 60 mm and 10 x 80 mm (Boston Scientific, Massachusetts, USA).

A search was performed of our endoscopic data for all post-ERCP bleeds (immediate or delayed) from January 2015 to June 2017. All those treated with FCSEBMS were included in this retrospective study.

A database with 40 variables was designed. Clinical data, laboratory results and endoscopic reports were collected. Clinical data included personal history (including cardiac, hepatic and renal diseases history, antiplatelet/anticoagulant treatment and withdrawal/non-withdrawal for the ERCP), ASA classification, hemodynamic status, the need for cardiac resuscitation and transfusion requirements. Endoscopic data included ERCP indication and the therapy performed, endoscopic findings, time of bleeding, severity of the bleed and additional hemostatic treatments (apart from stent placement).

Outcomes, data collection and definitions
The primary aim of the study was to evaluate the rebleeding rate after FCSEBMS placement. Secondary objectives included the safety of the procedure, technical success of the biliary stent placement, migration rate and mortality associated with post-ERCP bleeding.

Two different scenarios regarding when and in which situation the biliary stent was placed were established according to that described previously (Fig. 1): a) prophylactic stent placement after effective immediate endoscopic treatment; or b) a stent placed as a treatment of an active post-sphincterotomy bleed refractory to standard endoscopic treatment.

– Post-ERCP bleeding was defined as any bleeding during or after the ERCP, clinically significant (with overt gastrointestinal bleeding) and/or a drop in hemoglobin levels (≥ 3 gr/dl) and/or a bleed that involved hemodynamic instability and/or required endoscopic treatment. With regard to the time of bleed, this was classified as either immediate or delayed. The former refers to a bleed that occurred during the procedure and delayed bleeding refers to those that occurred from six hours up to 30 days after endoscopic sphincterotomy. Cotton’s bleeding severity grading classification (9) was used.

– Clinical success was defined as no signs of rebleeding after biliary stent placement.

– Clinical failure was defined as a rebleed after FCSEBMS placement confirmed by laboratory tests plus endoscopic or radiological evidence. Patients with a rebleed were managed by interventional radiology or surgery.

– Technical success was defined as the capacity of the correct deployment of the FCSEBMS in the patients. Stents were placed for 7-10 days and then removed endoscopically.

– Standard endoscopic therapy for post-ERCP bleeding included epinephrine injection, argon plasma coagulation ablation and/or hemoclip placement.

**Statistical data**

Data collection and statistical analysis was performed with the SPSS v24 package. The Student’s t-test and Chi-squared were used for comparisons where appropriate and a
p value less than 0.05 was considered as significant. Results are shown as the mean, standard deviation (SD), number and percentage.

RESULTS
In our center, 1,152 ERCPs were performed from January 2015 to June 2017. Sphincterotomy, sphincteroplasty and/or precut were performed in 699 procedures (60.7%). Post-ERCP bleeding events occurred in 29 patients (2.5%) and 22 patients (14 male, eight women) were treated with FCSEBMS placement (every patient received only one biliary stent). The technical success for stent placement was 100%. Patient characteristics are shown in table 1. Both groups were comparable and there were no statistically significant differences except for anticoagulant therapy, which was more frequent in the therapeutic group. The British Society of Gastroenterology (BSG) and European Society of Gastrointestinal Endoscopy (ESGE) guidelines recommendations (10) were followed for the withdrawal of these treatments in all patients. Biliary obstruction due to coledocolithiasis was the indication for ERCP in all procedures. Selective biliary sphincterotomy was performed in 14/22 patients, precut plus biliary sphincterotomy in 4/22, large balloon sphincteroplasty in 3/22 and any cannulation (or dilation) procedure was performed in one patient. A difficult cannulation was reported in nine patients according to the ESGE guidelines definition (11). According to the Cotton severity grading classification, bleeding was mild in 14/22 patients, moderate in 6/22 and severe in 2/22 patients. Seven patients with post-ERCP bleeding (7/29 patients) were treated only with standard therapy (epinephrine injection in all cases). Demographical data in this group was homogeneous compared to our cohort of stent-placed post-ERCP bleeding. However, the severity of bleeding was mild in 7/7 patients and there were no patients (0/7 patients) under anticoagulant or antiplatelet treatment, no relevant cardiologic pathology, liver and/or chronic kidney disease.
In relation to the two scenarios previously described (Fig. 1), the stent was placed once the initial bleeding was effectively treated with standard endoscopic treatment in 15 patients (prophylactic group, all in the initial ERCP). On the other hand, the stent was placed as treatment for a refractory post-ERCP bleeding in seven patients that did not respond to standard endoscopic therapy (1/7 stents were placed during the initial
ERCP and 6/7 of them in a second procedure due to the bleed). Clinical success was achieved in all but one patient (21/22 patients, 95.5%) within the prophylactic group that required angiographic embolization of the gastroduodenal artery as a rescue treatment, with a subsequent favorable outcome. No complications in relation to the stent placement were found (no acute pancreatitis or cholangitis were reported) and distal migration of the stent was described in 2/22 (9%) patients without any clinical relevance in the clinical course. There was no mortality associated with post-ERCP bleeding in our cohort. The mean time with stent placed was 24 days, which was 170 days in one patient who was excluded from the analysis.

DISCUSSION
Post-ERCP bleeding is a serious adverse event. The rate of post-ERCP bleeding reported in our cohort is consistent with the existing literature (12). First-line treatment is endoscopic but the most suitable management is not well established. We present our experience with a cohort of patients treated with biliary stents. The results showed that FCSEBMS can be a feasible and effective treatment for these patients. In a period of 30 months, 22 patients with a post-ERCP bleed were managed with biliary stents with a reported success rate of 95%; only one patient had a rebleed and angiographic embolization was required. Curiously, in this patient, the FCSEBMS was placed prophylactically after adequate immediate bleeding control with epinephrine injections. In relation to this fact, we clearly differentiated two situations for the placement of a stent. On one hand, those patients in which the bleeding was controlled after standard hemostatic therapy (15 patients) and on the other hand, a group of patients refractory to standard therapy (seven patients). Although we collected a heterogeneous cohort of patients, a high proportion had a high risk of post-ERCP bleeding. In fact, almost 2/3 of the cohort required antiplatelet and/or anticoagulant therapy had advanced liver or renal diseases or cardiopathy. The severity of the bleed (according to Cotton classification) (10) was mild in 63% of patients, in contrast to other classic studies (2). The fact that most of the patients had their biliary stent placed as a preventive measure surely had a significant influence on this result.
FCSEBMS was a highly safe procedure, as there were no related complications. In our cohort, no FCSEBM-related pancreatitis was reported, as described by previous authors (13). Migration was not a prominent issue (only distal migration in 2/22 patients), probably due to the short duration of the stent placement (mean time 24 days). Planned stent duration was established in seven to ten days, but the clinical situation of some patients prevented an early stent removal in these cases. Our study had some limitations. It is a not randomized retrospective cohort with a limited number of patients. A selection bias is almost certain. However, the patients selected for biliary stent placement to prevent a delayed bleed were considered as high risk for adverse events, according to the endoscopist. The cost of the stent treatment was not considered in our study.

In conclusion, post-ERCP bleeding is a serious adverse event and standard endoscopic treatment is often cumbersome. The temporary placement of FCSEBMS seems to be a technically feasible treatment option with a high clinical success rate. The complication rate of biliary stenting (including stent migration) in this situation seems to be low, due to the short duration of the stent placed. Further randomized studies are needed in order to identify the most suitable patients and the best management algorithm of this adverse event. Accordingly, evaluation of the bleeding risk should lead to an individualized plan of the cannulation technique in programmed ERCPs (14).

**COMPLIANCE WITH ETHICAL STANDARDS**

The authors declare that they have no conflict of interest related to this article. All procedures performed in our study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards. Formal consent is not required for this type of study. This article does not contain any studies with animals performed by any of the authors.

**REFERENCES**


Table 1. Patient baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Therapeutic group</th>
<th>Prophylactic group</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>22</td>
<td>7</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Age (mean [SD])</td>
<td>74.36 (14.1)</td>
<td>68.8 (20.2)</td>
<td>76.9 (10.0)</td>
<td>0.22</td>
</tr>
<tr>
<td>Male (%)</td>
<td>14 (63.6%)</td>
<td>4 (57.1%)</td>
<td>10 (66.7%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Cardiologic comorbidity* (%)</td>
<td>10 (45.5%)</td>
<td>5 (71.4%)</td>
<td>5 (33.3%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Cirrhosis (%)</td>
<td>1 (4.5%)</td>
<td>1 (14.3%)</td>
<td>0 (0%)</td>
<td>0.13</td>
</tr>
<tr>
<td>CKD† (%)</td>
<td>4 (18.2%)</td>
<td>2 (28.6%)</td>
<td>2 (13.3%)</td>
<td>0.38</td>
</tr>
<tr>
<td>Antiplatelet treatment (%)</td>
<td>7 (31.8%)</td>
<td>3 (42.8%)</td>
<td>4 (26.7%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Anticoagulant treatment (%)</td>
<td>8 (36.4%)</td>
<td>6 (85.7%)</td>
<td>2 (13.3%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Platelet count before procedure (mean [SD])</td>
<td>234,545 (104,762)</td>
<td>257,875 (96,005)</td>
<td>223,666 (110,064)</td>
<td>0.48</td>
</tr>
<tr>
<td>INR before procedure (mean [SD])</td>
<td>1.05 (0.2)</td>
<td>1.1 (0.2)</td>
<td>1.03 (0.8)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

*Defined as ischemic cardiomyopathy, atrial fibrillation or congestive heart failure. †
CKD: chronic kidney disease, defined as stage 3 or higher.
*Angiographic embolization was needed as a final treatment.