Hemostatic efficacy and clinical outcome of endoscopic treatment of Dieulafoy's lesions: comparison of endoscopic hemoclip placement and endoscopic band ligation

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Background: The most suitable mechanical endoscopic hemostasis for a bleeding Dieulafoy's lesion (DL) is not yet well established.

Objective: To compare the hemostatic efficacy and clinical outcome of endoscopic hemoclip placement (EHP) and endoscopic band ligation (EBL).

Design: Retrospective, single-center study.


Patients: Sixty-six patients who received mechanical endoscopic hemostasis for bleeding DLs.

Interventions: Endoscopic hemostasis.

Main Outcome Measurement: Primary hemostasis and rebleeding rates.

Results: DLs accounted for 3.8% of cases of acute nonvariceal upper GI bleeding during the study period. Active bleeding from DLs was noted in 34 patients (51.5%). EHP and EBL were performed as a method of endoscopic hemostasis in 34 and 32 patients, respectively. There were no significant differences between the 2 groups with respect to baseline characteristics (except comorbidities) and endoscopic features of DLs. Primary hemostasis was achieved in all 66 patients (100%). There were 6 cases of recurrent bleeding: 5 (14.7%) and 1 (3.1%) in the EHP and EBL groups, respectively. Secondary hemostasis was achieved with endoscopic treatment and angiographic embolization in 5 patients and 1 patient, respectively, and no patients required surgery. The mean procedure time of endoscopic hemostasis was significantly longer in the EHP group (19.1 vs 11.5 minutes, \( P = .015 \)). There was no bleeding-related mortality.

Limitations: Retrospective analysis.

Conclusions: Both EHP and EBL are suitable for the treatment of bleeding DLs. EBL can be used as an initial hemostatic method for bleeding DLs because of a favorable clinical outcome comparable to that with EHP and a shorter procedure time. (Gastrointest Endosc 2012;75:32-8.)
have a fatal clinical outcome unless adequate treatment is promptly initiated.5,6

With the advances in endoscopic techniques for locating and managing a bleeding site, endoscopic treatment has replaced surgery as the standard diagnostic and therapeutic approach for bleeding DLs.5,7 The rate of hemostasis with endoscopic treatment is known to reach 75% to 100%,1,5,6,8-19 and a good long-term prognosis after endoscopic treatment has been proved to date.1,6,9,14,15 Studies have shown that mechanical endoscopic methods, such as endoscopic hemoclip placement (EHP) and endoscopic band ligation (EBL), are more effective treatments than other endoscopic methods, such as injection and thermal therapy.5,8-12 However, few studies have compared the hemostatic efficacy of the different mechanical endoscopic methods, and the most suitable mechanical method for treating bleeding from DLs is not yet well established.

Our center has performed 2 mechanical endoscopic treatments (EHP and EBL) for patients with bleeding DLs, and the data on clinical outcomes of these patients have been collected prospectively. The aim of this study was to evaluate the clinical outcome of the mechanical endoscopic hemostasis for bleeding DLs and to compare the hemostatic efficacy and safety of EHP and EBL.

METHODS

Patients

From June 2003 to July 2010, patients who were admitted to the Emergency Unit in Seoul National University Bundang Hospital with acute upper GI bleeding from DLs were considered for inclusion in the current study. All patients were immediately resuscitated with intravenous fluids and blood transfusions and underwent emergent endoscopy within 24 hours of admission.

The diagnosis of DL was based on endoscopic findings. Findings accepted as specific for DLs were as follows: (1) active arterial spurting or micropulsatile streaming from a minute mucosal defect or through normal surrounding mucosa, (2) visualization of a protruding vessel with or without active bleeding within a minute mucosal defect or through normal surrounding mucosa, and (3) the appearance of a fresh, densely adherent clot with a narrow point of attachment to a minute mucosal defect or to normal-appearing mucosa.20

The data for enrolled patients were classified into 3 categories: preprocedural, procedural, and outcome data (Tables 1-3), which were then collected prospectively. Shock was defined as a systolic blood pressure of less than 90 mm Hg with symptoms or signs of organ hypoperfusion. The study protocol was reviewed and approved by the institutional review board of our institution.

Endoscopic procedure

All endoscopic procedures were performed by 2 experienced endoscopists with a standard upper endoscope (GIF-H260; Olympus, Tokyo, Japan). When the DL was verified as a bleeding focus on endoscopic findings, endoscopic hemostasis was performed immediately in the same procedure. At our institution, EHP had been performed as a primary method for endoscopic hemostasis from June 2003 to December 2006. However, based on the evidence from the previous reports showing favorable hemostatic efficacy of EBL,5,8 EBL, instead of EHP, has been performed as an initial hemostatic method at our institution since January 2007.

The processes of EHP and EBL are as follows: for EHP (Fig. 1), a hemostatic hemoclip (135-degree angle, HX-610-135; Olympus Optical Co, Ltd, Tokyo, Japan) was applied to the spurting or micropulsatile streaming vessels with surrounding tissue. When a lesion was identified, the bleeding site was initially approached carefully. In the second step, the loaded rotatable clip-fixing device was quickly applied to the normal mucosa through the endoscope channel. Third, the loaded hemoclip was released to clip the bleeding vessel and the surrounding mucosa. In the case of inactive bleeding, the normal surrounding mucosa was clipped with the protruding vessel or adherent clot. For EBL (Fig. 2), a Varioligator kit with a single-shot device (Top Corporation, Tokyo, Japan) was used without a flexible overtube. When a lesion was identified, the bleeding site was initially approached carefully. In the second step, the endoscope was removed and reinserted after the EBL apparatus had been attached. Third, the hood of the ligation device was then placed over the bleeding site, suction was applied, and ligation with an O ring was performed.

For DLs to which mechanical hemostasis could not be applied because of active bleeding, an injection of 0.9% NaCl (9 mL) and 1:1000 epinephrine (1 mL) mixture was applied to several sites around the DLs, if needed, to attenuate active bleeding and to allow better visualization of DLs. After the endoscopic procedure, clinical parameters such as vital signs, oxygen saturation, and laboratory values were monitored, and acid-suppressive therapy with intravenous proton pump inhibitors was administered. According to clinical parameters, additional blood transfusions were performed if needed. A follow-up endoscopic examination was performed in all patients within 7 days after initial hemostasis.
Clinical outcome

The primary outcome of the current study was defined as the primary hemostasis and rebleeding rates. The secondary outcome was defined as the number of endoscopic sessions for permanent hemostasis, the procedure time for endoscopic hemostasis, the need for angiographic embolization or emergent surgery, blood transfusion requirements, length of hospital stay, and bleeding-related mortality. These primary and secondary outcomes were compared between the 2 groups (EHP vs EBL).

Failure of primary hemostasis was defined as persistent active bleeding despite initial endoscopic management or any evidence of active bleeding such as hematemesis, hematochezia, and hemodynamic instability within 12 hours after primary hemostasis. Recurrent bleeding was
defined as ongoing bleeding signs such as fresh hematemesis, hematochezia, fresh blood aspirated via a nasogastric tube, instability of vital signs, or a reduction in hemoglobin by more than 2 g/dL after 12 hours after primary hemostasis. Patients with clinical evidence of recurrent bleeding received a prompt endoscopic examination. In case of recurrent bleeding that was not endoscopically amenable, angiographic embolization or emergent surgery was considered according to the individual clinical situation. After hemostasis was achieved, each patient with DL was followed as an outpatient for at least 1 year to evaluate the long-term outcome. For patients who were not available for clinical evaluation for the 1-year follow-up period, telephone contact was attempted to obtain information about the clinical outcome. Statistical analysis was performed by using the $\chi^2$ test, the Fisher exact test, and the unpaired 2-tailed test with $P$ values $<.05$ regarded as significant.

**RESULTS**

**Preprocedure data for enrolled patients**

A total of 1725 patients underwent emergent endoscopy for acute nonvariceal upper GI bleeding from June 2003 to July 2010. Among those patients, 66 (3.8%, mean age 62.5 ± 15.6 years, range 29-88 years) underwent endoscopic treatment of DLs. The presenting manifestation was hematemesis in 14 patients (21.2%), melena in 35

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**TABLE 3. Clinical outcomes of patients in the endoscopic hemoclip placement and endoscopic band ligation groups**

<table>
<thead>
<tr>
<th></th>
<th>EHP</th>
<th>EBL</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcomes, no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary hemostasis</td>
<td>34 (100)</td>
<td>32 (100)</td>
<td>NA</td>
</tr>
<tr>
<td>Recurrent bleeding</td>
<td>5 (14.7)</td>
<td>1 (3.1)</td>
<td>.20</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of endoscopic sessions: 1/2*</td>
<td>29/4†</td>
<td>31/1</td>
<td>.17</td>
</tr>
<tr>
<td>Procedure time ± SD, min</td>
<td>19.1 ± 15.8</td>
<td>11.5 ± 6.4</td>
<td>.02</td>
</tr>
<tr>
<td>Other treatment</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Embolization/surgery</td>
<td>1/0</td>
<td>0/0</td>
<td></td>
</tr>
<tr>
<td>Transfusion requirement ± SD, units</td>
<td>3.4 ± 3.5</td>
<td>2.8 ± 3.3</td>
<td>.45</td>
</tr>
<tr>
<td>Length of hospital stay ± SD, d</td>
<td>11.2 ± 3.5</td>
<td>9.0 ± 3.5</td>
<td>.59</td>
</tr>
<tr>
<td>Bleeding-related mortality</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
</tbody>
</table>

EHP, Endoscopic hemoclip placement; EBL, endoscopic band ligation; NA, not available; SD, standard deviation.
*The number of sessions of endoscopic treatments for permanent hemostasis.
†One patient who underwent angiographic embolization because endoscopic hemostasis failed was not included in this analysis.

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**Figure 1.** The process of endoscopic hemoclip placement. **A,** Dieulafoy’s lesion with spurting bleeding is visible in the upper part of the stomach, and a device loaded with a rotatable hemoclip approaches the bleeding lesion. **B,** Three hemoclips are placed to clip the bleeding vessel and the surrounding mucosa. No active bleeding was observed.
patients (53.0%), and both in 17 patients (25.8%). Shock was observed on initial admission in 8 patients (12.1%) and the mean hemoglobin level on initial admission was 9.8 ± 3.1 g/dL (range 2.3-16.4 g/dL). Thirteen patients (19.7%) were taking medications that adversely affected coagulation (antiplatelet agents, 8 patients; warfarin, 3 patients; nonsteroidal anti-inflammatory drugs [NSAIDs], 2 patients). The frequency of comorbidities was 71.2% (47 of 66 patients). The comorbidities in both the EHP group and EBL group included cardiovascular disease, arterial hypertension, chronic renal failure, liver cirrhosis, and malignancy. The mean value of the Rockall score was 5.8 ± 1.6 (range 3-9). The mean time from initial presentation of upper GI bleeding to endoscopy was 36.3 ± 42.0 hours (range, 3-242 hours). There were no significant differences between the 2 groups with respect to preprocedure data except the frequency of comorbidities (Table 1).

Procedure data for enrolled patients
A diagnosis was made at initial endoscopy in 92.4% (61 of 66 patients). Failure to make the correct diagnosis when the appropriate site was evaluated at the initial endoscopy was attributed to a large volume of blood in 4 patients and a missed lesion in 1 patient. Those 5 patients underwent a second endoscopy the following day, and the correct diagnosis of DL was made at this second endoscopy. The location of DL was the proximal stomach in 48 patients (72.7%), distal stomach in 8 patients (12.1%), and duodenum in 10 patients (15.2%). Active bleeding (arterial spurting or micropulsatile streaming) from the DLs was noted at endoscopy in 34 patients (51.5%).

Of a total of 66 patients, 34 underwent EHP and 32 underwent EBL. Injection therapy was performed in 26 patients (39.4%). The mean number of hemoclips used in the EHP group was 3.6 ± 1.7 (range 2-10 hemoclips), and only 1 band was used in all patients in the EBL group. There were no significant differences between the 2 groups with respect to procedure data (Table 2).

Primary outcome
Outcome data are summarized in Table 3. Primary hemostasis was achieved in all 66 patients. The recurrent bleeding after primary hemostasis occurred in 6 patients (9.1%), 5 in the EHP group and 1 in the EBL group. Among 5 patients with recurrent bleeding in the EHP group, 4 achieved successful secondary hemostasis with endoscopic treatment (EHP in 3 and thermal ablation in 1). However, in the other 1 patient, endoscopic hemostasis was not successful because of massive active bleeding, and this patient required angiographic embolization for hemostasis. In the EBL group, only 1 patient (3.1%) experienced recurrent bleeding. Bleeding recurred in this patient 18 days after the primary hemostasis. Endoscopic examination revealed an active ulcer crater with an exposed vessel at the previous band ligation site, and successful hemostasis was achieved with thermal ablation and EHP. The rate of recurrent bleeding tended to be higher in the EHP group than in the EBL group (14.7% vs 3.1%); however, this difference was not significant (P > .05, Table 3). No patient in either the EHP or the EBL group required surgery. During the 1-year follow-up, there was no further recurrence of bleeding in either group.

Secondary outcome
With respect to secondary outcome (Table 3), the mean procedure time for endoscopic hemostasis was significantly longer in the EHP group (19.1 vs 11.5 minutes, P = .015). Also, there was a trend toward a lower rate of the need for multiple endoscopic sessions to achieve permanent hemostasis in the EBL group, although this difference was not significant (12.1% vs 3.1%, P > .05). The number of blood transfusions and length of hospital stay were not
significantly different between the 2 groups. Endoscopic failure and the subsequent need for other treatments for hemostasis occurred in only 1 patient (angiographic embolization in the EHP group), and no patients required surgery. There was no bleeding-related mortality in the current study.

**DISCUSSION**

Although various endoscopic methods such as injection therapy, LASER, argon plasma coagulation, and cyanoacrylate have been applied to bleeding DLs, mechanical endoscopic methods such as EHP and EBL are considered to be the first option in the management of DL. Theoretically, mechanical hemostasis is associated with less damage to the surrounding tissue than injection or thermal therapy, and several reports have shown the superiority of the mechanical endoscopic methods (EHP or EBL) over injection or thermal therapy. The current study provides comparative results in the 2 mechanical endoscopic methods (EHP and EBL). This study confirms the good hemostatic efficacy and favorable clinical outcome with both EHP and EBL and suggests that EBL is one of the methods used in the initial approach for bleeding DLs.

One study reported the equivalent hemostatic efficacy and clinical outcome of EHP and EBL. In this prospective, randomized trial, the primary hemostasis rate and recurrent bleeding rate were 100% and 7.7%, respectively, in both groups. In our study, although the rate of primary hemostasis was also 100% in both groups, the rate of recurrent bleeding was 14.7% and 3.1% in the EHP and EBL groups, respectively. Other reports have shown the rate of recurrent bleeding in the case of EHP to range from 0% to 9.3%, and the frequency of comorbidities was significantly different between the 2 groups, and some of the other preprocedure data also tended to be different, despite statistical insignificance. However, because most of the data favored the EHP group (the frequency of comorbidities was significantly higher in the EBL group), those differences in preprocedure data do not seem to adversely affect the results showing that EBL is not inferior to EHP in hemostatic efficacy and clinical outcome.

The safety of endoscopic hemostasis should also be considered an important issue of clinical outcome. With respect to the safety, EBL has some problems such as delayed bleeding in the case of a residual vessel within a necrotic ulcer as well as perforation. In our study, 1 patient in the EBL group experienced delayed bleeding at the previous band ligation site. However, because the number of cases, including ours, showing this complication that have been reported to date is very small, the rate of those complications thus appears to be low. Therefore, we believe that this concern about the complications of EBL would not outweigh its advantages, such as a favorable clinical outcome and technical simplicity. However, in clinical practice, the possibility of incomplete occlusion of a vessel and subsequent delayed bleeding should be considered, especially in technically difficult cases.

A novel method of endoscopic hemostasis, hemospray with a clotting nanopowder, was investigated, and favorable hemostatic efficacy and safety in active peptic ulcer bleeding were reported in 1 pilot clinical study. It does not require direct tissue contact with the delivery device, which eliminates the risk of tissue damage. We think that this novel method could also be a promising option of endoscopic hemostasis for bleeding DL, especially in the case of recurrent bleeding after the initial mechanical hemostasis (ie, DL that is difficult to manage effectively with mechanical hemostasis). Studies would be required to apply this method to DL in clinical practice.

Our study has several limitations. First, although each mechanical method (EHP or EBL) was performed during a different period and the data were collected prospectively, this was a retrospective study. However, to the best of our knowledge, this study compares the hemostatic efficacy and clinical outcome between 2 mechanical endoscopic methods with the largest number of patients to date. Second, the frequency of comorbidities was significantly different between the 2 groups, and some of the other preprocedure data also tended to be different, despite statistical insignificance. However, because most of the data favored the EHP group (the frequency of comorbidities was significantly higher in the EBL group), those differences in preprocedure data do not seem to adversely affect the results showing that EBL is not inferior to EHP in hemostatic efficacy and clinical outcome.

In summary, both EHP and EBL are suitable in the treatment of bleeding DL. In most cases, permanent hemostasis can be achieved with those 2 mechanical endoscopic methods. In addition, EBL could be considered as one of the initial hemostatic methods for bleeding DLs in clinical practice because EBL, according to the results of our study, is not inferior to EHP in either the clinical outcome or technical aspect.
REFERENCES


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