

**Open Access**

Endoscopic Therapy for Acute Diverticular Bleeding

Masayuki Kato

Department of Endoscopy, The Jikei University Katsushika Medical Center, Tokyo, Japan

Diverticular bleeding accounts for approximately 26%–40% of the cases of lower gastrointestinal bleeding. Rupture of the vasa recta at the neck or dome of the diverticula can be the cause of this bleeding. Colonoscopy aids in not only the diagnosis but also the treatment of diverticular bleeding after a steady bowel preparation. Endoscopic hemostasis involves several methods, such as injection/thermal contact therapy, clipping, endoscopic band ligation (EBL), hemostatic powder, and over-the-scope clips. Each endoscopic method can provide a secure initial hemostasis. With regard to the clinical outcomes after an endoscopic treatment, the methods reportedly have no significant differences in the initial hemostasis and early recurring bleeding; however, EBL might prevent the need for transcatheter arterial embolization or surgery. In contrast, the long-term outcomes of the endoscopic treatments, such as a late bleeding and recurrent bleeding at 1 and 2 years, are not well known for diverticular bleeding. With regard to a cure for diverticular bleeding, there should be an improvement in both the endoscopic methods and the multilateral perspectives, such as diet, medicines, interventional approaches, and surgery. **Clin Endosc 2019;52:419-425**

Key Words: Diverticulum; Colon; Endoscopic; Hemostasis

INTRODUCTION

Epidemiology and pathogenesis

Diverticular bleeding accounts for approximately 26%–40% of the cases of lower gastrointestinal bleeding (LGIB).¹⁻⁴ Diverticular bleeding lowers the quality of life, although the mortality rate has been reported to be less than 5%.^{5,6} The occurrence of diverticular disease is increasing in Asia, including Korea and Japan, and the frequency of diverticular bleeding, particularly that of LGIB, has increased from 5.9% to 23.0%.⁷⁻⁹ The pathogenesis of colonic diverticula is believed to involve herniation of the mucosa and submucosa without the muscular layer at the sites of penetration by the vasa recta.⁵ The bleeding could be explained by rupture of the vasa recta at the

neck or dome of the diverticula (Fig. 1).⁶

Diagnosis

In the case of LGIB, including diverticular bleeding, colonoscopy should be the initial diagnostic procedure. The diagnostic yield of colonoscopy in patients presenting with LGIB is 90%, at the most.⁷⁻¹⁰ In contrast, a meta-analysis reported that the overall sensitivity and specificity of computed tomography (CT) angiography in patients with an episode of an acute gastrointestinal (GI) hemorrhage were 85.2% and 92.1%, respectively.¹¹ Another study showed that the diagnostic yield of multi-detector row CT for the site and etiology was higher than that of endoscopy.⁷ However, colonoscopy has the advantage of a diagnosis followed by an endoscopic hemostasis.^{8,10}

Bowel preparation

Diverticular bleeding usually occurs as a localized bleeding; thus, poor visualization not only prevents the identification of the bleeding point, but also increases the risk of perforation.⁹ Oral lavage approaches, such as polyethylene glycol, help in increasing the diagnostic yield and identifying the stigmata of recent hemorrhage (SRH), defining the bleeding site or the visible vessel after removing the adherent clot.^{4,12,13}

Received: April 3, 2019 **Revised:** May 25, 2019**Accepted:** June 24, 2019**Correspondence:** Masayuki Kato

Department of Endoscopy, The Jikei University Katsushika Medical Center, 6-41-2 Aoto, Katsushika, Tokyo 125-8506, Japan

Tel: +81-3-3603-2111, **Fax:** +81-3-3838-9943, **E-mail:** masakato89@gmail.com**ORCID:** <https://orcid.org/0000-0002-0338-2310>

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

A retrospective study showed that the visibility was superior in the lavage group when compared with that in the enema group.^{12,14} Thus, oral lavage may be important for identifying the hemorrhagic point.

Detection of the bleeding diverticulum

The rate of identification of the diverticulum responsible for the bleeding is relatively low (15%–25% of the cases) partly due to poor bowel preparation.^{4,15} To increase the detection rate of the bleeding diverticulum, the hood method and water jet scope should be used before colonoscopy.^{16,17}

Endoscopic findings for hemostasis

Endoscopic therapy can be performed in patients with an active bleeding, non-bleeding visible vessels, or SRH (Fig. 2).

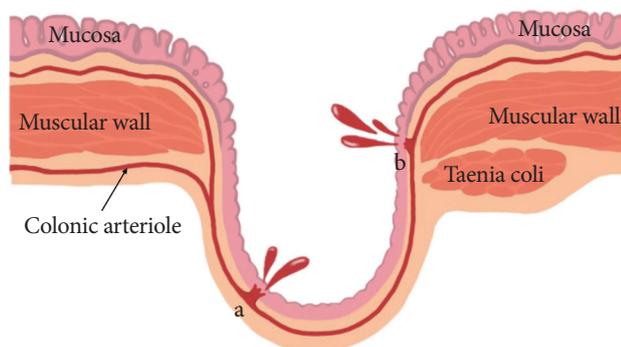


Fig. 1. Angioarchitecture of the diverticula. Diverticula are formed at the sites where the vasa recta penetrate the muscular wall of the colon. The arteriole is displaced over the dome. Diverticular bleeding is occasionally associated with a rupture of the vasa recta at the neck or dome of the diverticula.

Patients with SRH should be treated owing to the high risk of re-bleeding within 30 days.^{4,13}

METHODS OF ENDOSCOPIC HEMOSTASIS

Injection/thermal contact therapy

The effectiveness of epinephrine injections or thermal contact therapy for diverticular bleeding has been recognized in the last decade.^{4,18} Thermal contact therapies, such as heater probe therapy and bipolar coagulation, are usually indicated alone or in combination with an epinephrine injection for hemostasis in diverticular bleeding.^{4,18,19} Epinephrine injection therapy alone can show vasoconstrictive and mechanical effects, resulting in an insufficient treatment involving the risk of re-bleeding. Thermal contact therapy can lead to an increase in the incidence of perforation owing to the thermal influence on the thin wall of the colon or the mucosa and submucosa without the muscular layer.²⁰ It is highly recommended that excessive thermal injury be avoided, considering the thermal influences.²¹

Endoscopic clipping

Endoscopic clipping (EC) is a popular method because it induces less tissue injury than other endoscopic modalities and enables continued treatment without withdrawal of the colonoscope for re-setting to achieve hemostasis as well as injection/thermal contact therapy.²² Ideally, a direct placement (Fig. 3) of the hemoclips at the bleeding point is associated

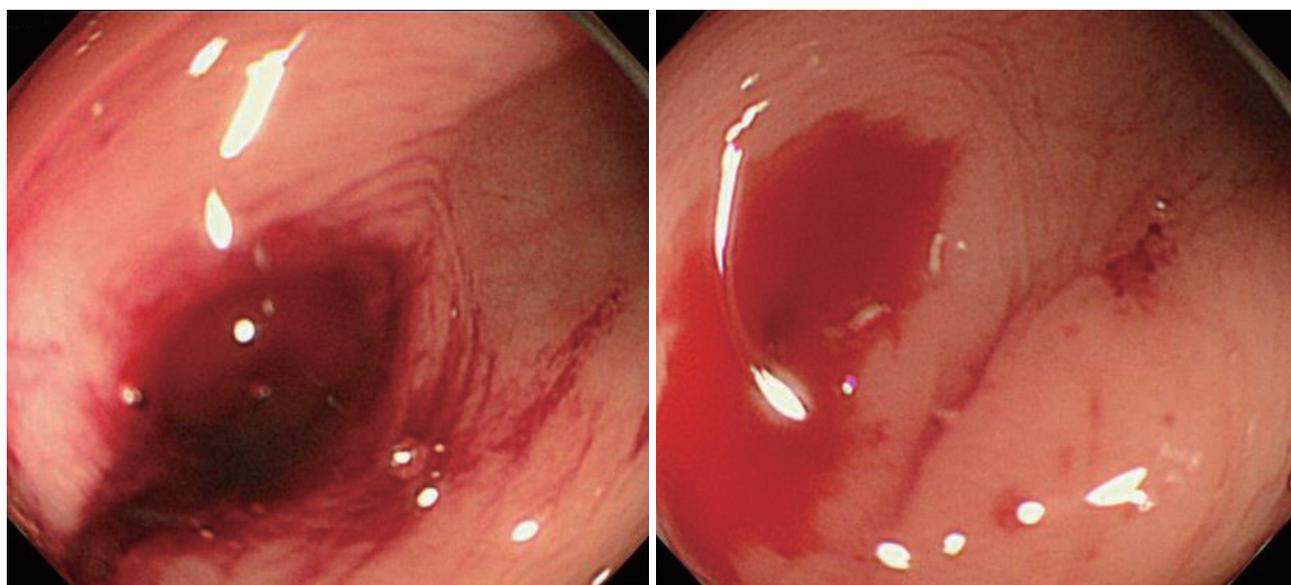


Fig. 2. A stigmata of recent hemorrhage defining the bleeding site or the visible vessel after removal of the adherent clot.

with a secure deployment.^{8,23} When a direct placement is not possible owing to a dome location, massive hemorrhage, or a small diverticular orifice, an indirect placement in a zipper fashion (Fig. 4) allows endoscopic hemostasis through compression.³ However, caution must be exercised in the indirect method because it may induce sepsis owing to the translocation of bacteria from the diverticulum to blood vessels in very rare cases.²⁴

Endoscopic band ligation

Endoscopic band ligation (EBL) can be a secure method with a tight closure for the muscularis propria compressed by an O-band involving the bleeding vessels.²⁵ After identifying the bleeding point, a marking clip is placed at the nearest point for preparation of EBL, followed by reinsertion of the

colonoscope with the application of a releasing O-ring for a tight ligation by an EBL device (Sumitomo Bakelite Co., Ltd., Tokyo, Japan). Subsequently, the colonic diverticulum is suctioned into the endoscopic ligator cup, and a syringe with air releases the elastic O-ring (Fig. 5). According to a recent meta-analysis, all three methods (i.e., EBL, coagulation, and clipping) exert beneficial effects on the initial hemostasis and early recurring bleeding. However, EBL has an advantage over coagulation and clipping in terms of the proportions of surgical treatment and transcatheter arterial embolization.²¹ With regard to the difference in the long-term outcomes between EBL and EC for the treatment of colonic diverticular bleeding, EBL has been proven to be more effective in decreasing re-bleeding when compared with EC.²⁶ However, a delayed perforation might develop as a rare complication of EBL.²⁷

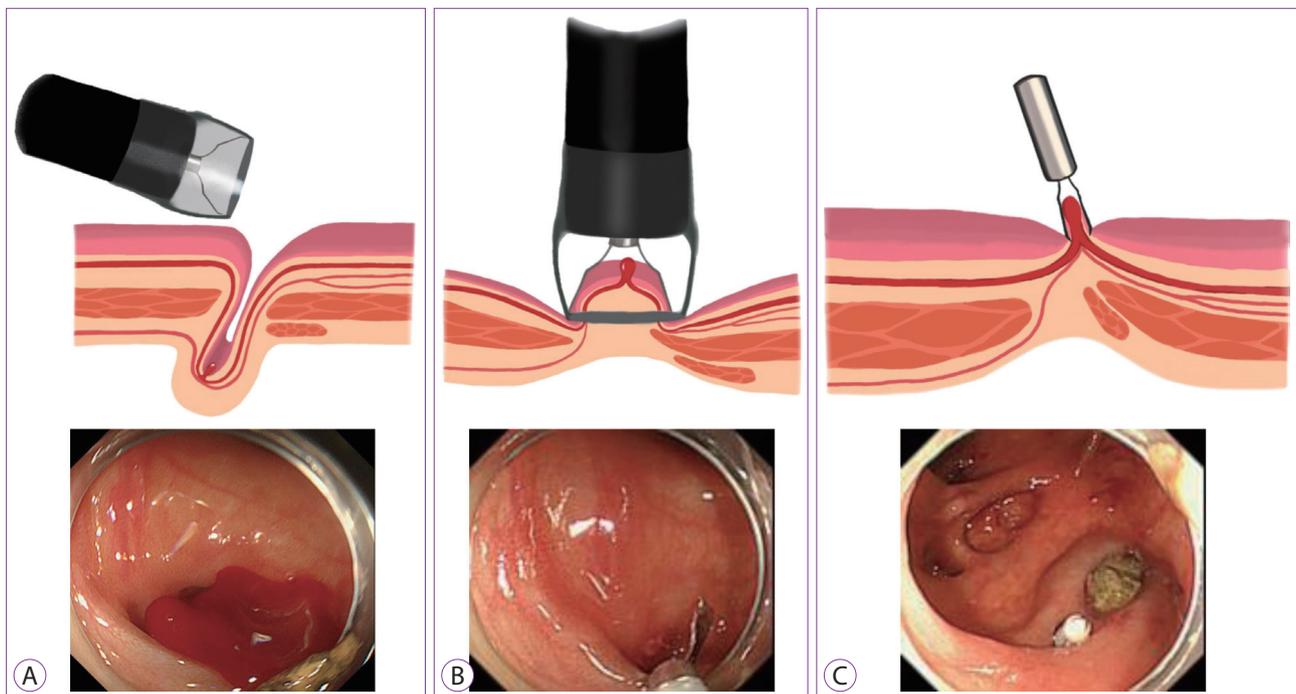


Fig. 3. Direct placement method. (A) Identification of the bleeding point using a distal attachment cap, which is useful for uncovering the bleeding point. The endoscope is fitted with a distal attachment cap. (B) Direct placement of the clip targeting the visible vessel with the cap. (C) Successful clipping.



Fig. 4. Indirect placement in a zipper fashion, which helps to stop the bleeding by compression.

Hemostatic powder

Hemostatic powder is not a popular hemostatic method for diverticular bleeding, and its usage in LGIB has not been licensed worldwide. Presently, the following three hemostatic powders are commercially available: Hemospray (Cook Medical, Winston-Salem, NC, USA), EndoClot (AMP; EndoClot Plus Inc., Santa Clara, CA, USA), and ABS (Ankaferd Health Products Ltd., Istanbul, Turkey). These hemostatic powders as topical sprays have been shown to be effective in the surgical field over the past 50 years.²⁸ In the recent years, this approach has been shown to be effective for achieving hemostasis in GI bleeding.²⁹⁻³⁵ With regard to hemostasis for diverticular bleeding, some case reports have shown the potency of the

hemostatic powder.^{36,37} It could be an important salvage therapy in case of an unidentified source of bleeding or bleeding that is untreatable with other endoscopic methods because it is simple and reliable for hemostasis.^{38,39}

Over-the-scope clip

The over-the-scope clip (OTSC) system (Ovesco Endoscopy AG, Tübingen, Germany) is designed for a full-thickness tight closure by using saw-like teeth of a shark (Fig. 6), and can treat a GI perforation or post-surgery leakage or fistula.⁴⁰⁻⁴² However, there are limited case reports on the use of the OTSC system for diverticular bleeding.⁴³ The OTSC system, which is a relatively complex and costly system, is not popular

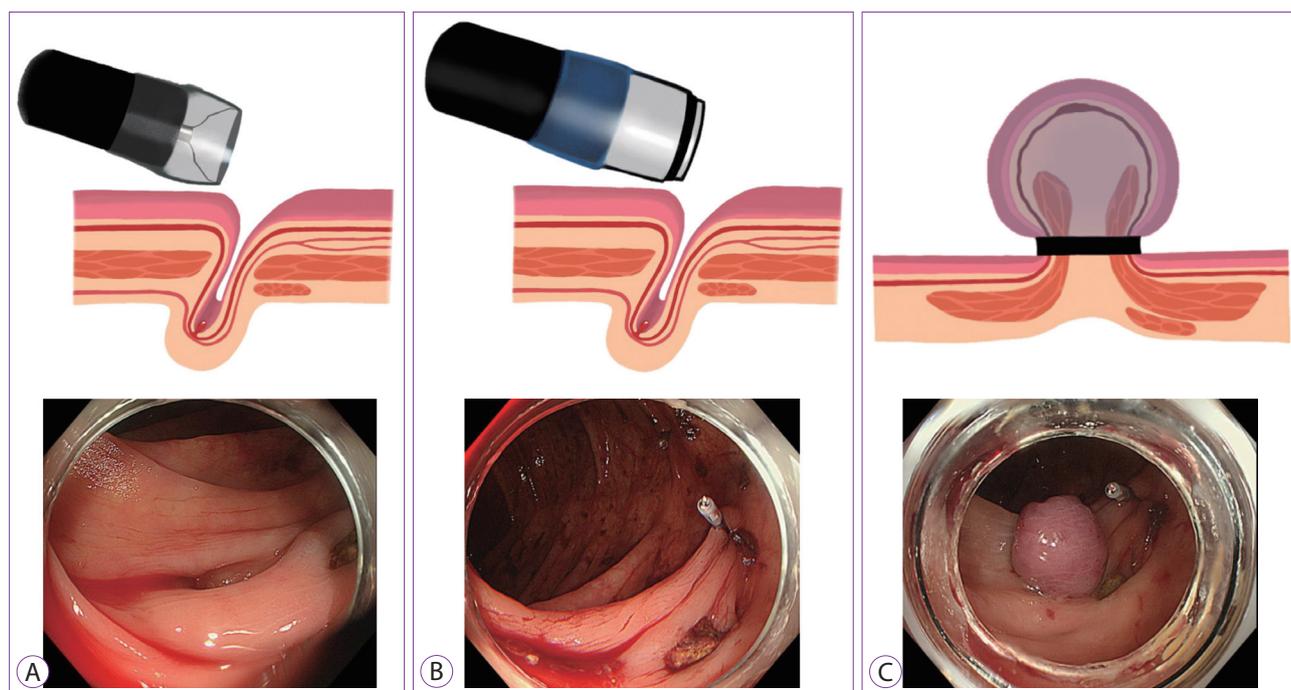


Fig. 5. Endoscopic band ligation. (A) Placement of a marking clip near the responsible diverticulum followed by reinsertion of the colonoscope with an endoscopic band ligation device. (B) Easy identification of the bleeding point with the marking clip. (C) View after releasing the O-ring, which ideally ligates both sides of the muscular wall involving the bleeding point.



Fig. 6. The over-the-scope clip (OTSC) system. (A) Type t and Type gc made of nitinol. (B) The OTSC system mounted onto the tip of an endoscope with a Twin Grasper as the application aid. (C) The OTSC system is applied at the perforation site.

for diverticular bleeding.

CLINICAL OUTCOMES AFTER ENDOSCOPIC TREATMENT

The issue of a high rate of late bleeding (0%–40%) from different diverticula remains unsolved. A long-term hemorrhage may occur if this issue is not solved under the existing conditions of hemostasis methods.^{8,44–46} Additionally, several studies have reported high recurrent bleeding rates of 30% and 40% at 1 and 2 years, respectively.^{47–49}

CHOOSING AN ENDOSCOPIC TREATMENT

After identifying the diverticulum responsible for the bleeding, there are three choices for endoscopic treatment: EBL, EC, or thermal contact therapy.

- (1) Whichever is selected, marking the clip deployment is required for subsequent treatment in the cases with an active bleeding. Such patients usually have multiple diverticula. Without the clip, an active bleeding or residual stool would make it difficult to identify the responsible diverticulum.

Table 1. Previous Studies of Endoscopic Treatment of Diverticular Bleeding

Study	Study design	Modalities	n	Initial hemostasis	Early re-bleeding (<30 days)	Late re-bleeding (>30 days)	Adverse events	Follow-up periods (mo)
Jensen et al. (2000) ⁴	Prospective	Epinephrine injection and/or bipolar probe coagulation	10	10 (100%)	0	0	0	Median 30 (range, 18–49)
Bloomfeld et al. (2001) ¹⁸	Retrospective	Epinephrine injection and/or contact coagulation	13	13 (100%)	5 (38%)	4 (31%)	0	Mean 35 (range, 1–74)
Couto-Worner et al. (2013) ²²	Retrospective	Endoscopic clipping with epinephrine injection	5	5 (100%)	1 (20%)	0	0	Mean 22 (range, 5–46)
Yen et al. (2008) ²³	Retrospective	Endoscopic clipping or/and epinephrine injection	11	11 (100%)	0	2 (18.2%)	0	Mean 15 (range, 1–22)
Kaltenbach et al. (2012) ⁸	Retrospective	Endoscopic clipping or/and epinephrine injection	24	21 (88%)	0	4 (19%)	0	Median 39 (range, 3–69)
Ishii et al. (2012) ³	Retrospective	Endoscopic clipping or/and epinephrine injection	89	87 (98%)	30 (34%)	0	0	N/A
Ishii et al. (2012) ²⁵	Retrospective	Endoscopic band ligation	29	27 (89%)	3 (11%)	0	0	Mean±SD 11±8
		Endoscopic clipping or/and epinephrine injection	3	3 (100%)	N/A	N/A	N/A	N/A
Nakano et al. (2015) ²⁶	Retrospective	Endoscopic band ligation	61	61 (100%)	9 (15%)	N/A	0	Median 30 (range, 12–65)
		Endoscopic clipping	39	39 (100%)	15 (38%)	N/A	0	Median 65 (range, 12–111)
Holster et al. (2014) ²⁶	Retrospective	Hemostatic powder	1	1 (100%)	1 (100%)	N/A	0	N/A
Aslan et al. (2013) ³⁷	Retrospective	Hemostatic powder	2	2 (100%)	0	0	0	2
Wedi et al. (2016) ⁴³	Retrospective	An over-the-scope clip	6	6 (100%)	2 (33%)	N/A	N/A	N/A

N/A, not available; SD, standard deviation.

- (2) Epinephrine injection might be effective for temporary hemostasis prior to the definitive treatment if massive bleeding occurs, owing to its vasoconstrictive and mechanical effects. Epinephrine injection therapy is insufficient for curative homeostasis.^{3,8,22,23,25,26}
- (3) Considering the long-term outcomes, EBL might be the best available option for endoscopic hemostasis. In some cases, the patients' anatomy makes the O-ring ligation difficult.^{25,26} In those patients, it is advisable to switch to EC or thermal contact therapy as the definitive treatment.^{3,4,8,18,22,23,25,26}

CONCLUSIONS

The present review indicates that various endoscopic therapies allow a secure initial hemostasis for diverticular bleeding. However, the existing endoscopic therapies have still not solved the issues of high rates of early and late re-bleeding (Table 1). With regard to a cure for diverticular bleeding, not only the endoscopic methods but also the multilateral perspectives, such as the diet, medicines, interventional approaches, and surgery, should be improved at present.

Conflicts of Interest

The author has no financial conflicts of interest.

Acknowledgements

I express my gratitude to Dr. Hiroko Inomata for her beautiful schema of the manuscript.

REFERENCES

1. Oakland K, Guy R, Uberoi R, et al. Acute lower GI bleeding in the UK: patient characteristics, interventions and outcomes in the first nationwide audit. *Gut* 2018;67:654-662.
2. Nagata N, Niikura R, Aoki T, et al. Role of urgent contrast-enhanced multidetector computed tomography for acute lower gastrointestinal bleeding in patients undergoing early colonoscopy. *J Gastroenterol* 2015;50:1162-1172.
3. Ishii N, Hirata N, Omata F, et al. Location in the ascending colon is a predictor of refractory colonic diverticular hemorrhage after endoscopic clipping. *Gastrointest Endosc* 2012;76:1175-1181.
4. Jensen DM, Machicado GA, Jutabha R, Kovacs TO. Urgent colonoscopy for the diagnosis and treatment of severe diverticular hemorrhage. *N Engl J Med* 2000;342:78-82.
5. Stollman N, Raskin JB. Diverticular disease of the colon. *Lancet* 2004;363:631-639.
6. Meyers MA, Alonso DR, Baer JW. Pathogenesis of massively bleeding colonic diverticulosis: new observations. *AJR Am J Roentgenol* 1976;127:901-908.
7. Frattaroli FM, Casciani E, Spoletini D, et al. Prospective study comparing multi-detector row CT and endoscopy in acute gastrointestinal bleeding. *World J Surg* 2009;33:2209-2217.
8. Kaltenbach T, Watson R, Shah J, et al. Colonoscopy with clipping is useful in the diagnosis and treatment of diverticular bleeding. *Clin Gastroenterol Hepatol* 2012;10:131-137.
9. Strate LL, Gralnek IM. ACG clinical guideline: management of patients with acute lower gastrointestinal bleeding. *Am J Gastroenterol* 2016;111:459-474.
10. Strate LL, Syngal S. Predictors of utilization of early colonoscopy vs. radiography for severe lower intestinal bleeding. *Gastrointest Endosc* 2005;61:46-52.
11. García-Blázquez V, Vicente-Bártulos A, Olavarria-Delgado A, Plana MN, van der Winden D, Zamora J. Accuracy of CT angiography in the diagnosis of acute gastrointestinal bleeding: systematic review and meta-analysis. *Eur Radiol* 2013;23:1181-1190.
12. Lim DS, Kim HG, Jeon SR, et al. Comparison of clinical effectiveness of the emergent colonoscopy in patients with hematochezia according to the type of bowel preparation. *J Gastroenterol Hepatol* 2013;28:1733-1737.
13. Jensen DM, Ohning GV, Kovacs TO, et al. Natural history of definitive diverticular hemorrhage based on stigmata of recent hemorrhage and colonoscopic Doppler blood flow monitoring for risk stratification and definitive hemostasis. *Gastrointest Endosc* 2016;83:416-423.
14. Saito K, Inamori M, Sekino Y, et al. Management of acute lower intestinal bleeding: what bowel preparation should be required for urgent colonoscopy? *Hepatogastroenterology* 2009;56:1331-1334.
15. Smoot RL, Gostout CJ, Rajan E, et al. Is early colonoscopy after admission for acute diverticular bleeding needed? *Am J Gastroenterol* 2003;98:1996-1999.
16. Shibata S, Shigeno T, Fujimori K, Kanai K, Yoshizawa K. Colonic diverticular hemorrhage: the hood method for detecting responsible diverticula and endoscopic band ligation for hemostasis. *Endoscopy* 2014;46:66-69.
17. Niikura R, Nagata N, Aoki T, et al. Predictors for identification of stigmata of recent hemorrhage on colonic diverticula in lower gastrointestinal bleeding. *J Clin Gastroenterol* 2015;49:e24-e30.
18. Bloomfeld RS, Rockey DC, Shetzline MA. Endoscopic therapy of acute diverticular hemorrhage. *Am J Gastroenterol* 2001;96:2367-2372.
19. Green BT, Rockey DC, Portwood G, et al. Urgent colonoscopy for evaluation and management of acute lower gastrointestinal hemorrhage: a randomized controlled trial. *Am J Gastroenterol* 2005;100:2395-2402.
20. Iqbal CW, Cullinane DC, Schiller HJ, Sawyer MD, Zietlow SP, Farley DR. Surgical management and outcomes of 165 colonoscopic perforations from a single institution. *Arch Surg* 2008;143:701-706; discussion 706-707.
21. Ishii N, Omata F, Nagata N, Kaise M. Effectiveness of endoscopic treatments for colonic diverticular bleeding. *Gastrointest Endosc* 2018;87:58-66.
22. Couto-Worner I, González-Conde B, Estévez-Prieto E, Alonso-Aguirre P. Colonic diverticular bleeding: urgent colonoscopy without purging and endoscopic treatment with epinephrine and hemoclips. *Rev Esp Enferm Dig* 2013;105:495-498.
23. Yen EF, Ladabaum U, Muthusamy VR, Cello JP, McQuaid KR, Shah JN. Colonoscopic treatment of acute diverticular hemorrhage using endoclips. *Dig Dis Sci* 2008;53:2480-2485.
24. Kume K, Yamasaki M, Yoshikawa I. Sepsis caused by endoscopic clipping for colonic diverticular bleeding: a rare complication. *World J Gastroenterol* 2009;15:3817-3818.
25. Ishii N, Setoyama T, Deshpande GA, et al. Endoscopic band ligation for colonic diverticular hemorrhage. *Gastrointest Endosc* 2012;75:382-387.
26. Nakano K, Ishii N, Ikeya T, et al. Comparison of long-term outcomes between endoscopic band ligation and endoscopic clipping for colonic diverticular hemorrhage. *Endosc Int Open* 2015;3:E529-E533.
27. Takahashi S, Inaba T, Tanaka N. Delayed perforation after endoscopic band ligation for treatment of colonic diverticular bleeding. *Dig Endosc* 2016;28:484.
28. Sundaram CP, Keenan AC. Evolution of hemostatic agents in surgical

- practice. *Indian J Urol* 2010;26:374-378.
29. Goker H, Haznedaroglu IC, Ercetin S, et al. Haemostatic actions of the folkloric medicinal plant extract Ankaferd blood stopper. *J Int Med Res* 2008;36:163-170.
 30. ASGE Technology Committee, Wong Kee Song LM, Banerjee S, et al. Emerging technologies for endoscopic hemostasis. *Gastrointest Endosc* 2012;75:933-937.
 31. Giday SA, Kim Y, Krishnamurthy DM, et al. Long-term randomized controlled trial of a novel nanopowder hemostatic agent (TC-325) for control of severe arterial upper gastrointestinal bleeding in a porcine model. *Endoscopy* 2011;43:296-299.
 32. Sung JJ, Luo D, Wu JC, et al. Early clinical experience of the safety and effectiveness of Hemospray in achieving hemostasis in patients with acute peptic ulcer bleeding. *Endoscopy* 2011;43:291-295.
 33. Smith LA, Stanley AJ, Bergman JJ, et al. Hemospray application in non-variceal upper gastrointestinal bleeding: results of the survey to evaluate the application of Hemospray in the luminal tract. *J Clin Gastroenterol* 2014;48:e89-e92.
 34. Chen YI, Barkun AN, Soulellis C, Mayrand S, Ghali P. Use of the endoscopically applied hemostatic powder TC-325 in cancer-related upper GI hemorrhage: preliminary experience (with video). *Gastrointest Endosc* 2012;75:1278-1281.
 35. Holster IL, Kuipers EJ, Tjwa ET. Hemospray in the treatment of upper gastrointestinal hemorrhage in patients on antithrombotic therapy. *Endoscopy* 2013;45:63-66.
 36. Holster IL, Brullet E, Kuipers EJ, Campo R, Fernández-Atutxa A, Tjwa ET. Hemospray treatment is effective for lower gastrointestinal bleeding. *Endoscopy* 2014;46:75-78.
 37. Aslan E, Akyüz Ü, Pata C. The use of Ankaferd in diverticular bleeding: two case reports. *Turk J Gastroenterol* 2013;24:441-443.
 38. Chen YI, Barkun AN. Hemostatic powders in gastrointestinal bleeding: a systematic review. *Gastrointest Endosc Clin N Am* 2015;25:535-552.
 39. Mourad FH, Leong RW. Role of hemostatic powders in the management of lower gastrointestinal bleeding: a review. *J Gastroenterol Hepatol* 2018;33:1445-1453.
 40. Matthes K, Jung Y, Kato M, Gromski MA, Chuttani R. Efficacy of full-thickness GI perforation closure with a novel over-the-scope clip application device: an animal study. *Gastrointest Endosc* 2011;74:1369-1375.
 41. Weiland T, Fehlker M, Gottwald T, Schurr MO. Performance of the OTSC system in the endoscopic closure of iatrogenic gastrointestinal perforations: a systematic review. *Surg Endosc* 2013;27:2258-2274.
 42. Shoar S, Poliakin L, Khorgami Z, et al. Efficacy and safety of the over-the-scope clip (OTSC) system in the management of leak and fistula after laparoscopic sleeve gastrectomy: a systematic review. *Obes Surg* 2017;27:2410-2418.
 43. Wedi E, von Renteln D, Jung C, et al. Treatment of acute colonic diverticular bleeding in high risk patients, using an over-the-scope clip: a case series. *Endoscopy* 2016;48:E383-E385.
 44. Longstreth GF. Epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage: a population-based study. *Am J Gastroenterol* 1997;92:419-424.
 45. Tanaka Y, Motomura Y, Akahoshi K, et al. Predictive factors for colonic diverticular rebleeding: a retrospective analysis of the clinical and colonoscopic features of 111 patients. *Gut Liver* 2012;6:334-338.
 46. Aytac E, Stocchi L, Gorgun E, Ozuner G. Risk of recurrence and long-term outcomes after colonic diverticular bleeding. *Int J Colorectal Dis* 2014;29:373-378.
 47. Niikura R, Nagata N, Yamada A, Akiyama J, Shimbo T, Uemura N. Recurrence of colonic diverticular bleeding and associated risk factors. *Colorectal Dis* 2012;14:302-305.
 48. Nishikawa H, Maruo T, Tsumura T, Sekikawa A, Kanesaka T, Osaki Y. Risk factors associated with recurrent hemorrhage after the initial improvement of colonic diverticular bleeding. *Acta Gastroenterol Belg* 2013;76:20-24.
 49. Okamoto T, Watabe H, Yamada A, Hirata Y, Yoshida H, Koike K. The association between arteriosclerosis related diseases and diverticular bleeding. *Int J Colorectal Dis* 2012;27:1161-1166.