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Outcomes of Regular-Dose Therapeutic Barium Enema as an Initial Treatment for Diverticular Hemorrhage

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Abstract

Purpose: Therapeutic barium enema (TBE) for hemostasis in diverticular hemorrhage was first reported in 1970. This retrospective study examines the outcomes of TBE use since 2008 at our hospital.

Methods: Fifty-four patients who presented with melena were diagnosed with diverticular hemorrhage based on computed tomography (CT) findings and subsequently underwent TBE between November 2008 and February 2017 (a period of approximately eight years and three months) at our hospital. Findings suggesting extravasation of a contrast agent, the number of TBE treatments received, and the hemostatic outcomes were retrospectively examined. Success or failures of the TBE were defined as the presence or absence of melena during the post-TBE hospital stay, respectively. Re-bleeding was defined as melena occurring after discharge from the hospital.

Results: Dynamic CT was performed in 48 of the 54 patients, and extravasation of the contrast agent was confirmed in 46% of the patients (25 patients). Among the 25 patients with active hemorrhage, only two patients did not achieve hemostasis, indicating that there is no difference in hemostasis outcome with and without extravasation. Only six of the 54 patients had re-bleeding during their post-TBE hospital stay.

Conclusions: TBE achieved a hemostatic rate of either 89% (excluding repeat TBE cases) or 94% (including repeat TBE cases) for diverticular hemorrhage. TBE is an effective therapy for the treatment of active hemorrhage when there are no contraindications due to severe systemic conditions, such as hemorrhagic shock.

Keywords: Diverticular hemorrhage; Extravasation; Barium; Enema; Hemostasis

Introduction

In industrialized countries with aging populations, the frequency of diverticular hemorrhage is increasing with the expanding use of non-steroidal anti-inflammatory drugs (NSAIDs), antiplatelet agents, and anticoagulants for the treatment of vascular diseases [1,2]. However, the rate of its endoscopic diagnosis is not high (21-55%) [1,3], and the presumptive diagnosis is currently made based on primary computed tomography (CT) findings (exclusion of other disorders, presence of a diverticulum, and presence of colonic hematoma). Despite the availability of several hemostatic treatments (e.g. endoscopic hemostasis, trans arterial embolization, and surgical resection), a treatment algorithm and gold standard for the management of diverticular hemorrhage have not been established to date.

Since its first report in 1970 [4], the hemostatic efficacy of therapeutic barium enema (TBE) using a barium sulfate contrast agent has been demonstrated [5-8]. However, high-dose suspensions (150-200 (w%/v%)) are used in most cases, and off-label concentrations are available in Japan, where 20-120 (w%/v %) barium suspensions are used for lower gastrointestinal series. In 2008, our hospital started performing TBE with a regular-dose barium suspension (70-100 (w%/v%) in accordance with the reimbursement rules) for hemostasis in patients presenting with melena who were diagnosed with diverticular hemorrhage based on CT findings (after exclusion of other disorders and confirmation of diverticulum and intracolonic hematoma (sometimes active bleeding)). This study retrospectively examined the outcomes of TBE.

Materials and Methods

Study design

This study received approval from the institutional review board. The subjects were 54 patients with a chief complaint of melena who were diagnosed with diverticular hemorrhage based on CT findings and subsequently received TBE at our hospital over a period of eight years and three months between November 2008 and February 2017. Fifty-seven percent of the subjects were men, and three subjects were under 50 years of age (**Table 1**). Contraindications for TBE included conditions requiring emergency treatment (e.g. Hemorrhagic shock or disturbance of consciousness) and those prohibiting changes in the patient's positions.

Table 1: Age and gender.

Age/Gender	Male	Female	Total
49	2	1	3 (5%)
5064	9	4	12 (22%)
6574	9	7	10 (19%)
75	11	11	14 (26%)
Total	31 (57%)	23 (43%)	54

Computed tomography (CT)

Plain, early phase, and equilibrium phase imaging of the area from the superior margin of the diaphragm to the inferior margin of the symphysis pubis was generally performed. Reconstruction was performed to obtain images of these three phases with axial (3-mm slice/3-mm pitch) and coronal (5-mm slice/5-mm pitch) slices. A non-ionic contrast agent (300 mg I/mL) at a dose of 2 mL/kg of body weight (100 mL in a patient weighing 50 kg) was auto-injected at 30s, and the artificial phase and equilibrium phase imaging was started 50s and 150s after injection of the contrast agent, respectively **Figure 1**.

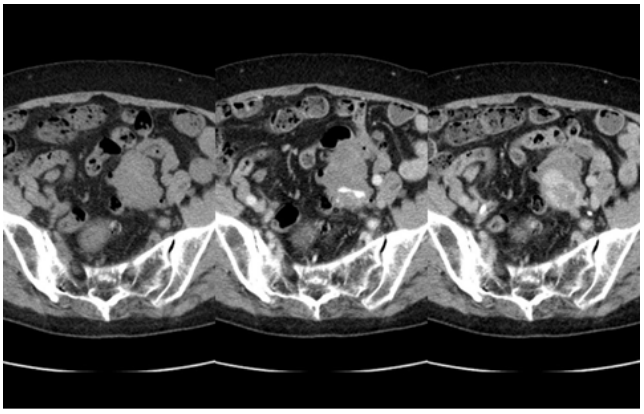

Figure 1: Dynamic CT shows extravasation from a diverticulum.

Diagnosis of diverticular hemorrhage

Diverticular hemorrhage was diagnosed when the CT findings excluded the possibility of small bowel disease, ischemic colitis, large tumour of the colon, intussusception, and infectious colitis, confirmed the diverticular structure, and confirmed an intracolonic hematoma with a density similar to or higher than that of the soft tissue. Additionally, the site of extravasation of a contrast agent adjacent to the diverticulum (if observed) was regarded as the site of active hemorrhage. When extravasation was not observed, the location of the hematoma was used to predict the bleeding site.

Patients with bronchial asthma, an iodine allergy, and/or renal dysfunction underwent plain imaging only, and diverticular hemorrhage was diagnosed when the above criteria were met.

Enema

A radiologist diagnosed diverticular hemorrhage and informed the doctor in charge of the diagnostic outcome. Then, TBE was urgently performed after consent was obtained from the patient. In principle, a resident radiologist performed the TBE. A 75 (w%/v%) barium sulfate suspension was prepared, of which 800 mL was placed in an enema bag (enema unit), and 400 mL of a 75 (w%/v%) suspension or 300 mL of a 100 (w%/v%) suspension was added when needed during the procedure. A urethral balloon catheter (24 Fr) was used as an enema tube when digital palpation confirmed anal dilation.

After insertion of the tube, the barium suspension was injected after moving the patient into the prone position. The enema bag was placed at a one-meter height from the patient to allow the intracolonic pressure to be maintained below the systolic blood pressure. Air was not injected, and a barium-filling method was used. A contrast agent was injected under fluoroscopic guidance until it reached the ileocecum, and the patient's position was changed in the following order: right lateral decubitus position, supine position, and head-up tilt position. The contrast agent was retained for 15 min each in the spine position and the prone position and finally recovered from the rectum (**Figure 2**).

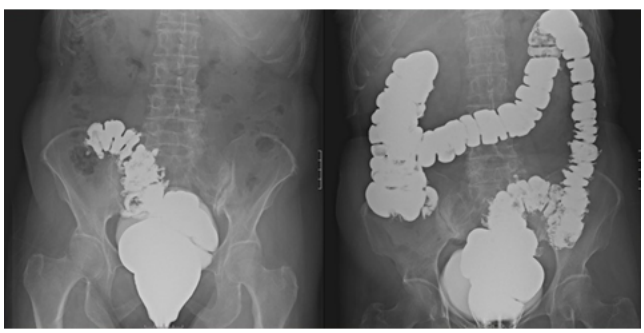

Figure 2: Therapeutic barium enema (TBE). Barium is filled in the diverticulums.

Outcome parameters

Success or failures of the TBE were defined as the presence or absence of melena during the post-TBE hospital stay, respectively. Re-bleeding was defined as melena that reoccurred after discharge from the hospital that led to a revisit to our hospital. The characteristics of the patients who were examined were age, gender, CT scans (performed or not), dynamic study (performed or not), findings suggesting extravasation of the contrast agent (present or absent), site of diverticulum, NSAIDs, antiplatelet agents and anticoagulants (administered or not), amount of barium sulfate used, surgery (performed or not), and duration of the hospital stay. The hemostasis rates (overall and in extravasation cases), the rate of patients who underwent a pre-TBE endoscopy, and details of re-bleeding (if appropriate) were also examined.

Statistical analysis

Data were tested by using the Mann-Whitney test according to the normality assumption. We compared between two groups with or without extravasation. The statistical significance level was set at $P<0.05$.

Results

CT was performed on the day of hospital admission. A dynamic study was performed in 48 cases (89%), 46% of which (25 cases) were the result of extravasation of a contrast agent. A source of bleeding was located by endoscopy in three of the six cases without a dynamic study. The ascending colon (28 cases, 52%) was the most common site of diverticulum formation, followed by the sigmoid colon (12 cases, 22%), descending colon (five cases), and cecum (one case); the site was not identified in six cases (i.e., the dynamic study did not confirm the site of bleeding).

The success rate of TBE was 89% (48/54). Among the six cases of hemostasis failure, three cases achieved hemostasis via a repeat TBE, whereas bleeding was stopped without any treatment in two cases. In the remaining case, the post-TBE course was good, the hospital discharge was scheduled, and planned rivaroxaban therapy in the hospital was restarted. However, re-bleeding occurred one day after restarting rivaroxaban therapy, and an emergency colectomy was performed to treat hemorrhagic shock. NSAIDs, antiplatelet agents, or anticoagulants were used in 25 cases (60%). Hemostasis was achieved in 23 of 25 extravasation cases, indicating no differences in the hemostatic outcome in this group (**Table 2**).

Pre-TBE endoscopy was performed in 11 of the 36 cases with a difficult differential diagnosis, including those in the early stage of TBE introduction at our hospital and those with an absence of imaging findings suggesting extravasation. A diverticulum was confirmed in all cases. Hemostatic intervention was performed to treat a diverticulum with active bleeding (two cases) or suspected previous bleeding (two cases). Melena continued after endoscopic hemostasis in these cases. The endoscope could not reach the bleeding site in two cases, and endoscopy did not confirm active diverticular bleeding in five cases. TBE was performed after endoscopy, and hemostasis was achieved in all 11 cases.

Table 2: Characteristics of two group with or without Extravasation (*Calculated with Mann-Whitney test).

	Extravasation (+) (n=25)	Extravasation (-) (n=23)	P Value
Age (y)	73 ± 36	67 ± 27	0.137
Male to female ratio	14:11	15:08	0.518
Bleeding site			
Cecum	1	0	
A-Colon	14	14	
D-Colon	3	3	
S-Colon	7	5	
unknown	0	6	
Antiplatelet or anticoagulant agents + : -	11:14	11:12	0.792
Success : Failure	24:01:00	19:04	0.133

The mean follow-up period was approximately 32 months. Post-discharge re-bleeding was confirmed in three cases. NSAID, antiplatelet, or anticoagulant therapy was restarted in all three cases; the shortest and longest intervals were approximately one month and three years and five months, respectively **Table 3**.

Table 3: Rebleeding cases after discharge.

Period until rebleeding			Back ground and progress
1	88M	39 days	After discharge Rivaroxaban therapy was restarted → TBE
2	75F	75 days	After discharge Trapidil was restarted→TBE
3	54M	3 years 5 months	After discharge 3 anticoagulant agents therapy was restarted → TBE

The volume of the barium suspension used was less than 800 mL in 21 cases (39%), 800-1,200 mL in 25 cases (46%), >1200 mL in seven cases (13%), and unknown in one case. The volume was greater than 800 mL in approximately two-thirds of the cases. Complications after TBE were absent, and catheter or balloon dislocation was not observed. A colonoscopy was performed to confirm the absence of a malignancy before hospital discharge when the patient's condition was stable or at an outpatient visit otherwise.

Discussion

Diverticular hemorrhage accounts for 17-40% of total lower gastrointestinal hemorrhage cases in adults and is the most common cause of lower gastrointestinal hemorrhage in adults

aged 60 years and over [9]. In patients presenting with melena, CT is beneficial for narrowing down the cause of melena and the site of bleeding [10]. Furthermore, a dynamic study that enabled visualization of active bleeding confirmed the bleeding site in 43% of the cases. Diverticular formation in the right colon is more common in Japan, and bleeding is heavier in a bilateral diverticular haemorrhage [11]. The success rate of standard endoscopy in confirming the bleeding site represented by stigmata of recent hemorrhage (SRH) is low (30-40%) [12,13], which is attributed to the considerable distance between the bleeding site and the anus and poor visibility due to bleeding; the re-bleeding rate after clipping and band ligation is reported to be 11-22% [14,15]. Surgery and vascular embolization are effective when endoscopic hemostasis is difficult [16]. Colectomy is a reliable hemostatic intervention when the bleeding site is identified. However, this procedure is invasive and is associated with a high rate of complications, because the resection area becomes larger if the bleeding site is not identified, and mortality can be as high as approximately 33% [17]. Formation of another diverticulum post-colectomy can also occur. Regarding vascular embolization, a total of three or fewer vasa recta adjacent to the bleeding vessel should be embolized, because inclusion of a wider area will cause bowel ischemia that requires intestinal resection in many cases [18]. A bleeding site may remain unknown after angiography. A specificity of 100% and sensitivities of 47% and 30% for primary bleeding and re-bleeding, respectively, have been reported [19]. There is no gold standard established for treatment of diverticular hemorrhage, and the current therapies used vary among medical institutions.

In this study, the hemostasis rate of TBE for the treatment of diverticular hemorrhage was 89% and rose to 94% when cases of repeat TBE for re-bleeding were included. Hemostasis was achieved in 23 of 25 cases of dynamic CT-confirmed extravasation (92%), and there was no significant difference in hemostasis rate with or without extravasation, indicating its benefit (TBE was not completed in one case). The tamponade effect of barium and the hemostatic effect of barium sulfate itself were implicated in the hemostasis achieved by TBE, but the details were unclear [4,20-22]. The benefits of TBE on the failure of endoscopy to identify SRH have also been reported [5]. The entire colon was filled with barium, and thus, the hemostatic effect could be expected to be equal across all diverticula even if the sites of bleeding were unidentified in cases of multiple diverticula. Furthermore, TBE can be performed in patients with contraindications (e.g. renal dysfunction and iodine allergy) for use of an iodine contrast agent and in those who cannot undergo surgery.

TBE is strictly indicated for diverticular hemorrhage and cannot be performed in patients with conditions requiring emergency treatment (e.g. hemorrhagic shock or disturbance of consciousness) and those with conditions prohibiting changes in their position. Repeat TBE is performed in re-bleeding cases, because endoscopy and vascular embolization are difficult to perform due to residual barium within the colon. Surgery is chosen when the patient's condition deteriorates and requires urgent treatment. Nagata et al. performed a randomized controlled study to compare the prognosis of high-dose TBE (barium concentration 200 (w%/v%); volume 400 mL) for diverticular hemorrhage between a TBE hemostasis group and a natural hemostasis group (case number ratio: 27:27) and showed that the re-hospitalization rate, duration of the hospital stay, number of transfusion units, and rate of colonoscopy performed were significantly lower in the former group than in the latter group, indicating the efficacy of TBE [7].

Diverticular hemorrhage frequently occurs in the elderly, which was confirmed in this study. Most of the patients had a concomitant disease, and 46% were on NSAID, antiplatelet, or anticoagulant therapy. These therapies reduce the thromboembolic risk, but the possibility of inducing cerebral and acute gastrointestinal hemorrhage cannot be eliminated. This study showed that the hemostasis rate of initial TBE using a regular dose of barium was 89%, which demonstrated a hemostatic effect versus the 70-80% dose for the rate of spontaneous hemostasis [23]. The efficacy of high-dose TBE was reported by Nagata et al. and regular-dose TBE, although it was retrospectively examined in this study, was likely to have a similar level of hemostatic effect. In addition, our lower dose barium hemostatic rate was superior to the previous high dose barium report [8]. This is presumed to be due to the low consistency of barium, easy to reach the ascending colon, easy to fill the diverticulum and the high pressure due to the large injection volume itself.

We employed a barium-filling method without air injection, and thus, tube dislocation rarely occurred. Additionally, use of a barium suspension at a regular concentration may have made filling of the colon easier. To the best of our knowledge, only one case of ileus and one case of perforation have been reported after TBE [8,24]. However, no complications were observed in this study, indicating the safety of TBE. Our study was limited by its retrospective nature, and we could not exclude the selection bias on the study outcomes, because we could not calculate the total number of diverticular bleeding in our institution. Therefore, another limitation was that we could not directly compare TBE and other treatments.

Reports of TBE outcomes are currently being accumulated, but the procedure has not been standardized to date. Standardization of a less complicated procedure together with investigation and elucidation of the mechanisms involved in hemostasis in acute bleeding is crucial for wider recognition of TBE as a first-line option for the treatment of diverticular hemorrhage. Regular-dose TBE is likely to be safer and easier to perform, and thus, more clinical data need to be accumulated.

Conclusion

The outcome of regular-dose TBE for the treatment of diverticular hemorrhage was favourable at our hospital, achieving an overall hemostasis rate of 94%. TBE does not require sophisticated technology, repeatable, and can be performed in patients who cannot undergo surgery as long as they have a certain level of mobility on a medical fluoroscopy table. When it can be performed, regular-dose TBE is likely to serve as a sufficient effective initial therapy even in active diverticular hemorrhage, as confirmed by the presence of extravasation by diagnostic imaging.

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