

Gastrointestinal bleeding from Dieulafoy's lesion: Clinical presentation, endoscopic findings, and endoscopic therapy

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tract which become progressively smaller in caliber peripherally, Dieulafoy's lesions maintain a large caliber despite their peripheral, submucosal, location within gastrointestinal wall. Dieulafoy's lesions typically present with severe, active, gastrointestinal bleeding, without prior symptoms; often cause hemodynamic instability and often require transfusion of multiple units of packed erythrocytes. About 75% of lesions are located in the stomach, with a marked proclivity of lesions within 6 cm of the gastroesophageal junction along the gastric lesser curve, but lesions can also occur in the duodenum and esophagus. Lesions in the jejunoleum or colorectum have been increasingly reported. Endoscopy is the first diagnostic test, but has only a 70% diagnostic yield because the lesions are frequently small and inconspicuous. Lesions typically appear at endoscopy as pigmented protuberances from exposed vessel stumps, with minimal surrounding erosion and no ulceration (visible vessel sans ulcer). Endoscopic therapy, including clips, sclerotherapy, argon plasma coagulation, thermocoagulation, or electrocoagulation, is the recommended initial therapy, with primary hemostasis achieved in nearly 90% of cases. Dual endoscopic therapy of epinephrine injection followed by ablative or mechanical therapy appears to be effective. Although banding is reportedly highly successful, it entails a small risk of gastrointestinal perforation from banding deep mural tissue. Therapeutic alternatives after failed endoscopic therapy include repeat endoscopic therapy, angiography, or surgical wedge resection. The mortality has declined from about 30% during the 1970's to 9%-13% currently with the advent of aggressive endoscopic therapy.

Key words: Dieulafoy's lesion; Gastrointestinal bleeding

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Core tip: Dieulafoy's lesion is an important cause of acute gastrointestinal bleeding. Dieulafoy's lesions maintain an abnormally large caliber despite their

Abstract

Although relatively uncommon, Dieulafoy's lesion is an important cause of acute gastrointestinal bleeding due to the frequent difficulty in its diagnosis; its tendency to cause severe, life-threatening, recurrent gastrointestinal bleeding; and its amenability to life-saving endoscopic therapy. Unlike normal vessels of the gastrointestinal

peripheral, submucosal, location. Dieulafoy's lesions typically present with severe, active, gastrointestinal bleeding. About 75% of lesions are located in the stomach, most commonly close to the gastroesophageal junction, but lesions can occur in duodenum and esophagus. Endoscopy is the first diagnostic test (70% diagnostic yield). Lesions typically appear at endoscopy as pigmented protuberances from exposed vessel stumps, with minimal surrounding erosions. Endoscopic therapy, including clips, sclerotherapy, argon plasma coagulation, thermocoagulation, or electrocoagulation, is the recommended initial therapy, with primary hemostasis achieved in nearly 90% of cases. Mortality of bleeding from this lesion is 9%-13%.

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INTRODUCTION

Although relatively uncommon, Dieulafoy's lesion represents an important etiology of acute gastrointestinal (GI) bleeding because of its propensity to cause massive, life-threatening, and recurrent bleeding; and its amenability to life-saving endoscopic therapy. It most commonly causes upper GI bleeding^[1], but can also cause middle GI bleeding (defined as bleeding localized between the ampulla of Vater and the cecum^{[2],[3]}), and rarely cause lower GI bleeding^[4], depending upon the location of the lesion. Numerous, recent, small, retrospective studies have analyzed the efficacy and safety of individual endoscopic therapies for this lesion, but these studies generally lack a comprehensive review of the literature. This work comprehensively reviews the pathophysiology, epidemiology, clinical presentation, endoscopic diagnosis, and endoscopic therapy of Dieulafoy's lesions, with an emphasis on recent studies of endoscopic therapy.

BRIEF HISTORY

Although first reported by Gallard^[5] in 1884, Dieulafoy's lesion was more precisely described 14 years later by the French surgeon, Georges Dieulafoy^[6]. He reported fatal GI hemorrhage in three, asymptomatic, young, male patients caused by large, actively bleeding, blood vessels within the stomach associated with small ulcers, which he called "exulceratio simplex", as he erroneously believed these lesions were early peptic ulcers. Since then, a multitude of cases of Dieulafoy's lesions have been reported throughout the world^[7,8]. The lesion nomenclature has been variable, including the following alternative names: caliber-persistent

artery, gastric arteriosclerosis, cirroid aneurysm, and submucosal arterial malformation^[9]. However, the most commonly accepted name is Dieulafoy's lesion, even though the term caliber-persistent artery has the virtue of aptly summarizing its pathophysiology. The term gastric arteriosclerosis is to be avoided because the pathophysiology does not involve arteriosclerosis or atherosclerosis. Likewise, the term cirroid aneurysm should be avoided because the pathophysiology does not involve an aneurysm.

PATHOPHYSIOLOGY

The lesion is defined anatomically as a dilated, aberrant, submucosal artery that erodes overlying GI mucosa in the absence of an underlying ulcer, aneurysm, or intrinsic mural abnormality^[10]. Unlike the normal arterial tree, which like branches of a tree, progressively narrows when approaching distal branches, Dieulafoy's lesion maintains constant arterial caliber, of approximately 1-3 mm, despite its very distal, submucosal location within the GI wall^[7]. This caliber is up to ten-fold larger than the normal maximal caliber of such submucosal vessels. The aberrant artery can protrude through a small mucosal defect, become susceptible to even minor mechanical trauma (e.g., passage of food bolus in stomach or solid stool in colon), and eventually erode into the lumen to cause severe acute GI bleeding. Each arterial pulsation transmits mechanical pressure that may traumatize the fragile, thin layer of mucosa overlying the vessel. Alternatively, enhanced blood flow through the enlarged artery may cause hypoperfusion, ischemia, and erosion of overlying mucosa from shunting and redistribution of blood perfusion^[11]. This hypothesized "vascular steal" phenomenon resembles that which produces a pale mucosal halo that sometimes surrounds angiodysplasia^[12]. Chronic age-related mucosal wear and tear and atrophy may explain the tendency for this bleeding to generally present in older age^[8].

About 70% of lesions occur in the stomach^[8,9]. The proximal stomach, in particular within 6 cm from the gastroesophageal junction and along the lesser gastric curve, is the most common gastric location, accounting for about 75% of all gastric lesions (Table 1)^[13,14]. This proclivity is attributed to the blood supply to this area coming directly from the arterial chain running along the lesser gastric curve because the usual submucosal, arterial anastomotic gastric plexus is absent in this area^[15]. Other common lesion locations include duodenum (15% prevalence)^[7,9], distal stomach (12% prevalence)^[8], and esophagus (8% prevalence)^[16]. However, recent publications, consisting mostly of case reports or limited case series, also report Dieulafoy's lesions of the jejunum^[3,17], ileum^[17-21], cecum^[22], appendix^[23], colon^[24,25], rectum^[26], and anal canal^[27] which present with lower GI bleeding. Figure 1 summarizes the approximate distribution of bleeding Dieulafoy's lesions within the GI tract. Also,

Table 1 Clinico-epidemiologic characteristics of Dieulafoy lesion

Anatomy	Dilated, aberrant, submucosal artery eroding overlying gastrointestinal mucosa in absence of either underlying ulcer or local aneurysm
Location	70% of ulcers in stomach In stomach most commonly located within 6 cm of gastroesophageal junction along lesser curve Can occur moderately commonly in esophagus or duodenum, occasionally in jejunum or ileum, and rarely in colon
Epidemiology	Generally presents clinically in older age, but can occur at any age Male:female ratio = 2:1 No known epidemiologic risk factors or clinically associated diseases
Clinical presentation	Typically presents with overt GI bleeding, often with hematemesis or melena, or both Bleeding typically severe No prodromal symptoms Typically bleeding is painless Frequent presentation with signs or laboratory tests of hemodynamic instability, including: tachycardia, hypotension, orthostasis, and acute prerenal azotemia Frequently requires transfusion of multiple units of packed erythrocytes Frequent recurrent bleeding if undetected or not treated at initial endoscopy

GI: Gastrointestinal.

extra-gastrointestinal locations of Dieulafoy-like lesions can present with acute non-gastrointestinal bleeding, such as bronchial Dieulafoy's lesion presenting with hemoptysis^[28].

It is unknown if this lesion is inherited or acquired^[29]. It has not been associated with genetic mutations. The generally older age of patients with Dieulafoy's lesion might suggest an acquired defect. Contrariwise, the propensity of these lesions to be located within 6 cm of the gastroesophageal junction might reflect a congenital defect. While the pediatric literature suggests that the tortuous, dilated artery with a variable course length may represent a congenital anomaly^[30], scant data supports familial predisposition in adults^[7].

EPIDEMIOLOGY

Dieulafoy's lesion is responsible for approximately 1.5% of acute upper GI bleeding^[14,31], and is responsible for approximately 3.5% of jejunoileal GI bleeding^[17]. For example, in a recent, retrospective, multicenter, study of 284 patients with suspected overt or occult small intestinal bleeding who underwent 317 double-balloon and 78 single-balloon enteroscopies, 10 patients (3.5%) had Dieulafoy's lesion in the jejunum or ileum as the bleeding etiology^[17]. Most of the small bowel lesions were located in the jejunum. Colonic Dieulafoy's lesion is presumably rare; less than 30 cases have been reported since three patients with colonic Dieulafoy's lesion were first reported in 1985^[24,32,33].

Epidemiologic characteristics of patients with Dieulafoy's lesions have been described. The lesion

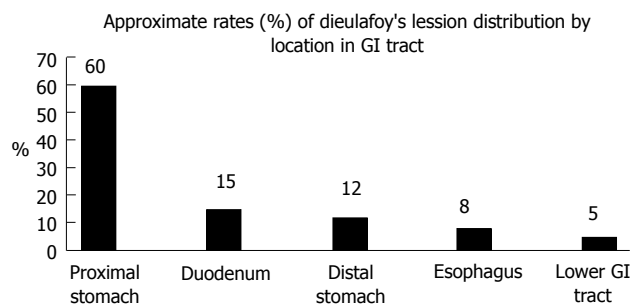


Figure 1 Segmental distribution of Dieulafoy's lesion within the gastrointestinal tract in patients presenting with acute gastrointestinal bleeding. GI: Gastrointestinal.

is reportedly more common in males than females, with a sex ratio of 2:1^[8,20,34]. It can occur at any age^[7,8], although older series reported a predisposition towards advanced age, with most cases presenting in the sixth or seventh decades^[14,35]. Affected patients often have non-gastrointestinal comorbidities such as cardiovascular disease, hypertension, diabetes, and chronic renal insufficiency. Also, affected patients are often administered non-steroidal anti-inflammatory drugs (NSAIDs) or anticoagulants most likely because these drugs promote bleeding from underlying Dieulafoy's lesions which results in clinical detection^[10,36]. No causal link has, however, been found between Dieulafoy's lesions and use of NSAIDs, alcohol or tobacco; or the presence of peptic ulcer disease or *Helicobacter pylori* infection^[10,15,36-38].

CLINICAL PRESENTATION

Patients are typically asymptomatic before presenting with acute, profuse GI bleeding, which can manifest as hematemesis, melena, or hematochezia^[39,40]. Approximately half of patients present with both hematemesis and melena^[9]. For example, in a review of 177 cases, 51% presented with hematemesis and melena, 28% of patients presented with hematemesis, and 18% presented with melena alone^[40]. Patients with colonic Dieulafoy's lesions typically present with profuse bright red blood per rectum. The bleeding is typically severe, attributed to the arterial nature of the bleeding and the enlarged arterial vessel (Table 1). Patients rarely present with chronic, occult, GI bleeding. Signs of hemodynamic instability such as tachycardia, hypotension, and orthostasis, or laboratory abnormalities of acute prerenal azotemia frequently occur because of the severity and acuity of the GI bleeding^[41,42]. For example, 10 (50%) of 20 Mexican patients presented with signs of hemodynamic instability^[40]. The mean hemoglobin on admission for bleeding is about 9 g/dL^[43]. The bleeding is frequently recurrent, with recurrence < 72 h after initial presentation if it is left untreated at the initial endoscopy^[7]. Recurrent bleeding is often extremely severe, which emphasizes the importance of accurate diagnosis and appropriate therapy at the initial

Table 2 Diagnosis of Dieulafoy's lesion

EGD
Small, relatively inconspicuous pigmented protuberance with minimal surrounding erosion and no ulceration
Lesion often actively bleeding or oozing at EGD
Gastric lesions most commonly within 6 cm of GE junction along lesser curve
Initial EGD may be nondiagnostic in up to 30% of cases due to relatively small lesion size
Avoid endoscopic biopsies of lesion
Colonoscopy or enteroscopy
May be useful to diagnose colonic or jejunoileal lesions, respectively, if EGD was negative in setting of severe, acute GI bleeding
Angiography
May be helpful in setting of rectal bleeding after negative EGD and colonoscopy

EGD: Esophagogastroduodenoscopy; GI: Gastrointestinal.

endoscopy. Other GI symptoms, especially abdominal pain, are uncommon and their presence suggests alternative diagnoses such as peptic ulcer disease or complications from the bleeding such as mesenteric ischemia from hemorrhagic shock^[14].

The clinical presentation of patients with jejunoileal lesions is similar to that of patients with upper GI Dieulafoy's lesions^[17]. Among 10 patients diagnosed with small-intestinal Dieulafoy's lesions, all presented with overt bleeding and all had severe, transfusion-dependent, anemia^[17]. Eight of the ten Dieulafoy's lesions were actively bleeding at enteroscopy. Most patients were elderly (mean age = 69.7 years), but the disease occurred at younger ages as well (youngest patient = 35 years old).

Dieulafoy's lesion is also an important cause of obscure GI bleeding because it frequently bleeds intermittently, it occasionally involves unusual GI bleeding sites that are relatively inaccessible to conventional endoscopy, such as the jejunum or ileum; and the lesions are frequently relatively small, subtle, and inconspicuous despite repetitive use of standard diagnostic techniques^[44]. Conversely, alternative diseases can sometimes mimic a Dieulafoy's lesion in the setting of acute GI bleeding. For example, two recent reports from Japan describe patients whose initial clinical presentation and endoscopic findings suggested gastric Dieulafoy's lesions, but who were subsequently diagnosed with GI stromal tumors^[45,46].

Dieulafoy's lesions are apparently not associated with other GI vascular lesions, such as angiodysplasia or hemangiomas. Although syndromes with multiple vascular lesions occur with angiodysplasia (in hereditary hemorrhagic telangiectasia), syndromes with multiple or disseminated Dieulafoy's lesions have not been reported. One patient, however, had two GI Dieulafoy's lesions^[47]. Unlike the genetic mutations associated with hereditary hemorrhagic telangiectasia^[48], no genetic mutations have been associated with Dieulafoy's lesions. Hereditary hemorrhagic telangiectasia is occasionally associated with high-output cardiac failure^[49], or individual organ

(e.g., liver) failure^[50], from extensive shunting of blood. However, Dieulafoy's lesion is not associated with high-output cardiac failure or individual end-organ failure because it produces minimal individual organ or systemic vascular shunting due to its relatively moderate size and single lesion status.

DIAGNOSIS

Esophagogastroduodenoscopy (EGD) is usually the first diagnostic test performed for acute, upper, GI bleeding. Dieulafoy's lesion is, therefore, usually diagnosed by EGD, which reveals a pigmented protuberance from the vessel stump, with minimal surrounding erosion and no ulceration (visible vessel sans ulcer; Figures 2A, 3A and 4A). The pigmented protuberance has a variable color, including reddish, purple, blue, or greyish-white. The protuberance is usually relatively inconspicuous at EGD; it is approximately 10-15 mm wide and about 5-10 mm high (Table 2). Approximately 50%-60% of identified upper GI Dieulafoy's lesion are actively bleeding at the initial EGD, typically with spurting or oozing of blood from a miniscule (1-5 mm in diameter) point source on the GI mucosa^[40,42]. For example, in a study of 29 patients, 66% had oozing, and 28% had spurting bleeding at endoscopy^[51]. Spurting bleeding is often micro-pulsatile reflecting the underlying arterial breach. Other patients typically have a fresh adherent clot or visible (non-actively bleeding) Dieulafoy's lesion at the initial endoscopy. Dieulafoy's lesion should be strongly considered, when a lesion is located in proximal stomach and/or has a small mucosal defect connected by a narrow attachment point to an adherent clot^[9]. Dieulafoy's lesion may not be detected when covered by an adherent clot, and the lesion may be exposed by washing away an adherent clot with moderate endoscopic perfusion. The authors do not recommend guillotining an adherent clot covering a Dieulafoy's lesion because of the risk of inducing severe hemorrhage.

Dieulafoy's lesion should be endoscopically distinguished from other clinical entities with a similar clinical presentation and endoscopic appearance, including: arteriovenous malformations, hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome), or vascular neoplasms. Additionally, when located close to the gastroesophageal junction, the lesion has to be distinguished from a Mallory-Weiss tear, in which the bleeding originates from a superficial mucosal tear instead of a superficial protruding blood vessel. A history of vomiting before hematemesis may suggest a Mallory-Weiss tear. However, given their frequently similar anatomical location, endoscopic misdiagnoses of Dieulafoy's lesions as Mallory-Weiss tears have been reported^[7]. It is important to differentiate a colonic Dieulafoy's lesion from an adenomatous colonic polyp to prevent massive hemorrhage from performing "polypectomy" of a Dieulafoy's lesion^[52].

Initial EGD is diagnostic in only about 70% of cases

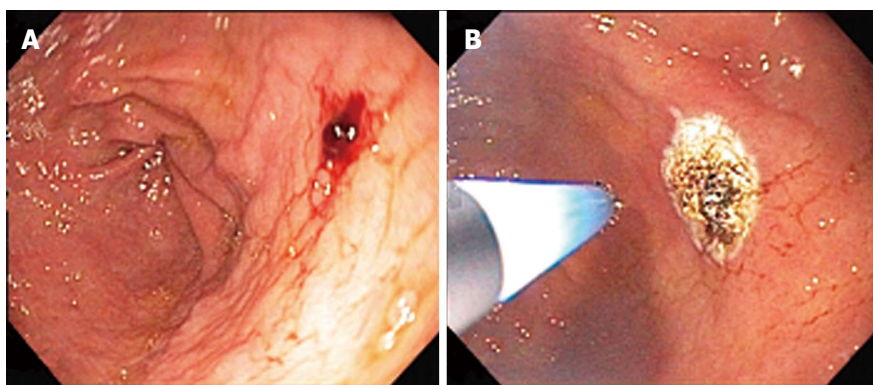


Figure 2 An 86-year-old woman who had undergone two esophagogastroduodenoscopies in the prior 2 years for 2 episodes of acute upper gastrointestinal bleeding that had not revealed any upper gastrointestinal lesions, presented with acute onset of melena and an acute hemoglobin level decline from 11.0 g/dL to 8.6 g/dL. Esophagogastroduodenoscopy revealed an actively oozing, darkly red, 6-8 mm wide, raised, lesion without surrounding erosions or ulceration that was actively oozing along the greater curvature of the gastric body (A), findings characteristic of a Dieulafoy lesion. The lesion was successfully cauterized using 50 watts of argon plasma coagulation at 1 L/min (note probe hovering over cauterized lesion in (B) with cessation of active oozing). The patient was discharged four days later with no evidence of recurrent bleeding during the hospitalization and no further gastrointestinal bleeding during 4 mo of follow-up.

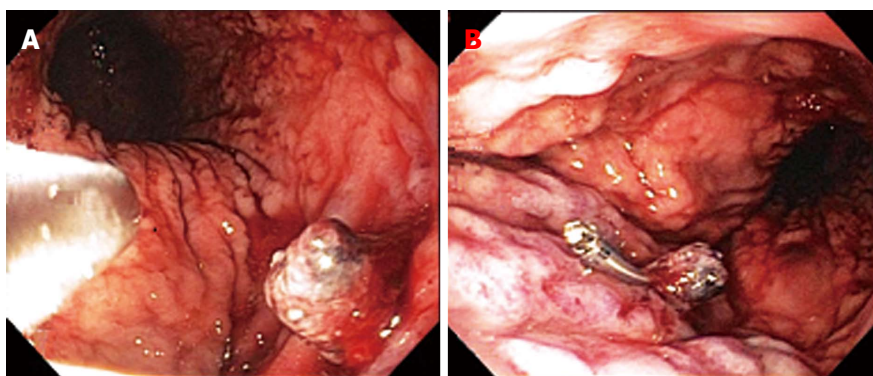


Figure 3 An 88-year-old woman with prior bleeding duodenal ulcer 40 years earlier, and actively administered aspirin, presented with acute onset of hematemesis and melena, with an acute decline in the hemoglobin level from 11.2 g/dL to 9.2 g/dL. Esophagogastroduodenoscopy revealed an actively oozing, darkly red, 8-10 mm wide, raised, lesion without surrounding erosions or ulceration that was actively oozing in the gastric cardia (A), findings characteristic of a Dieulafoy lesion. The lesion was first injected with 7 mL of epinephrine (1:10000 solution), followed by successful placement of a single hemoclip around the protruding vessel (B), with cessation of active oozing. The patient was discharged three days later with no evidence of recurrent bleeding during the hospitalization.

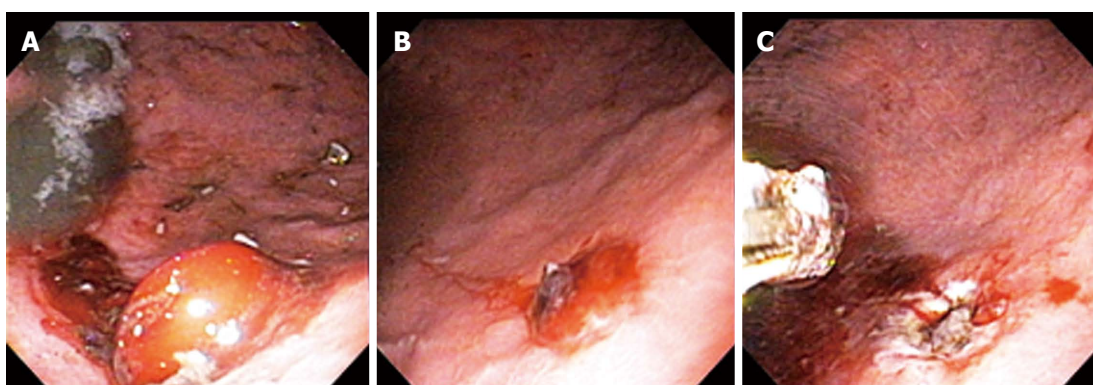


Figure 4 An 81-year-old woman presented with nausea, coffee-ground emesis, and dizziness. She underwent urgent esophagogastroduodenoscopy (EGD), despite a normal initial hemoglobin level of 13.0 g/dL, because of the hematemesis. EGD revealed a small blood clot, overlying a lesion without surrounding ulceration, located in proximal gastric body, which was slowly oozing red blood (A). After detachment of the blood clot with irrigation, a raised, darkly red, blood vessel was visualized consistent with a Dieulafoy lesion (B). The lesion was treated with 4 mL of 1:10000 solution of epinephrine and thermocoagulated via heater probe 5 pulses of 30 Joules/pulse without post-procedural bleeding (C). Patient remained stable after the EGD with no further bleeding and she was discharged 3 d later.

due to relatively small lesion size; intermittently active bleeding; lesion location between folds; or lesion

location underneath gastric contents, an adherent blood clot, or a pool of blood from massive bleeding^[53]. For

example, in a retrospective study of 177 patients with Dieulafoy's lesions causing acute GI bleeding, repeat endoscopic evaluation was needed in 33% of cases, due to nondiagnostic initial examinations^[37]. Indeed, about 6% of patients require three or more endoscopies to establish the diagnosis^[8]. This diagnostic yield at EGD is significantly lower than that of about 95% for other lesions causing upper GI bleeding^[54]. Gastric insufflation may expose a Dieulafoy's lesion previously buried between gastric rugae. Careful aspiration of the gastric lake may demonstrate an underlying Dieulafoy's lesion. Cautious removal of an adherent clot may reveal an underlying Dieulafoy's lesion. Lesion identification may require careful gastric retroflexion due to its predilection to be near the gastroesophageal junction. As with EGD, repeat enteroscopic examinations, after initially nondiagnostic enteroscopy, are frequently required to diagnose jejunoileal lesions. In one study 40% of cases required a second or even a third enteroscopy to establish the diagnosis^[17].

Several small reports suggest that, supplemental methods such as endoscopic ultrasound or bleeding provocation with intravenous heparin, may help increase the diagnostic yield of Dieulafoy's lesions at endoscopy^[55,56]. Typical endosonographic features include an abnormally large (2-3 mm wide) caliber, pulsatile, high-flow, submucosal artery, usually located along the lesser gastric curve near the gastroesophageal junction. Endosonography has been used to confirm endoscopic hemostasis of a bleeding Dieulafoy's lesion by demonstrating absent blood flow after therapy^[55]. However, combining endoscopy with such costly, advanced technology is currently not recommended for routine clinical practice due to insufficient data concerning efficacy. Endoscopic biopsies of suspected Dieulafoy's lesion are generally contraindicated because of the risk of inducing severe bleeding by biopsying the exposed artery and the lack of pathologic diagnosis from endoscopic biopsies.

Colonoscopy is usually indicated following a negative EGD for acute GI bleeding. Multiple individual cases of bleeding Dieulafoy's lesion diagnosed at colonoscopy have been reported during the past 30 years. However, the diagnostic yield of colonoscopy for this entity is unknown^[24-27,56-61].

Enteroscopy is often indicated for acute GI bleeding after nondiagnostic EGD and colonoscopy. It enables viewing of the small bowel up to about 150 cm beyond the pylorus, to identify distal duodenal or proximal jejunal lesions. There is limited data on the diagnostic yield of enteroscopy for acute bleeding from small bowel Dieulafoy's lesions^[3,17-21]. Single-balloon and double-balloon enteroscopies permit intubation of more distal small intestine, thereby permitting detection of more distal Dieulafoy's lesions.

Several Dieulafoy's lesions have been diagnosed by capsule endoscopy^[34,62]. While noninvasive, capsule endoscopy lacks therapeutic capabilities, and a positive test still requires a subsequent invasive therapeutic

modality. Still, capsule endoscopy may be diagnostically helpful for Dieulafoy's lesion causing obscure GI bleeding, especially from the distal small intestine^[62].

If endoscopy is nondiagnostic, angiography may help establish the diagnosis in the setting of acute bleeding, especially for lower GI Dieulafoy's lesions, because detailed colonoscopic examination of mucosa may be difficult to achieve due to overlying blood or the performance of colonoscopy on an unprepared colon because of severe, acute bleeding (Table 2)^[10,35,37]. No angiographic pattern is specific for Dieulafoy's lesions, but features such as visualization of a non-tapering (caliber-persisting), ectatic (tortuous), artery at the bleeding site may suggest this entity^[7,63,64]. Often, however, only extravasation is visualized at an eroded site of an otherwise normal appearing artery^[65]. Angiography may also suggest an underlying Dieulafoy's lesion when extravasation of contrast is visualized from a point source in the proximal stomach. Angiodysplasia, another point source of bleeding, may be distinguished from Dieulafoy's lesion by its characteristic angiographic features, such as an early filling vein, that are inconsistent with Dieulafoy's lesion^[8,66]. In one study, angiography was diagnostic in 11 of 14 patients with Dieulafoy's lesions who underwent nondiagnostic endoscopic examinations^[37].

Technetium 99-m-labeled erythrocytes scanning is reportedly useful to locate a bleeding Dieulafoy's lesion after nondiagnostic endoscopies^[67,68]. This test may permit diagnosis at lower rates of active GI bleeding, because the threshold to detect blood extravasation is less than half that required for angiography^[69].

TREATMENT

As for any severe, acute, GI bleeding, pre-endoscopic therapy for a recently bleeding Dieulafoy's lesion focuses on volume resuscitation to prevent systemic hypotension and consequent end-organ damage to heart, brain, or kidneys from hypoperfusion. Multiple, reliable, large-bore, intravenous lines are inserted. Volume resuscitation is initially performed with crystalline solution, with normal saline or Ringer's lactate, but transfusion of packed erythrocytes is often required, after typing and crossing of blood, as guided by the tempo of the GI bleeding and serial hematocrit determinations. Patients with Dieulafoy's lesions often require transfusion of three or more units of packed erythrocytes due to the severity of the bleeding^[9]. Electrolyte abnormalities are assessed and appropriately corrected. Treatment to reverse a severe coagulopathy is important before endoscopy, particularly when endoscopic therapy is contemplated.

Hemostatic therapy is important because of the bleeding severity from Dieulafoy's lesion, the propensity for bleeding to recur without therapy, especially within 72 h after an initial bleed, and the high mortality if it is left untreated. Minimally invasive therapies are derived from their respective diagnostic tests, including

Table 3 Therapy for Dieulafoy's lesion

Pre-endoscopic therapy
Secure IV access using multiple, large bore catheters
Volume resuscitation initially using crystalloid followed by transfusions of packed erythrocytes as dictated by serial hematocrit determinations and tempo of bleeding
Endoscopic therapies
Mechanical therapies
Hemoclips
Band ligation
Injection therapies
Epinephrine injection
Absolute alcohol
Ablative therapies
Heater probe
Electrocoagulation: Bicap, gold probe, <i>etc.</i> ,
APC (argon plasma coagulation)
Combination therapies
Usually epinephrine injection therapy followed by:
Heater probe
Hemoclip
Or APC
Interventional angiography
Embolization
Pledgelets
Metal coils
Balloon occlusion
Surgery
Mostly salvage therapy after failure of other interventional therapies

APC: Argon plasma coagulation.

therapeutic endoscopy immediately after diagnostic endoscopy, and therapeutic angiography immediately after diagnostic angiography (Table 3). While no consensus recommendations on treatment exist, there has been increased use of endoscopic therapy and therapeutic angiography, with decreasing use of surgery during the last few decades^[10,70]. As Dieulafoy's lesions are relatively uncommon, most data on treatment modalities consist of small, retrospective, case-series, or individual case-reports^[7,8,10].

Therapeutic endoscopy is the primary treatment modality for acute GI bleeding. It can achieve initial hemostasis in about 90% of accessible lesions with a < 10% rate of rebleeding during the next 7 d^[36,71-73]. Therapeutic endoscopy for recently bleeding peptic ulcers depends upon the Forrest criteria, with endoscopic therapy recommended only for lesions that are actively bleeding or oozing, that have a visible vessel, or perhaps have an adherent clot^[74]. Endoscopic therapy is not recommended for peptic ulcers that have a flat, pigmented spot or have a clean, homogeneous, flat base. Contrariwise, therapeutic endoscopy is recommended for virtually all Dieulafoy's lesions, whether actively bleeding, oozing, or without any stigmata of recent bleeding. The difference in therapeutic strategies reflects the natural history of Dieulafoy's lesion as compared to peptic ulcers. Peptic ulcers with a flat pigmented spot have a low risk of rebleeding of about 8%-10% without endoscopic therapy and peptic ulcers with a clean,

homogeneous, flat, base have only about a 3% risk of rebleeding without endoscopy therapy^[74]. This low risk of rebleeding with these two types of peptic ulcers does not justify incurring the approximately 1% or more risk of major, life-threatening, complications from endoscopic therapy including, gastrointestinal perforation, massive bleeding, pulmonary aspiration, and cardiovascular complications^[74]. In contrast, the risk of continued bleeding or rebleeding within 72 h from an untreated Dieulafoy's lesion is very high. This high risk of rebleeding justifies undertaking the risks of therapeutic endoscopy to prevent further bleeding from Dieulafoy's lesion.

Although initially developed for EGD for upper GI Dieulafoy's lesions, endoscopic therapy is now performed using the same techniques and devices during colonoscopy for colonic Dieulafoy's lesions^[22-25], and during single or double balloon enteroscopy for jejunoileal lesions^[17]. The current modalities of endoscopic therapies include injection, ablation, and mechanical therapy. Injection therapy most commonly involves local injection of epinephrine, sclerosing agents (sclerotherapy), or cyanoacrylate. Epinephrine therapy promotes hemostasis *via* vasospasm and tamponade/mechanical pressure from interstitial injection that leads to stasis of blood and thrombus formation. Relative contraindications to epinephrine therapy may include severe tachycardia, cardiac arrhythmias such as atrial flutter, unstable vital signs from severe, uncorrected hypovolemia, and recent myocardial infarction or unstable angina. Sclerotherapy promotes vascular inflammation and thrombosis from local irritation, whereas cyanoacrylate promotes gluing to plug a bleeding artery. Ablation modalities include thermocoagulation, electrocoagulation, and argon plasma coagulation (APC). Photocoagulation using the yttrium aluminum garnet laser to ablate tissue has been discontinued due to an unacceptably high risk of gastrointestinal perforation. Ablation modalities can stem bleeding by destroying and devitalizing tissue. Thermocoagulation and electrocoagulation involve point contact with the lesion with apposition of the probe against the bleeding vessel. Contrariwise, APC involves hovering the probe over the lesion without lesion contact^[74]. Mechanical therapy, including band ligation or endoscopic clips, can arrest bleeding by mechanically closing off the bleeding vessel. Mechanical therapy likely requires greater endoscopic skill and experience than injection or ablative therapies because correct placement of the band or clip directly around the lesion is critical for successfully strangulating the vessel within Dieulafoy's lesion.

These therapies are generally effective for most Dieulafoy's lesions, when used individually or in combination^[17,35,38,71-75]. Successful cases of hemostasis of bleeding Dieulafoy lesions using various modalities of endoscopic therapy are illustrated in Figures 2-4. Available data suggest that mechanical hemostasis may be more effective than other endoscopic modalities in

Table 4 Efficacy of endoscopic mechanical monotherapies for bleeding Dieulafoy's lesions

Endoscopic procedure (No. of patients)	Lesion location	Type of study	Follow-up	Outcome	Ref.
Hemoclips					
EGD (34)	Stomach/duodenum	Prospective	54 mo	initial hemostasis 32/34 pts (94%), 3 pts (9%) rebled	[75]
EGD (18)	Stomach	Retrospective	36 mo	1 (5%) rebled	[77]
EGD (16)	Stomach/duodenum	Prospective, randomized	1 wk	1 (6%) rebled	[78]
Mostly EGD (14)	Mostly stomach/duodenum	Retrospective	Hospitalization	No rebleeding	[36]
EGD (8)	Stomach	Retrospective	19 mo	1 (12%) rebled	[73]
Colonoscopy (1)	Rectum				
EGD (6)	Stomach/duodenum	Retrospective	47 mo	1 (17%) rebled, unclear if single/combination therapy	[79]
Colonoscopy (3)	Rectum	Retrospective	5 mo	No rebleeding	[80]
Double balloon enteroscopy (3)	Jejunum	Retrospective, multicenter	14.5 mo	1 (33%) rebled 69 d after hemoclip	[17]
Single balloon enteroscopy (2)	Ileum	Retrospective	2 mo	No rebleeding	[18]
Colonoscopy (1)	Colon	Case report	6 mo	No rebleeding	[33]
Band ligation					
EGD (24)	Stomach 23 Jejunum 1	Retrospective	18 mo	1 (4%) hemostasis failure, 1 (4%) rebled (jejunum)	[81]
EGD (13)	Stomach Esophagus	Prospective	24 wk	No rebleeding	[82]
EGD (13)	Stomach/duodenum	Retrospective	30 d	No rebleeding	[83]
EGD (10)	Stomach	Prospective	30 d	No rebleeding	[76]
EGD (7)	Stomach	Retrospective	8 mo	No rebleeding	[84]
EGD (3)	Upper GI	Retrospective	19 mo	No rebleeding	[73]
"Mostly" EGD (2)	Stomach	Retrospective	Hospitalization	No rebleeding	[75]
EGD (1)	Stomach	Retrospective	2 d	No rebleeding	[35]
Colonoscopy (4)	Rectum	Retrospective	2-5 d	2 (50%) rebled	[85]
Colonoscopy (3)	Rectum	Retrospective	5 mo	No rebleeding	[80]

Pts: Patients; EGD: Esophagogastrroduodenoscopy; GI: Gastrointestinal.

patients with GI bleeding from Dieulafoy's lesion^[73,76]. A review of the published literature on application of endoscopic hemoclips in 106 patients and on application of band ligation in 80 patients as monotherapies for bleeding Dieulafoy lesions reveals that both techniques are almost uniformly effective to achieve initial hemostasis and both techniques have low re-bleeding rates, generally $\leq 10\%$ (Table 4)^[17,18,33,36,73,75-85]. They are particularly effective in the hands of expert endoscopists with extensive experience with these techniques. However, endoscopic band ligation may be less desirable than clips because it can cause perforation from banding too deep tissue. This is a particular concern in GI segments with thin walls such as gastric fundus, small bowel, or right colon. Also bleeding may occur from an ulcer after the band falls off^[86,87].

A literature review of endoscopic injection encompassing 68 cases of epinephrine injection and 13 cases of sclerotherapy (12 with injection of absolute ethanol and 1 with injection of ethanolamine) appears to show a somewhat lower rate of achieving hemostasis for injection therapy than mechanical therapy (Table 5)^[35,36,40,72,73,78,88,89]. However, this therapy may be particularly useful for initially treating massive bleeding. This therapy is technically easier than mechanical therapy and can be performed rather quickly. Also, injection therapy, especially with epinephrine, may slow down massive bleeding so that the lesion can be more readily visualized to apply mechanical therapy.

A literature review of endoscopic ablation therapies for Dieulafoy's lesion encompassing 40 cases, including 18 cases with thermocoagulation, 7 cases of APC, and 15 cases of electrocoagulation shows a high rate of initial hemostasis (Table 6)^[17,35,36,40,72,77,82]. However, the data on efficacy for this therapy is less reliable than that for the mechanical or injection therapies because the individual studies on ablative therapies are all retrospective and relatively small and the total number of studied patients is only 40.

Combined endoscopic mechanical hemostasis with injection or ablation therapeutic endoscopy are highly effective therapeutic modalities (Table 7)^[17,35,36,40,59,71,72,79,88-90]. Although combined endoscopic treatment modalities are recommended as more effective in the setting of non-variceal acute upper GI bleeding, there is contradictory evidence on such practice when it comes to Dieulafoy's lesions; some studies found no added benefit from endoscopic dual therapy vs monotherapy^[10,36]. The overall risk of short-term (< 72 h) recurrent bleeding after endoscopically-achieved initial hemostasis is about 10%^[10,37,61]. Dieulafoy's lesions treated with single-modality endoscopic therapy may be more likely to rebleed compared to lesions treated with dual endoscopic therapy^[51,72].

Other potential risk factors for rebleeding after endoscopic therapy include administration of NSAIDs, administration of anticoagulants, and Dieulafoy's lesions with actively spurting blood at the time of initial

Table 5 Efficacy of endoscopic injection monotherapy for bleeding Dieulafoy's lesions

Endoscopic procedure (No. of patients)	Lesion location	Type of study	Follow-up	Outcome	Ref.
Epinephrine injection					
EGD (16)	Stomach/duodenum	Prospective	1 wk	2 (12%) hemostasis failure, 5 (31%) rebled	[78]
EGD (11)	Stomach	Retrospective	22 mo	3 (27%) hemostasis failure, 4 (36%) rebled	[73]
Colonoscopy (1)	Rectum				
EGD (11)	Stomach/duodenum	Retrospective	18 mo	3 (27%) hemostasis failure, 2 (18%) rebled	[88]
"Mostly" EGD (8)	Mostly stomach/duodenum	Retrospective	Hospitalization	No rebleeding	[36]
EGD (8)	Stomach	Prospective	30 d	6 (75%) rebled	[76]
EGD (6)	Stomach	Retrospective	60 d	2 (33%) hemostasis failure	[40]
EGD (3)	Stomach/duodenum	Retrospective	14 mo	No rebleeding	[35]
Colonoscopy (1)	cecum (1)				
EGD (3)	Stomach	Retrospective	32 mo	2 (66%) rebled	[72]
Absolute ethanol injection					
EGD (12)	Stomach/duodenum	Retrospective	69 mo	1 (8%) hemostasis failure, no rebleeding	[89]
Ethanolamine injection					
EGD (1)	Stomach	Retrospective	8 mo	Rebled	[72]

EGD: Esophagogastroduodenoscopy.

Table 6 Effectiveness of endoscopic ablation monotherapies for bleeding Dieulafoy's lesions

Endoscopic procedure (No. of patients)	Lesion location	Type of study	Follow-up	Outcome	Ref.
Heater probe coagulation					
EGD (6)	Stomach/duodenum	Retrospective	14 mo (2/3 of pts)	No rebleeding	[35]
EGD (6)	Stomach	Retrospective	36 mo	2 (33%) rebled	[77]
Mostly EGD (5)	Mostly stomach/duodenum	Retrospective	Hospitalization	No rebleeding	[36]
EGD (1)	Stomach	Retrospective	40 mo	No rebleeding	[72]
Argon plasma coagulation					
Double balloon enteroscopy (3)	Jejunum-2, Ileum-1	Retrospective / multicenter	14 mo	1 (33%) rebled	[17]
EGD (3)	Stomach	Retrospective	2 mo	No rebleeding	[40]
EGD (1)	Likely upper GI	Retrospective	Hospitalization	No rebleeding	[36]
Multipolar electrocoagulation					
EGD (14)	Stomach	Retrospective	24 mo	1 (7%) hemostasis failure, 1 rebled	[82]
EGD (1)	Likely upper GI	Retrospective	Hospitalization	Rebled	[36]

EGD: Esophagogastroduodenoscopy.

endoscopy^[42,51]. The data in Tables 4-7^[17,18,33,35,36,40,59,71-73,75-85,88-90] on initial hemostasis and re-bleeding rates with single-modality and combination-modalities endoscopic therapy for both upper and lower Dieulafoy's lesions should be interpreted cautiously; most reported studies are retrospective, have relatively small sample-size, and generally lack controls to exclude potential confounding variables.

Recurrent bleeding after attempted endoscopic hemostasis can be treated by repeat endoscopic hemostasis, angiographic embolization, or surgical wedge resection. Subtotal gastrectomy is unnecessary if the lesion has been properly localized preoperatively or intraoperatively. Successful hemostasis with angiographic embolization has been reported in scattered case reports^[65,91], but requires specialized angiographic expertise. Embolization of a too large and too central vessel feeding the Dieulafoy lesion can occasionally cause GI ischemia leading to GI perforation^[92].

The mortality of GI bleeding from Dieulafoy's lesions

prior to the era of flexible diagnostic endoscopy was up to 80%, due to the frequent need for emergency surgery for severe, refractory GI bleeding, but declined to about 30% with the advent of flexible diagnostic endoscopy in the 1970's, and has declined to about 9%-13% currently with the advent of therapeutic endoscopy^[93].

FUTURE TRENDS

Although the anatomic basis of Dieulafoy's lesion and the pathophysiology of bleeding from this lesion is fairly well understood, the etiology of lesion formation is poorly understood. Why does the lesion most commonly occur within 6 cm below the gastroesophageal junction along the lesser curve? Is this a developmental defect during organogenesis? Do genetic mutations play any role? Is there a familial predisposition to this lesion? Hopefully, the molecular mechanisms and developmental origin of this lesion will be elucidated. Such an understanding might provide a mechanism to

Table 7 Effectiveness of various combination endoscopic therapies for bleeding Dieulafoy's lesions

Endoscopic therapies (No. of patients)	Endoscopy: lesion location	Type of study	Mean length of follow-up	Study outcome	Ref.
Epinephrine and polidocanol (27)	EGD: stomach/duodenum	Retrospective	28 mo	5 (18%) rebled	[71]
Epi and heater probe (28)	EGD: stomach/duodenum	Retrospective	14 mo (2/3 of patients)	2 (7%) rebled	[35]
Epi and heater probe (10)	EGD: stomach/duodenum	Retrospective	18 mo	No rebleeding	[88]
Epi and heater probe (9)	"Mostly" EGD; Mostly stomach/duodenum	Retrospective	Hospitalization	1 (11%) rebled	[36]
Epi and heater probe (8)	EGD: stomach/duodenum	Retrospective	32 mo	No rebleeding	[72]
Epi and heater probe (6)	EGD	Retrospective	2 mo	No rebleeding	[40]
Epi and heater probe (2)	Colonoscopy	Retrospective	1 and 7 mo	No rebleeding	[59]
Epi and hemoclip and ethanol injection (21)	EGD: stomach/duodenum	Retrospective	47 mo	1 (4%) rebled	[79]
Epi and hemoclip (19)	EGD: Stomach	Retrospective	47 mo	1 (5%) rebled	[79]
Epi and hemoclip (16)	"Mostly" EGD: mostly stomach/duodenum	Retrospective	During hospitalization	1 (6%) rebled	[36]
Epi and hemoclip (3)	EGD: Stomach	Retrospective	2 mo	No rebleeding	[40]
Epi and multipolar electrocoagulation (5)	"Mostly" EGD: Mostly stomach/duodenum	Retrospective	During hospitalization	1 (20%) rebled	[36]
Epi and banding (1)	EGD: stomach	Retrospective	During hospitalization	No rebleeding	[36]
Epi and ethanol (52)	EGD: Stomach/ duodenum	Retrospective	69 mo	Approximately 9% hemostasis failure, 10 (20%) rebled	[89]
Epi and ethanol (11)	EGD: stomach duodenum	Retrospective	47 mo	1 rebled	[79]
Epi and ethanolamine (5)	EGD: stomach/duodenum	Retrospective	32 mo	2 (40%) rebled	[72]
Injection therapy and clip (2)	Double balloon enteroscopy: jejunum	Retrospective, multicenter	14 mo	No rebleeding	[17]
Injection therapy and APC (1)	Double balloon enteroscopy: jejunum	Retrospective, multicenter	14 mo	Rebled after 9 d	[17]
Injection and heater probe and clips (1)	Colonoscopy: colon	Case report	NA	No rebleeding	[90]

Epi: Epinephrine; APC: Argon plasma coagulation; NA: Not available.

prevent lesion formation.

Currently the ideal endoscopic therapy for recently bleeding Dieulafoy's lesion is uncertain. Large, prospective, head-to-head clinical trials are needed of different endoscopic modalities are needed but these are difficult to perform and complete due to the relative rarity of this lesion. It is reasonable, therefore for gastroenterologists to adopt particular techniques based on personal and local experience and technologies available within their endoscopy suite. Use of a spray to stem bleeding is an exciting technology because of ease of use but is experimental and unproven^[94].

Therapeutic angiography is likely to become a more viable alternative to endoscopic therapy, with greater experience with this technology for this indication, but it is likely to remain a second option after failed endoscopic therapy due to the easy availability of therapeutic endoscopy at the same session when performing the initial diagnostic endoscopy and the very high success rate of therapeutic endoscopy. It is expected that endoscopic therapy will evolve with even better techniques for lesion ablation or mechanical occlusion of vascular lesions, such as the development of clinically applicable endoscopic micro-suturing devices^[95].

Although endoscopic ultrasound may potentially prove very useful in identifying whether a vessel in a Dieulafoy's lesion has active flow through it, widespread adoption of this technique awaits lowering

the cost of this technology, greater availability of endosonographers, and demonstration of its clinical benefits through clinical trials. CT angiography may assume a greater diagnostic role after nondiagnostic endoscopy in the face of severe, active bleeding, but its role is likely to remain limited due to a lack of therapeutic capabilities.

Currently, single-balloon and double-balloon enteroscopy are generally limited to tertiary hospitals, but should become more available in the future with lowering of costs. This may offer a new technology for diagnosing and treating small bowel Dieulafoy's lesions that are otherwise difficult to reach and treat. Capsule endoscopy may become more helpful in diagnosing jejunoileal lesions with development of capsules with active propulsion, better camera resolution, and longer-lasting and more powerful batteries, but its role will likely remain limited for bleeding from jejunoileal Dieulafoy's lesions because of a lack of therapeutic capabilities^[96].

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