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When all else fails - Radiological management of severe gastrointestinal bleeding

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ABSTRACT

Although most cases of acute nonvariceal gastrointestinal bleeding (GIB) either spontaneously resolve or respond to medical management and endoscopic therapy, there are still a significant proportion of severe patients who require emergency angiography and endovascular treatment. Over the past three decades, transcatheter arterial embolization (TAE) has become the first-line therapy for the management of acute nonvariceal GIB that is refractory to endoscopic hemostasis. Advances in catheter-based techniques and newer liquid embolic agents, as well as recognition of the effectiveness of minimally invasive treatment options, have expanded the role of interventional radiology in the treatment of bleeding for a variety of indications. TAE is a safe and effective minimally invasive alternative to surgery, when endoscopic treatment fails to control acute bleeding from the gastrointestinal tract. In this article we review the current role of angiography and TAE in the management of acute nonvariceal GIB.

Introduction

Most cases of acute nonvariceal gastrointestinal bleeding (GIB) resolve spontaneously and of those that do not, the majority respond to conservative medical management. Endoscopy remains the mainstay for diagnosis and treatment in bleedings refractory to medical management [1]. However, there is a small group of patients (5–15%) in whom endoscopic hemostasis is ineffective, requiring alternative treatment [1–3]. Localization and characterization of the bleeding source are important in determining the appropriate intervention, as treatment options range from minimally invasive catheter-directed therapy to extensive surgical resection [3]. Transcatheter arterial embolization (TAE) has been performed for at least three decades and has been shown to be effective at controlling bleeding and decreasing mortality [3–7]. The alimentary system is subdivided into the upper and lower GI tracts and thus GIB is subcategorized according to the location of bleeding. The upper GI system extends from the esophagus to the ligament of Treitz, while the latter includes the small bowel, colon and rectum [1]. The distinction is important, as there are some characteristics that are relatively unique to each location and these may affect and determine the therapeutic approach to the particular bleeding source. Embolization techniques have evolved with the use of microcatheters and new embolic agents [3–7]. The purpose of this review is to summarize data on techniques and outcomes of TAE for acute severe nonvariceal GIB.

Indications for angiography

The typical candidate patient presents with the following: (1) massive bleeding (transfusion requirement of at least 4U blood/24 h) or hemodynamic instability (hypotension with systolic pressure <100 mm Hg and heart rate of 100 min^{-1} or clinical shock secondary to blood loss), (2) bleeding that has failed to respond to conservative medical treatment, including volume replacement, antacids, H2-receptor blocking agents, or proton pump inhibitors, and (3) bleeding that has failed to respond to one or two attempts at endoscopic control. Lastly, endovascular treatment can be used after open surgery has failed and bleeding recurred [8,9].

The most common cause of acute upper GIB is peptic ulcer disease. Other causes include acute gastroduodenal erosions, esophagitis, Mallory-Weiss tears, tumors, Dieulafoy's lesions, vascular malformations and iatrogenic lesions. Approximately 80% of LGIB derives from a colorectal source, 5–10% from a small bowel

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source and 10–15% of LGIB is blood of upper gastrointestinal origin. The most common cause of acute lower GIB is diverticular disease. Other causes include colitis, anorectal lesions, neoplasia, post-polypectomy lesions, and angiodysplasia. The source of small bowel bleeding is more apt to be obscure/occult as compared to bleeding from a colorectal source [10,11].

Angiographic evaluation

Timing of angiography

Endoscopy is usually performed before angiography. Endoscopic diagnosis and therapy can render angiography unnecessary. Endoscopy also helps in planning the timing and approach of angiography. For example, inability to determine the cause of bleeding at endoscopy because of severe bleeding should prompt urgent angiography. Even endoscopic localization of the bleeding site without determination of the cause helps guide which artery to catheterize first at angiography [9,10]. Negative endoscopic information, such as excluding esophageal bleeding, is valuable to the angiographer. On the other hand, it has been shown that longer time to angiography is a predictor of early rebleeding after TAE [9,10]. Thus, the ability to achieve bleeding control in critically ill patients seems to depend chiefly on early intervention. There is much discussion about the necessity of diagnostic studies preceding angiography. Certainly, endoscopy has a diagnostic and therapeutic role in the management of upper GIB (UGIB) and can almost replace the need for computed tomography angiography (CTA) of the abdomen in most patients. However, endoscopy has been almost replaced with CTA for pre-angiography evaluation of patients with lower GIB (LGIB) because of the absence of colon preparation in the emergency setting [11]. CTA is more sensitive than angiography to depict vascular abnormalities and guide treatment. However, most of the controversy involves the need for nuclear scintigraphy before diagnostic angiography in patients with LGIB [12,13]. Despite more sensitive than angiography, nuclear scintigraphy may be recommended before angiography only in cases of episodic bleeding. The decision to proceed directly to angiography without nuclear scintigraphy depends on the clinical situation and the degree of bleeding [13]. The clinical presentation of LGIB may be episodic or continual. The former ranges from minor episodes that resolve, to chronic intermittent bleeding, to severe life-threatening hemorrhage. Angiography is warranted in the latter group and may play a diagnostic role in the second. It remains the primary diagnostic imaging tool in those patients with continual active hemorrhage, however, and delaying angiography for scintigraphy is not warranted [12–14]. Intermittent LGIB deserves special attention. Wireless capsule endoscopy may be used in such a setting. At the present time, however, it is not a practical modality to use in acute UGIB. Finally, the amount of bleeding may affect treatment strategy, continued active bleeding demands for emergency angiography primarily without any pre-procedural imaging.

Technique of angiography

In the advent of UGIB, the source for bleeding is usually identified by endoscopy and regarding LGIB, the source of bleeding is usually identified by CTA, in the absence of hemodynamic instability. Therefore, angiography is most often performed as a precursor to TAE based on the knowledge of the vascular supply to the abnormal area. Thus, for suspected UGIB, the celiac artery should first be evaluated, followed by the superior mesenteric artery (SMA), as the latter may contribute to a site of UGIB through the pancreaticoduodenal arcade. The lower GI tract, however, is the primary territory within the distribution of the SMA [13,14]. It supplies the small bowel and the ascending and transverse portions of the colon, while the inferior mesenteric artery (IMA) supplies the splenic flexure, descending and sigmoid colonic segments as well as the rectum and anus. An additional arterial supply to the rectosigmoid and anus arises from the internal iliac arteries and this may become a dominant vascular pathway if there is IMA occlusion. The SMA becomes another collateral pathway in the presence of IMA occlusion and may provide the entire arterial supply to the descending and sigmoid colon via either the arcade of Riolan or the marginal artery of Drummond. One should be aware of the numerous mesenteric circulatory variations that may occur in the presence of occlusive disease. Furthermore, congenital variant vascular anatomy must be considered during the angiographic evaluation of GIB [13,14]. A transfemoral approach is generally used and with placement of a 5-French sheath in the common femoral artery. For selective catheterism, the most widely used catheters are the cobra, hook and short- and long-curve sidewinder with a 4-French diameter. Once access is secured, angiogram then is performed to delineate the anatomy. If no extravasation is seen, then superselective angiography is advised. Depending on endoscopic or CTA findings that offer information on the likely location of the bleeding source, superselective catheterization of the gastroduodenal artery (GDA), left gastric artery (LGA) or splenic artery (SA) may be performed. A microcatheter is always recommended for a distal superselective approach to the bleeding vessel [15,16]. The use of carbon dioxide as contrast medium has been almost abandoned because of the risk of bowel ischemic complications despite improved sensitivity for small bleeds. Localization of contrast extravasation into the bowel lumen is considered as a direct angiographic sign of active GIB. Extravasation signifies a breach in the integrity of the arterial wall that permits the angiographic contrast to freely exit from the vessel. Extravasated contrast, therefore, does not have the typical tubular appearance of a vascular structure but instead distributes irregularly and often without a pattern. Commonly encountered indirect angiographic signs of GIB include visualization of an aneurysm, pseudoaneurysm or a submucosal vessel and early venous drainage of angiodysplasia [15,16]. Other angiographic signs include neovascularity in oncologic cases, mucosal or extramucosal hyperemia, intramural pooling of contrast or arterial wall abnormalities. Arterial aneurysms may be seen in patients with chronic occlusive disease of the celiac artery, and involve the pancreaticoduodenal arteries. Arterial pseudoaneurysms occur most frequently in patients who have chronic pancreatitis [15,16].

Provocative angiography

There is no enough data to provide guidelines to perform provocative mesenteric angiography or pharmaco-angiography. This technique has been mainly used to provoke LGIB, which is more challenging than UGIB [17,18]. Indeed, contrary to LGIB, almost all upper GI bleeders have undergone endoscopy in an attempt to identify, localize and treat the source of bleeding. Several prior studies have shown that empiric embolization based on endoscopic findings, in the absence of contrast extravasation, may be performed safely and successfully [15,16]. Thus, the absence of angiographic extravasation is less problematic at the level of the upper GI tract and does not prevent from embolizing the artery that supplies the bleeding site. However, this technique can be applied in situations where conventional angiography is nondiagnostic, especially at the lower GI tract. The addition of pharmacologic agents to standard angiographic protocols in order to increase the diagnostic yield has been reported in case reports and small series [17–20]. Provocative mesenteric angiography is defined as the use of thrombolytics, vasodilators, and anticoagulants intra-arterially to elicit active bleeding from a source that may have recently ceased hemorrhaging. Unfortunately, the available literature on this technique is limited [19,20]. Although reasonably successful and without any reported major hemorrhagic complications, provocative mesenteric angiography is not a commonly used examination in clinical practice. The precise reasons for this are unknown but likely relate to fear of potential uncontrollable hemorrhagic complications and lack of familiarity with this procedure by interventional radiologists. Currently, provocative angiography is rarely needed for the diagnosis of GIB and only limited reports for use in difficult and recurring nonvariceal GIB have shown to be beneficial [19,20].

Transcatheter arterial intervention

Over the past three decades, angiographic interventions have shifted from playing a purely diagnostic role to being a major therapeutic option in the management of nonvariceal GIB [21,22]. Endovascular interventions to control GI bleeding takes two forms: the infusion of a vasoconstricting medication and the mechanical occlusion of the arterial supply responsible for the bleeding.

Intra-arterial vasopressin infusion

Selective infusion of intraarterial vasoconstrictors was one of the first angiographic treatments for GIB [23,24]. Vasopressin, a posterior pituitary hormone, elicits smooth muscle contraction in the mesenteric bed, thereby decreasing the perfusion pressure to the bowel and potentially resulting in thrombosis of the bleeding site. Vasopressin infusion is easy to perform, most often by placing a 5-French diagnostic catheter into the artery most suspected of bleeding. Vasopressin is then infused at a rate of 0.2–0.4 U/min until successful control of bleeding is observed on angiography. Then, the mesenteric intraarterial infusion is continued for 12–48 h. Vasopressin infusion has lost favor for two main reasons: necessary catheterization times can require several days and, more importantly, the emergence of embolotherapy. Given that embolotherapy replaced vasopressin infusion early in the treatment of GIB, there is little recent data on the use of this technique. Finally, the use of vasopressin in the treatment of nonvariceal GIB is empiric as there is no substantial data to support its use.

Selective arterial embolization

Standard technique

When a dual supply of the bleeding area is suspected, both arterial sources must be embolized to assure that all of the inflow ceases. This is typically noted in bleeding secondary to an ulcer that erodes into the GDA [25]. Embolization in this case must start distally to prevent persistent "backdoor" bleeding from the right gastroepiploic and superior pancreaticoduodenal arteries and then proceed to the proximal side of the erosion. In cases of active bleeding with extravasation of contrast, the bleeding vessel is identified by superselective catheterization with a microcatheter and embolized with microcoils or glue if arterial flow is not blocked by the microcatheter [26]. If no evidence of bleeding is found on pre-embolization arteriography, then blind embolization, defined as embolization without angiographic proof of extravasation, is advised and is typically guided by endoscopic information regarding the location of the bleeding vessel (Fig. 1). Coils and gelatine sponge are then used in such a situation. Finally, "sandwich" occlusion can be used at the level of the GDA: the catheter is pushed to the origin of the right gastroepiploic artery, and coils are introduced as the catheter is withdrawn to the proximal GDA. Complete embolization of the GDA, which inlcudes proximal and distal embolization and exclusion of its two side branches, is the end point in this case (Fig. 1). A selective superior mesenteric arteriogram is made after embolization to ensure that no collateral supply to the bleeding site is present. If extravasation is identified, superselective catheterization of the inferior pancreaticoduodenal artery and the side branch responsible for the collateral circulation is performed with the microcatheter [25,26]. TAE with microcoils of the bleeding site is performed as distal as possible. The risk of ischemic complications is very rare at the upper GI tract thanks to the rich collaterality [11]. Regarding embolization of LGIB, the use of smaller microcatheters is usually needed to reach distal bleeding sites. It is admitted that the risk of ischemic complications post-embolization is higher than that of embolization of UGIB. This risk is almost nil if less than three vasa recta are embolized at the

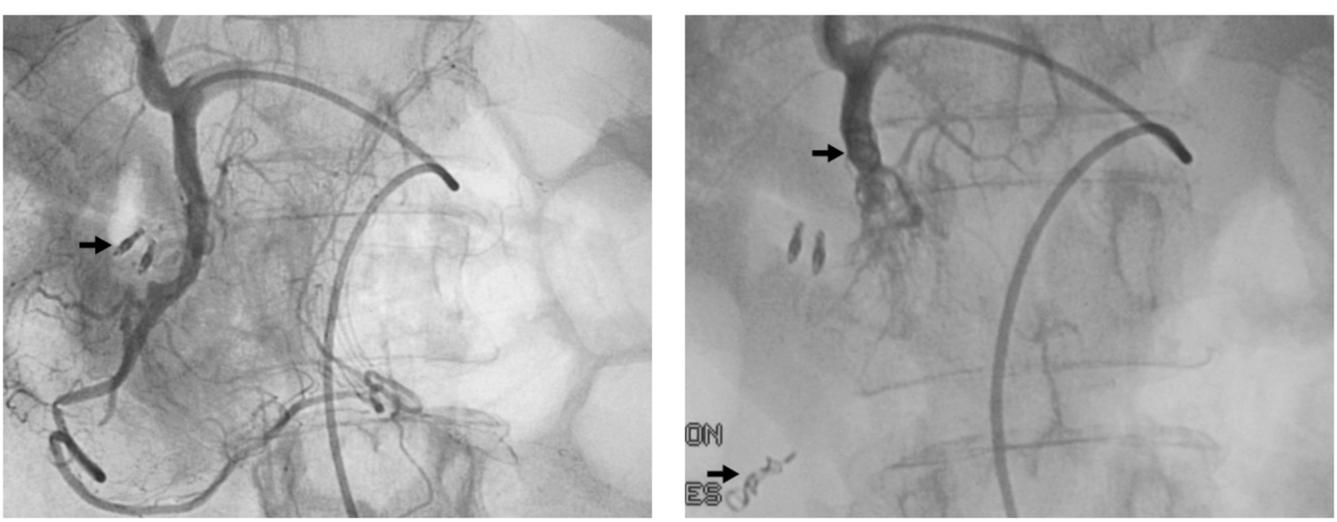

Fig. 1. Typical sandwich embolization in a 75-year-old woman with bleeding from a postbulbar duodenal ulcer at endoscopy. Angiography before embolization, guided by clip position (arrow): no evidence of active bleeding **(a)**. Coil embolization of the distal and proximal gastroduodenal artery (with gelatine sponge in the arterial trunk), including the anterior and posterior superior pancreaticoduodenal arteries and the right gastroepiploic artery, to prevent retrograde flow (arrows) **(b)**. Bleeding stopped and no ischemic complications were reported.

colon level [11,27]. Embolization must then be conducted very selectively (Fig. 2).

Empiric or blind embolization

Blind embolization is a matter of debate. Because massive bleeding is often intermittent, most teams have adopted a policy to embolize on the basis of endoscopic findings even where no extravasation is seen angiographically at the upper GI tract [15,16,28]. In the main reported series, no difference in outcomes were found between patients who underwent empiric embolization and those who underwent embolization after a bleeding site had been demonstrated angiographically [15,16]. The practice of endoscopy-directed empiric embolization is nowdays consiederd as appropriate for patients with UGIB. No data exist about its use for LGIB based on CTA findings, endoscopy being impossible in most cases.

Choice of embolic material

Many embolic agents have been used successfully: mainly coils, resorbable gelatin sponge particles and nonresorbable particles [7–12,25–28]. Liquids such as *n*-butyl 2-cyanoacrylate (NBCA) glue (Glubran®, GEM, Viareggio, Italy) or ethylene-vinyl alcohol copolymer (Onyx®, MicroTherapeutics, Inc., Irvine, CA, USA) are less popularly used but have recently gained acceptance. The choice of

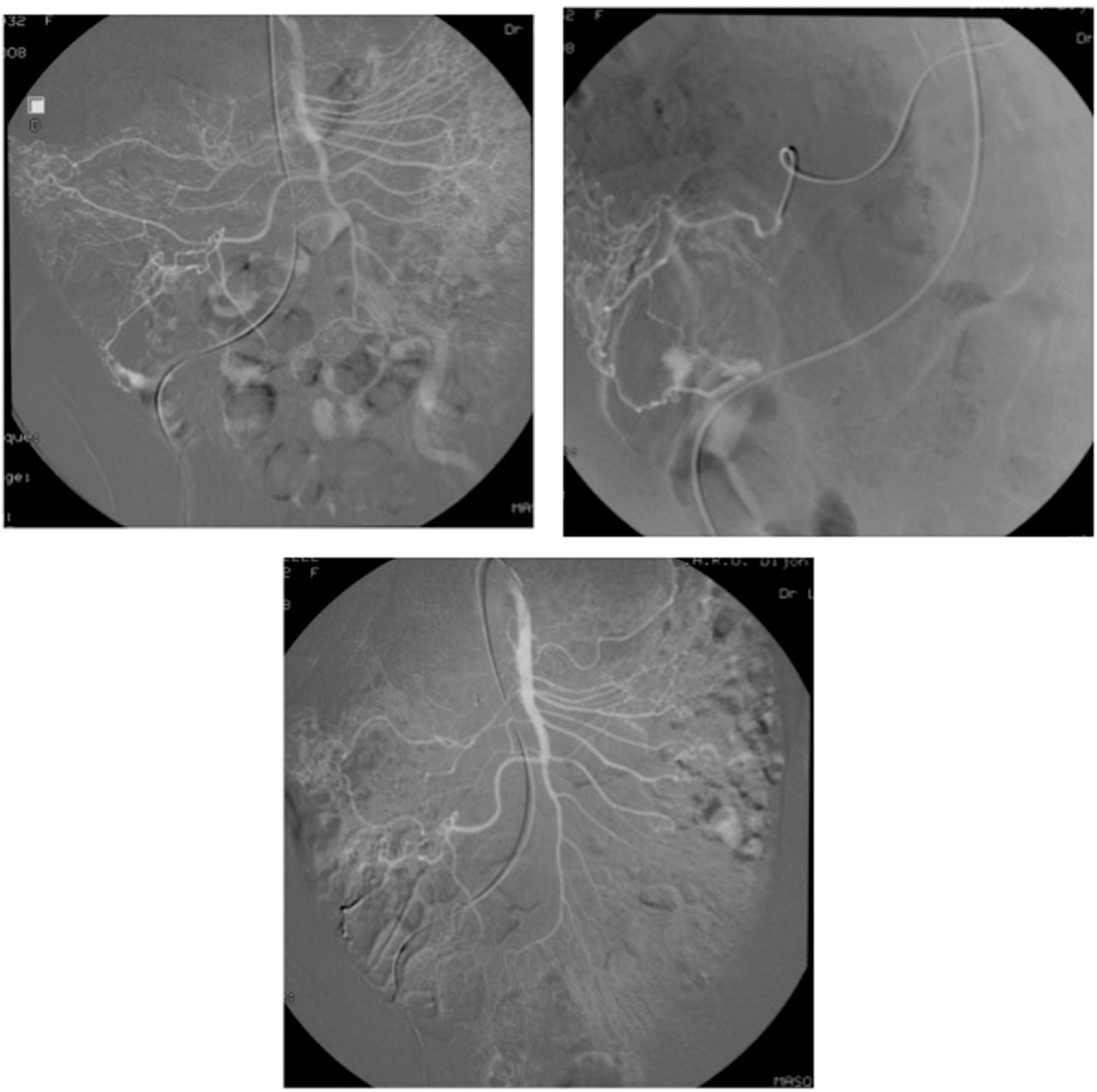

Fig. 2. Bleeding Dieulafoy's lesion in an 87-year-old man. Extravasation of contrast medium from the left gastric artery at the celiac trunk **(a)** and superselective angiography **(b)** indicates continuing bleeding (arrows). After arterial microcatheterization, bleeding was controlled after embolization of the left gastric artery using a Glubran®2 glue/lipidol mixture (1:3) (arrows) **(c)**.

the best embolic agent is still controversial. Coils alone inserted for both UGIB and LGIB have been used with success [10–12]. The main advantages of using coils are that they can be delivered in a very precise fashion and carry low risk of infarction because of the preservation of the distal microvasculature. Coils and microcoils of different size and length may be used. They may have thrombogenic fibers to facilitate occlusion of the vessel, and they may offer the option of detachability and retrievability. The main drawback is that they are permanent and may preclude reaccessing the vessel in the future should it prove necessary. Another disadvantage is that coil application is dependent upon vessel diameter and intrinsic blood clotting. The use of coils alone has been shown to be associated with the incidence of bleeding recurrence, especially in patients with coagulopathy. The advantages of use of gelatin sponge in association with coils when choosing a strategy for this subgroup of patients cannot be over stressed. Gelatin sponge is the main temporary embolic agent used worldwide. It has the advantage that after resorption, flow will be restored weeks after embolization. Furthermore, it is readily available, cheap, and unlikely to cause ischemia. The disadvantages are that it requires some time to prepare appropriate-sized particles, and the risk of recanalization is unpredictable. Data from the literature confirm that the use of gelatin sponge as the only embolic agent guarantees only short-term results and should probably be avoided [29].

Particles such as poly-vinyl-alcohol particles and tris-acryl gelatin microspheres may be of advantage when a flow-directed strategy is favourable, e.g. when diffuse tumor vascularization is to be excluded from the arterial supply. These agents have been used successfully in treating GIB, usually through a microcatheter and at a site distal to major vessels [30]. Only larger particles (>500 μm) should be used to decrease the risk of ischemia from normal tissue devascularization.

More recently, very good results have also been reported with NBCA for both UGIB and LGIB [31–33]. TAE using NBCA allows rapid hemostasis. This is important especially in cases of massive bleeding. Indeed, the use of NBCA glue is particularly of interest in hemodynamically unstable patients and in cases of underlying coagulopathy (Fig. 3). However, the use of NBCA glue requires training and considerable experience, given the risk of bowel infarction and glue reflux into other vessels. Reflux of NBCA may also result in its polymerization to the catheter tip. This bit of NBCA may then be stripped from the catheter during catheter retraction, resulting in nontarget embolization. The use of a proper technique, including prompt removal of the catheter after injection as well as

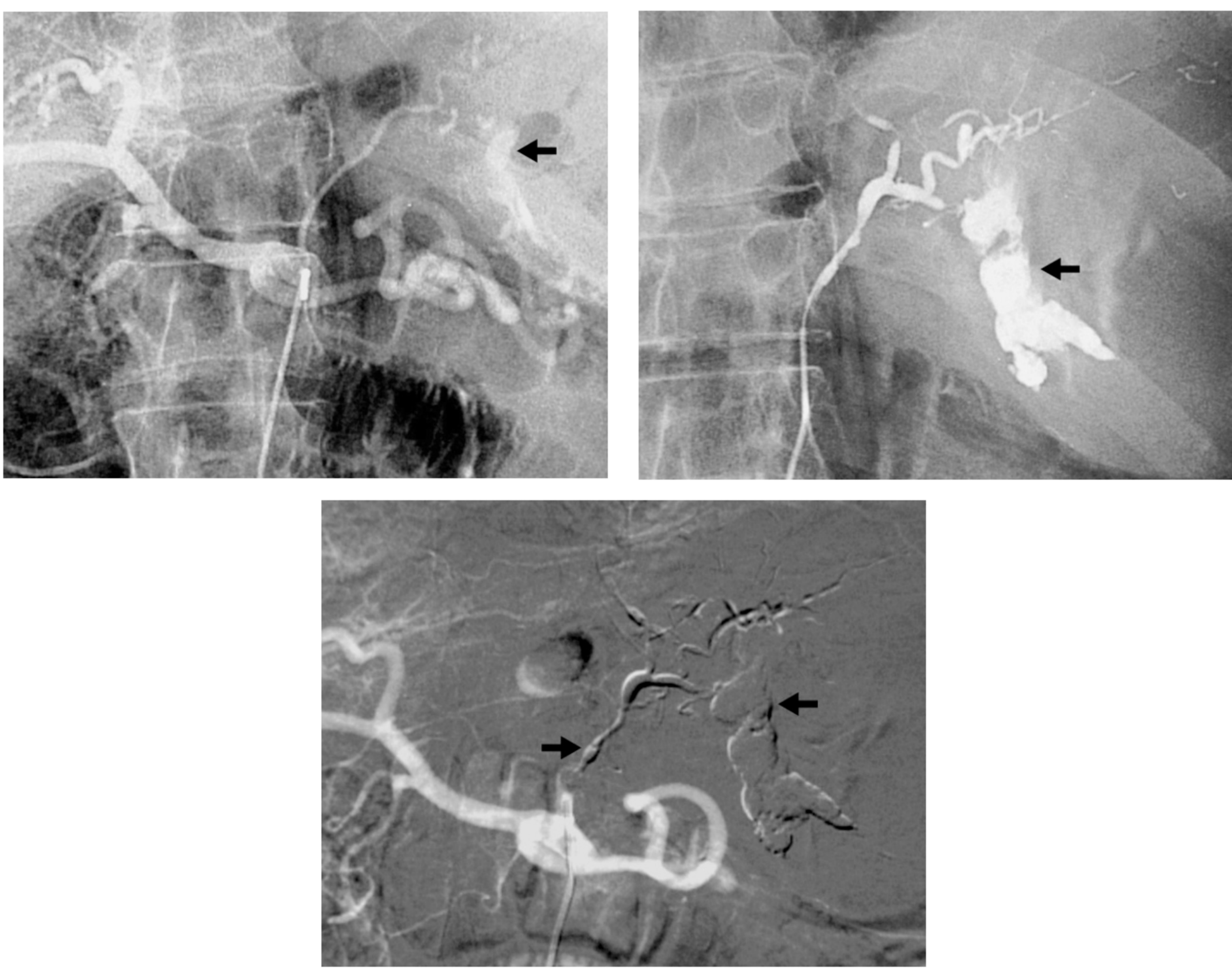

Fig. 3. Lower gastrointestinal bleeding after endoscopic ablation of polyps of the caecum in a 76-year-old patient. Superior mesenteric artery arteriogram shows contrast extravasation arising from the ileocecal artery **(a)**. Superselective arteriogram confirms active bleeding. This extravasated contrast medium denotes the site of lower gastrointestinal bleeding **(b)**. The bleeding branch was successfully coil embolized using microcoils through a microcatheter **(c)**.

aspiration of the guide catheter after microcatheter removal, can significantly reduce this risk [34]. Onyx® seems to have great potential as a liquid embolic agent in embolotherapy of acute GIB. Few studies reported to date results on TAE with Onyx® as an embolic agent in the GI tract. The success rate is high (81%) and the complication rate almost nil. The main advantages of Onyx® are its nonadhesive properties, high radiopacity, and long solidification periods. These properties of Onyx® compared to acrylic glues, make the embolization procedure more controllable and predictable [27,34,35]. However, Onyx® has some disadvantageous characteristics. First, DMSO can cause severe vasospasm if injected rapidly. Secondly, DMSO is volatile and is excreted via respiration and sweat. This has a typical smell not unlike that of diabetic ketoacidosis and may last a few days. The patient and ward staff should be warned to expect this. Lastly, the use of Onyx® has cost implications as it is much more expensive than alternative embolic materials and requires specific DMSO-compatible microcatheters [29,35]. These factors explain its restricted use in neuroradiology in most of the institutions around the world. In some situations, specific endovascular techniques maybe useful to stop bleeding as coil packing of a pseudoaneurysmal sac or implantation of a covered stent, in order to preserve the patency of the parent vessel [36].

Finally, it is not clear if careful selection of the embolic agents according to the bleeding vessel may play a role in a successful outcome. It would be worth comparing the different embolic agents for TAE in the GI tract in a prospective randomized multicenter trial. However, data from the literature suggest that coils probably should not be used as the only embolic agent, but rather in association with gelatin sponge, particles or glue for the treatment of gastroduodenal hemorrhage. Furthermore, surgical glue should probably be used more often, especially in patients with coagulopathy, because it provides a better and faster hemostasis and does not cause more ischemia for both UGIB and LGIB [31–34].

Outcomes of embolization

Technical and clinical success

The current technique of TAE in the treatment of acute GIB successfully controls bleeding in about 80%–90% of patients [11,25,30,33,34]. Recurrent hemorrhage is infrequent, with the exception of angiodysplasia, AVMs and inflammatory lesions. Recurrences can usually be angiographically reevaluated and, if a bleeding source is identified, treated with repeat embolization. Since the beginning of its use in the management of UGIB, TAE has shown increasing technical and clinical success rates. With a goal of hemostasis, most studies since 2000 show technical success rates greater than 90% and clinical success rates greater than 70% [15,26,32,37,38]. Additionally, studies suggest comparable clinical results for empiric (endoscopically, but not angiographically, identified) embolization versus angiographically identified bleeding site embolization [15,16]. And clinical results are comparable with surgical treatment, even in patients deemed poor surgical candidates and those with more severe comorbid conditions. TAE is also highly effective in treating acute LGIB with technical success rates as high as 96.4%–100%. Clinical success rates are somewhat lower, ranging from 63% to 91.2%, often due to rebleeding following embolization [11,27,30,35].

Complications

TAE for the treatment of acute GIB is safe, with major adverse events (those requiring subsequent treatment) occurring in less than 5% of patients [11,34]. Most major adverse events seem to occur in individuals with preexisting vascular compromise: prior surgery or radiation treatments. A fraction of patients embolized superselectively will develop minor, asymptomatic and self-limited ischemic changes such as small ulcers that can only be detected incidentally via objective follow-up methods such as endoscopy, pathologic surgical specimen or by a radiographic imaging examination [39,40]. Arterial embolization in the upper GI tract above the ligament of Treitz is generally considered very safe because of the rich collateral supply to the stomach and duodenum. The risk of ischemic complications is considered higher after TAE for LGIB. However, if less than three vasa recta are embolized in the colon area, this risk is very low [11,30,35]. Overall, mild ischemic complications, ranging from transient abdominal pain to asymptomatic ischemic stricture, are shown in 10% of patients. The use of cyanoacrylate glues has gained acceptance over the last 5 years, without any more risk of ischemic complications but with many advantages as described previously [41]. Few studies reported results of TAE with Onyx® for GIB [27,35]. The largest series reported no major complications and no ischemic complications in patients treated for LGIB [35]. Non-target embolization with microcoils is rare, as the coils are introduced only after a microcatheter has been successfully negotiated into the target vessel. One must carefully choose appropriate sized microcoils however, as a coil that is oversized relative to the target vessel may displace the microcatheter from its superselective position. This could lead to deployment of the microcoil in a non-target location. Similarly, undersized coils may fail to adequately occlude the target vessel or may lodge distal to the lesion that is to be treated.

Prognostic factors

Although few series analyzed factors predicting TAE failure, some factors that may influence the outcome of patients who have undergone TAE for acute UGIB or LGIB have been identified [9,15,25,42].

Among clinical factors predicting rebleeding, coagulopathy has been shown to adversely affect the success rate for embolization, with an increase in the odds ratio for clinical failure, which ranges from 2.9 to 19.6 [9,15]. Subsequently, every effort should be made to correct coagulopathy before, during, and after endovascular procedure. Other clinical variables have been identified as predictors of early rebleeding after TAE: a longer time from shock onset to angiography, a larger number of RBC units transfused before angiography, and having $\geq$2 comorbid conditions [9]. Thus, the ability to achieve bleeding control in critically ill patients seems to depend chiefly on early intervention and severity of the underlying disease. Previous surgery for bleeding is also a well-documented independent predictor of poor TAE outcome [25]. Clinical signs of shock and active bleeding at admission are known risk factors for rebleeding after endoscopic therapy; hence, they are probably risk factors for early recurrence after embolization as well [25,42]. Regarding LGIB, thrombocytopenia and coagulopathy prior to TAE are also strongly associated with clinical failure [42].

Factors influencing mortality include advanced age, trauma or sepsis, recent major operation, lung or liver disease, and massive blood transfusions. One of the most important factors influencing post-TAE mortality and frequently encountered is the absence of early rebleeding. Laslty, a strong correlation exists between coagulopathy, clinical failure, and mortality after TAE [25,26,34].

Specific topics of interest

Marking with a metallic clip

Marking with a metallic clip during pre-embolization endoscopy can assist with localization of the vessel feeding the bleeding site even if there is no contrast medium extravasation after injection with the catheter in the common hepatic or the main trunk of the GDA. This is also important when the bleeding artery arises separately from the proper hepatic artery or the GDA. The clips remain in position for several hours and allow for an educated guess of the location of the culprit vascular branch [43]. If no extravasation is seen despite the injection of contrast, then the branches terminating to the clip are superselected using microcatheter techniques and embolized. Arteriography at multiple projections is necessary at this step to ensure the relation between the clip and the adjacent branches. Superselective angiography guided by clip position has better chances to demonstrate the extravasation, making blind coil placement unnecessary, thus increasing the efficacy of the procedure and decreasing the risk of coil misplacement and inadvertent hepatic embolization [43].

Embolization versus surgery

To date, no controlled trial has compared angiographic embolization with surgery as a salvage procedure for failed endoscopic therapy. A randomized study comparing TAE and surgery in peptic ulcer bleeding uncontrolled by endoscopy is currently recruiting patients in Hong Kong [44]. Its primary outcome is 30-day mortality, and the secondary outcomes are recurrent bleeding, need for further intervention in terms of either surgery or interventional radiology, and postprocedural complications. However, the trial was registered in 2007 and has yet to recruit its target of patients. This could be in part related to problems gaining consent in the emergency situation. The wide array of alternatives for the treatment of GIB after endoscopic failure make the decision of when to resort to emergency surgery more difficult, especially in patients with risk factors for recurrent bleeding and death, which are also related to high surgical risk. Law et al. in a randomized controlled study, showed no differences in bleeding control between a second endoscopic treatment and surgery after initial endoscopic treatment failure for bleeding peptic ulcers [45]. During endoscopy, active bleeding, large ulcer size, location of ulcer at posterior bulbar duodenum, and lesser curve have been identified as predictors for endoscopic failure [45]. TAE may be particularly attractive in such a setting because it is not as invasive as surgery and has few complications [45]. Another advantage of TAE is that most patients with recurrent bleeding after initial treatment with surgery or TAE can be effectively treated with TAE, thus avoiding a second surgical procedure. Results of the largest review comparing the use of surgery or TAE in major UGIB are based on nine nonrandomized studies of variable quality, including 711 patients (347 who had embolization and 364 who had surgery) [46]. When compared with surgery, TAE had a significant increased risk of rebleeding rates after TAE; however, there were no differences in mortality rates. These findings are subject to multiple sources of bias due to poor quality studies. These findings support the need for a well-designed clinical trial to ascertain which technique is superior. The technological advances in the management of GIB via interventional radiology have improved rapidly, whilst the experience of surgeons in the management of upper GI hemorrhage is dwindling. Over the past few decades the number of patients requiring surgical intervention for UGIB has decreased enormously. In the 1990s, up to 13% of patients required surgery to control bleeding from peptic ulcer disease [45]. However, with improved endoscopic hemostatic techniques and intravenous proton pump infusions, the rate of surgical procedures has dropped to less than 2% in the present day [47]. Most of individual series indicate that TAE compares favorably with surgery regarding prognosis after refractory peptic ulcer bleeding, and the shorter length of hospital stay and fewer complications outweigh a higher risk of re-bleeding [48,49]. Finally, TAE could be recommended as first-line treatment for these patients with co-morbidities and coagulation disorders, making them poor surgical candidates.

Prophylactic embolization in high-risk peptic ulcers

One of the major challenges in peptic ulcer bleeding is rebleeding which is associated with up to a five-fold increase in mortality [47]. Recently, Lau et al. evaluated in a randomized controlled trial the role of prophylactic angiographic arterial embolization performed after achieved endoscopic hamostasis in the management of patients with high-risk ulcer bleeding [47]. The authors' hypothesis was that added angiographic embolization performed within 12 h from successful endoscopic therapy may reduce the rate of rebleeding in patients with bleeding from high-risk peptic ulcers. Unfortunately, the authors failed to demonstrate any statistically significant impact of added embolization on outcomes of these patients, as a consequence of lack of power. However, if added angiographic embolization after.

Endoscopic hemostasis did not improve clinical outcomes in most high-risk patients.

With bleeding peptic ulcers, in a posthoc analysis, the authors found that patients with bleeding ulcers 15 mm in size or greater would benefit from added angiographic embolization [47]. The risk of recurrent bleeding was then reduced by around fivefold. The results show that in patients with exigent bleeding from gastroduodenal ulcers 15 mm or greater, angiographic embolization to the bleeding artery may be considered after initial hemostasis with endoscopic methods. Further studies are needed in order to confirm these findings but technical advances combined with a better selection of patients could probably broaden the indications for prophylactic embolization of peptic ulcer bleeding after achieved endoscopic hemostasis.

Summary

Endoscopy has been very successful in the treatment of GI bleeding. However, in a small but challenging proportion of patients, endoscopy cannot achieve hemostasis or is not able to identify the source of bleeding. For these patients, additional diagnostic and therapeutic tools are required. CT angiography (CTA) may be considered in patients with upper GI bleeding but is often unnecessary, especially if the actively bleeding site has been marked with a metallic clip during endoscopy. On the other hand, CTA is mandatory before angiography for lower GI bleeding, endoscopy being often times impossible or unconclusive in the emergency setting. TAE is a viable option for cases of nonvariceal GI bleeding failing endoscopy, particularly in the setting of massive acute bleeding in poor surgical candidates. Advances in microcatheter technology, the development of a wide range of embolic agents, and modern interventional radiology angiography suites have extended the ability of this technique. Liquid embolic materials as NBCA and Onyx® should be more frequently used, given the rapidity and efficacy of hemostasis, especially in the setup of coagulation disorders. Given success rates that are comparable with surgical treatment, TAE should be considered the first option after failure of endoscopic treatment. In patients successfully treated endoscopically for hemorrhage related to ulcer disease, prophylactic additional TAE of the bleeding artery could become a viable option to decrease the rate of rebleeding. Further studies are warranted. Additional technical developments expected to become more widespread in the future include the use of newer liquid embolic agents, CT angiography fusion guidance, and endovascular robotics.

Practice points

- For persistent or intermittent bleeding that cannot be localized by gastroscopy or colonoscopy, further diagnostic evaluation with computed tomography angiography should be considered
- Patients with active bleeding that is refractory to endoscopic treatment should undergo transcatheter arterial embolization
- The choice of the best embolic agent remains controversial but liquid embolic agents provide rapid hemostasis not affected by coagulopathy and, therefore, should probably be used more frequently

Research agenda

- The best embolic material to be used in the treatment of severe gastrointestinal bleeding needs to be defined
- Detailed controlled studies are necessary to define the efficacy of liquid embolic agents in acute nonvariceal gastrointestinal bleeding
- More studies are necessary to define the role of prophylactic embolization based on endoscopic findings in high risk peptic ulcers

Conflicts of interest

None.

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