Endovascular therapy of gastrointestinal bleeding
Die endovaskuläre Therapie gastrointestinaler Blutungen

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Key words
abdomen, angiography, embolization, interventional procedures, hemorrhage

received 15.12.2018
accepted 19.03.2019

Bibliography
DOI https://doi.org/10.1055/a-0891-1116
Published online: 2019
Fortschr Röntgenstr
© Georg Thieme Verlag KG, Stuttgart - New York
ISSN 1438-9029

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ABSTRACT
Background Gastrointestinal (GI) bleeding is a frequently occurring disease pattern, with a broad variety of possible causes. The most acute bleeding responds well to conservative, medicinal and endoscopic therapies. Nevertheless, a certain amount of endoscopically not-identifiable or controllable non-varicose GI-bleeding requires alternative, sometimes surgical, therapy concepts. The updated S2k guideline “gastrointestinal bleeding” makes the case for interventional radiology with its minimally invasive endovascular techniques.

Methods This review article discusses the role of interventional radiology in the therapy of non-variceal upper and lower gastrointestinal bleeding according to the current literature and updated guideline. In this regard it covers the indications, technical performance, results and complications of endovascular therapy.

Results and conclusion Considering interdisciplinary therapy options, the guideline-oriented endovascular treatment of gastrointestinal bleeding, using embolization and implantation of covered stents, shows to be a reasonable option with good technical and clinical success rates and a low rate of complications. In this context solid knowledge of vascular anatomy is essential to acquire adequate hemostasis.

Key points:
- Interventional radiology contributes significantly to the diagnosis and treatment of non-variceal bleedings of various etiologies.
- In this context the S2K guideline “gastrointestinal bleeding” is the foundation for the decision-making process for hemostatic therapy.
- Embolization is the first choice when it comes to endovascular treatment of gastrointestinal bleeding.
- Adequate periinterventional management increases the success rate of endovascular therapy.

ZUSAMMENFASSUNG

Methodik In dieser Übersichtsarbeit wird die Rolle der interventionellen Radiologie in der Therapie nichtvarikeröser und unterer gastrointestinaler Blutungen anhand der aktuellen Literatur sowie der neuen Leitlinie diskutiert. In diesem Kontext werden Indikationen, technische Durchführung, Ergebnisse und Komplikationen endovaskulärer Therapieverfahren thematisiert.

**Introduction**

Non-variceal gastrointestinal bleeding is often an urgent, potentially life-threatening emergency [1]. In 75 – 85 % of cases they are located in the upper gastrointestinal tract [2, 3]. Treatment generally requires a structured interdisciplinary approach with therapeutic options ranging from conservative, surgical, endoscopic to endovascular procedures. The indication for endovascular therapy is closely oriented to the recently published S2k guideline of the German Society for Gastroenterology, Digestive and Metabolic Diseases (DGVS) [4].

**Classification, Epidemiology and Etiology**

Upper gastrointestinal bleeding (UGIB) is bleeding above the ligament of Treitz. With an incidence of 50 to 100 per 100 000 population, it is a common pathology with a median disease age of 60 – 70 years [5]. In 70 – 75 % of cases an upper GI bleed ceases spontaneously. The mortality rate is between 3 and 14 %, for intensive care patients between 42 and 64 % [1]. In approximately 50 % of cases, UGIB results from an ulcer disease such as a gastric ulcer or duodenal ulcer. Other causes include esophageal or gastric tumor bleeding, Mallory-White syndrome, erosive gastritis or duodenitis, reflex esophagitis, angiodysplasia and iatrogenic or post-traumatic changes.

A special case of UGIB is acute hemorrhage of the peripancreatic vessel branches or collaterals, which etiologically often result from pancreatitis, tumors and trauma. Hemorrhages after pancreatic surgery due to pancreatic jejunostomy or biliodigestive anastomosis, with a mortality rate of 11 – 38 %, are among the most complex and difficult to treat complications due to vascular congestion. In many cases, such postoperative complications of endovascular therapy are easily accessible, which can significantly reduce morbidity and mortality rates [6].

Lower gastrointestinal bleeding (LGIB) beyond the ligament of Treitz, with an incidence of about 20 to 30 per 100 000 population and a median age of 65 – 80 years increases dramatically with age [7]. In 80 – 85 % of cases LGIB ceases spontaneously. Recent studies indicate the mortality between 2 and 5 % [1]. Etiologically, LGIB can be attributed to causes such as diverticulitis, angiodyplasia, polyps, tumors, proctitis or chronic inflammatory bowel disease [8].

**Anatomy**

The upper gastrointestinal tract contains pronounced vascular anastomoses and physiological collaterals, which on the one hand make the intestinal segments less susceptible to post-embolic ischemia, but on the other hand can make bleeding control more difficult due to the maintenance of bleeding via the "back door" and the necessity of occlusion of the feeder vessel proximal and distal to the bleeding source or due to the occurrence of recurrent bleeding. These vascular anastomoses consist of branches of the pancreaticoduodenal arteries between the celiac trunk and the superior mesenteric artery. The arch of Riolan and the Drummond anastomosis connect the superior and inferior mesenteric arteries. Anastomoses exist between branches of the superior mesenteric artery and the internal iliac artery via branches of the superior and medial rectal arteries. A large number of anatomical variants, in particular the branches of the celiac trunk, require a thorough evaluation of the vascular anatomy before planned embolization [9].

**Symptomology**

The clinical presentation of gastrointestinal bleeding varies as a function of the severity and localization of bleeding. Occult bleeding can manifest itself as iron deficiency anemia or lead to a positive hemoccult test if there are other symptoms. In the case of heavy bleeding of the upper GI tract, clinical signs such as regurgitation of blood or hematemesis are evident; melena may also occur. Hematochezia is indicative of heavy bleeding of the upper or lower GI tract. In chronic forms, non-specific signs such as fatigue, tiredness or shortness of breath may occur. Depending on its severity, acute bleeding leads to symptoms of circulatory insufficiency or a hypovolemic shock with tachycardia, hypotension and collapse.

**Clinical Evaluation and Diagnosis**

Initial and pre-interventional management includes the anamnesis of clinical manifestation and bleeding duration as well as the assessment of accompanying symptoms, medication, concomitant and pre-existing conditions and interventions such as polypectomy or surgery.

Further procedure depends on the hemodynamic status of the patient and the suspected location of bleeding. The hemoglobin value and the (modified) Glasgow-Blatchford score, in which vital parameters, laboratory values and pre-existing conditions are taken into account for risk stratification (open recommendation, strong consensus), can be used for the initial assessment of the severity of bleeding and for clinical decision making [4, 10 – 12].

According to the guideline, hemodynamically unstable patients with non-variceal UGIB should receive intensive medical care, after stabilization, should be examined promptly (< 12 h) using EGD (strong recommendation, strong consensus) [4, 12]. In hemodynamically stable patients, endoscopy should be performed within the first 72 hours after continuous monitoring of the vital parameters (open recommendation, strong consensus) [4, 13]. Since severe consequences of LGIB are less frequent and mortality and bleeding-related mortality are lower, outpatient treatment is often possible [14]. Severe hemorrhages of the lower GI tract with hemodynamic compromise should be promptly colonoscoped after drug stabilization (recommendation, strong consensus). Detection of the source of bleeding in these situations is only possible in about 42 % of cases due to inadequate intestinal preparation in emergency management and the limited visibility of the colon and proximal ileum [15].

Depending on the bleeding type and genesis, endoscopic hemostasis can be achieved by various mechanical methods...
(rubber band ligation, hemoclips) and thermal procedures (electrocoagulation), injection therapy (e.g. with adrenalin) and the use of Hemospray (open recommendation, strong consensus) [4]. If an endoscopic hemostasis attempt remains unsuccessful, endoscopy can nevertheless contribute to precise endovascular intervention planning and facilitate superselective catheterization of the corresponding bleeding vessel branch by means of clip marking of the detected bleeding source, especially if no active contrast extravasation can be detected angiographically [16].

In the case of frustrated identification of the bleeding source during endoscopy, further diagnostic procedures are available, depending on the bleeding dynamics and availability of other diagnostic procedures, provided that the affected patients concerned are hemodynamically stable or stabilized. Detection using contrast-enhanced multi-line computed tomography can be performed at bleeding rates of 0.5 ml/minute and above [17]. In multi-phase technology, CT as non-invasive imaging allows rapid diagnosis with good sensitivity and specificity and can contribute to the planning of further therapy regimes in addition to localization of bleeding [18]. According to current data, due to its high spatial resolution, digital subtraction angiography (DSA) allows the identification of a bleeding source at bleeding rates between 0.5 and 1 ml/minute [21]. There is high variability in the literature with respect to regard to sensitivity and specificity of catheter angiography [22]. The invasive character of DSA, which can be considered disadvantageous, is countered by the possibility of simultaneous treatment of GI bleeding. In a direct comparison with CTA, several studies showed its superiority with regard to the sensitivity of the detection of the bleeding source and the cause of bleeding [22, 23]. In summary, it can be recommended that patients, after a frustrated endoscopic search for the source of hemorrhage, should first be referred to multi-phase CT diagnostics in the case of hemodynamic stability, since important information can be obtained regarding the cause of the bleeding, possible vascular anomalies and variants. This can contribute to an exact planning of the subsequent (endovascular) therapy and a consecutive temporal shortening of the intervention time [19, 22]. In addition, this approach is in line with the recommendations of the current S2k guideline [4]. A blood cell scintiscan using $^{99m}$Tc-marked red blood cells with a sensitivity of 93 % and specificity of 95 % enables the localization of intermittent GI bleeding from low bleeding rates of 0.2 ml/minute [20].

Pre-interventional Preparation

In the case of hemodynamic instability, hypovolemia should be balanced with erythrocyte concentrates, crystalloids or colloids and catecholamine or vasoconstrictor therapy prior to intervention [12, 24, 25].

In addition, the relevant coagulation parameters (INR, PTT) should be determined and, if necessary, optimized, since mechanical embolic agents in particular often only cause sufficient vessel occlusion if the coagulation cascade is intact [21]. Administration of glucagon or buscopan may be considered to reduce intestinal peristalsis.

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Contraindications

Contraindications for endovascular therapy – such as contrast agent allergy, hyperthyroidism, pregnancy, sepsis, acute kidney failure and consumption coagulopathy – are to be regarded as relative, especially in acute threatening situations. Depending on the intensity of the bleeding, the possible superiority of surgical therapy must be considered.

Technique

As a rule, endovascular treatment of upper GI or lower GI bleeding is performed under local anesthesia via a transfemoral access pathway, although transbrachial access can also be considered, especially in the case of an unfavorable angle of descent of the visceral vessels. Depending on the vascular anatomy, insertion of a long reinforced guide sheath for catheter stabilization may be useful. Especially in the absence of pre-interventional imaging, mechanical preparation of a survey angiography via a multi-hole pigtail catheter allows evaluation of the vascular anatomy for subsequent targeted vascular exploration. The most suspicious or identified visceral vessel is probed using a preferred selective catheter, and a selective angiography is performed. For UGB, the celiac trunk and then the superior mesenteric artery are probed; in the case of LGB the superior and inferior mesenteric arteries are examined. The use of approximately 50 ml 1:1 diluted contrast agent at a flow rate of 15 ml/s is recommended for a proper aortography; for selective angiography of the celiac trunk, the superior and inferior mesenteric arteries, 30 – 50 ml 1:1 diluted contrast agent at flow rates of approximately 6 – 7 ml/s is recommended [32]. In case of rectal bleeding and inconclusive presentation of the inferior mesenteric artery, angiography of the internal iliac artery including the middle and inferior rectal arteries should be performed [33]. In this case, care must be taken to ensure sufficient exposure time to distinguish contrast agent extravasation and venous washout. Angiographic evidence of GI bleeding in the active bleeding interval presents as contrast extravasation in the arterial phase with pooling in the venous phase. However, indirect signs such as evidence of pseudoaneurysms, vascular spasms or – in the case of inflammatory changes – blushing and focal hyperemia can also be interpreted as angiographic evidence of (intermittent) GI bleeding [34]. Early venous discharge may indicate angiodysplasia.

Superselective vascular probing and thus the use of coaxial or triaxial microcatheter technique is often necessary to identify an upper or lower GI bleed. The coaxial technique involves the use of a microcatheter within a selective catheter; the triaxial technique involves the use of a microcatheter and a selective catheter within a reinforced guide sheath or guide catheter.

The frequently intermittent character of gastrointestinal bleeding may lead to a negative angiographic result despite recent relevant bleeding. In these cases, repeated angiography at a later stage or bleeding provocation by selective intra-arterial application of nitroglycerin, heparin or tPA may be considered [35].

In the absence of evidence of active contrast extravasation, blind or empirical embolization based on an endoscopic finding may be possible, although prior endoscopic clip marking may be helpful [16, 36].

The patient should promptly undergo surgery in the event of technically frustrated intervention due to feeder vessels that cannot be probed, or even in the case of diffuse bleeding. Until the patient is transferred to the OR, balloon occlusion can be used to achieve preoperative hemodynamic stabilization. Additional options for facilitating, identifying and accelerating surgical therapy include catheter-assisted staining of the bleeding intestinal segment with methylene blue.

Once angiographically identified, the location of the upper or lower GI bleeding (distal vs. proximal) determines the endovascular procedure to be used.

Embolization

In more distal hemorrhages, embolization is performed by coaxial or triaxial microcatheterization (Fig. 1 – 4). The choice of the appropriate embolic material to stop the respective hemorrhage is at the discretion of the interventionist and is influenced by practical experience, local availability of material, the cause of bleeding, coagulation situation and extent of the angiographic findings. The use of a temporary embolic agent such as a gelatin sponge as the sole embolization material has been associated with an increased rate of secondary bleeding and should therefore be avoided [34]. Microspirals are the most commonly used mechanical embolization material in the treatment of GI bleeding. With technical success rates between 80 – 90 % for upper gastrointestinal bleeding and 40 – 88 % for the lower gastrointestinal bleeding, microspirals support practicable placement with good radiopacity and, precisely because of their good visualization properties, reliable embolization [37]. However, the use of microspirals alone has been associated with a significantly increased rate of recurrent bleeding compared to a combination with cyanoacrylates or particles [34]. Cyanoacrylates as the sole liquid embolic material or in combination with other agents have been shown to be particularly effective in patients with impaired coagulation [34, 38, 39]. Especially in the case of hemodynamic instability, they offer the advantage of a significantly shorter procedure time [40] The likelihood of reflux, misembolization or adherence of the catheter tip to the polymerized adhesive or vessel wall is considered a relative risk. Ethylene-vinyl alcohol copolymer can be used as an alternative liquid embolization material [41, 42]. Particulate embolic agents such as polyvinyl alcohol particles or microspheres have a particle diameter of less than 250 µm and therefore carry the risk of intestinal ischemia due to reaching the intramural vascular bed [7]. Nevertheless, particles have been shown to be effective in controlling bleeding due to malignant tumors without increasing the incidence of post-embolic-ischemic complications [43]. The low radiopacity – despite combination with contrast medium – thus providing only indirect visualizability requires a limited control of embolization and necessitates a certain amount of experience for this embolic agent as well.

Due to pronounced vascular anastomoses, especially of the upper GI tract, the front door-back door technique with occlusion
**Fig. 1** Lower GI bleeding with unidentified genesis in a 55-year-old male. 

a. An axial CTA in the arterial contrast phase shows an intraluminal contrast extravasation within a jejunal loop in the left lower abdomen. 

b. Superselective DSA using coaxial microcatheter technique allows the identification of the related feeder vessel. 

c. Superselective DSA using coaxial microcatheter technique allows the identification of the related feeder vessel. 

d. Selective DSA after microspiral embolization, in which active bleeding can no longer be detected.

**Fig. 2** Iatrogenic upper GI bleeding after PEG placement in a 55-year-old female. 

a. Overview of the non-selective DSA shows a pronounced contrast extravasation from the left gastric artery. 

b. In superselective DSA, a microcatheter is used to identify the true extent of active bleeding from the left gastric artery. 

c. Superselective DSA after microspiral embolization shows the successful elimination of active bleeding. 

d. Selective final DSA again documents cessation of the iatrogenic upper GI bleeding from the left gastric artery.

**Fig. 3** Lower GI bleeding as a consequence of ulceration in a 57-year-old male under intensive care. 

a. Coronal CTA shows active contrast extravasation in the arterial contrast phase at the level of the cecum. Evidence of abundant fresh blood within the ascending colon. 

b. Selective DSA impressively shows active bleeding in the final flow area of the ileocolic artery. 

c. Superselective DSA via a microcatheter after spiral embolization identifies a further, circumscribed active bleeding from another vasum rectum of the ileocolic artery. 

d. Selective control DSA demonstrates successful hemostasis in the final flow area of the ileocolic artery.
of the feeder vessel proximal and distal to the bleeding source is often necessary for sufficient embolization. Alternatively, embolization of two supplying vessels (initially branches of the celiac trunk, then the superior mesenteric artery or vice versa) may be necessary.

The level of embolization plays a significant role here. Since the risk of territorial ischemia increases with too proximal vascular occlusion, distal, super-selective probing of the vessel supporting the bleeding should be sought. This applies in particular to endovascular treatment of lower gastrointestinal bleeding and especially to bleeding of the colon, as this has a much lower collateralization compared to the upper GI tract [44].

Post-interventional Procedure

The focus here is on the patient’s hemodynamic status to determine the extent of the effectiveness of the endovascular measure. In addition, regular monitoring of lactate levels should be carried out, the increase of which, in combination with abdominal symptoms, may be indicative of intestinal ischemia. If necessary, a control endoscopy can be useful. The utility of antibiotic treatment with first generation cephalosporins depends on the respective clinical conditions and should therefore be decided on a case-by-case basis.

Results

The body of data regarding endovascular treatment of upper and lower GI bleeding, in particular embolization using coaxial or triaxial microcatheter technology, is constantly increasing, but must be viewed cautiously due to the inhomogeneity of the underlying pathologies. In this context, the data published so far are often based on retrospective results, often small to medium case series and with at most short to medium-term follow-up periods. It is relevant for the interpretation of the clinical results that corresponding published studies are partly based on differing reporting standards.

According to current clinical literature, bleeding of the upper gastrointestinal tract can be treated with technical success using endovascular procedures in 69 – 100 % of cases [34, 45 – 49]. In contrast, clinical success rates are between 58 and 91 % [34, 49, 50]. Compared to surgical procedures, interventional radiological strategies in the treatment of upper GI bleeding show similar efficacy in terms of technical success and rate of recurrent bleeding, but with lower mortality [51 – 53]. In the respective cohorts, however, patients treated with interventional therapy had a higher rate of comorbidity as well as higher age, which could explain the relatively high mortality rate of up to 33 % [34]. Recurrent bleeding, which occurred in about one-third of cases, was accessible for a new intervention in 50 % of the cases; in 20 % of the patients, surgical measures were necessary for definitive bleeding control [34]. Apparently selective, empirical arterial embolization without angiographically-detectable contrast extravasation may also be
effective. Thus, in different study cohorts, no difference was found with regard to the outcome among patients in whom blind embolization was performed based on endoscopic or surgical findings and those in whom embolization relied on an angiographic image of the bleeding [24, 26, 47]. In contrast, if one considers the publication by Schenker et al. [48], who blindly embolized 103 of 163 patients (63%) within their patient cohort due to different bleeding etiologies, the question arises to what extent this therapeutic approach might have contributed to the high recurring bleeding rate of 42% (68 out of 163 patients) and mortality rate of 33% (54 out of 163 patients).

These results are based on only sparse data if one considers the endovascular results of acute bleeding of the peripancreatic vessels, which is difficult to treat and is often based on erosion due to released proteolytic enzymes in the course of acute pancreatitis or surgical intervention. Nevertheless, technical success rates of up to 93% have been described in this respect, while clinical success rates of up to 91% have been described, with mortality rates being reduced by up to 60% compared with surgical procedures [54–57].

There is agreement that the survival of patients after endovascular upper GI bleeding therapy is highly influenced by the general condition of the patient at the time of intervention [48, 58]. Thus, patients with multi-organ failure exhibit significantly higher mortality rates. In this context, mortality is highly dependent on the primary technical success of endovascular treatment with mortality rates of up to 96% in the event of treatment failure [48].

Endovascular treatment of LGIB is possible with technical success between 89 and 100% and clinical success rates between 81 and 90%, especially after failure of an endoscopic attempt to stanch bleeding [7, 21, 29, 44]. The improvement of the super-selective embolization technique through the development of microcatheter systems with an external diameter down to 1.8 French plays a major role in this context, as this enables the precise probing of the smallest feeder arteries (vasa recta). This minimizes the rate of misembolization, especially as the treatment is mainly performed in the terminal branches. In this context, it appears to be highly significant that recurrent bleeding in the sense of clinical failure is often located in intestinal segments other than the actual area of embolization [59, 60]. This may be primarily due to the relevant bleeding etiology. Diverticular bleeding responds better to embolization than those of the lower gastrointestinal tract with other etiologies such as tumors or bleeding resulting from angiodysplasia [60]. In this context, the distinction between early recurrent bleeding within 30 days and late recurrent bleeding >30 days after embolization may be useful, as suggested by d’Othee et al. [59].

Various studies have identified technical and clinical predictors for a negative outcome with respect to technical failure and recurrent bleeding in the endovascular treatment of upper and lower GI bleeding. Previously untreated coagulopathy showed a strong influence on the treatment outcome, underlining the importance of adequate peri-interventional treatment of coagulation disorders [48, 61]. Other risk factors for interventional treatment failure include multimorbidity, low hemoglobin levels, hemorrhagic shock, corticosteroid treatment, prolonged duration of intervention and increased need for transfusion of blood products [46, 47].

Complications

Potential complications include general risks of endovascular therapy such as hematomas in the access area, vascular dissections or contrast-associated complications (allergy, nephropathy) [34]. In addition, fever, leukocytosis, sepsis and abdominal pain may occur as part of post-embolization syndrome. The risk of related intestinal ischemia after embolization shows a clear dependence on the localization and embolization agent used, and lies between 0 and 20% for UGIB and between 0 and 22% for LGIB [29, 33, 34, 44, 59, 62].

Due to distinct alternative circulatory routes, arterial embolization of the upper gastrointestinal tract can be described as very safe and rarely leads to ischemic complications. Agents reaching the distal vascular bed, such as liquid embolic agents or small particles, are associated with an increased risk of significant ischemia with gastroparesis, intestinal gangrene and necrotizing pancreatitis [63]. In addition, prior surgical procedures at the embolization site have been associated with increased
rates of severe ischemic complications following embolization of upper GI bleeding [46]. In addition, symptomatic duodenal stenosis could be observed as a long-term complication after embolization of terminal branches of the upper gastrointestinal tract [45].

The lower GI tract is significantly more sensitive to post-procedural intestinal ischemia due to less pronounced collateralization, which depending on the extent of the embolization area, may manifest as minor ischemia (mucosal ischemia) with transient abdominal discomfort and increase in lactate levels, or in approximately 1 – 5 % of cases as major ischemia (transmural infarction) with the need for surgical resection [29, 64, 65]. Nevertheless, the development and improvement of microcatheter technology and embolization has led to a minimization of the rates of post-embolic minor and major ischemia [44, 66]. Distal embolization at the level of the vasa recta or marginal arteries contributes to a significant reduction of the risk of critical ischemic complications [41 – 43]. Major ischemic complications requiring surgery occur here only in isolated cases and are mostly due to necessary super-selective probing of the feeder branch in question, especially in the context of generalized atherosclerosis [67]. In exceptional cases, however, the clinical relevance of intestinal ischemia should be put into perspective, i. e. when hemostasis is used for pre-operative bridging. Within such a scenario, endovascular intervention with hemodynamic stabilization can be followed by medical optimization of the patient’s general condition and risk stratification.

Summary

Endovascular therapy of upper and lower GI bleeding is a minimal-invasive measure that should be carried out according to guidelines and with close interdisciplinaty cooperation. The underlying etiology of bleeding, the localization and dynamics of bleeding, as well as the structural, staff and equipment conditions of the respective site, are all factors that influence the choice of diagnostic and therapeutic measures. Previous data indicate that endovascular strategies may be beneficial for morbidity and mortality in patients with high surgical risk.

Conflict of Interest

The authors declare that they have no conflict of interest.

References


