

Endovascular Therapy of Severe Non-Variceal Gastrointestinal Bleeding – One Decade Experience.

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Abstract

Introduction Severe non-variceal gastrointestinal bleeding is a life-threatening condition with complicated treatment if endoscopic rescue fails. In that case, transcatheter arterial embolization is recommended to stop the bleeding. The technical and clinical effects of this technique were analyzed in this group of patients, as well as its complication rate and 30-day mortality.

Method Patient data of the one-decade period (from 2010 to 2019) were analyzed retrospectively. Twenty-seven patients (18 men and nine women, median age 61 years) treated by endovascular embolization in our institution with clinically significant gastrointestinal hemorrhage after unsuccessful or impossible endoscopic treatment were identified.

Results The source of bleeding was found in 88% of patients, but embolization was performed in 96% of them. The technical success rate in the sample was 100%, and the clinical favorable outcome rate was 88.5%. The bleeding recurrence occurred in eight cases, five of whom had technically successful re-embolization in four cases. The incidence of recurrent bleeding was significantly higher in patients with two or more comorbidities with ($p = 0.043$). There was one serious complication (4%) in the group and minor difficulties occurred in 18% of patients; 30-day mortality reached 22%. Mortality was significantly higher in the group of patients with re-bleeding ($p = 0.044$).

Discussion Our documented results in common are in the established rank of previously published results, which range from 62-100% for technical success, 52-94% for the clinical favorable outcome, 9-66% for re-bleeding and 4-46% for 30-day mortality.

Conclusion Transcatheter arterial embolization is a safe mini-invasive method with high technical and clinical success in patients with endoscopically untreatable gastrointestinal bleeding. It is also suitable for high-risk cases. Mortality (to a significant extent) typically depends on the re-bleeding presence and the patient's comorbidity.

Introduction

The nonvariceal gastrointestinal tract (GIT) bleeding is often a sudden, life-threatening condition. In 85% of patients, we encounter bleeding from the upper GIT [1], which includes part of the GIT from the esophagus to the ligament of Treitz. To simplify the study, an older classification was used, and only the upper and lower GIT bleeding (which includes bleeding from the small intestine, colon, and rectum) were evaluated separately. Most bleeds are resolved spontaneously or after conservative treatment. The endoscopy is a method of choice for the diagnosis and treatment of GIT bleeding refractory to drug treatment. Nevertheless, there is a 5-10% group of patients in whom it is not possible to achieve hemodynamic stability or endoscopy is ineffective or unfeasible after surgery. These patients require endovascular or surgical intervention [2]. Technical improvement of transcatheter arterial embolization (TAE) based on possibility to use microcatheters and new embolic agents enables targeted superselective embolization with high technical and clinical success.

Methods

The patients underwent angiography and embolization for clinically significant GIT bleeding, which was nonresponsive to a medical, endoscopic or, in some documented cases, surgical treatment, were retrospectively identified in the period from 2010 to 2019 in the local database of Clinic of Radiology.

Twenty-seven hospital patients (18 men and nine women) aged 2 to 94 years (median 61 years) met the inclusion criteria of the study group. One-third of the specific cases were older than 70 years. In all, 78% of them had severe

comorbidity, and 55% in common were polymorbid ill patients with two or more comorbidities.

Clinically, bleeding was present in 30% as enterorrhagia (n = 8), in 22% as hematemesis (n = 6), in 15% as melena (n = 4) and in 18% as a combination of hematemesis with melena (n = 5) or in 15% enterorrhagia followed by melena (n = 4). The mean hemoglobin (Hb) value before embolization was 85 g/l (45-121).

Etiologically the hemorrhage originated from a duodenal ulcer in five patients, inoperable cancer in seven patients, bleeding after endoscopic drainage of a pancreatic pseudocyst in two cases (Fig. 1), and three times from pancreatic pseudoaneurysm. One case of Mallory-Weiss syndrome and two cases of jejunal angiodysplasia were also occurred. In seven patients, GIT bleeding occurred after previous surgery: 1 × total gastrectomy, 2 × laparoscopic biopsy of the liver followed by radiofrequency tumor ablation, 1 × enucleation of NET of the head of the pancreas, 2 × proximal duodenopancreatectomy with cholochojejunal anastomosis, and 1 × resection of ductus hepatocholedochus with cholochojejunal anastomosis. The median time interval between initial clinical manifestations and angiography was 5.5 days (14 hours to 22 days).

A transfemoral approach was typically used to perform splanchnic angiography. In one specific case, in a patient with an advanced rectal tumor, the approach was promptly changed to transaxillary during the procedure, due to the technical unavailability of the inferior mesenteric artery. Angiography was satisfactorily performed using diagnostic catheters. After vascular pathology confirmation, a coaxial system with a guiding catheter was used, and embolization was performed selectively through a microcatheter. Coils, liquid embolic agent (LEA), and microparticles or Spongostan foam were used as embolic material. In selected patients with negative angiographic findings, empirical embolization was performed, or embolization was oriented by an endoscopically placed clip close to the area of the bleeding lesion.

Technical success was typically determined as the angiographic disappearance of extravasation or the occlusion of pseudoaneurysm or other embolized vascular pathology at the end of embolization. Clinical success was precisely defined as the ultimate disappearance of the original symptoms of bleeding after the endovascular procedure. Recurrent bleeding was defined as a repeatedly significant decrease of Hb after embolization in the period of monthly follow-up. Potential complications were traditionally classified as serious if caused time prolongation in medical institution or required surgical treatment; or classified as minor if they did not affect the time of hospital stay.

Data were analyzed by using the Fisher exact test and Wilcoxon signed-rank test. Statistical significance was determined at $p = 0.05$. Statistical software® [3], version 4.0.2, was used for data processing.

Results

Pathological angiographic findings were confirmed in 24 out of 27 patients (88%). Active bleeding was identified in nine cases, pseudoaneurysms in seven patients, diseased tumor enhancement was found four times, pathological hypervascularization in the ulcer area in two cases, one arterioportal fistula, and one pseudoaneurysm with arteriovenous fistula in the liver. In three cases, it was not possible to angiographically identify the source of hemorrhage. Despite a negative angiographic finding, two of these studied patients also underwent empiric embolization of the gastroduodenal artery with continued bleeding from the duodenal ulcer, which was initially treated endoscopically. In total, embolization was performed in 26 selected patients.

The following arteries were treated: gastroduodenal artery (GDA) (n = 7), left gastric artery (n = 4), superior pancreaticoduodenal artery (n = 3), inferior pancreaticoduodenal artery (n = 3), hepatic artery or its branches (n = 3), rectal artery (n = 3), jejunal branches and superior mesenteric artery (SMA) (n = 3), splenic artery (n = 2), great pancreatic artery (n = 1). Embolization was performed by using coils (n = 15), LEA (n = 5), microparticles (n = 2), and

Spongostan (n = 1). A combination of embolic material was applied three times (coils + microparticles, coils + LEA, and microparticles + LEA). The technical success rate of embolization in our group of patients reached 100%. Clinical success or cessation of clinical signs after embolization reached 88.5% (23/26). Recurrent bleeding occurred in eight sick person (29.6%), after the primary session. In five exceptional cases, repeat embolization was carefully performed, which was technically and clinically successful among four patients. The summary characteristics of patients with re-bleeding are summarized in Table 1.

A significantly higher risk of re-bleeding occurred in polymorbid patients (p = 0.043). In the group of patients with re-bleeding, there is a tendency, although insignificant, of patients being of older age, with a median age of 70 (SD 63-76) years, compared to patients without re-bleeding, with a median age of 58 (SD 35-68) years (p = 0.067).

Table 1: Characteristics of patients with recurrent bleeding.

Patient	Time to re-bleed (days)	Primary diagnosis	Primary endovascular treatment	Secondary treatment	Technical success	Clinical success	30-day mortality
No. 2	3	Rectal cancer	Spongostan	TAE - LEA	successful	successful	
No. 4	3	NET	Coils	Surgical revision, conservative treatment	-	successful	
No. 7	11	Jejunal angiodysplasia	Coils	conservative treatment	-	successful	
No. 9	3	Post-surgery - Klatskin TU	Coils	TAE - LEA	successful	successful	Death
No. 10	10	Post-surgery – pancreatic cancer	No pathology revealed, no treatment	TAE - Coils and LEA	successful	successful	
No. 11	1	Duodenal ulcer	Coils	TAE technically unsuccessful	unsuccessful	unsuccessful	Death
No. 17	9	Gastric cancer	Coils and particles	TAE - Coils	successful	successful	Death
No. 27	17	Pancreatic cancer	LEA	conservative treatment	-	unsuccessful	Death

TAE – transcatheter arterial embolization, LEA – liquid embolic agent, NET – neuroendocrine tumor

There was only one major procedure related complication in the patient group (4%). Splenic necrosis transformed to abscess occurred in one patient after embolization, the because of extravasation after surgery (proximal duodenopancreatectomy), which was managed by surgical splenectomy. Other complications, classified as minor, were diagnosed in a total of five patients (18.5%) – three periprocedural dissections of the artery without hemodynamic effect and clinical manifestation, one ulceration of the gastric mucosa after embolization of the left gastric artery, and one puncture site bleeding managed by prolonged compression and a hemostatic bandage.

The 30-day mortality reached 22% (six patients). The median age of selected patients who died was 68 years vs. 58 years in the remaining ones. The 30-day mortality was significantly increased by the presence of re-bleeding (11% vs.

50%; $P = 0.044$). Two critical patients died from persistent bleeding. These were a polymorbid 94-year-old patient with a duodenal ulcer bleeding and a 67-year-old patient with inoperable pancreatic cancer. Premature deaths, in the patient group without persistent bleeding, were caused by 1 × myocardial infarction, 1 × hepatorenal failure, and 2 × multiorgan failure due to malignancy.

Discussion

In practice, bleeding from the upper GIT accounts for 70% of GIT bleeding [4] and ulcer disease being the most common cause [5]. In hemodynamically unstable patients with upper gastrointestinal bleeding, intensive care is needed for patient stabilization, followed by subsequent endoscopic examination, which is a remarkably successful treatment option. In direct contrast, hemodynamically significant bleeding into the lower GIT is less common. Hemodynamic instability and insufficient bowel cleansing are relative complications of colonoscopy. Despite stabilization, colonoscopy can, in the acute phase for insufficient patient preparation, prove the possible source of bleeding in only 42% of cases [6]. CT examination aimed at detecting GIT bleeding performed with the correct protocol can accurately detect an extravasation with a higher sensitivity compared to that in conventional angiography (0.3 ml/min vs. 0.5 ml/min) [4]. CT examination is therefore recommended before digital subtraction angiography (DSA) in case of bleeding from the lower GIT and endoscopically non-localized bleeding from the upper GIT. Its practical implementation remains questionable in the case of localized, endoscopically untreatable bleeding from the upper GIT, when endoscopy should provide sufficient necessary information before DSA [7]. Indications for endovascular treatment traditionally include technical failure of endoscopic treatment, recurrent bleeding despite a second endoscopic treatment and an endoscopically non-localizable source of bleeding [8]. Contraindications to standard angiographic examination are only relative in life-threatening bleeding. The modern development of embolic material has provided various practical possibilities of proper use, according to the required properties and nature of embolization. The procedures were performed by using coils at our institution in most cases. Coils as the only embolic agent have been successfully used in several studies [7, 9 and 10]. Their advantage is precise placement, saving of the distal vasculature and the minimal risk of ischemia. Coil embolization is permanent, therefore blocking re-access to the target vessel or to its more distal branches in the future. The potential disadvantage in common is their effectiveness depends on the patient's own blood clotting. The exclusive use of coils as the sole embolic material is naturally associated with an increased risk of recurrent bleeding in critical patients with coagulation disorders [2]. In our group of patients, coil embolization was performed in 12 cases and four of these patients suffered repeated bleeding. An example is the recanalization of a pseudoaneurysm of the hepatic artery in a patient with consumption coagulopathy. The pseudoaneurysm was occluded with liquid embolic material in the second treatment session. This is a certain advantage of LEAs, providing immediate hemostasis that is especially needed in hemodynamically unstable patients and vulnerable patients with coagulopathy. Several agents are available, such as n-butyl cyanoacrylate, ethylene vinyl alcohol copolymer (Onyx, Medtronic or Squid, Balt), and biocompatible polymer agents (PHIL, MicroVention). Their use has also recently proved successful in the effective treatment of GIT bleeding [11–16]. The LEA (Onyx or PHIL) was utilized solo five times and twice in the proper combination. Its local application has been technically and clinically successful without ischemic complications. Other embolic agent, e.g. a Spongostan, was carefully applied for treatment of GIT lesions exclusively. It is a temporary occlusion material, and its usage as a stand-alone embolic agent is naturally associated with increased re-bleeding rate [17]. The Spongostan was optionally used in our cohort only once in a selected patient with a rectal tumor due to the probable risk of post-ischemic neuropathy. This patient developed re-bleeding, which was carefully managed by Onyx application, after a negative Mesocaine test, with technical and clinical success. Microparticles are considered frequent use in the embolization of bleeding tumors. In case of intestinal embolization, the use of particles with diameter larger than 500 µm is recommended because of the risk of ischemia. Ischemic complications are uncommon in the upper GIT area thanks to the extensive collateral

network. To prevent the so-called backdoor bleeding in the specific case of dual arterial supply, embolization of both dominant sources is necessary. A typical example of such embolization is the so-called sandwich technique of embolization of the GDA. In our documented case of a bleeding duodenal ulcer, the right gastroepiploic artery and pancreatic arcade were embolized primary, promptly followed the proximal GDA occlusion. This is efficient technique to prevent continued bleeding through the collateral branches from the splenic artery and SMA [17]. The embolization is associated with a higher risk of ischemic complications in the lower GIT. Due to superselective embolization and occlusion of less than three rectal artery branches, this terrible risk is minimal [18]. Empirical or blind embolization refers to embolization based on endoscopic findings without confirmed extravasation during angiographic examination. This valuable method is traditionally accepted in the upper GIT bleeding, and do not differ in published results of its use compared to targeted embolization with proven hemorrhage [19]. The empirical embolization was performed by us in two cases of refractory bleeding ulcer with technical and clinical success. The procedure can be facilitated by an endoscopically placed clip on the edge of a suspicious lesion. This helps the radiologist target the local treatment of the bleeding area (Fig. 2). Recent findings powerfully suggest the potential benefits of the preventive embolization in bleeding duodenal ulcers in patients at significant risk of recurrent blood loose [20]. In a published analysis that included 15 studies (a total of 829 patients) focusing on the TAE in the upper GIT bleeding, the technical success rate was 93% (62-100%), the clinical success rate was 67% (52-94%), the risk of re-bleeding was 33% (9-66%) and the 30-day mortality was 28% (4-46%) [21]. The results of embolization from the lower GIT range with a technical success rate above 90%, a clinical favorable outcome rate of 86% and an occurrence of ischemic complications of 4-6% [22, 23]. In our study, all pathological lesions detected by angiography were treated. Notable clinical success with an acceptable re-bleeding rate of 29.6% was confirmed by our analysis, which depended significantly on the occurrence of comorbidities. In addition to the number of comorbidities, other studies have identified next risk factors for early recurrent hemorrhage, like coagulopathy, prolonged time from bleeding to angiography and a higher number of transfusions [21]. The total 30-day mortality was 22%, and it was significantly higher in the group of patients with recurrent bleeding.

Conclusion

Transcatheter embolization is the recommended treatment option in the case of endoscopically untreatable gastrointestinal bleeding. It has high technical and clinical success and an acceptable level of complications. It is also suitable for high-risk patients; whose mortality mostly depends on the occurrence of early recurrent hemorrhage and comorbidities.

List Of Abbreviations

GIT – gastrointestinal tract, TAE – transcatheter arterial embolization, RFA – radiofrequency ablation, NET – neuroendocrine tumor, Hb – hemoglobin, LEA – liquid embolic agent, DSA – digital subtraction angiography, GDA – gastroduodenal artery, SMA – superior mesenteric artery, TU – tumor

Declarations

Authors' contributions

ZK supervised the entire study, participated in the study design, wrote, and reviewed the manuscript. VM, SJ analyzed and interpreted the data. GM performed statistical analyses. VM wrote the manuscript. DM, BP reviewed the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and analyzed in the current study are available from the corresponding author on a reasonable request.

Ethics approval and consent to participate

This study was approved by the University Hospital Martin institutional review board. Consent to participate was waived by the institutional review board due to the retrospective nature of this study and the fact that patients were deidentified.

Consent for publication

Not applicable.

Competing interests

The authors have no conflicts of interest to declare.

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Figures



Figure 1

Embolization of superior anterior pancreaticoduodenal artery pseudoaneurysm. A - Superior anterior pancreaticoduodenal artery pseudoaneurysm after pancreatic pseudocyst endoscopic treatment. B – Embolic agent – Coils. C – Final angiogram confirmed pseudoaneurysm occlusion.



Figure 2

Gastroduodenal artery embolization in the managed patient with the endoscopically untreatable duodenal ulcer bleeding. A – Duodenal wall hypervascularity. B – The final angiogram with the occlusion of the gastroduodenal artery. C – Embolic material – coils positioned next to the endoscopically placed clip, which facilitates endovascular treatment precisely targeting.