REVIEW

An upper gastrointestinal ulcer still bleeding after endoscopy: what comes next?

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ABSTRACT

Introduction: Recurrent bleeding from an upper gastrointestinal ulcer when endoscopy fails is a reason for radiological or surgical treatment, both of which have their advantages and disadvantages.
Case: Based on a patient with recurrent gastrointestinal bleeding, we reviewed the available evidence regarding the efficacy and safety of surgical treatment and embolisation, respectively.
Discussion: Transarterial embolisation (TAE) and surgical treatment are both options for recurrent gastrointestinal bleeding when endoscopy fails. Both therapies have serious complications and a risk of rebleeding. Choosing the therapy depends on the capability of the patient to tolerate haemodynamic instability, resuscitation and hypotension.
Conclusion: Choosing between TAE and surgery depends a great deal on the case presented, haemodynamic stability and the skills and tools available at that moment.

KEYWORDS

Gastrointestinal bleeding, failed endoscopy, TAE, surgery

INTRODUCTION

A bleeding upper gastrointestinal ulcer is a potentially fatal disease, and immediate treatment is necessary. The primary treatment of a bleeding ulcer is endoscopic, but with persistent or recurrent bleeding, rescue treatment may be necessary or even life saving. In this report, we describe a patient with recurrent massive bleeding where initial endoscopic treatment failed. Based on a literature review we discuss the treatment options.

CASE

A 58-year-old male was admitted to the GI department of the hospital with gastrointestinal bleeding. He was mentally impaired and his medical history revealed nephrotic syndrome and hypertension. Because of his mental impairment, endoscopy had to be performed under sedation. He was admitted to the ICU where he was intubated. The endoscopy revealed multiple lesions in the bulbus duodeni, one of them being the source of the bleeding. This large semi-circumferential ulcer was coagulated and then the patient started esomeprazole therapy (80 mg iv twice daily). The patient showed no signs of persistent bleeding. After extubation he was haemodynamically stable and was discharged to the ward. He had a rebleed six days later. Endoscopy revealed that the same ulcer was bleeding from a visible vessel, and the treatment was coagulation around the ulcer. The performing endoscopist stated that there where no further options for endoscopic therapy in case of rebleeding. In that case, surgical or radiological consultation should be sought. The patient was discharged to the ward again, in a good condition.
Two days later, the patient had to be resuscitated because of haemorrhagic shock due to recurrent bleeding. The patient could be stabilised initially. The decision was made to do an interventional angiography because he was judged to be stable enough. During the decision-making process, the patient became unstable again with abdominal distension, high pressure ventilation and hypotension.
Despite this, he underwent an interventional angiography. The bleeding site was seen, marked by extravasation of contrast in the lumen of the bowel. The gastroduodenal artery and the proximal gastroepiploic artery were embolised. The procedure was difficult due to the size and anatomy of the lesion, and was further complicated due to ongoing bleeding requiring continuous resuscitation.

But ultimately haemostasis was reached. After the angiography, intra-abdominal hypertension developed reaching a maximum pressure of 40 mmHg. It decreased after several hours to 15 mmHg. The following night systemic hypotension developed without signs of further bleeding. The patient underwent a laparotomy where an ischaemic colon and gall bladder were seen with open arterial blood supply. Both were removed. The operation was complicated by massive blood loss. The next day he showed gastrointestinal blood loss again. An endoscopy revealed a necrotic stomach. The ulcer showed no signs of healing and the radiologically placed coils could be seen intraduodenally (*figure 1*). The patient died shortly after, without further therapy for shock.

DISCUSSION

In upper gastrointestinal bleeding, endoscopy is the diagnostic modality of choice. It has a high sensitivity and specificity for locating and identifying bleeding lesions in the upper GI tract. In addition, once a bleeding lesion has been identified, therapeutic endoscopy can achieve acute haemostasis, by thermal coagulation or haemoclip placement. This prevents recurrent bleeding in most patients. In most cases, endoscopy achieves haemostasis, but 10-30% of the patients have repeated bleeding for various reasons.[1,2] When haemostasis is not (expected to be) achieved with endoscopic techniques, other options are surgery or transarterial embolisation (TAE). Surgery has long been the standard of care but, with the development of intervention radiology, coiling a bleeding artery has gained a prominent role.

Figure 1. *Endoscopic view during the third endoscopy of the bulbus duodeni with the intra-arterial coil visible in the intestinal lumen*

Surgery

Surgery, the classical therapy, is effective in patients with uncontrolled bleeding. The aim of emergency surgery is not to cure the disease but rather to stop the haemorrhage when endoscopic therapy is unavailable or has failed. Generally accepted indications for surgery are failures of endoscopic techniques, haemodynamic instability despite resuscitation, recurrent bleeding after two endoscopic attempts, and continued slow bleeding (three transfusion units per day). It is an option in patients who may not tolerate recurrent or worsening bleeding. High-risk patients may not tolerate prolonged resuscitation, large volume transfusion, or periods of hypotension.[3,4]

Several surgical approaches are possible. In peptic ulcer disease, emergency surgery includes over-sewing the ulcer plus truncal vagotomy and pyloroplasty. Another approach for a gastrointestinal bleed is removing the bleeding site (e.g. performing a (partial) gastrectomy or duodenectomy), or ligating the bleeding vessel with a non-absorbable suture.[5,6] In a multicentre randomised prospective trial, Poxon *et al.* compared minimal surgery (ligating the vessel or ulcer excision) with conventional ulcer surgery (vagotomy and pyloroplasty or partial gastrectomy) for the treatment of a bleeding ulcer. The patients were randomised to undergo either minimal surgery, in which case the artery that supplied blood to the ulcer was ligated or where the ulcer itself was removed, or they underwent conventional surgery, in which case a vagotomy with pyloroplasty or a partial gastrectomy was added to vessel ligation. They found more fatal rebleeding in the minimal surgery group.[7] This finding is supported by the study of Billat *et al.* who found that gastrectomy with ulcer excision is the procedure of choice for emergency surgical treatment, because postoperative bleeding recurrence is lower, and the overall mortality rate and duodenal leakage is the same as with over-sewing and vagotomy.[8] Barkun *et al.* recommend that surgical consultation should to be sought for patients at risk for rebleeding after endoscopic retreatment, because salvage surgery can be required.[9,10] Emergent surgery is associated with mortality rates of up to 36%.[6] Surgical therapy is not always definitive. Recurrent bleeding rates following surgery vary from 3 to 23%, depending on the kind of surgery performed.[7,8]

Interventional angiography

TAE of gastrointestinal bleeding vessels has become the first choice in some centres for patients who do not to respond to medical and/or endoscopic therapy. Before intervention the bleeding locus can be identified. This can be done by clipping during endoscopy, CT angiography or standard angiography.[11]

Depending on the suspected location of the bleeding lesion the coeliac artery and either the superior mesenteric artery or the lower mesenteric artery are selectively filled with

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contrast. Extravasation of contrast in the lumen (blush) of the bowel marks the bleeding site. In the absence of a blush, indirect evidence is sought, which includes visualisation of an aneurysm or pseudo-aneurysm, filling of spaces outside the bowel lumen (diverticula), early draining vessels (angiodysplasia), neovascularity (tumours), arterio-venous fistulas and hyperaemia (colitis). Once the bleeding site is identified, the therapy can be delivered. In upper GI bleeding, the therapy can be given in the suspected vessel, even when the bleeding is not seen during angiography, when the bleeding site was identified during endoscopy.

Angiographic therapy consists of infusion of vasoconstrictive medication (vasopressin) at the bleeding site, or embolisation. In embolisation the arterial blood supply to the bleeding site is occluded. Materials used for embolisation can be gelatine sponges, polyvinyl alcohol (in small microspheres or sheets), liquid agents e.g. N-butyl 2-cyanoacrylate (NBCA) or ethylene-vinyl alcohol copolymer (Onyx, Micro Therapeutics, Inc, Irvine, CA). Once delivered, liquid agents solidify, leading to embolisation. The mechanical blocking devices, such as coils, platinum microcoils, balloons and silk threads, induce blood flow reduction and coagulation. These mechanical blocking agents are best suited for patients bleeding from varices, a large visceral artery or the gastroduodenal artery. The coils are placed proximally and distally from the bleeding site to prevent back-bleeding from collateral vessels.

Complications of embolisation include complications from the angiography itself (haematomas, arterial thrombosis, dissection, embolism, formation of pseudo-aneurysm) and bowel infarction. In their systematic review, Mirsadraee *et al.* found complications from embolisation in 5-9% of the patients, with ischaemia and infarction accounting for the majority of the complications.[12] They occur even though the GI tract has a rich collateral blood supply. Risk factors for these complications include previous surgery, pancreatitis, radiation therapy and concurrent vasopressin infusion. In their study, which included 95 patients with GI bleeding, Yap *et al.* found complications to be technical (migration of coils from the gastroduodenal artery into proper hepatic artery (3%), non-target embolisation of splenic artery (1%)), and they found four patients (4%) to have post embolisation ischaemia, all of the upper GI tract.[13]

Angiography with TAE for persistent or recurrent peptic ulcer bleeding is a less invasive alternative to surgery. Initial success rates for patients with acute peptic ulcer bleeding have been reported from 52% up to 98%, with recurrent bleeding rates ranging from 10% up to 38%.[13,14] Indications for interventional angiography for acute non-variceal upper gastrointestinal bleeding have been

suggested in a consensus statement from the American College of Radiology[15]:
- Endoscopy is the best initial diagnostic and therapeutic procedure
- Surgery and transcatheter arteriography/intervention are equally effective following failed therapeutic endoscopy, but transcatheter arteriography/intervention should be considered particularly in patients at high risk for surgery
- Transcatheter arteriography/intervention is less likely to be successful in patients with impaired coagulation
- Transcatheter arteriography/intervention is the best technique for treatment of bleeding in the biliary tree or pancreatic duct

TAE versus surgery in the literature

TAE and surgery have only been compared in retrospective studies of patients with peptic ulcer bleeding that could not be controlled endoscopically. No randomised trials have been performed and will probably never be done.

Ripoll *et al.* analysed the outcome of 70 patients with refractory peptic ulcer bleeding. Although the patients in the TAE group were older and had more comorbidity, the incidence of rebleeding (29 *vs* 23%) and mortality (26 *vs* 21%) was similar to the surgical group.[16]

Eriksson *et al.* found a trend towards lower 30-day mortality in the TAE group (3%) compared with the surgical group (14%) (p<0.07). However, the patients in the TAE group were older and had more comorbidity. The repeat bleeding frequency after TAE was slightly higher (25 *vs* 18%). There were no complications related to TAE, and TAE could prevent unnecessary resection of the upper gastrointestinal tract. Although the study has several limitations, they suggested that TAE might be superior to surgery.[17]

Wong *et al.* found TAE to be a safe procedure, with no ischaemic complications, although there is a high rate of recurrent bleeding. They state that TAE should at least be considered as an alternative to surgery. The high percentage of recurrent bleeding is supported by the data of Yap *et al.* who found rebleed percentages of up to 38%.[13,18]

Loffroy *et al.* state that embolisation is effective in patients for whom surgery is not a realistic option, even when extravasation is not visualised by angiography. The radiologist should be well informed about the patient's condition, the procedure should take place shortly after onset of bleeding, and coagulation disorders should be corrected. The choice of embolic agent in relation to the characteristics of the bleeding vessel is important.[19]

TAE versus surgery; the clinical balance

No decisive data were found in the literature. Therefore the choice for an individual patient has to be based on other arguments. Some of these are patient based. In

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older fragile patients, in patients with massive bleeding leading to deep hypotension, surgery might be preferable because the bleeding is, at least perceived to be, more quickly controlled. In rather stable patients or patients with previous abdominal surgery, TAE might be the first choice. Other arguments are institutional. Performing upper gastrointestinal tract surgery for benign reasons has diminished in frequency and not every surgeon is equally experienced. TAE also requires skills that not every radiologist possesses. The limited possibilities for resuscitation and monitoring in the angiography room during procedures that are sometimes lengthy can defer the choice to the operating theatre.

CONCLUSION

Our patient died of ischaemic complications after ongoing haemodynamic instability. An extensive literature search did not reveal convincing evidence for an alternative therapy. The initial treatment of an upper gastrointestinal bleed is endoscopy and an attempt at local control of bleeding. If endoscopic treatment fails there are two options: TAE or surgery. The available evidence from a limited number of retrospective studies suggests that there is a similar outcome in TAE and surgery to control gastrointestinal bleeding. Recurrent bleeding rates might be higher in patients treated with TAE, but complications might be more frequent in patients treated with surgery. As for surgery, there are different techniques for the procedure without any one proving superior. There seems to be no place for minimal surgery in this setting. The best way to proceed in patients with upper GI bleeding that cannot be controlled endoscopically is determined by patient related and institutional arguments.

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