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Embolization and its Limits: Tips and Tricks

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Nowadays, non-operative management is the preferred strategy, when possible. During recent years, an improvement in embolic techniques and agents, make non-operative management more feasible and effective. In the present paper, current indications, technical requirements, advantages and disadvantages, and contraindications are discussed. Moreover, particular attention is given to the limits of the embolization procedure, suggesting some tips documented by data in the literature to overcome these limits. The most feared limit or complication is the risk of non-target embolization, especially when target tissues are noble organs. Skilled interventional radiologists, embedded into an adequate multidisciplinary team, have the available tricks to limit risks, complications, and failures.

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INTRODUCTION

Nowadays, non-operative management (NOM) is a strategy for most hemodynamically stable blunt trauma patients, whereas patients who are hemodynamically unstable despite initial resuscitation are directly transported to the operating room for exploration [1]. The mini-invasive approach and NOM certainly expedite patient recovery and minimize hospital management, which is attractive in the current era of requiring the cost-effective use of hospital facilities.

Embolization is an interventional radiology (IR) procedure involving the intentional endovascular occlusion of an artery or vein which is usually performed on patients who are hemodynamically stable, or whose hemodynamic status is stabilized with initial resuscitation [2].

Although embolization was initially employed to diminish vascular inflow in neoplastic lesions and/or to facilitate surgical excision, with the development of endovascular techniques, procedures in IR allow most of these patients to be treated effectively, sparing the need for surgery [3,4].

Since embolization should be as selective as possible, interventional radiologists can precisely identify the bleeding vessel (as well as the presence of collaterals or anatomical variants) thanks to imaging modalities such as ultrasound or contrast-enhanced computed tomography (CT) angiography, and effectively occlude it [5]. Signs of clinical improvement are often evident as soon as the procedure has been completed [1].

Although NOM is preferred if possible, many cases require damage control surgery or a combination of surgery and IR techniques [6]. In hemorrhage settings, IR and damage control surgery are indeed complementary techniques. Moreover, during NOM and mini-invasive procedures, some limits may be encountered [7] and relative contraindications should always be considered (for instance, pregnancy, renal failure, and contrast allergy) [6,8–11].

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Table 1 Embolization key-points.

Main indications	– Treatment/stopping internal bleeding
	– Treatment of uterine fibroid tumors
	– Palliative treatment of some tumors
	– Treatment of aneurysms by blocking an artery supplying the aneurysm
	– Treatment of varicoceles
	– Administration of chemotherapy.
Limits	– Non-target embolization
	– Coagulopathy
	– Lack of time
Alternatives	– Open surgical repair
	– Correction of coagulopathy if any
Meds	– 1% Lidocaine
	– Moderate sedation
	– Antibiotics may be necessary (solid organ embolization)
Equipment	– Regular needle or micro-puncture kits
	– Guidewires/diagnostic and microcatheters
	– Embolization agents
How to perform	1. Prep and drape
	2. Local anesthesia and skin nick
	3. Seldinger technique - Guidewire, sheath, place catheter into
	4. Imaging (e.g. angiogram) to visualize target vessel
	5. Microcatheters may be used to access target vessel
	6. Deploy appropriate embolization agent
	7. Post-embolization imaging
	8. Remove catheter, obtain hemostasis
	9. Clean site and sterile bandages
Contraindications	– Hemodynamic instability
	– Pregnancy
	– Renal failure
	– Contrast allergy
	– Compartment syndrome, skin ischemia or necrosis
Adverse reactions	– Post-embolization syndrome (fever, pain, leukocytosis, nausea, vomiting)
Complications	– Puncture site: bleeding, hematoma, pseudoaneurysm, infection
	– Damage to healthy adjacent organs
	– Ischemia
	– Contrast allergy/nephropathy
Follow-up	– Bed rest per protocol
	– Evaluate puncture site
	– Keep clean and dry

In the present study, we discuss the indications, the main limits, and contraindications of embolization, with a focus on patients with hemorrhage in an emergency setting. Additionally, we analyze some challenging conditions in which embolization is required and feasible but the risk of non-target ischemia prevents execution. Finally, some tips to overcome ischemic damage will be reported.

The key-points of embolization are shown in Table 1.

INDICATIONS AND CONTRAINDICATIONS

Embolization has been used extensively in clinical practice because it may avoid the need for surgery, which has high mortality and morbidity rates in an emergency setting [6]. With technological improvements in the last decades, NOM has become the preferred first-line therapy for acutely injured patients [7, 12].

Although embolization was initially used to diminish vascular inflow in neoplastic lesions or to facilitate surgical excision, especially when the tumor is difficult or impossible to remove, this procedure can be applied to almost any part of the body to control or prevent abnormal bleeding [13].

In the acute setting, the workflow starts with a clinical evaluation. If the patient is hemodynamically stable, embolization should be promptly performed by interventional radiologists. On the contrary, if the patient is hemodynamically unstable, surgery is the gold standard and IR may have a role as embolization to reduce flow (such as in spleen or kidney hemorrhages) or as resuscitative endovascular balloon occlusion of the aorta in abdominal trauma patients [14].

Common indications include bleeding resulting from a traumatic injury, from gastrointestinal tract lesions (such as an ulcer or diverticular disease) or from vascular malformations [1]. Additionally, embolization is a technique used largely in IR to arrest small and medium-sized arteries of the peripheral system where preservation is not critical [15], whether due to penetrating or blunt injuries (for example, a patient with traumatic brain injury and pelvic trauma may require decompressive craniectomy prior to pelvic angiography and embolization; likewise, an unstable pelvic fracture may require external fixation or pre-peritoneal packing prior to embolization) [16].

Currently, NOM is the standard of care for most hemodynamically stable patients because it reduces the time of hospitalization, transfusion requirements, and costs while reducing the pain associated with tumor bleeding, preserving splenic function, and improving overall survival rates [8,17]. Furthermore, arterial embolization is also performed to treat aneurysms by either blocking an artery supplying the aneurysmal sac or closing the aneurysmal sac itself as an alternative to surgery [18–21].

Hemodynamic instability is the only absolute contraindication to NOM in traumatic patients with hemorrhage [6]. Provided that in an emergency setting there are no contraindications to carrying out embolization; pregnancy, renal insufficiency, and contrast allergy are relative contraindications in elective cases [1,5].

TECHNICAL REQUIREMENTS

Image-guided, minimally invasive procedures such as embolization should be performed by a specially trained interventional radiologist in an IR suite or occasionally in the operating room [6]. Moreover, effective integration of IR into the trauma management paradigm requires a multidisciplinary team composed of an interventional radiologist with an assistant, a nurse skilled in critical care, an interventional radiology technologist, and the availability of surgeons [22].

In an emergency setting, the primary goal of embolization is to arrest hemorrhage [12] and, hence, to minimize non-target embolization, thereby preserving organ function and limiting ischemic sequelae. Because procedures in IR can be time-consuming, it is crucial that life and limb threatening injuries are recognized and prioritized.

The multidisciplinary team decision to perform embolization rather than conventional surgical repair is typically made on the basis of imaging findings [23]. Prior to the procedure, ultrasound (US), CT, contrast-enhanced angiography, or magnetic resonance imaging (MRI) may be performed. Aside from their specialized training in the delivery of trans-catheter therapies, interventional radiologists receive broad-based multimodality imaging training, which renders them highly capable of correlating findings from pre-procedural imaging studies to speed diagnosis and the treatment of trauma patients [1,13]. The multidisciplinary team should also choose how to use the permanent or temporary (namely, resorbable) embolization material (Table 2). Resorbable in addition to permanent material may be used to aid the action of coils/plugs-occlusion [24]. Resorbable material should be the first choice in post-partum hemorrhages to spare the uterus, arresting acute bleeding while providing an early restoration of uterine artery flow, or in massive hepatic hemorrhage (when the portal vein is patent) to restore pressure and vital function of the patient with acute and massive abdominal (or even pelvic) bleeding [24–27].

A pre-procedural imaging evaluation must be complete, not only to identify injured vessels but also to document the presence of collaterals and variant anatomy [5]. Findings of vascular injury on angiography include contrast extravasation, occlusion, intimal irregularity, pseudoaneurysm (PSA), arteriovenous malformation, and dissection [12].

Currently, thanks to the rapid acquisition of CT imaging, angiography is no longer required for diagnosis and characterization of solid organ and major vascular injuries and contrast-enhanced CT (CECT) is routinely performed in most patients with blunt abdominal- and pelvic trauma, while angiography is now reserved essentially for therapeutic or problem-solving scenarios [1,6].

The length of an embolization procedure varies from 30 minutes to several hours depending on the complexity of the condition, but in the case of an emergency issue, the team response time should be within 60 minutes [13]. Moreover, the availability of contemporary angiographic equipment with digital subtraction capabilities and a complete array of IR instruments (angiographic catheters, microcatheters, guidewires, stents, stent-grafts, and embolic agents) are required [12].

The importance of rapid patient assessment and resuscitation prior to and during the embolization procedure is essential and, although CECT is highly sensitive and specific, this technique may be a time-consuming procedure that involves a considerable risk of deterioration during CT scanning itself and/or patient transfer to

Table 2 Embolization agents.

Embolic Agent	*Indications*	*Advantages*	*Disadvantages*
Permanent			
Coils	blush, PSA, AVF	super-selective, rapid effective	effectiveness in coagulopathy
Standard coils			
Detachable coils			
Active coils			
Particles	injury terminal vessel	permanent	non-target embolization, reflux
Gelfoam			
Polyvinyl alcohol particles			
Spherical particles			
NBCA (N-butyl-2-cyanoacrylate)	alternative to coil/ +++rebleeding	rapid; alternative in rebleeding	non-target embolization, microcatheter entrapment
Plugs	large vessel	1 device (vs multiple coils)	proximal embolization; angiographic catheter
Detachable balloon			
Vascular plug (AVP)			
EVOH (Onyx)	conform to complicated network of vessels	not influenced by vasospasm; not adhesive	cost
Temporary			
Gelatin sponge	rapid non-selective control of hemorrhage	cheap	poor effectiveness (+++ in impaired hemostasis)
Autologous clot		rapid	non-target embolization
Starch/swine skin gelatin particles		effective	
		uniform distribution	

AVP: Amplatzer vascular plug; EVOH: Ethylene vinyl alcohol copolymer.

CT suites. In this scenario, the hybrid emergency room is a novel trauma management system that is potentially suitable for the evaluation and care of patients with severe multiple injuries [28]. The key component of this system is a trauma resuscitation room that is designed for the completion of all the examinations and treatments in a single place and includes angio-CT equipment, anesthesiologic equipment and surgical, neurosurgical, and IR instruments.

Innovations in microcatheters, embolic agents, and stent graft technology have broadened the scope and improved the efficiency and efficacy of NOM for traumatic hemorrhage.

Procedural Consideration

Standard arterial access using the Seldinger technique should be achieved through a common femoral artery approach preferably using the side opposite any unilateral pelvic or lower extremity injury [29]. Given the extent and location of these injuries, as well as the presence of orthopedic fixation devices, axillary or brachial arterial access might be required [1]. Although sheaths are not absolutely required, many angiographers use them because multiple catheter changes are often needed. In addition, if a catheter becomes occluded or if an embolic agent deployment is compromised, arterial access can still be maintained if a sheath is used [5].

A careful selection of microcatheters is required, and end-hole catheters should be used to overcome the main limitation of this procedure, namely, non-target embolization, as discussed above. Selection of a catheter or coaxial system with an inner diameter and taper large enough to prevent occlusion by the embolic material is also crucial [6] (Table 2). Coaxial systems and microcatheters allow a more accurate selection of injured vessels and hence a more selective embolization [30]. Accordingly, a super-selective embolization technique allows rapid hemostasis in an injured vessel while preserving as much tissue as possible.

The choice of embolic agents will vary based on the site and nature of the injury, the desire to preserve collateral flow, and operator reference, as well as the inherent properties and behavior of the agent [22]. Although modern embolic agents may be either temporary or permanent, permanent agents are more common, and there are many applicable subsets including liquid agents, particulates, coils, and detachable plugs and balloons [4]. Some liquid agents, such as ethylene vinyl alcohol copolymer (EVOH), have been used in several indications (e.g., the embolization of selected traumatic injuries, renal arteriovenous malformations, renal aneurysms, and

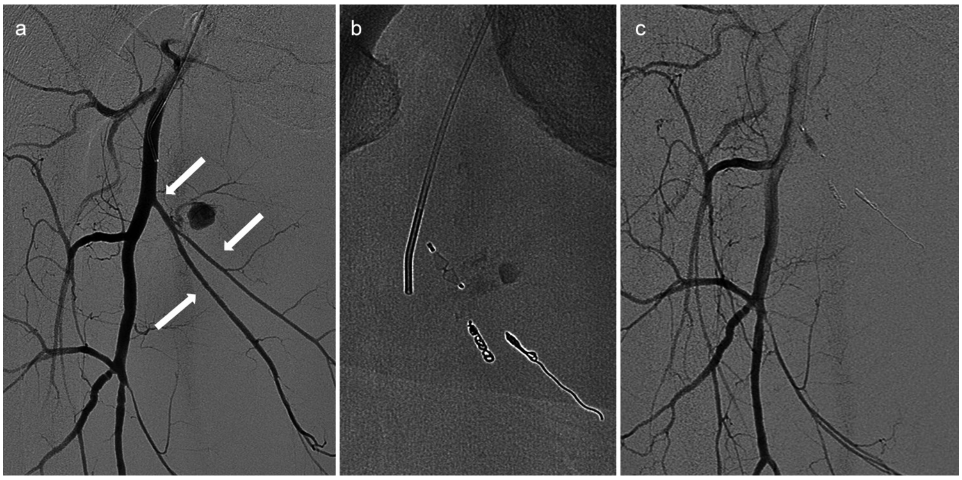

Figure 1 (**a**) Pseudoaneurysm of profunda femoral artery; (**b**) embolization performed with sandwich technique to prevent retrograde flow; (**c**) final angiogram documented complete embolization.

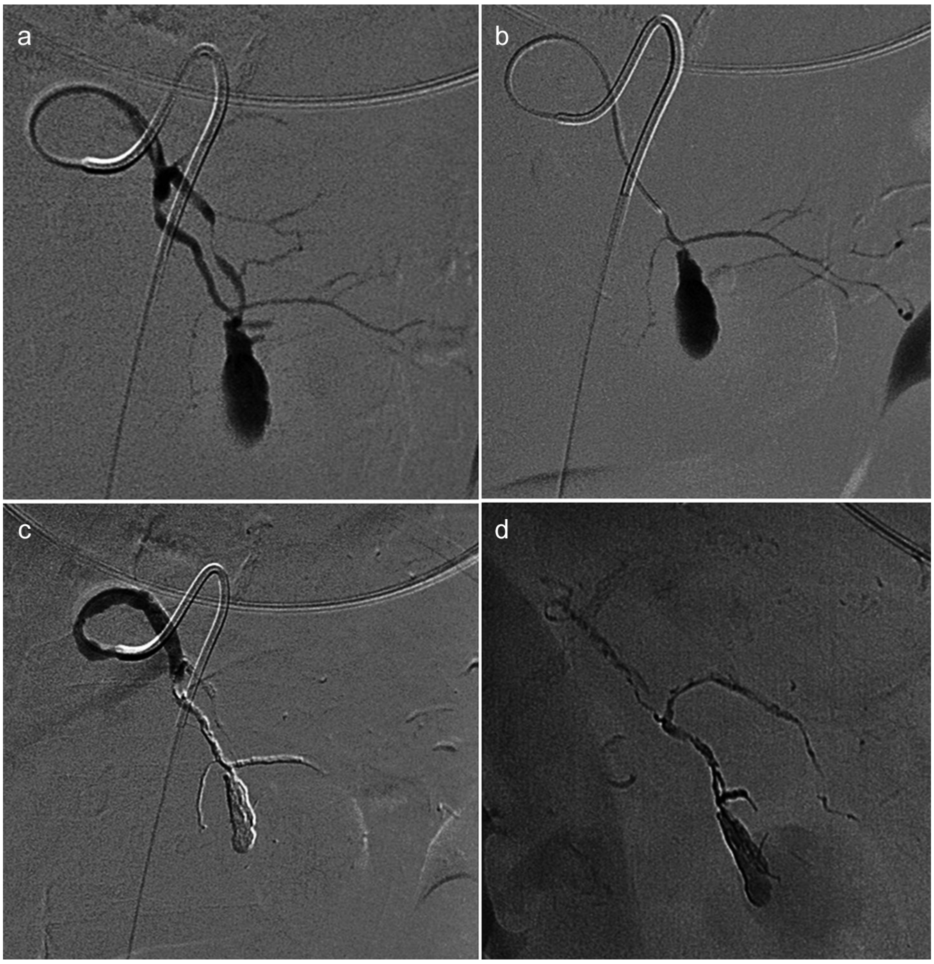

Figure 2 (**a**) Pseudoaneurysm (PSA) of left gastric artery; (**b**) selective arteriogram; (**c,d**) embolization was performed with Onyx that reached a distal vessel, filled the PSA and embolized the feeder.

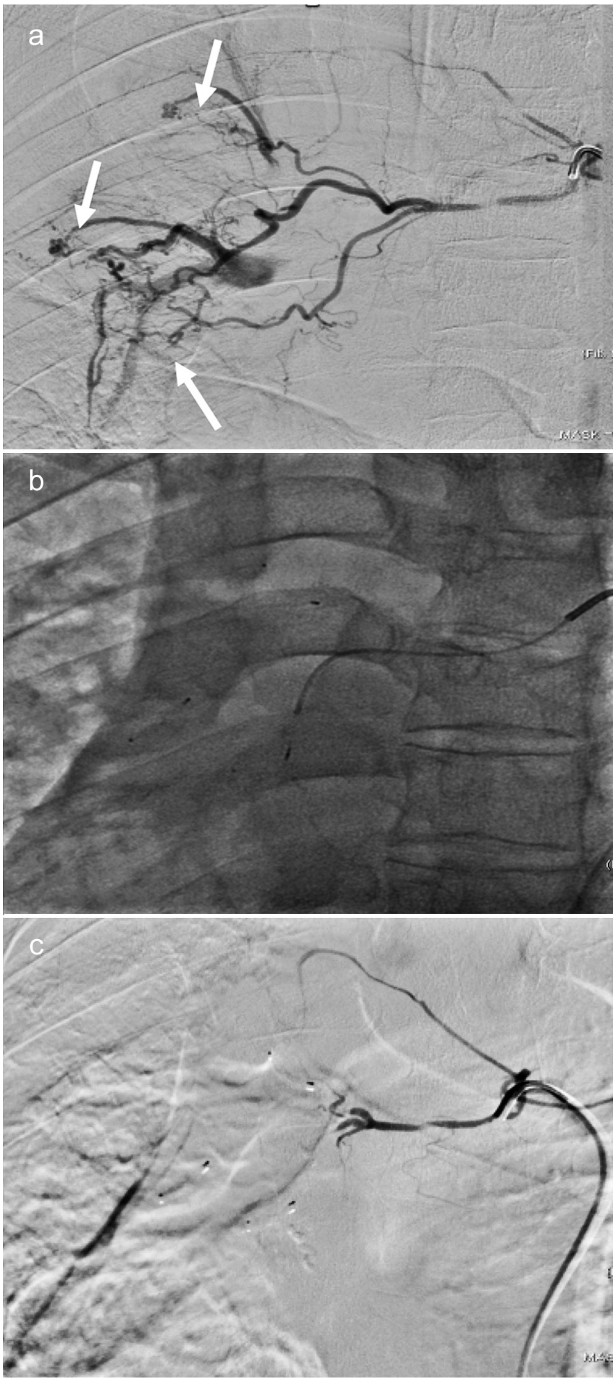

Figure 3 (**a**) Selective angiogram of the right bronchial artery reveals communication with pulmonary arteries (white arrows); (**b**) selective embolization of fistulas with micro-plugs (white arrows); (**c**) final angiogram following embolization of bronchial artery with particles.

PSAs) [3,31–35], especially in patients with coagulopathy [3]. Accordingly, Onyx (Covidien, Plymouth, MN) is the embolic agent of choice to overcome the problems of endovascular navigation and to first obtain a distal occlusion, and then a proximal occlusion [31, 36].

Clearly, the clinical condition of the patient also determines how selective a distal embolization is performed. In the stable patient, a more super-selective technique is usually undertaken, whereas in a patient who is more unstable or has massive bleeding a more non-selective proximal embolization technique is used as the main aim is the cessation of hemorrhage in a more timely manner [37].

LIMITS

Prompt, effective, and safe embolization requires good knowledge of the available equipment, arterial anatomy, role of collateral arterial flow, and possible risks. A clear understanding of the target vessel is critical, especially if it contains extensive collateral supply (e.g., via muscular branches) as these can provide distal flow and supply to the bleeding vessel and therefore result in continued bleeding if they are not also embolized. Accordingly, both the proximal and distal segments of the artery, in relation to the site of injury, are routinely embolized to prevent this complication [37].

Broadly speaking, the non-target embolization and the ischemia caused by embolization of the vital area may be considered the main limits of the embolization [1]. A technically successful embolization requires the (micro)-catheter be placed in a precise position to prevent injuring normal tissue. In a small percentage of cases, the procedure is not technically possible because the (micro)-catheter cannot be positioned to appropriately deposit embolic material in the target blood vessels [30].

The risk of non-targeted embolization should be reduced by EVOH with good radio-opacity and its injection under continuous fluoroscopy [4,31,36]. Nevertheless, symptomatic EVOH migration in pulmonary arteries has been described after embolization of cerebral vascular malformations, in the graft limb during embolization of type I endoleak, and during gastrointestinal bleeding causing non-target embolization [38,39]. Accordingly, considering its ability to penetrate, it is essential to pay extreme attention to the progression of EVOH when potentially dangerous anastomoses and/or fistulas are present [40].

The intraprocedural impossibility to reach the distal branch during an endovascular exclusion of a PSA represents an example of a condition that is a common challenge [6]. As opposed to actively bleeding vessels, PSAs require slightly different considerations. Firstly, if the vessel is non-vital, it might be sacrificed. Secondly, many vessels cannot be completely embolized [19]. When considering embolization of PSA, an interventional radiologist needs to prevent retrograde flow in the embolized vessel from collaterals, occluding vessels both distal and proximal to the injury [5] (Figure 1*a*–*c*). If the proximal embolization is inadequate, the PSA is revascularized by collateral vessels. If the distal embolization is inadequate, bleeding may occur in retrograde fashion via collateral blood flow. Should retrograde bleeding occur, re-embolization usually cannot be performed

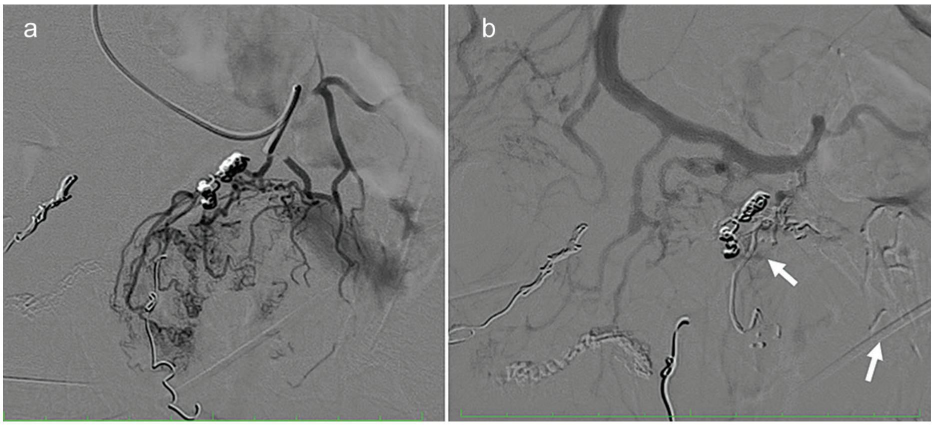

Figure 4 (**a**) Voluminous colic angiodysplasia first embolized with coils; (**b**) rebleeding after one week, embolized with Onyx (white arrows).

through the same vessel because of the more proximal embolization. Therefore, it is necessary to consider the achievable percutaneous puncture of the PSA or the use of embolizing agents (such as Onyx) which can transit into the vessels going into terminal vessels [19,41] (Figure 2*a–d*) A major limitation is the embolization of bleeding vessels that supply noble organs, such as embolization of the following vessels: medullary arteries (during embolization of intercostal arteries or bronchial arteries) (Figure 3*a–c*), mesenteric artery branches that supply parts of the intestine, hepatic artery proper when the door is thrombosed, dorsal pancreatic arteries (during splenic embolization) that would revascularize the spleen [30]. In order to facilitate distal super-selective catheterization of a microcatheter for embolization, it is preferable to place a guiding catheter as distal as possible, which may, however, increase the risk of vessel injury by manipulation of the guiding catheter [31,36].

Gentle manipulation of a guiding catheter or a microcatheter as well as a guidewire is essential to avoid vessel injuries during catheterization. Once an injury occurs, early recognition and appropriate management minimize the clinical sequelae. It is noteworthy that many dissections heal spontaneously with only conservative management [42]. For the treatment of simple vasospasm, the use of intraarterial injection of nitroglycerin is commonly performed [42]. The use of inappropriate (namely, liquid) agents into the gastrointestinal arteries may not be sufficient (e.g., the embolization of angiodysplasias coils are often not sufficient and Onyx is necessary) (Figure 4*a*,*b*) or may involve the risk of pancreatitis [1,12,43–45].

Notably, most of the embolization agents requiring a relatively intact coagulation cascade with embolization are ideally performed before severe coagulopathy develops [37]. This is noteworthy since trauma patients have frequently altered coagulation profiles [5,7,30]: one-third of patients with hypothermia and major hemorrhage require multiple blood transfusions [2,7,12,30]. Accordingly, embolization should be performed before the onset of coagulopathy [2,7,12]. Although EVOH is a notable exception—because it is effective even in the setting of coagulopathy—costs, availability, time-consuming preparation, and a technical learning curve preclude the widespread use of these embolic agents in the trauma setting [3, 39].

Finally, time is another possible limit to consider. Embolization requires skilled operators and should be available within a short time. However, no matter how quickly the procedure is conducted, it must be understood that embolization requires a significant amount of time [5].

ADVANTAGES AND DISADVANTAGES

Prospective randomized trials, which show advantages and disadvantages of embolization are difficult to perform because the trauma patient population varies widely with respect to the extent and type of injuries, clinical status on presentation, presence of comorbidities, and patient demographics. Moreover, the hyper-acute treatment scenario creates an additional obstacle to randomization [46].

In Table 3 the main benefits and risks of the embolization procedure are shown.

Pregnancy

The radiation exposure of an unborn child should be principally avoided, whenever it is medically reasonably possible. However, in cases of emergency saving the life of the patient has a higher priority than the radiation protection of the unborn child [47]. The effects of fetal radiation are highly dependent on both the administered dose and developmental stage at the time of exposure. Beyond 25 weeks, the risks of physical deformity and mental retardation are believed to be minimal unless exposure levels exceed 500 mGy [48]. The other concern is regarding the administration of contrast media as

Table 3 Main benefits and risks of embolization.

Benefits	*Risks*
It is a highly effective way of controlling bleeding, especially in an emergency situation.	Slight risk of an allergic reaction if contrast material is injected.
It can be used to treat tumors and vascular malformations that either cannot be removed surgically or would involve great risk if surgery was attempted.	Any procedure that involves placement of a catheter carries certain risks, including damage to the blood vessel, bruising or bleeding at the puncture site, and infection. However, precautions (such as antibiotic prescription) are taken to mitigate these risks.
It is less invasive than conventional open surgery. As a result, there are fewer complications and the hospital stay is relatively brief.	There is always a chance that an embolic agent can lodge in the wrong place and deprive normal tissue of its oxygen supply.
Blood loss is less than with traditional surgical treatment, and no surgical incision is needed.	The risk of kidney damage due to the contrast material, particularly in patients with diabetes or pre-existing kidney disease, is reported.

iodinated contrast agent crosses the human placenta and enters the fetus [49]. However, the intravascular administration of non-ionic iodinated contrast agent has been reported to have no effect on neonatal thyroid function unlike that administered intravenously [8].

The above considerations have no sense if the patient is a pregnant woman with a life-treating hemorrhagic condition without any other indication for alternative treatments. Moreover, embolization minimizes morbidity related to surgery. Close relatives and the patient (when it is possible) have to be informed and radiation to the fetus must be limited as much as possible. Intraprocedural radiation monitoring and dose documentation are important, particularly when a future review of fetal exposures will be performed by the patient and multidisciplinary team [9].

Renal Failure

The post-contrast–acute kidney injury (PC-AKI) incidence following direct intraarterial contrast media administration with first-pass renal exposure is frequently reported to be higher than after intravenous administration, but this remains controversial [50]. Currently, the identification of high-risk patients, appropriate hydration regimens with either isotonic sodium chloride or sodium bicarbonate, withdrawal of nephrotoxic drugs, and the use of the minimum contrast medium volume represent the preventive measures which can be suggested for daily clinical practice [51].

In life threatening hemorrhages, renal insufficiency is not a contraindication to the administration of non-ionic iodinated contrast agent; when possible the appropriate precautions described above may be adopted. Morbidities related to a surgical approach in renal failure patients should be compared with PC-AKI and its sequelae. To the best of our knowledge, no randomized studies are available, and they appear difficult to organize in this cohort of patients, as discussed above.

However, when trans-arterial procedures may be life-saving, all the other concerns should be considered secondary.

Contrast Allergy

Adverse reactions to contrast media are not uncommon, but they are usually mild and caused by toxicity or hypersensitivity [52]. Common minor adverse reactions include rash, pain at the injection site, nausea, vomiting, and minor hemodynamic changes, which are all usually self-limiting. Acute severe reactions are likely anaphylactoid in nature, and patients with asthma, atopy, or a history of an acute reaction to a contrast media are at greatest risk [53].

Known hypersensitivity to non-iodinated contrast media must alert the entire staff of the operating theater (angiographic suite or hybrid room). Pretreatment with corticosteroids can reduce the risk of, but not prevent, severe reactions. If a reaction occurs, the airway, breathing, and circulation should be managed. Administration of epinephrine and intravenous fluids is critical [53]. In the most severe cases, anaphylactic shock and acute coronary syndrome (Kounis Syndrome) can occur [52]. First-line drugs for the treatment of anaphylaxis must always be available, as should the equipment and trained personnel required for its management.

COMPLICATIONS

The inadvertent distal infarction of nonexpendable vessels and the continued bleeding distal to the point of embolization secondary to collateral flow [16,54] are the complications that may follow the embolization procedure. Occlusion of a normal territory may occur during embolization due to misinterpretation of vascular anatomy, distal migration of the embolic material during an "en passage feeder embolization," reflux of embolic material or migration of the embolic material through the artery-to-artery anastomosis. To protect a normal territory for embolization, liquid coils may be placed in the vessel, which is distal to the malformation [42].

Figure 5 and Figure 6 show the migration of glue as a complication of embolization in two different patients, probably due to an incorrect dilution of the embolization

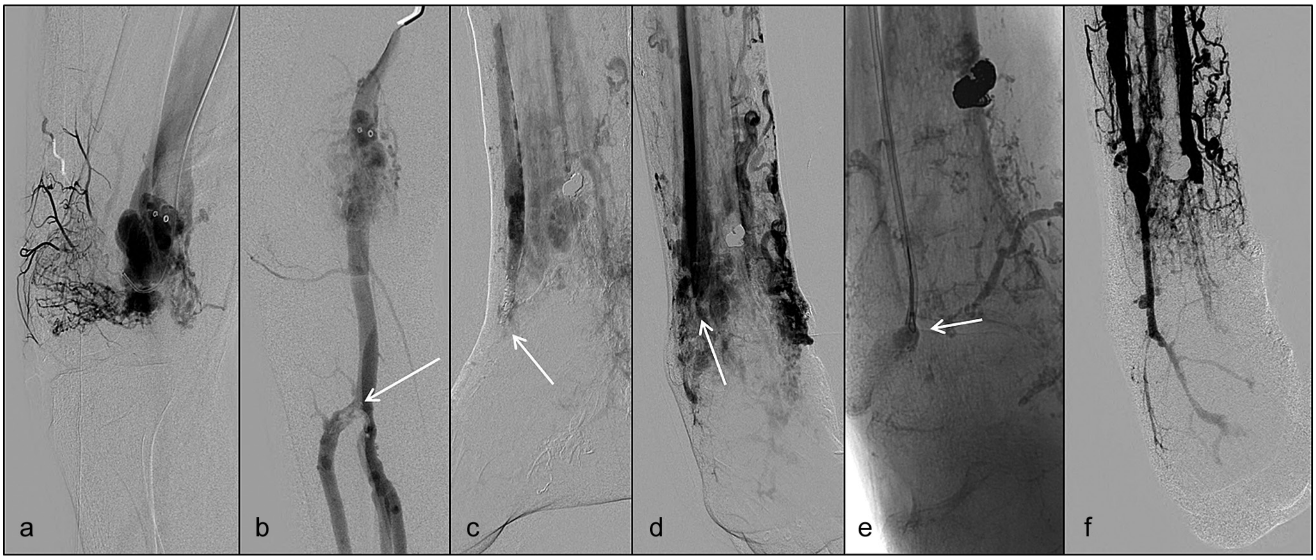

Figure 5 (**a**) Arteriovenous malformation; (**b–d**) migration of glue in anterior tibial artery and dorsal pedis artery; (**e**) recovery with snare of the migrated glue; (**f**) final angiogram.

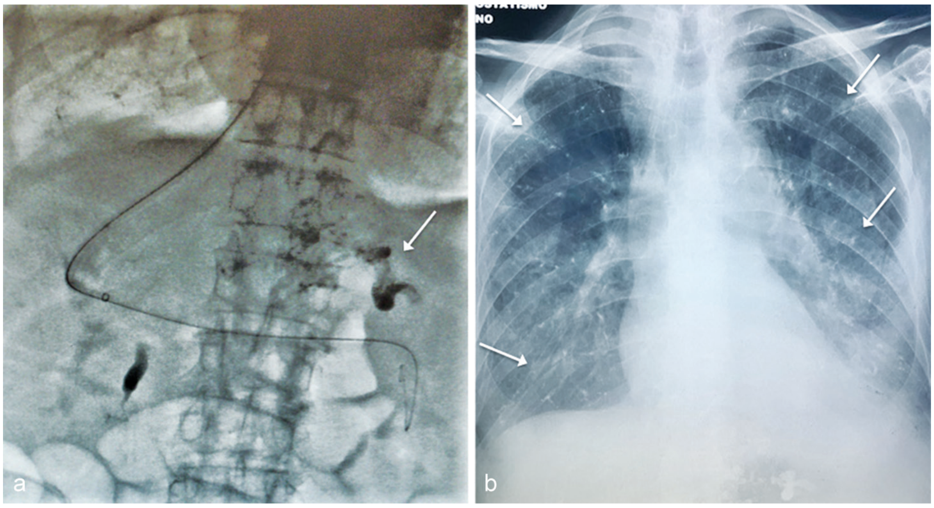

Figure 6 (**a**) Previous embolization of gastric varices with glue (white arrow). (**b**) Thorax radiograph shows diffuse migration of glue in both lungs (white arrows).

glue material. Among major complications, damage in adjacent organs has been reported [11,54,55]. Minor complications occur in approximately 10–20% of cases and include fever, pain, injuries in the puncture site (bleeding, hematoma, infection or, rarely, PSA).

Prevention is the best solution for any kind of complication [42]. Once a technical complication occurs, however, its early recognition and proper management are critical to minimize the clinical sequela. Knowledge of the disease, vascular anatomy, potential complications (and their management), the skill of interventional radiologists to handle catheters, guidewires, and embolic materials safely, and adequate equipment are the most important elements in preventing and managing technical complications that may occur during such procedures [1,30,54,56].

CONCLUSIONS

As a safe and effective first-line therapeutic approach for the majority of hemodynamically stable patients, NOM improves the clinical outcomes with acceptable low post-procedural complication rates.

Interventional radiologists have a central role in modern trauma management protocols, and their integration of intervention requires adequate and available staffing and equipment, and importantly, rapid multidisciplinary assessment and direct communication.

Limits and adverse events, among which the most feared is non-target embolization, may often be overcome using techniques and materials or a combination of them by skilled operators.

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