

Received:  
7 November 2015

Revised:  
6 January 2016

Accepted:  
12 January 2016

<http://dx.doi.org/10.1259/bjr.20150934>

Cite this article as:

Ierardi AM, Urbano J, De Marchi G, Micieli C, Duka E, Iacobellis F, et al. New advances in lower gastrointestinal bleeding management with embolotherapy. *Br J Radiol* 2016; **89**: 20150934.

## EMERGENCY RADIOLOGY SPECIAL FEATURE: COMMENTARY

# New advances in lower gastrointestinal bleeding management with embolotherapy

<sup>1</sup>ANNA MARIA IERARDI, MD, <sup>2</sup>JOSÈ URBANO, PhD, <sup>1</sup>GIUSEPPE DE MARCHI, MD, <sup>1</sup>CAMILLA MICIELI, MD, <sup>1</sup>EJONA DUKA, MD, <sup>3</sup>FRANCESCA IACOBELLIS, MD, <sup>1</sup>FEDERICO FONTANA, MD and <sup>1</sup>GIANPAOLO CARRAFIELLO, PhD

<sup>1</sup>Interventional Radiology Unit, Radiology Department, Uninsubria, Varese, Italy

<sup>2</sup>Vascular and Interventional Radiology Department, Jiménez Díaz Foundation University Hospital, Madrid, Spain

<sup>3</sup>Institute of Radiology, Second University of Naples, Napoli, Italy

Address correspondence to: Gianpaolo Carrafiello

E-mail: [gcarraf@gmail.com](mailto:gcarraf@gmail.com)

### ABSTRACT

Lower gastrointestinal bleeding (LGIB) is associated with high morbidity and mortality. Embolization is currently proposed as the first step in the treatment of acute, life-threatening LGIB, when endoscopic approach is not possible or is unsuccessful. Like most procedures performed in emergency setting, time represents a significant factor influencing outcome. Modern tools permit identifying and reaching the bleeding site faster than two-dimensional angiography. Non-selective cone-beam CT arteriography can identify a damaged vessel. Moreover, sophisticated software able to detect the vessel may facilitate direct placement of a microcatheter into the culprit vessel without the need for sequential angiography. A further important aspect is the use of an appropriate technique of embolization and a safe and effective embolic agent. Current evidence shows the use of detachable coils (with or without a triaxial system) and liquid embolics has proven advantages compared with other embolic agents. The present article analyses these modern tools, making embolization of acute LGIB safer and more effective.

### KEY POINTS

- To describe new tools available to facilitate endovascular treatment of lower gastrointestinal bleeding (LGIB).
- To suggest to interventional radiologists how best to manage procedures to increase safety and to reduce non-target embolization.

### INTRODUCTION

LGIB is defined as bleeding distal to the ligament of the Treitz. The incidence is approximately 36 per 1,00,000 population,<sup>1</sup> and it is associated with significant morbidity and mortality. Most cases are self-limited in elderly population and may be approached medically by correction of coagulation or endoscopy. Patients with significant bleeding for which these methods fail are candidates for endovascular treatment before surgical treatment.<sup>1</sup>

First, radiological and nuclear medicine methods can be extremely useful for the diagnosis. Scintigraphy is a consolidated method in the identification of obscure gastrointestinal bleeding. On the basis of literature data, the reported success rates for detecting exact locations of bleeding range from 19% to 96%.

In future, correlation with further diagnostic tests such as capsule endoscopy and double-balloon enteroscopy scintigraphy is necessary.<sup>2</sup>

Multidetector CT angiography (CTA), using the correct protocol, is able to detect bleeding from an amount of  $\sim 0.3 \text{ ml min}^{-1}$ , to depict surrounding anatomical structures and to determine not only the place, but also the possible cause of bleeding; for this reason, multidetector CT became the diagnostic method of choice in massive LGIB, where colonoscopy is not useful or cannot be performed.<sup>3,4</sup>

In addition, CTA can be used as a suitable selection agent for angiographic intervention,<sup>5,6</sup> allowing avoidance of the extra risks associated with this invasive technique.<sup>1,5</sup> It can allow for pre-assessment of differences in a patient's particular vascular anatomy, and it makes subsequent vessel selection easier for embolization during formal angiography.<sup>1,5</sup>

The indication for the procedure of embolization is usually based on a multidisciplinary consensus between the gastroenterologist, radiologist and surgeon. In particular, endovascular embolization is an established treatment for

managing patients who are haemodynamically unstable or patients who are stabilized with fluid resuscitation.<sup>1,7</sup>

Surgical treatment is considered suitable in patients with bleeding gastroduodenal peptic ulcer or recurrent bleeding from colonic diverticula and after endoscopy and embolization therapy failure.

Contraindications to embolization are relative, generally related to general contraindications for iodine-contrast examinations (allergy and renal insufficiency).<sup>7</sup>

In view of the criticality of the patients who arrive in the angiographic suite, the procedure of embolization requires great care and attention, and it must be performed in the shortest possible time, using the most appropriate device to prevent non-target embolization.

Below, we analyse these two important topics: imaging guidance and safe embolization.

#### Advances in imaging guidance

Accurate and prompt identification of the bleeding site during the treatment session is fundamental for timely control of haemorrhage.

However, procedures are sometimes challenging even for skilled operators and require several sequential angiographic runs for the manual identification of the leaking artery on two-dimensional angiographic images.

Nowadays, software to facilitate and improve procedure are available. In particular, cone-beam CT (CBCT) capable of

providing more information than standard two-dimensional angiography in localizing and/or visualizing target vessel and subsequently reach it.<sup>8</sup>

Identifying the specific artery responsible for the bleeding is difficult, when the arterial vasculature has a complex branching pattern.

CBCT is performed with a catheter in a principal vessel (superior or inferior mesenteric artery), using correct parameters (in terms of amount and flow), for the injection of contrast medium. The protocol described below is used in our angiographic suite (Allura Xper FD20; Philips Healthcare, Best, Netherlands).

Depending on the catheter/microcatheter tip location, dual-phase cone-beam CT (DP-CBCT) may be obtained. Different volume of contrast medium and flow rate may be used. Pressure limit is usually 900 psi, but when the microcatheter tip is located in a very small vessel (<3-mm diameter), a pressure of 600 psi is chosen.

When a catheter is used, a volume of 10–60 ml of non-diluted contrast medium may be injected (300 mg of iodine per millilitre) (for example, 10 ml in a branch of the mesenteric artery, 40 ml in the mesenteric artery and 60 ml in the abdominal aorta above the carrefour), with a flow rate that is adapted to the selected arterial district, ranging from 1 to 6 ml s<sup>-1</sup>; if a microcatheter is used, a volume of 5–20 ml of non-diluted contrast medium may be injected, with a flow rate adapted to the selected arterial district, ranging from 1 to 5 ml s<sup>-1</sup>. In both cases, a delay time before imaging must be considered, according to the duration of acquisition. Delayed-phase CBCT may be triggered 15 s after the end of the first CBCT scan in order to identify late

Figure 1. Dual-phase non-selective cone-beam CT arteriography performed with a catheter in the superior mesenteric artery (a–d). First acquisition revealing active arterial bleeding in the caecum (arrow) (a); delayed second acquisition showing accumulation of contrast medium in the lumen (arrow) (b); coronal view showing afferent vessels to the bleeding (arrow) (c); accumulation of contrast medium in the lumen (arrow) documented by second acquisition: coronal view (d).

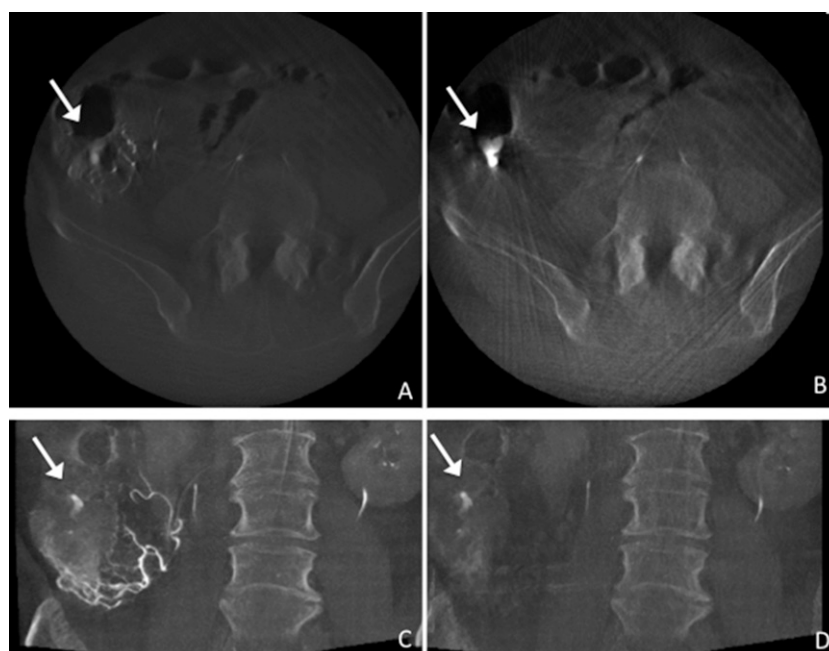
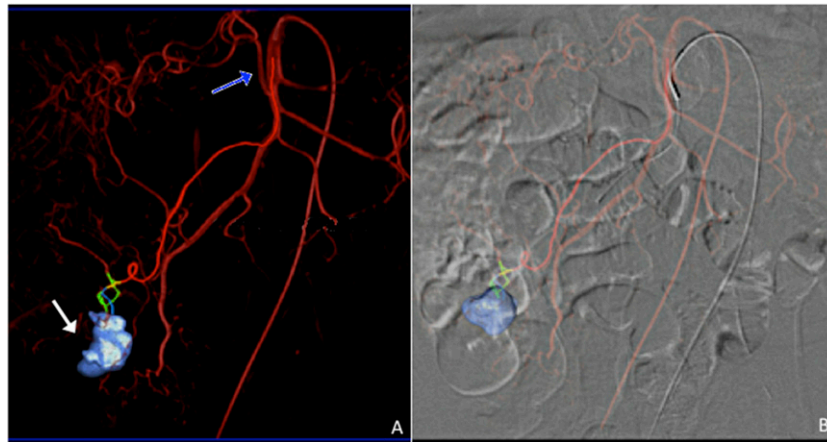


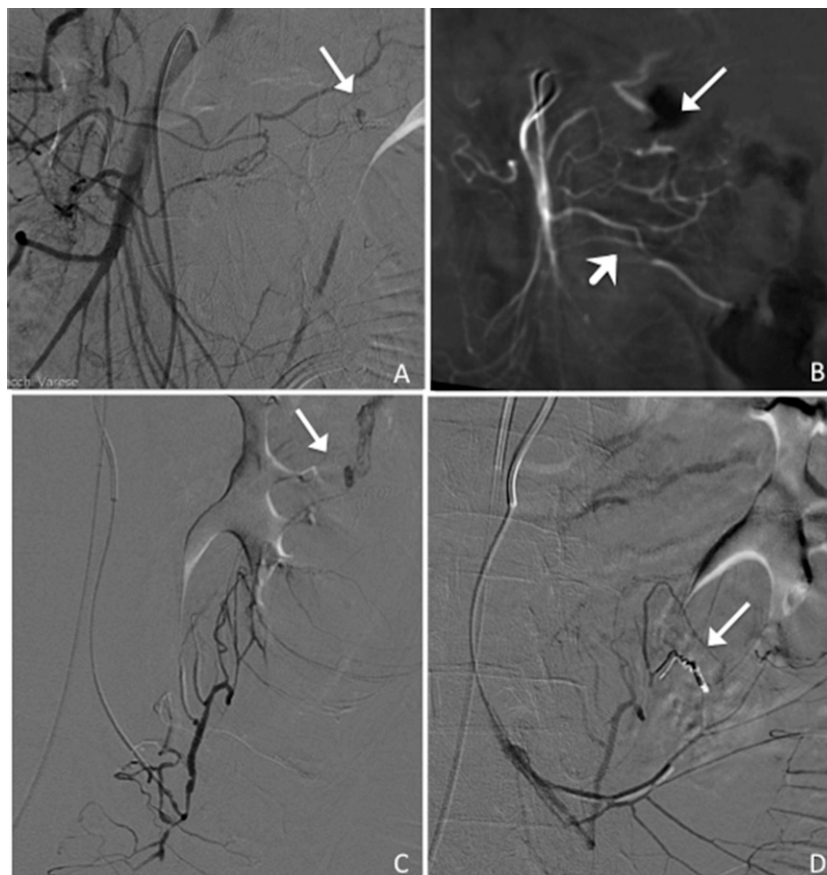
Figure 2. The software permits “segmentation” of the bleeding site (white arrow) and a starting point, normally the catheter tip (blue arrow): all the afferent vessels were detected (a). Arterial route determined using the software could be overlaid on live fluoroscopy and exploited during the intervention to facilitate catheter navigation to the damaged vessel (b).



enhancing bleedings. Breathing artefacts may be avoided, asking patients to hold their breath or breathe shallowly, whenever possible. The volumetric data sets are automatically transferred to a three-dimensional (3D) workstation (XtraVision 8.8; Philips Healthcare), where 3D reconstruction may be performed and

displayed as cross-sectional images. When the bleeding site is identified, automatic vessel detection (AVD) software (Embo-Guide; Philips Healthcare) is used to determine the most appropriate arterial route leading to the haemorrhage. The AVD software applies a minimal path using a “segmentation” of the

Figure 3. Preliminary non-selective angiography of an uncooperative patient (a): bleeding is documented (arrow) but the culprit vessel is not clear. Non-selective cone-beam CT angiography was performed (b): automated vessel detection was not applied because of breathing artefacts, but the operator intuited the feeder (short arrow) of the bleeding site (arrow). Selective catheterization of that vessel confirmed bleeding (arrow) (c); final angiogram performed with detachable microcoil (d).



bleeding site and a starting point, normally the catheter tip. If the bleeding site was not correctly depicted on DP-CBCT images, CTA data sets could be imported into the 3D workstation and CBCT–CT fusion can be performed: target segmentation may be performed on the CTA data set. Once the target culprit artery is reached, a selective angiogram is performed to confirm correct position<sup>9</sup> (Figure 1a–d).

The application described should reduce the number of image acquisitions and overall procedure time, because the software can identify a damaged vessel from non-selective CBCT arteriography images and facilitate direct placement of a microcatheter into the culprit vessel without the need for sequential angiography.<sup>8,9</sup>

Further, the software visualizes the arterial path from the catheter tip to the target site on a 3D vascular map at the optimal working angle, enabling easier, quicker and more accurate target catheterization (Figure 2a,b).

When multiple bleeding sites are present, each leaking artery could be determined from a single acquisition of a non-selective CBCT image, during contrast injection of the proximal artery. Multiple software processes are necessary to detect the artery responsible for each bleeding site.

Since volumetric CBCT data sets are acquired in a calibrated coordinate space and are synchronized with the C-arm, flat-panel detector and angiographic table displacements, the arterial route determined using the software could be overlaid on live

fluoroscopy and exploited during intervention, to facilitate catheter navigation to the damaged vessel (Figure 2b).

One limitation could be the increased susceptibility of C-arm CT to patient motion compared with conventional CT. Even transient movement during image acquisition negatively affects the quality of the entire image, resulting in risk of misinterpretation.<sup>9,10</sup> However, in our experience, the combination with the AVD software helps in the interpretation of the CBCT data set and provides the correct path to the bleeder also in the case of mild motion artefacts (Figure 3a–d).

Moreover, in some cases, previous CTA data sets could be imported into the 3D workstation, and target segmentation may be performed on the basis of the CTA data set after CBCT–CT fusion.

Some authors reported as limitation the field of view, but in our opinion, in accordance with preliminary experience,<sup>9,10</sup> contrast-enhanced C-arm CT is performed with the catheter in the superior or inferior mesenteric artery and the field of view is selected on the basis of previous CT; in particular, if the bleeding is localized in the ascending colon, C-arm CT is aimed to the study of that region: field of view is enough.

These computer software, specifically designed to assist in planning embolization, have reported significant advantages in terms of sensitivity for detecting feeders to the target with a shorter processing time (~2 min) than manual angiographic assessments.<sup>10</sup>

Figure 4. Contrast-enhanced CT revealed arterial bleeding of a diverticulum (arrow) of the descending colon previously treated endoscopically (a); coronal view of the contrast-enhanced CT showing the bleeding (arrow) (b); angiography performed after super-selective catheterization of the vasa recta near clips, confirmed bleeding (arrow) (c); final angiogram of the inferior mesenteric artery revealed complete embolization and detachable microcoil (arrow) in the bleeder (d).

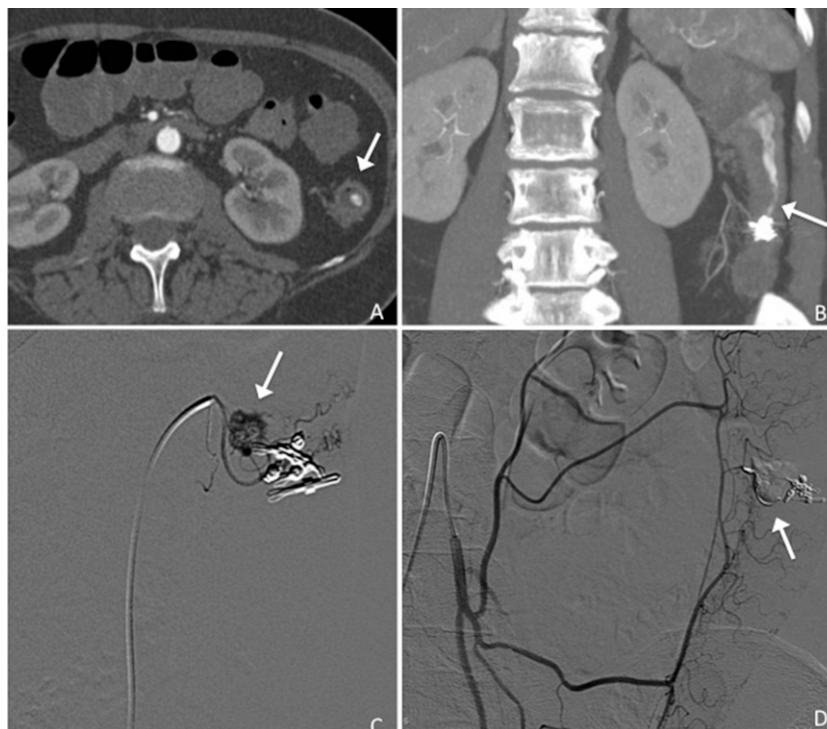
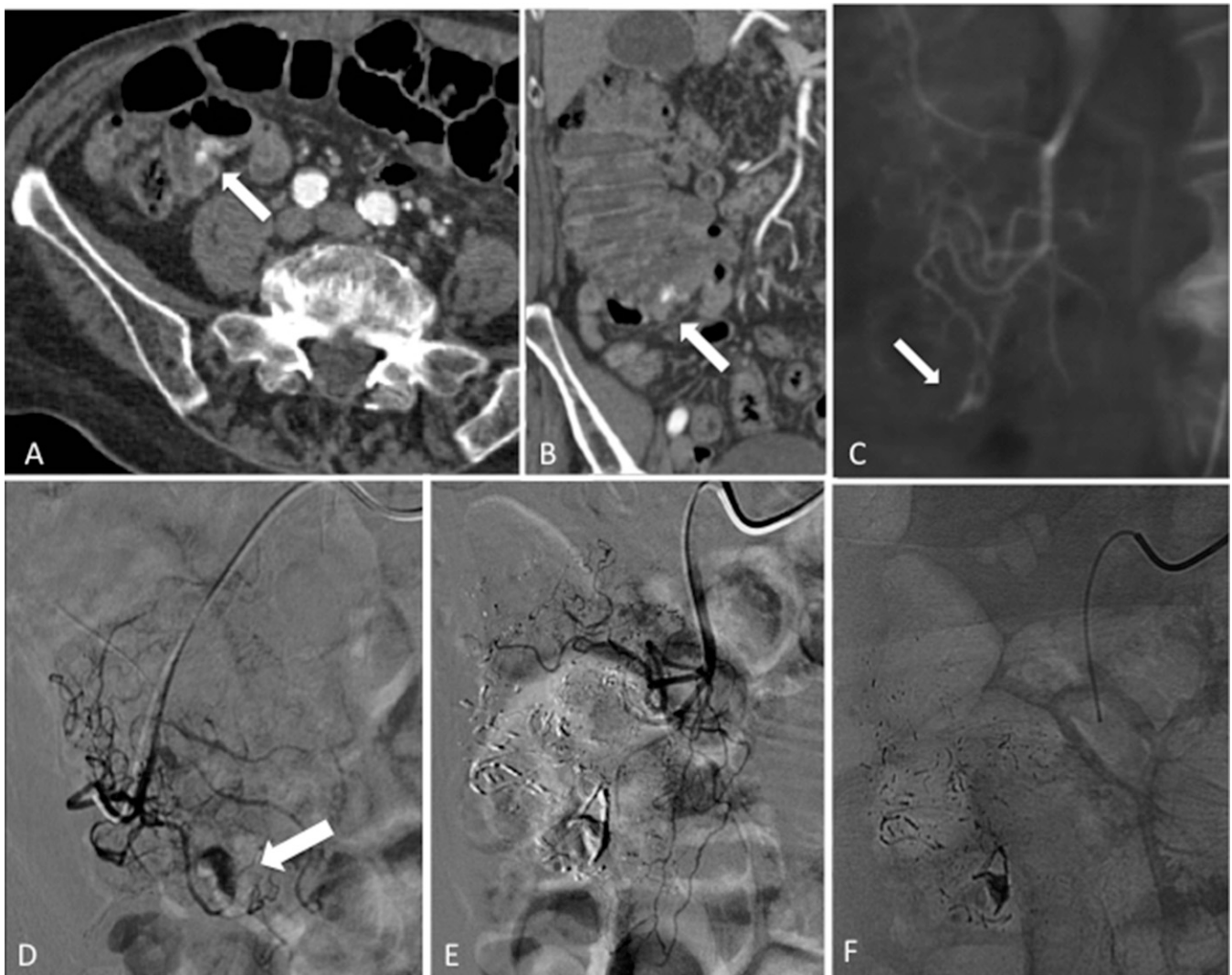




Figure 5. Contrast-enhanced CT revealed arterial bleeding of the colonic angiodysplasia (arrows) (a–f). Axial (a) and coronal (b) view; non-selective cone-beam CT arteriography showing the bleeder (arrow) (c); angiography performed after super-selective catheterization of the feeder that reveals the bleeding (arrow) (d); final angiogram performed after embolization with Onyx (e); plain image showing the Onyx distribution in the previous bleeding site (f).



The feasibility and utility of CBCT and vessel-tracking software has primarily been proven in targeted chemoembolization of liver malignancies and benign prostate hyperplasia, with a reported detection accuracy of around 90% in detecting feeding branches.<sup>8–10</sup> Iwazawa and Carrafiello reported first experiences in emergency transarterial embolization.<sup>9,10</sup>

On the basis of the data reported above, the use of angiographic CBCT and AVD software during embolization of arterial bleedings can improve operator confidence with embolization techniques in emergency settings, reduce overall procedural time and total contrast media administration and ultimately have an impact on treatment outcome.

#### Advances in embolotherapy

The second aspect in which improvements are available is embolization technique and tools. Embolization may be performed with gelatin sponges; particles; coils; and microcoils; and, more

recently, glue. There are no guidelines for the choice of embolic material used, and the final decision is usually made by the operator on the basis of his experience and compliance. There are two main concerns with LGIB embolization. Rebleeding after endoscopy or embolization of LGIB is a key point and it has been described to be as high as 25%. Rebleeding has an impact on the outcome and is a negative-predictive factor for survival.<sup>11</sup> The second main concern in LGIB embolization is the risk of secondary bowel ischaemia because bowel irrigation is terminal with no collateral circulation; so, embolization must be very accurate at the bleeding site, and non-target embolization should always be avoided.

The goal is to embolize selectively at the level of the vasa recta, avoiding the marginal artery; some authors suggested less-selective flow-directed particle embolization.<sup>12</sup> However, the particles are associated with an increased risk of bowel infarction because they cannot be visualized or precisely deposited and may reflux into non-target arteries. Cyanoacrylates are very effective

in terms of bleeding control and rebleeding but are not controllable and require high operator expertise otherwise their use is associated with high risk of non-targeted embolization and severe intestinal ischaemia.<sup>13</sup> Another potential risk related to cyanoacrylates is microcatheter entrapment.<sup>12,13</sup>

For this purpose, in most centres, detachable coils were introduced,<sup>14</sup> sometimes using a triaxial system.<sup>14</sup> Vessels may sometimes be too thin and/or tortuous and, super-selective catheterization can still be difficult to perform safely. Shimohira et al<sup>14</sup> indicated that the 2.7-Fr microcatheter provides good support for the 1.9-Fr non-tapered microcatheter to advance into even thin tortuous vessels. Detachable coils have been recommended for these situations<sup>14</sup> (Figure 4a–d).

Microvascular plug (Medtronic, Irvine, CA) is a new embolic device, recently introduced, which enables the treatment of distal, super-selective vessels; but, at the moment, no data are available for selective embolization of LGIB.

Ethylene-vinyl alcohol copolymer, Onyx® (Medtronic), is increasingly used as embolization agent in peripheral interventional radiology.<sup>15</sup> Ethylene-vinyl alcohol copolymer is a liquid embolization agent which is a plastic polymer dissolvable in a potent organic solvent, dimethyl sulfoxide. It does not have adhesive properties in contact with arterial walls but only properties of “filling” the vascular lumen. The major advantages of this liquid compared with glue are its controlled release, non-adherence, progressive solidification, cohesiveness, high vascular penetration and a weak inflammatory effect on the endothelium.<sup>16</sup> Unlike cyanoacrylates, it does not polymerize into a block but solidifies gradually from the periphery out towards the centre.<sup>15,16</sup> Onyx® is not carried by blood flow but is conversely displaced by pressure applied by the operator on the syringe. This makes the procedure safer, enables the operator to stop the injection at any time leaving the distal tip of the catheter *in situ* and to start again even a few minutes later.

Time is essential in cases of acute arterial haemorrhage. The bottles need to be shaken for 20 min to obtain a consistent mixture of the tantalum powder. In our experience, it is advisable to start stirring Onyx as soon as it is suspected that its use may be necessary, and if finally not used, it can be returned to the shelves to be used another time.<sup>12</sup>

Coagulopathy is a negative-predictive factor for survival, bleeding control and rebleeding in patients with LGIB.<sup>9,10</sup> Onyx has the remarkable advantage of acting independently of any underlying coagulopathy or low platelet count.<sup>9,10</sup>

On the basis of the characteristics described above, Onyx could present some advantages in the embolotherapy of LGIB. Moreover, we never registered ischaemic damage of the bowel requiring surgery: we hypothesized a decrease of blood flow more than a complete occlusion, especially when Onyx does not make the cast in the vessel (Figure 5a–f). Clearly, before affirming this concept, more clinical evidences are necessary.

We described techniques designed to improve procedures of embolization. In our opinion, early identification of the leaking vessel, fast reaching of the site of bleeding and use of an embolic agent that reduces risks of non-target embolization and bowel ischaemia may be considered fundamental for fast and precise LGIB embolization.

In conclusion, nowadays modern tools for diagnosis and also for endovascular treatment are available to make embolization of acute massive LGIB safer and more effective.

## ACKNOWLEDGMENTS

The scientific guarantor of this publication is Gianpaolo Carrafiello. The authors of this article declare no relationships with any companies whose products or services may be related to the subject matter of the article.

## REFERENCES

- ASGE Standards of Practice Committee; Pasha SF, Shergill A, Acosta RD, Chandrasekhara V, Chathadi KV, Early D, et al. The role of endoscopy in the patient with lower GI bleeding. *Gastrointest Endosc* 2014; **79**: 875–85. doi: [10.1016/j.gie.2013.10.039](https://doi.org/10.1016/j.gie.2013.10.039)
- Brünnler T, Klebl F, Mundorff S, Eilles C, Reng M, von Korn H, et al. Significance of scintigraphy for the localisation of obscure gastrointestinal bleedings. *World J Gastroenterol* 2008; **14**: 5015–19.
- Martí M, Artigas JM, Garzón G, Alvarez-Sala R, Soto JA. Acute lower intestinal bleeding: feasibility and diagnostic performance of CT angiography. *Radiology* 2012; **262**: 109–16. doi: [10.1148/radiol.11110326](https://doi.org/10.1148/radiol.11110326)
- Romano S, Scaglione M, Tortora G, Martino A, Di Pietto F, Romano L, et al. MDCT in blunt intestinal trauma. *Eur J Radiol* 2006; **59**: 359–66. doi: [10.1016/j.ejrad.2006.05.011](https://doi.org/10.1016/j.ejrad.2006.05.011)
- Moss AJ, Tuffaha H, Malik A. Lower GI bleeding: a review of current management, controversies and advances. *Int J Colorectal Dis* Oct 2015. Epub ahead of print. doi: [10.1007/s00384-015-2400-x](https://doi.org/10.1007/s00384-015-2400-x)
- Scaglione M, de Lutio di Castelguidone E, Scialpi M, Merola S, Diettrich AI, Lombardo P, et al. Blunt trauma to the gastrointestinal tract and mesentery: is there a role for helical CT in the decision-making process? *Eur J Radiol* 2004; **50**: 67–73. doi: [10.1016/j.ejrad.2003.11.016](https://doi.org/10.1016/j.ejrad.2003.11.016)
- Valek V, Husty J. Quality improvement guidelines for transcatheter embolization for acute gastrointestinal nonvariceal hemorrhage. *Cardiovasc Intervent Radiol* 2013; **36**: 608–12. doi: [10.1007/s00270-012-0462-5](https://doi.org/10.1007/s00270-012-0462-5)
- Tacher V, Radaelli A, Lin M, Geschwind JE. How I do it: cone-beam CT during transarterial chemoembolization for liver cancer. *Radiology* 2015; **274**: 320–34. doi: [10.1148/radiol.14131925](https://doi.org/10.1148/radiol.14131925)
- Carrafiello G, Ierardi AM, Duka E, Radaelli A, Floridi C, Bacuzzi A, et al. Usefulness of cone-beam computed tomography and automatic vessel detection software in emergency transarterial embolization. *Cardiovasc Intervent Radiol* Oct 2015. Epub ahead of print. doi: [10.1007/s00270-015-1213-1](https://doi.org/10.1007/s00270-015-1213-1)
- Iwazawa J, Ohueo S, Hashimoto N, Mitani T. Feasibility of using vessel-detection software for the endovascular treatment of visceral

- arterial bleeding. *Diagn Interv Radiol* 2014; **20**: 160–3. doi: [10.5152/dir.2013.13267](https://doi.org/10.5152/dir.2013.13267)
11. Newman J, Fitzgerald JE, Gupta S, von Roon AC, Sigurdsson HH, Allen-Mersh TG. Outcome predictors in acute surgical admissions for lower gastrointestinal bleeding. *Colorectal Dis* 2012; **14**: 1020–6. doi: [10.1111/j.1463-1318.2011.02824.x](https://doi.org/10.1111/j.1463-1318.2011.02824.x)
  12. Urbano J, Manuel Cabrera J, Franco A, Alonso-Burgos A. Selective arterial embolization with ethylene-vinyl alcohol copolymer for control of massive lower gastrointestinal bleeding: feasibility and initial experience. *J Vasc Interv Radiol* 2014; **25**: 839–46. doi: [10.1016/j.jvir.2014.02.024](https://doi.org/10.1016/j.jvir.2014.02.024)
  13. Yata S, Ihaya T, Kaminou T, Hashimoto M, Ohuchi Y, Umekita Y, et al. Transcatheter arterial embolization of acute arterial bleeding in the upper and lower gastrointestinal tract with N-butyl-2-cyanoacrylate. *J Vasc Interv Radiol* 2013; **24**: 422–31. doi: [10.1016/j.jvir.2012.11.024](https://doi.org/10.1016/j.jvir.2012.11.024)
  14. Shimohira M, Hashizume T, Ohta K, Suzuki K, Kurosaka K, Muto M, et al. Triaxial coil embolization using Guglielmi detachable coils with the voltage-dependent coil-detaching technique. *Acta Radiologica* 2015; **56**: 51–5. doi: [10.1177/0284185113518771](https://doi.org/10.1177/0284185113518771)
  15. Guimaraes M, Wooster M. Onyx (ethylene-vinyl alcohol copolymer) in peripheral applications. *Semin Intervent Radiol* 2011; **28**: 350–6. doi: [10.1055/s-0031-1284462](https://doi.org/10.1055/s-0031-1284462)
  16. Saeed Kilani M, Izaaryene J, Cohen F, Varoquaux A, Gaubert JY, Louis G, et al. Ethylene vinyl alcohol copolymer (Onyx®) in peripheral interventional radiology: indications, advantages and limitations. *Diagn Interv Imaging* 2015; **96**: 319–26. doi: [10.1016/j.diii.2014.11.030](https://doi.org/10.1016/j.diii.2014.11.030)