Diagn Interv Radiol DOI 10.5152/dir.2019.19348
Diagn Interv Radiol 2020; 26:216–222

INTERVENTIONAL RADIOLOGY
ORIGINAL ARTICLE

Transarterial embolization with n-butyl cyanoacrylate for the treatment of abdominal wall hemorrhage

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PURPOSE
We aimed to evaluate the effectiveness and safety of n-butyl cyanoacrylate (n-BCA) in the context of the transarterial embolization (TAE) of abdominal wall hemorrhage in an urgent scenario.

METHODS
A retrospective study of cases admitted from January 2008 to December 2017 in the emergency unit of our institution revealed 11 patients with abdominal wall hemorrhage who underwent digital subtraction angiography and TAE with n-BCA. We analyzed the sex, age, hemorrhagic risk factors, etiology, embolized vessel, technical success (no rebleeding in the embolized area), clinical success (hemoglobin level control and hemodynamic stability after the procedure), complications inherent to the procedure, and clinical outcome (mortality in 30 days).

RESULTS
The mean age was 63.4 years (52–83 years), with a predominance of the female sex (64%). The majority (91%) of patients presented hemorrhagic risk factors (chronic hepatopathy and anticoagulation drug usage). Spontaneous hemorrhage was present in 18% of patients, and the other 82% had an iatrogenic etiology. Technical success was achieved in 100% of the patients, which required the embolization of inferior epigastric artery in 10 patients (91%), circumflex iliac artery in 2 (18%), and superior epigastric artery in 1 (9%). Five patients were hemodynamically unstable, and despite achieving technical success, 4 (36%) died in less than 30 days due to decompensation of their clinical comorbidities caused by the acute phase. There were no complications inherent to the procedures.

CONCLUSION
The present study concludes that TAE with n-BCA is a safe and effective treatment for abdominal wall hemorrhage in an urgent scenario, with high rates of technical and clinical success.

Abdominal wall hemorrhage (AWH) is a rare condition that is most commonly caused by an injury in the inferior epigastric artery and is frequently associated with rectus abdominis sheath hematoma (1–4). The condition most often has traumatic, spontaneous or iatrogenic etiology and usually presents as acute abdominal pain and a palpable mass in the inferior quadrants that does not cross the midline (5–8). Nearly always, AWH is self-limiting following noninvasive and symptomatic care such as analgesia, fluid resuscitation, blood transfusion and optimizing the coagulation status (1, 9, 10).

The growing number of elderly patients and the increasing exposure of the population to hemorrhagic risk factors has made AWH not only a more frequent entity but also a more dangerous condition. The spread of anticoagulation and antiplatelet therapies and clinical situations such as chronic liver disease can cause bleeding to be severe and uncontrollable with conservative measures (3, 6, 9–12).

The presence of a life-threatening hemorrhage, refractory to clinical measures or massive bleeding leading to hemodynamic instability, indicate that surgical or endovascular intervention is necessary to avoid a worsened outcome (1, 5, 9, 13). Endovascular therapies with the embolization of the injured arteries for hemorrhage control have become a fast and efficient treatment option, decreasing the morbidity and mortality rates (13). The techniques that are most frequently described in the literature and most widely used are microcoils, particle

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Received 01 July 2019; revision requested 21 July 2019; last revision received 06 September 2019; accepted 16 September 2019.

Published online 28 February 2020.

DOI 10.5152/dir.2019.19348

You may cite this article as: Albuquerque TVC, Monsignore LM, Castro-Afonso LH, Elias-Junior J, Muglia VF, Abud DG. Transarterial embolization with n-butyl cyanoacrylate for the treatment of abdominal wall hemorrhage. Diagn Interv Radiol 2020; 26:216–222.

agents and gelatin sponge hemostatic embolization (2, 3, 5, 7, 9–11, 14–17). Despite being effective in the majority of cases, there are some details to consider; for example, it can be difficult to navigate and place coils in distal and tortuous vessels, the retrograde flow in the collateral circulation can maintain the bleeding site and re-bleeding can occur due to recanalization (1, 9, 13).

To overcome these difficulties, selective artery embolization using n-butyl cyanoacrylate (n-BCA) is the first choice for patients presenting with abdominal wall life-threatening hemorrhage at our institution. The n-BCA is an adhesive liquid embolization agent that is practical, effective, and associated with low rates of complications in acute hemorrhage (1, 9, 13, 18).

Our primary objective in this retrospective study of a single center's experience was to evaluate the technical and clinical effectiveness and feasibility of the n-BCA transarterial embolization (TAE) of AWH.

Methods

Patient selection

We performed a single center retrospective review of the clinical and demographic characteristics of patients diagnosed with abdominal wall hemorrhage between 2008 and 2017 in the emergency unit of our institution. We examined the system database and then selected the patients who underwent TAE with n-BCA, representing 11 cases. We reviewed the medical records and relevant imaging studies to evaluate the etiology of the bleeding, method of diagnosis, injured artery, clinical and therapeutic effectiveness of treatment, and mortality within 30 days. Before all procedures, informed consent was obtained from the patients or their legal guardians. This study complied with the ethical standards of the Institutional and National research committee.

After the suspected AWH, both hemodynamically stable and unstable patients received immediate clinical management and underwent enhanced computed tomography (CT), except for two patients: one underwent ultrasonography (US) due to equipment unavailability and the other was a stable patient who underwent magnetic resonance imaging (MRI). Signs of vessel injury, active bleeding and presence of muscular hematoma were evaluated. Hemodynamic instability was considered as hypotension or need for vasoactive drugs for blood pressure control or any lowering in Glasgow coma scale associated with any other signs of hypovolemic shock, such as tachycardia, sweating, and pallor.

The endovascular intervention was indicated in AWH when there was hemodynamic instability in the acute presentation, regardless of the presence of signs of active bleeding in imaging exams; or in stable patients with signs of active bleeding when conservative treatment was considered unsuccessful in hemorrhage control (Fig. 1). Study inclusion criteria were: AWH diagnosed by any imaging study (CT, US or MRI); signs of active bleeding prior to the procedure; TAE with n-BCA as the embolic agent. Exclusion criteria were: resolution of active bleeding and clinical improvement with conservative management; TAE procedure with an embolization agent other than n-BCA.

Main points

- Abdominal wall hemorrhage (AWH) is a rare entity, but with increasing incidence, especially in elderly patients. Patients with hemorrhagic risk factors (chronic liver disease or anticoagulation therapy) are more prone to severe evolution of AWH with higher morbidity and mortality.
- Transarterial embolization has been shown to be superior to surgery in controlling hemorrhage site and decreasing morbidity and mortality in patients with AWH with hemodynamic instability in the urgent scenario.
- As an embolic agent, n-butyl-cyanoacrylate (n-BCA) is described as safe, fast and feasible for AWH, with superior characteristics in comparison to coils and particulate agents such as better placement visualization, greater facility in deploying in small tortuous vessels and the possibility of adjusting more proximal or distal embolization capacity depending on the n-BCA:Lipiodol dilution used.
- Complications of n-BCA embolization that are most relevant in AWH scenario include occlusion of normal territory and microcatheter entrapment, which must be minimized with proper technique and careful handling of the material.

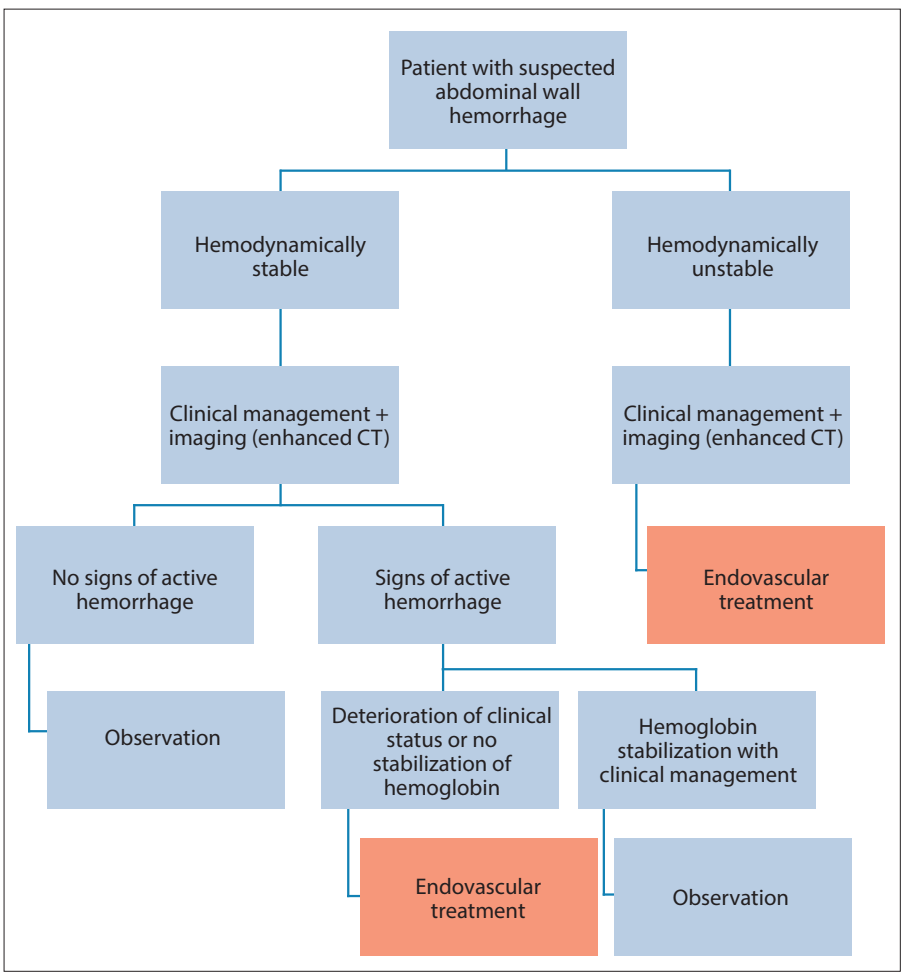

Figure 1. Flowchart of workup in patients suspected of having abdominal wall hemorrhage and simplified clinical and imaging criteria for endovascular treatment indication.

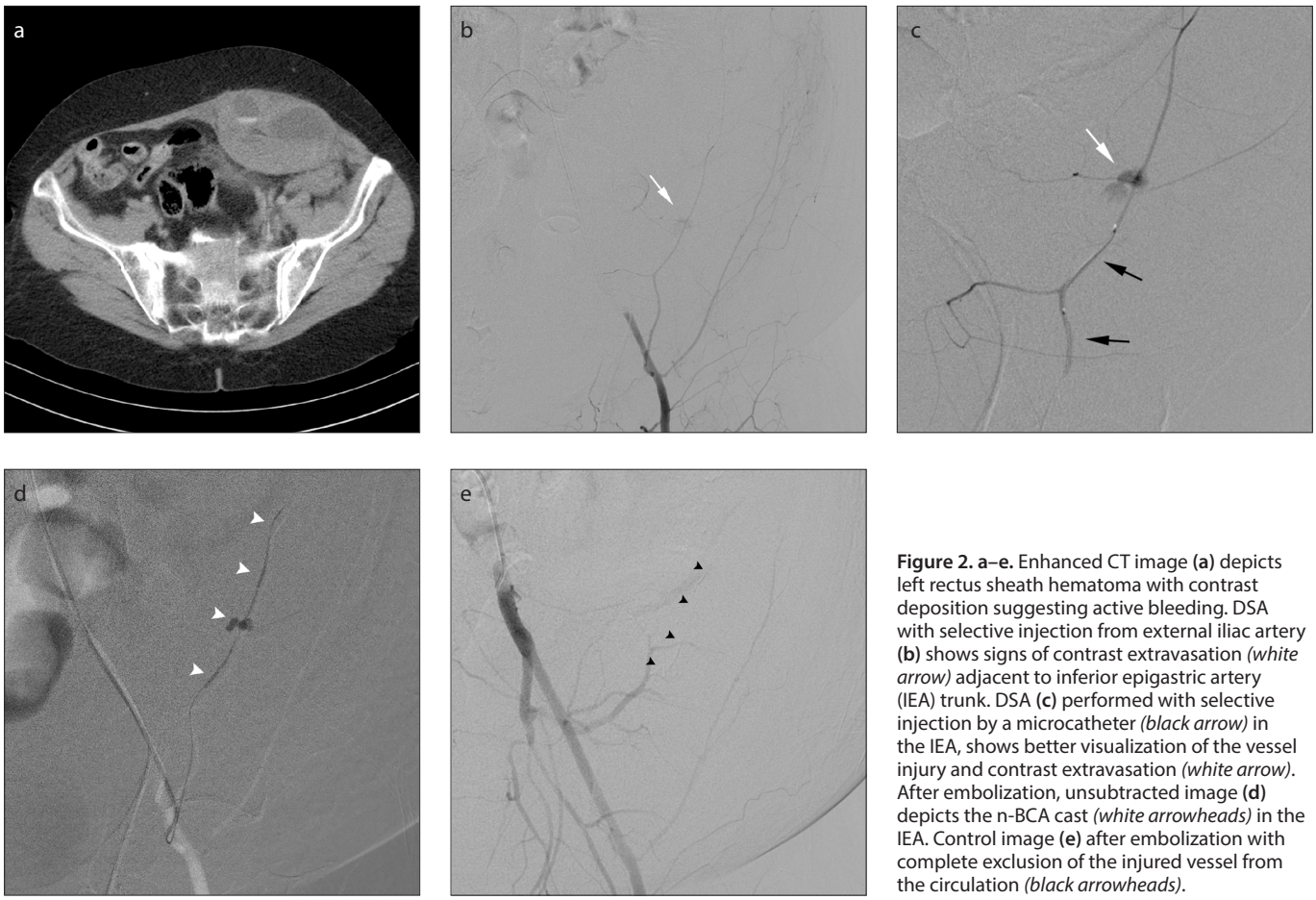

Figure 2. a–e. Enhanced CT image **(a)** depicts left rectus sheath hematoma with contrast deposition suggesting active bleeding. DSA with selective injection from external iliac artery **(b)** shows signs of contrast extravasation *(white arrow)* adjacent to inferior epigastric artery (IEA) trunk. DSA **(c)** performed with selective injection by a microcatheter *(black arrow)* in the IEA, shows better visualization of the vessel injury and contrast extravasation *(white arrow)*. After embolization, unsubtracted image **(d)** depicts the n-BCA cast *(white arrowheads)* in the IEA. Control image **(e)** after embolization with complete exclusion of the injured vessel from the circulation *(black arrowheads)*.

TAE procedure

The procedures were performed by one interventional radiologist with at least 5 years of experience and one or two interventional radiology residents (first or second year). Standard percutaneous transfemoral access was performed contralateral to the side of the suspected injury in the abdominal wall with a 5 F sheath. All patients were submitted to aortography to analyze possible splanchnic artery injury in association with abdominal wall injury. Angiography of the iliac artery and selective angiography in the suspected vessel was then performed with a selective Cobra 2 or Internal Mammary 5 F catheter (Merit Medical). The microcatheters used were Echelon 10 or Echelon 14 (Medtronic) in Avigo or Silverspeed guidewires (Medtronic) or Progreat microcatheter (Terumo Corporation). All affected arteries were embolized with n-BCA (Glubran 2, NBCA-MS GEM Srl or Histoacryl, B. Braun AG) in solution with ethiodized oil (Lipiodol UF, Guerbet). The solution of n-BCA:Lipiodol was used in ratios between 1:2 and 1:5, depending on the location of the injury and the operator's preference. One patient did not have active bleeding during angiography, even though previous imaging exams depicted it. In this patient we empirically embolized the feeding artery to the target territory based on previous imaging findings. The microcatheter was flushed with 5% dextrose solution before n-BCA injection, which was performed under fluoroscopic monitoring, until the expected findings were obtained and the microcatheter was subsequently removed. Post-embolization angiograms were performed to show the exclusion of the injured arteries from circulation. Additionally, after embolization, selective angiography in possible collateral territories was performed to avoid potentially untreated collateral bleeding (Fig. 2).

Study end-points

Our main purpose with the study was to determine the safety and technical effectiveness (hemorrhage control) of TAE with n-BCA in AWH in urgent scenario. Also, we evaluated immediate and late clinical outcome based on the mortality observed immediately and 30 days after the procedure.

Results

Mean age of the patients was 63±8.2 years (range, 52–83 years) with the predominance of female sex (64%). Hemorrhagic risk factors were present in 10 patients (91%); 8 of them had chronic hepatopathy (72%) and two received anticoagulation therapy (18%), both due to atrial fibrillation. The etiology was, in most cases, iatrogenic, with 7 cases after paracentesis (64%) and two cases after enoxaparin application (18%). Only two cases presented with spontaneous bleeding (18%).

Before the endovascular procedure, 5 patients (45%) showed hemodynamic instability; the most common clinical presentations were intense abdominal pain and an abdominal mass. Due to the comorbidities seen in our group, most of the patients already had chronic anemia, presenting be-

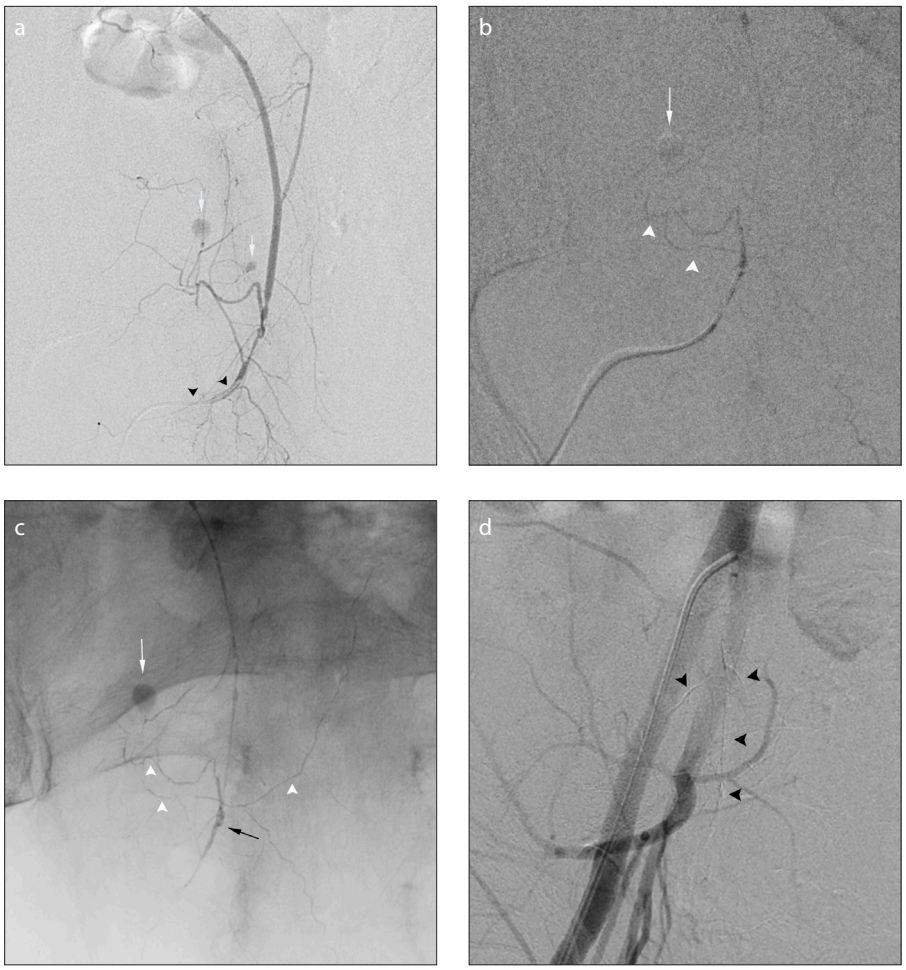

Figure 3. a–d. Image **(a)** shows DSA performed with selective injection by a microcatheter *(black arrowheads)* in right IEA with two hemorrhage points from small branches of the main artery trunk *(white arrows)*. These small and tortuous branches preclude the microcatheter from reaching the injured point, and therefore from being embolized using coils. In this situation, if the IEA trunk had been embolized with coils in an attempt to stop hemorrhage, there would be a high chance that it would be maintained by collaterals. Also, if particulate agents were used, the capillary bed of other branches not involved in the hemorrhage would be embolized, predisposing to other complications such as ischemia. Image **(b)** during n-BCA injection proximal to the hemorrhage focus shows the distribution among the small branches *(white arrowheads)* and reaching the target hemorrhage point *(white arrow)* but not reaching the capillary bed due to the n-BCA viscosity and fast polymerization time. Unsubtracted image **(c)** after embolization with the n-BCA cast filling the IEA trunk *(black arrow)* and the small branches *(white arrowheads)*, including the hemorrhagic point *(white arrow)*. Control angiography **(d)** with injection from iliac artery demonstrates complete exclusion of the hemorrhage from the circulation and the n-BCA cast *(black arrowheads)*. After the procedure, this patient achieved hemoglobin level stabilization and clinical improvement.

fore the hemorrhagic event with a mean basal hemoglobin level of 10.2±2.46 g/dL (range, 7.1–14.0 g/dL) and immediately after bleeding with a mean hemoglobin level of 6.3±1.77 g/dL (range, 3.8–9.2 g/dL).

Upon clinical suspicion of AWH, imaging was performed before procedure indication (CT, n=9; US, n=1; MRI, n=1) depicting abdominal wall hematomas in 8 patients (73%) and peritoneal hemorrhage in 3 (27%), all with signs of active bleeding at that moment. Table 1 summarizes the demographic, etiology and imaging data and Table 2 summarizes the clinical status and findings before the procedure.

After the procedure, all 11 patients presented stabilization of the hemoglobin level, representing technical success in 100% of the cases. None of the patients presented new hemorrhages or required more than one session of TAE. Of the 5 patients with hemodynamic instability, 4 patients died within 30 days after the intervention; the earliest death occurred 2 days after the procedure, due to comorbidities and decompensation of the clinical parameters, despite complete resolution of bleeding. Thus, clinical failure occurred in 37% of the cases. No deaths were observed as a result of immediate bleeding or in patients who did not present with hemodynamic instability before the intervention. The inferior epigastric artery was embolized in 10 of 11 patients (91%), the circumflex iliac artery in two (18%) and the superior epigastric artery via the internal mammary artery in one (9%).

None of the patients developed hematoma or pseudoaneurysm at the puncture site or any other complications inherent to the procedure. The technical and clinical results after the procedure, as well as the arteries involved, the lesions observed in angiography and the glue dilution in each patient are shown in Table 3.

Discussion

This study concludes primarily the feasibility, safety and technical effectiveness of TAE with n-BCA as embolic agent for AWH. The hemorrhage was controlled in all patients after one session of TAE with stabilization of hemoglobin level, even under anticoagulation therapy. Despite the rareness of this condition, the recent increase in the number of people with certain hemorrhagic risk factors, such as chronic liver disease patients and those who are receiving anticoagulant therapy, makes patients not only more susceptible to bleeding events but also prone to the more severe evolution of the condition, with higher morbidity and mortality rates, regardless of its etiology (3, 6, 9–12). As mentioned above, the outcomes were also dependent on patient's comorbidities, and clinical deterioration could occur even after endovascular technical success and hemoglobin stabilization was achieved. There were no complications inherent to procedures, such as tissue ischemia or infection, vessels injury, access site hematomas, or pseudoaneurysms.

The most common lesion in the anterior abdominal wall is an inferior epigastric artery injury that induces rectus abdominis sheath hematoma formation (1–4). Some studies have also reported associations between arteriosclerosis, chronic renal failure, coronary disease and arterial hypertension and an increased risk of spontaneous bleeding (9, 19), because these factors predict more weakness in the vessel wall (18). Aside from these risk factors, our study was consistent with previous findings that women

Table 1. Demographic data, mechanism of injury and imaging

Patient no.	Age (years)	Sex	Hemorrhagic risk factor	Mechanism of injury	Imaging diagnosis
1	70	F	Chronic hepatopathy	Spontaneous	MRI
2	66	M	Chronic hepatopathy	Paracentesis	CT
3	66	F	Chronic hepatopathy	Paracentesis	CT
4	65	F	Chronic hepatopathy	Paracentesis	CT
5	61	F	Chronic hepatopathy	Paracentesis	CT
6	58	F	Chronic hepatopathy	Paracentesis	CT
7	54	M	Chronic hepatopathy	Paracentesis	CT
8	52	M	Chronic hepatopathy	Paracentesis	US
9	65	F	Anticoagulation therapy	Enoxaparin application	CT
10	83	F	Anticoagulation therapy	Enoxaparin application	CT
11	57	M	None	Spontaneous	CT

F, female; M, male; MRI, magnetic resonance imaging; CT, computed tomography; US, ultrasonography.

Table 2. Clinical status and findings before the procedure

Patient data	Value
Clinical status, n (%)	
Hemodynamic instability	5 (45)
Abdominal pain	10 (91)
Abdominal mass	8 (73)
Hemoglobin level (g/dL), mean±SD (range)	
Before bleeding	10.2±2.46 (7.1–14.0)
After bleeding	6.3±1.77 (3.8–9.2)
Imaging findings, n (%)	
Abdominal wall hematoma	8 (73)
Peritoneal hemorrhage	3 (27)

SD, standard deviation.

are more prone to developing AWH, with a mean proportion of 2–3:1 (8, 20, 21), as well as elderly individuals (8), as they usually have a lower muscular mass (20).

The etiologies of AWH are usually divided into iatrogenic, traumatic, and spontaneous. In accordance with some studies, the most common etiology of inferior epigastric artery injury was iatrogenic manipulation of the abdominal wall (14), especially after paracentesis in patients with chronic liver disease and following minor surgeries, retention sutures, subcutaneous injections, peritoneal dialysis and catheter insertions or removals (3, 5, 22). In our series, there was a high incidence of paracentesis as the catalyst of the hemorrhage. We assume that technical details may be one explanation. Other uncommon mechanisms have also been described, such as acupuncture (23). On the other hand, spontaneous AWH usually occurs after incidences of forceful muscular strain or extensive contraction, such as coughing, weight lifting and vomiting (9, 10, 20).

The anatomy of the abdominal wall seems to be closely related to the anterior lower quadrants being a preferential target for bleeding (8). First, the lowest part of the rectus abdominis muscle is the longest, where there is the greatest shortening with contraction, predisposing the area to injuries secondary to tensional forces (8). Second, the inferior epigastric artery originates medially from the external iliac artery, just superior to the inguinal ligament, and has an upward path between the rectus abdominis muscle and the posterior leaf of the rectus sheath. This artery forms an anastomosis network with superior epigastric artery, which comes from the internal mammary arteries, at the umbilical level (21) and with the superficial epigastric artery, which arises anteriorly from the common femoral artery, immediately inferior to the inguinal ligament. Third, and last, the circumflex iliac arteries, both deep and superficial, originate laterally from the external iliac and common femoral arteries, respectively, and then extend along the crest of the ilium bone. These locations are common targets of unguided small procedures and even minor local surgeries.

As in the literature, the most common clinical features in AWH were acute abdominal pain followed by an inferior abdominal mass when hematoma formation was present (7, 8, 10, 13, 24). Depending on the volume, hemorrhage can also lead to hemodynamic instability. Additionally, when most patients are of an elderly age, there are presentations of their comorbidities, with or without decompensation, due to the acute hemorrhagic status. In our study, chronic renal failure, arterial hypertension and coronary artery disease were the most frequent comorbidities, consistent with previous studies (9). The diagnosis can be difficult and is not infrequently mistaken for other causes of abdominal pain or acute abdominal injury. The typical presentation of pain tends to be localized and to have a gradual evolution over a few hours; however, it can also be abrupt (20). If a mass is present, it would not move with respiration and remains palpable with anterior abdominal wall contraction or becomes more prominent or fixed (Fothergill's sign) (20).

Several reports have focused on the endovascular approach in cases of AWH in patients undergoing anticoagulation therapy or with some kind of coagulopathy, such as chronic liver disease. Most of those studies showed embolization effectiveness with gelfoam, microspheres, polyvinyl alcohol (PVA) particles or coil embolization (3, 5, 9, 25, 26). Few reports mentioned embolization with n-BCA (9, 18, 27–30). Our study showed that TAE with n-BCA for AWH is a feasible, effective, and safe treatment, including in patients using anticoagulant therapy or with chronic liver disease. A single intervention was sufficient to control the hemorrhage in all patients with the stabilization of the hemoglobin level and no complications inherent to the procedures were observed. Five patients with advanced comorbidities who experienced decompensation and/or delayed clinical management of the bleeding developed hemodynamic instability and despite the

Table 3. Procedures and results

Pt no.	Involved artery(ies)	Angiography findings	Glue dilution (n-BCA:Lipiodol)	Technical success	Hemodynamic instability before/after procedure	Mortality in 30 days
1	IEA, SEA and CIA	Contrast extravasation	1:3	Yes	Yes/Yes	Yes
2	IEA	Contrast extravasation	1:3	Yes	Yes/No	No
3	IEA	Pseudoaneurysm	1:3	Yes	No/No	No
4	CIA	Pseudoaneurysm	1:2	Yes	No/No	No
5	IEA	Pseudoaneurysm	1:2	Yes	No/No	No
6	IEA	Pseudoaneurysm	1:5	Yes	No/No	No
7	IEA	Pseudoaneurysm	1:4	Yes	Yes/Yes	Yes
8	IEA	Pseudoaneurysm	1:3	Yes	Yes/Yes	Yes
9	IEA	Contrast extravasation	1:5	Yes	No/No	No
10	IEA	No active bleeding	1:4	Yes	Yes/Yes	Yes
11	IEA	Contrast extravasation	1:3	Yes	No/No	No

n-BCA, n-butyl cyanoacrylate; IEA, inferior epigastric artery; CIA, circumflex iliac artery; SEA, superior epigastric artery.

technical procedural success, four of those patients died within 30 days.

Endovascular treatment has been described as a better choice than open surgery in acute hemorrhages, not only because it is less invasive but also because fewer complications are reported and better management is possible in patients with comorbidities and a poor surgical status (9, 24, 26, 27, 29–31), markedly reducing the mortality and morbidity associated with hemorrhage treatment (13, 32). Moreover, endovascular treatment can be performed without general anesthesia if the patient maintains a good status of orientation and cooperation.

Metallic coils and particulate agents are effective in controlling bleeding in most cases. However, in some cases, homeostasis is not reached, because the bleeding site is not reached or due to rebleeding resulting from collaterals or recanalization. Coils are ideal for bleeding in a single vessel, usually with a larger diameter, and when embolization requires precision (13). In cases of AWH in the presence of small and tortuous vessels and a rich collateral net, coil embolization may not only be more difficult but also may not be resolutive. Particulate agents cannot be precisely placed in the site of the vessel injury, may clump, and may occlude the microcatheters and vessels proximal to the bleeding site. Other described complication is skin necrosis after embolization (33), usually present when the occlusion happens at the capillary level, making it impossible for collateral vessels to supply that region. Other cofactors that increase the possibility of skin necrosis are diabetes, acidosis, hemodynamic shock and vasoactive drugs, all conditions that reduce capillary perfusion (33, 34).

TAE with n-BCA is our institution's first choice approach for AWH due to its characteristics: a liquid agent, fast-acting polymer chain, which can be used in small microcatheters, does not necessarily need to be administered at the bleeding site and can be mixed with ethiodized oil in different ratios that alter its polymerization time (13, 30, 35). This allows the operator to embolize more distally or proximally depending on the n-BCA:ethiodized oil ratio (Fig. 3). Moreover, ethiodized oil is radiopaque and permits the more controlled placement of embolic agent with the documentation of the occluded site. Another advantage is that the viscosity and polymerization speed of n-BCA do not allow it to progress to the capillary level and to promote tissue ischemia (13), which can occur with particulate agents. To our knowledge, there is no report of target tissue ischemia after AWH embolization with n-BCA. The n-BCA can also promote complete vessel occlusion in patients with coagulopathies, which must be considered in patients with AWH.

There are some complications related to n-BCA embolization (36–38). The most relevant in the AWH scenario are the unwanted arterial territory embolization and catheter entrapment and they may occur due to distal glue migration or to reflux during the administration. Occlusion of normal territory may lead to organ ischemia. Microcatheter entrapment is relatively rare and in this peripheral circulation generally does not lead to adverse clinical consequences (36, 37). There are some factors that must be considered to minimize those risks: size of target vessel, direction and speed of blood flow through catheter tip, n-BCA:Lipiodol dilution and the technique during injection (36).

The operator must understand the strategy involved in each territory and use refined embolization techniques: adjust the best projection to monitor the n-BCA progression, remove redundant loops in microcatheter to guarantee more control if pullback maneuver is required, select the most suitable dilution and injection speed and avoid forceful movements of the catheter (36–38).

The major limitation in our study is the retrospective nature. We point that TAE with n-BCA can be considered as primary strategy in AWH to aim better technical and clinical success with lower rates of recurrent hemorrhage and complications.

In conclusion, TAE with n-BCA in patients with AWH was shown to be feasible, safe and efficient in hemorrhage control and for the stabilization of the hemodynamic status in urgent scenarios, when clinical treatment is not sufficient, including in patients with coagulopathies or who use anticoagulation therapy. Proper technique should be employed to avoid complications.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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