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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Urgent percutaneous transcatheter embolization of hemorrhagic hepatic lesions with N-butyl cyanoacrylate

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PURPOSE
To report on our clinical experience with and the success rate and safety of percutaneous transcatheter embolization with N-butyl cyanoacrylate (NBCA) as the lone primary embolic agent used for arterial embolization of hemorrhagic liver lesions.

MATERIALS AND METHODS
This retrospective study enrolled all patients who presented to the emergency room with hemorrhagic liver lesions during a two-year period and were treated by percutaneous transcatheter embolization with NBCA.

RESULTS
Eight consecutive patients were evaluated, and 13 lesions were embolized exclusively with NBCA: eight pseudoaneurysms and five active bleeds. All patients were treated successfully using percutaneous transcatheter embolization with NBCA without re-bleedings or major complications.

CONCLUSION
Percutaneous transcatheter embolization with NBCA is a safe and effective method for treating hemorrhagic lesions.

Key words: • *liver* • *hemorrhage* • *therapeutic embolization* • *interventional radiology*

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Hepatic lesions may bleed as much from their blood supply (hepatic artery or portal vein) as they do through their drainage vein (hepatic vein). Hepatic arterial bleeding is a life-threatening condition with many etiologies; trauma is the most common, followed by iatrogenic and spontaneous lesions.

The hepatic artery anatomy is quite variable (1). In the most common pattern (Michels type 1 configuration), the common hepatic artery is the right branch of the trifurcation of the celiac trunk. After the gastroduodenal artery arises, the common hepatic artery is called the proper hepatic artery, which bifurcates into the right and left hepatic arteries. Posteriorly, they divide and subdivide into segmental and subsegmental arteries.

Currently, the treatment of choice for hepatic lesions is an endovascular approach, which can use a wide range of embolic materials. The most commonly used materials are coils and absorbable gelatins, followed by polyvinyl alcohol (PVA) particles, stent grafting, AMPLATZER plugs, and N-butyl cyanoacrylate (NBCA), either alone or in combination (2–7). Given the dual blood supply to the liver, the hepatic artery and its branches can be embolized, and there is only a low risk of hepatic necrosis as long as the portal vein shows no abnormalities on splenoportography (8).

This preliminary study describes our experience treating hemorrhagic hepatic lesions using arterial embolization with NBCA alone as the first option.

Material and methods

This was a retrospective study of patients treated for hemorrhagic hepatic liver with NBCA as the lone embolic agent in urgent situations. The Quality Improvement Guidelines for Percutaneous Transcatheter Embolization (9) were used to define the terms used here. This study was performed according to the World Medical Association Declaration of Helsinki. Informed consent was obtained from all patients.

Patients and presentations

Eight consecutive patients with hemorrhagic lesions in the liver who presented in the emergency room from October 2008 to November 2010 were studied retrospectively; these patients were treated by percutaneous transcatheter embolization with NBCA (Histoacryl, B. Braun AG, Melsungen, Germany). Patients were seven men and one woman, with ages ranging from 3 to 61 years (mean, 39.5 years). All patients presented with symptoms of hypotension and falling hemoglobin levels; the lowest mean hemoglobin was 6.75±1.6 g/dL. Each patient received a blood transfusion before embolization.

The hemorrhage was post-traumatic in four patients, and postvideolaparoscopic cholecystectomy, postduodenopancreatectomy, spontaneous intratumor bleeding, and multiple spontaneous pseudoaneurysms were the cause in one patient each. The initial diagnosis of liver bleeding was made with computed tomography in five patients, scintigraphy in two, and Doppler ultrasonography in one. Four patients needed a transfusion after the procedure: three patients with post-traumatic etiology and one with spontaneous tumor bleeding.

All of the patients who presented with active bleeding had an abnormal platelet count or coagulogram (prothrombin time/international normalized ratio and activated partial thromboplastin time ratio), as shown in Table 1.

Angiographic evaluation

All interventional procedures were done via a femoral approach (11-cm-long 5 F sheath introducer) with selective angiography of the celiac trunk, common hepatic artery, and superior mesentery artery, along with a delay phase for splenoportography with a 5 F diagnostic angiography catheter. The target areas were characterized as active bleeding or pseudoaneurysm according to the angiographic findings, and each target area was classified according to its location. When the common, proper, right, or left hepatic artery was involved, the targets were classified as truncal or proximal lesions; when segmental or subsegmental branches of the right or left hepatic arteries were involved, they were classified as distal.

All eight patients underwent an angiographic evaluation, and 13 lesions were detected. Eight lesions were characterized as pseudoaneurysms, and five as active bleeding. All active bleeding lesions were distal. Of the pseudoaneurysms, two were truncal and six were distal.

Embolization technique

The target areas classified as truncal or proximal and characterized as pseudoaneurysm were treated by selective embolization of the false lumen, sparing the affected artery (Fig. 1). A microcatheter (Renegade 18, Boston Scientific, Natick,

Table 1. Clinical findings of eight patients

Patient number	1	2	3	4	5	6	7	8
Age (years)	48	61	21	3	51	60	15	57
Gender	Male	Male	Male	Male	Male	Female	Male	Male
Lowest serum hemoglobin level before embolization (g/dL)	7.7	8.6	5.1	7.9	4.5	8.4	5.5	6.3
Serum hemoglobin level at discharge (g/dL)	9.1	10.3	10.9	11.8	9.3	11.8	13.3	8.7
Platelet count (10^3 platelets/μL)	318	541	79	532	331	550	128	72
International normalized ratio	0.98	0.99	1.86	1.59	1.03	1.13	1.79	1.56
Activated partial thromboplastin time ratio	0.77	1.15	1.22	1.65	1.12	1.16	2.41	1.36
Blood tranfusion before embolization	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Blood transfusion after embolization	No	No	Yes	Yes	No	No	Yes	Yes
NBCA concentration	50%	50%	33%	50%	50%	50%	25%	25%
Patient presentation	Recurrent hemobilia after cholecystectomy	Abdominal pain and hypotension after spontaneous rupture of intrahepatic pseudoaneurysms	Motorcycle vs. car collision	Car vs. car collision	Melena two months after truck vs. car collision	Hemobilia after biliodigestive anastomosis	Bicycle vs. car collision	Spontaneous intratumoral bleeding (gastrointestinal stromal tumor metastasis)
Initial imaging method for diagnosis	Scintigraphy	Doppler ultrasonography	Computed tomography	Computed tomography	Computed tomography	Scintigraphy	Computed tomography	Computed tomography
Number of lesions	1	4	1	2	2	1	1	1
Angiographic presentation	Pseudoaneurysm	Pseudoaneurysm	Active bleeding	Active bleeding	Pseudoaneurysm	Pseudoaneurysm	Active bleeding	Active bleeding
Localization	Distal	Distal	Distal	Distal	Distal / truncal	Truncal	Distal	Distal
Etiology	Iatrogenic	Spontaneous	Traumatic	Traumatic	Traumatic	Iatrogenic	Traumatic	Spontaneous
Hospitalization time (days)	7	26	16	47	13	7	11	6

NBCA, N-butyl cyanoacrylate.

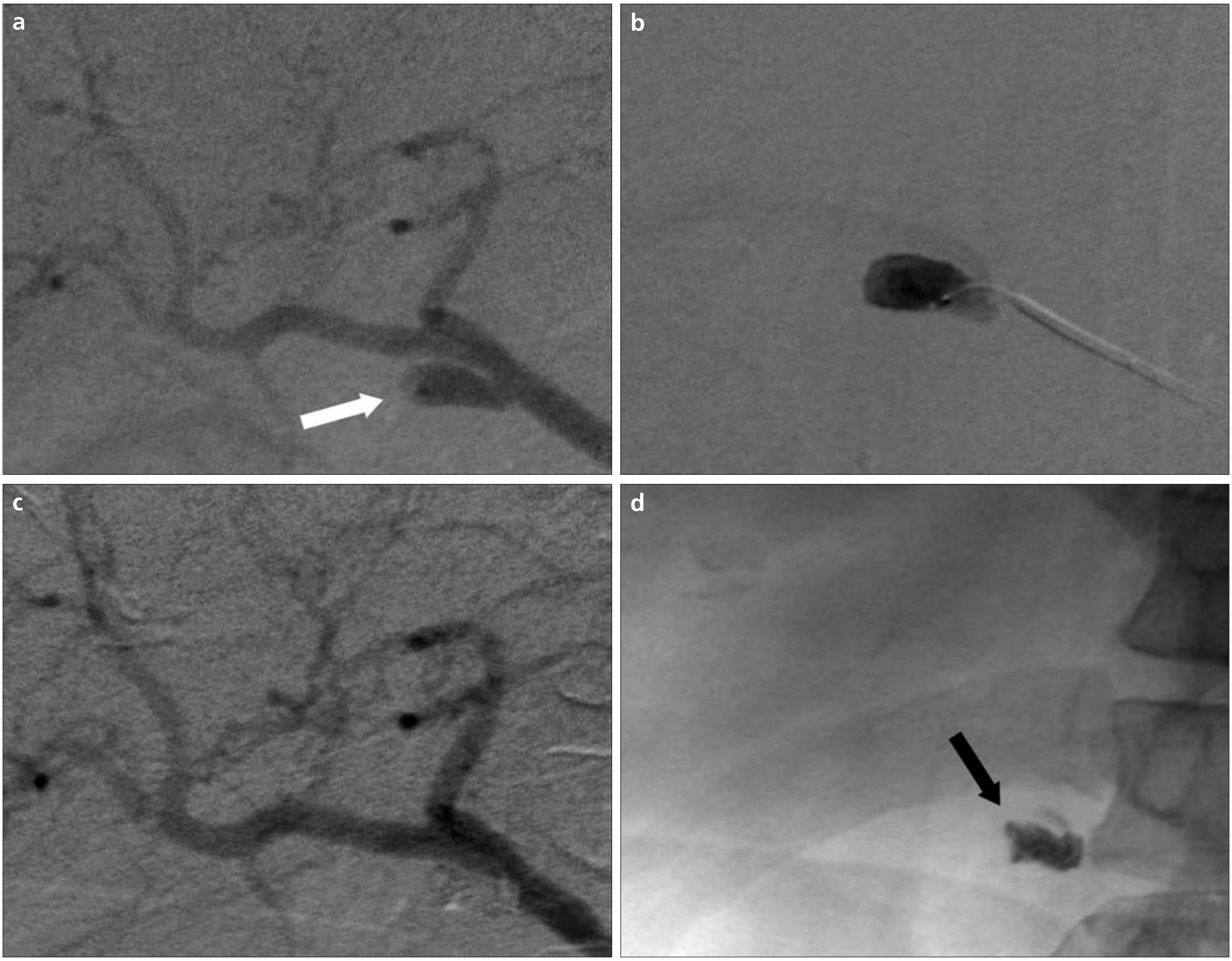

Figure 1. a–d. Truncal lesion embolization. The patient presented with melena two months after a motor vehicle collision. Selective angiographic evaluation of the celiac trunk showed a pseudoaneurysm in the proper hepatic artery **(a,** *white arrow***)**. Microcatheterization of the pseudoaneurysm **(b)**, which resolved with angiographic control, sparing the proper hepatic artery **(c)**. Cast of NBCA selectively injected inside the pseudoaneurysm **(d,** *black arrow***)**.

Massachusetts, USA) with an inner lumen diameter of 0.021" and a 0.014" micro-guidewire (ChoICE, Boston Scientific) were navigated coaxially into the 5 F catheter until they reached the lumen of the pseudoaneurysm.

Truncal/proximal lesions

The tip of the microcatheter was placed inside the pseudoaneurysm and close to its visible limits. Then, the microcatheter was flushed exhaustively with 5% dextrose solution; this was followed by injecting a mixture of NBCA and iodized oil (Lipiodol, Laboratoire André Guerbet, Aulnay-sous-Bois, France) in a 1:1 ratio (50% NBCA) until the pseudoaneurysm was obstructed completely; this spared the feeding artery. We avoided injections lasting more than 1 min. After the injection, the microcatheter was removed quickly under aspiration to prevent potential non-target embolization and was discarded. Then, the 5 F angiographic catheter was aspirated and flushed, and postembolization angiography was performed.

Distal lesion

Target areas that were classified as distal, both pseudoaneurysms (Fig. 2) and active bleeding (Fig. 3), were treated by embolizing the lesion, together with the affected artery, proximal and distal to the lesion. A microcatheter and a micro-guidewire were navigated coaxially into the 5 F catheter until they reached the segmental or subsegmental hepatic artery that was responsible for the bleeding or that supplied the pseudoaneurysm. The microcatheter was flushed with 5% dextrose solution; this was followed by the injection of a mixture of NBCA and iodized oil in a 1:1 to 1:3 ratio (50%–25% NBCA), depending on the velocity of blood flow, until the lesion and affected artery were obstructed completely. For patients with more than one target area, different microcatheters were used and then discarded, repeating the steps described above.

Clinical follow-up

All patients were hospitalized for clinical and laboratorial evaluations and discharged after an average of 16.6 days (range, 6–47 days). The longest

Figure 2. a–c. Multiple distal pseudoaneurysm embolization. The patient presented with abdominal pain and hypotension after spontaneous rupture of intrahepatic pseudoaneurysms. Selective angiography of the proper hepatic artery showed four lesions in the intrahepatic branches of the right hepatic artery consistent with pseudoaneurysms **(a,** *white arrows***)**. Superselective microcatheterization of each pseudoaneurysm was performed with microcatheters **(b,** *white arrow***)**. At angiography after the NBCA treatment, the pseudoaneurysms are no longer seen **(c)**.

stays were for patients with a traumatic etiology, as other organs were affected or there were surgical complications. The mean hemoglobin at discharge was 10.6±1.6 g/dL.

Results

Technical success using percutaneous transcatheter embolization with NBCA was achieved in all patients for both techniques, which included complete exclusion of the pseudoaneurysm from the circulation. Complete clinical success was also achieved for all patients: no clinical recurrence was observed during the hospital stay or follow-up, with progressive recovery of the hemoglobin level following the intervention (Table 1). Non-target embolization, inside or outside the liver, was not observed in this series.

In a patient who had two pseudoaneurysms, a truncal pseudoaneurysm in the right hepatic artery and a distal pseudoaneurysm in a segmental right hepatic artery, the latter was perforated during microcatheterization. The treatment proceeded with an NBCA injection to obstruct the pseudoaneurysm and the affected artery so that the bleeding was resolved. This patient was awake during the procedure and did not develop new symptoms or a decrease in hemoglobin.

No major complications were observed during the hospital stay or in the follow-up in our patient series. One patient developed a large asymptomatic peritoneal pseudocyst, which was seen on the one-month magnetic resonance imaging follow-up, but the pseudocyst had resolved spontaneously by the three-month follow-up and was believed to be secondary to previous intra-abdominal bleeding.

Discussion

The hepatic artery or its branches can hemorrhage due to a number of etiologies, including traumatic, iatrogenic, or spontaneous. Trauma is the most common etiology and accounts for approximately 85% of cases; this includes active bleeding from a liver

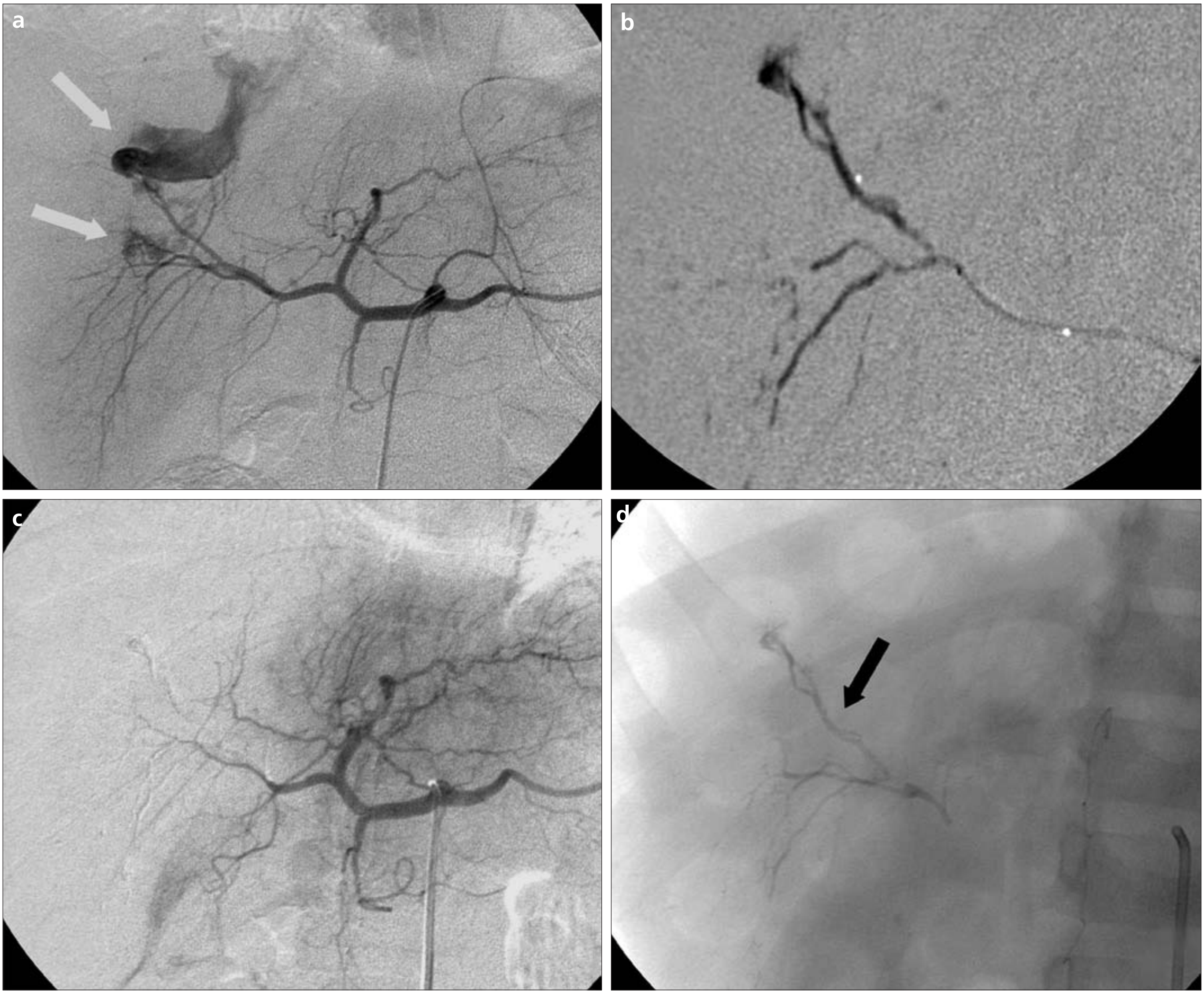

Figure 3. a–d. Post-traumatic active bleeding embolization. Following an automobile collision, the patient presented with blunt abdominal trauma with free abdominal fluid at ultrasonography and hypovolemic shock. Two different spots of active bleeding were seen in the right liver lobe from distal branches of the right hepatic artery (**a**, *white arrows*). NBCA injection after microcatheterization **(b)** and postembolization angiography **(c)** are seen. Cast of NBCA is inside the distal branches of the right hepatic artery (**d**, *black arrow*).

laceration, usually after blunt trauma, or a liver contusion with pseudoaneurysm formation (2). Iatrogenic lesions to the hepatic artery can occur during surgical (e.g., cholecystectomy, duodenopancreatectomy, and liver transplantation) or percutaneous (e.g., biliary drainage and liver biopsy) procedures (3, 4). Spontaneous hepatic artery bleeding is uncommon and includes aneurysm and pseudoaneurysm ruptures, tumors, pre-eclampsia, and other rare causes.

Endovascular embolization is currently the treatment of choice for a life-threatening liver hemorrhage of any etiology (5, 6, 10–13). The reported success rates of embolization of liver bleeding are from 53% to 92% (2, 14, 15), depending on the site of the bleed and which embolic material was used (Table 2). A wide range of materials has been used for treatment, including coils (4–6), absorbable gelatins (2–4), PVA particles (2), stent grafting (16), and NBCA (4–7), either exclusively or in combination. Coils are considered the best embolic material for active bleeding from pseudoaneurysms. However, coils are inconvenient because superselective catheterization is always required, and the proximal occlusion of a vessel may not successfully treat the bleeding lesion due to the presence of collateral vessels (6) or in patients with coagulopathy. Absorbable gelatin and PVA particles are often used in combination with coils, but they have a high rate of technical failure, especially when used alone.

NBCA is a non-absorbable liquid ester that polymerizes rapidly in the presence of ionic substances like blood and saline. When mixed with Lipiodol, NBCA becomes radiopaque, and its polymerization is retarded to a timescale of seconds; the polymerization time is inversely proportional to the amount of Lipiodol in the mixture (17). It has been used in interventional radiology for more than three decades and primarily for neuro-interventional procedures, e.g., cerebral and medullar arteriovenous malformations (AVMs)

Table 2. Embolization of liver hemorrhagic lesions in the literature

Study, year	Number of patients	Etiology	Embolization material	Success (excludes technical failure, re-bleeding, and death)	Major complications
Hidalgo et al. 1995 (2)	12	Iatrogenic trauma (n=7), blunt external trauma (n=3), septic emboli (n=1), and lupus vasculitis (n=1)	Coils (n=12), gelatin sponge (n=8), polyvinyl alcohol particles (n=2)	7/12 (58%)	Ischemic necrosis of the gallbladder (n=1), liver failure (n=1), biliary sepsis (n=1), death (n=2)
Görich et al. 1999 (14)	26	Hemobilia following percutaneous biliary drainage (n=12) or biliary stenting (n=3), vascular tumor bleedings (n=3), iatrogenic trauma post biopsy or postoperative (n=4), posttraumatic (n=1), cumarin therapy (n=1), hepatic aneurysm (n=1), or unknown (n=1)	Coils (n=22), ethibloc (n=4), NBCA (n=3), gelatin sponge (n=1)	24/26 (92%)	Hepatic abscess (n=1), gallbladder necrosis (n=1)
Srivastava et al. 2006 (15)	32	Iatrogenic trauma (n=6), car accident (n=13), vasculitis (n=6), vascular malformation (n=2), hepatobiliary tumors (n=5)	Coils (n=19), gelatin sponge (n=15), polyvinyl alcohol particles (n=1)	17/32 (53%)	Septicemia with multiorgan failure (n=1), death (n=1)

NBCA, N-butyl cyanoacrylate.

(18, 19) or head and neck tumors (20). Recently, its use outside the central nervous system was approved; case reports and series have been published on the treatment of gastrointestinal bleeding (21–23), varicoceles (24), peripheral arteriovenous fistulas and AVMs (25), tumor lesions (26), and portal vein embolization (27) with NBCA alone or with other embolic material.

As a liquid embolic material, NBCA has the advantage of promoting the occlusion of an entire vessel and the bleeding lesion or being extremely selective inside a truncal pseudoaneurysm of the hepatic artery, depending on its dilution with Lipiodol. It is prepared and delivered quickly, relative to absorbable gelatin and PVA particles, resolving the bleeding rapidly. As the vessel occlusion does not depend on the patient's coagulation state, it can be used safely in cases of severe coagulopathy. Although non-target embolization can occur, NBCA is considered safe and effective for treating hemorrhagic liver lesions because of the dual blood supply to the liver and the low rate of hepatic necrosis when there is normal portal venous flow (8, 28). Onyx (ethylene-vinyl-alcohol-copolymer) is a permanent nonadhesive liquid embolic agent with behavior comparable to acrylic glue. Some authors have used Onyx to treat acute bleeding with good results (29). We feel that Onyx is indicated for situations in which long injections of material are needed to achieve better filling of the lesion, usually for intracranial (30, 31) and peripheral (32) vascular malformations. With active bleeding, although Onyx can be used, we consider NBCA superior due to the ability to alter its concentration and hence the polymerization time. In summary, the indications for the use of NBCA and Onyx differ; we consider NBCA more controllable when the occlusion of a vessel is needed.

The presence of anatomical variation in the arterial supply of the liver and gallbladder and physiological anastomoses to adjacent organs (33) can lead to undesirable and potentially dangerous non-target embolization outside of the liver.

Most interventional radiologists avoid the use of liquid embolic agents because they consider their delivery difficult to control. The main technical limitation of the use of NBCA is its management. Its polymerization characteristics, dilution with Lipiodol, velocity of delivery, reflux control, and anatomical familiarity are important aspects linked to its use, and the clinician must know these well to perform safe, successful procedures. Interventional radiologists must be attentive to some physiological anastomoses, called dangerous anastomoses, during the use of NBCA in specific locations, such as external carotid artery-ophthalmic artery-internal carotid artery in the treatment of epistaxis (34) and bronchial artery-anterior spinal artery in the treatment of hemoptysis (35), due to the possibility of neurological complications.

Our study has several limitations. First, it was a retrospective study examining preliminary results and included a small number of patients, which prevents additional statistical analysis. Second, all of the procedures were performed by two experienced interventional radiologists in a single center, which may bias the results. A multicenter study with more patients must be performed to confirm our findings.

In conclusion, this preliminary study demonstrated that endovascular embolization with NBCA as a single embolic agent is a feasible and effective method for treating hemorrhagic liver lesions. NBCA occludes the embolized artery or the pseudoaneurysm definitively, without recurrent bleeding during follow-up. Interventional radiologists must become familiar with the use of NBCA in lesions outside the central nervous system. In trained hands, NBCA can be used as the primary or sole embolic agent in many situations, particularly for hemodynamically unstable patients who require fast, effective resolution of bleeding, truncal pseudoaneurysms of the hepatic artery to spare the affected artery, and patients with severe coagulopathy in whom other embolic procedures are less effective.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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