BJR
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Received: 11 May 2014 | Revised: 7 July 2014 | Accepted: 14 July 2014

doi: 10.1259/bjr.20140347

Cite this article as:
Park SY, Kim J, Kim BW, Wang HJ, Kim SS, Cheong JY, et al. Embolization of percutaneous transhepatic portal venous access tract with *N*-butyl cyanoacrylate. Br J Radiol 2014;87:20140347.

FULL PAPER

Embolization of percutaneous transhepatic portal venous access tract with *N*-butyl cyanoacrylate

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Objective: To evaluate the safety and feasibility of *N*-butyl cyanoacrylate (N-BCA) embolization of percutaneous transhepatic portal venous access tract and to establish an appropriate technique.
Methods: 40 consecutive patients underwent percutaneous transhepatic portal venous intervention for various reasons. Embolization of percutaneous transhepatic portal venous access tract was performed after the procedure in all of the patients using N-BCA and Lipiodol® (Lipiodol Ultra Fluide; Laboratoire Guerbet, Aulnay-sous-Bois, France) mixture. Immediate ultrasonography and fluoroscopy were performed to evaluate perihepatic haematoma formation and unintended embolization of more than one segmental portal vein. Follow-up CT was performed, and haemoglobin and haematocrit levels were checked to evaluate the presence of bleeding.
Results: Immediate haemostasis was achieved in all of the patients, without development of perihepatic haematoma or unintended embolization of more than one segmental portal vein. Complete embolization of percutaneous access tract was confirmed in 39 out of 40 patients by CT. Seven patients showed decreased haemoglobin and haematocrit levels. Other complications included mild pain at the site of embolization and mild fever, which resolved after conservative management. 16 patients died during the follow-up period owing to progression of the underlying disease.
Conclusion: Embolization of percutaneous transhepatic portal vein access tract with N-BCA is feasible and technically safe. With the appropriate technique, N-BCA can be safely used as an alternate embolic material since it is easy to use and inexpensive compared with other embolic materials.
Advances in knowledge: This is the first study to investigate the efficacy of N-BCA for percutaneous transhepatic portal venous access tract embolization.

Percutaneous transhepatic approach for portal venous intervention is used in various procedures, such as portal vein angioplasty, partial portal vein embolization before hemihepatectomy, variceal embolization for upper gastrointestinal bleeding and pancreatic islet cell transplantation.[1–6] After performing these procedures, life-threatening bleeding may occur from transhepatic tracts and, as a result, lead to morbidity and mortality. According to the literature, various embolic materials, including gelatin sponge particles, biological tissue adhesives, coils and plugs, have been utilized to prevent bleeding from the tracts.[7–13] Among these materials, gelatin sponge particles and coils are the two most commonly used embolic materials. However, most of these embolic materials have one or more drawbacks, such as incomplete tract embolization when using gelatin sponge particles, which may be the cause of delayed bleeding, and longer procedure time when using coils or plugs.[14,15] On the contrary, *N*-butyl cyanoacrylate (N-BCA) is a permanent, fast-acting and inexpensive embolic material, which is associated with a low possibility of rebleeding or migration. There are several reports on embolization of percutaneous biopsy tracts or biliary access tracts with N-BCA.[16–21] However, to the best of our knowledge, none of the studies has evaluated the outcome of embolization of portal venous access tracts with N-BCA. Therefore, the purpose of this study was to evaluate the safety and feasibility of N-BCA embolization of percutaneous transhepatic portal venous access tracts.

METHODS AND MATERIALS

Patients

From June 2007 to August 2013, a total of 40 consecutive patients underwent 42 sessions of percutaneous transhepatic portal venous interventions for various reasons.

The patient population included 29 males and 11 females, with a mean age of 59 years (median, 60 years; range, 29–80 years). 24 patients had undergone pre-operative portal vein embolization before sequential hemihepatectomy for underlying hepatocellular carcinoma (HCC), cholangiocarcinoma or gall bladder cancer. Embolization surpassing one segmental level of the accessed portal vein was intentionally performed in patients who underwent pre-operative portal vein embolization. In one patient, a large arterioportal shunt in the liver had been embolized via percutaneous transhepatic access. Ten patients had undergone transhepatic stent insertion in the portal vein owing to post-operative portal vein stenosis or thrombosis after liver transplantation or hemihepatectomy, three of whom had also undergone thrombolysis with thrombectomy. Two patients with hypercoagulability associated with protein S deficiency and antiphospholipid antibody syndrome had undergone thrombolysis with thrombectomy for thrombosis of the superior mesenteric vein and portal vein. Three patients had undergone direct portal venography during the process of portal venous pressure measurement; after liver transplantation in one patient, for evaluation of the cause of haemobilia after percutaneous transhepatic biliary drainage in another patient and for assessment of the extent of portal vein thrombosis in the third patient with HCC, in whom pre-operative portal vein embolization prior to hemihepatectomy was originally planned but subsequently aborted owing to the discovery of tumour thrombosis within the portal vein at the planned site of embolization. Embolization of the transhepatic access tract was accomplished in all of the patients using N-BCA and Lipiodol® (Lipiodol Ultra Fluide; Laboratoire Guerbet, Aulnay-sous-Bois, France) mixture. This retrospective study was approved by our institutional review board, and the requirement for informed patient consent was waived.

Techniques

On completion of transhepatic portal venous intervention, the introducer sheath was withdrawn from the portal vein under fluoroscopic guidance until the tip of the sheath was positioned within the liver parenchyma adjacent to the punctured segment of the portal vein. By injecting contrast media through the sheath, the absence of any large communication between the transhepatic tract and hepatic vein was confirmed prior to tract embolization in order to prevent inadvertent embolization of the hepatic vein or pulmonary artery embolism. Thereafter, the introducer sheath and dilator were flushed with 5% dextrose in water (D5W) to prevent polymerization of N-BCA inside the sheath. The introducer sheath dilator was then inserted through the introducer sheath, and a mixture of N-BCA and Lipiodol (prepared in ratios of 1:1 or 1:2) was injected via the sheath dilator using a 1-ml syringe. The sheath was withdrawn carefully while simultaneously injecting the N-BCA and Lipiodol mixture through the sheath dilator under fluoroscopic guidance until the tract was completely embolized up to the skin. Additional techniques such as manual compression were not performed for achieving haemostasis.

Follow-up

Follow-up data were collected up to 28 February 2014, or up to the point of the patient's death. The duration of the follow-up period ranged from 12 to 2014 days (median, 170 days; mean, 434 ± 613 days). Before the procedure, platelet count, prothrombin time (PT), international normalized ratio and activated partial thromboplastin time (aPTT) were pre-evaluated in each patient to assess the possible presence of any underlying haemostatic disorder. The presence of perihepatic haematoma formation was evaluated by ultrasonography immediately after the transhepatic procedure, which was on standby, while the extent of N-BCA within the tract and portal vein was evaluated under fluoroscopy immediately after the procedure.

In patients who underwent follow-up CT, the images were reviewed in order to evaluate the completeness of tract embolization and the presence of any complications. The accessed lobe of the liver, size of the introducer sheath and amount of N-BCA and Lipiodol mixture were recorded. Baseline haemoglobin and haematocrit levels were checked before the procedure, and follow-up levels were checked 1–4 days after the procedure and were compared for detecting the presence of possible bleeding. Decrease in haemoglobin and haematocrit levels by $<2\,\mathrm{g\,dl^{-1}}$ and 4%, respectively, was defined as a mild decline.

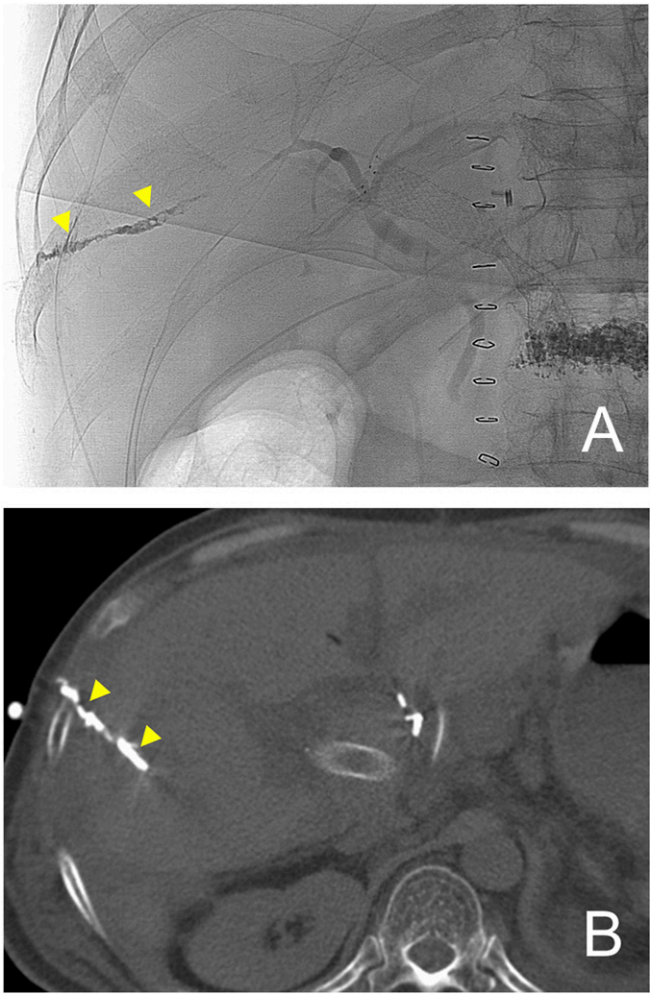
Technical success was defined as the absence of haematoma on the penetrated liver surface on immediate ultrasonography and visualization of a compact N-BCA cast along the tract without wash out on fluoroscopy. Major complications were defined as prolonged hospitalization owing to procedure-related complications, uncontrollable pain, massive bleeding, inadvertent extensive portal vein embolization, severe liver injury, permanent adverse sequelae and death. Minor complication was defined as mild pain that could be controlled with conservative care. These complications were evaluated by reviewing the medical records, laboratory findings and CT examination.

RESULTS

Immediate haemostasis was achieved in all of the patients. Perihepatic haematoma was not observed in any of the patients on immediate ultrasonography. The presence of N-BCA and Lipiodol mixture within the portal venous access tract was confirmed in all of the patients on post-procedural fluoroscopic imaging (Figure 1a). The size of the introducer sheath ranged from 5 to 9 French. For portal vein embolization, 5-French sheaths were the most commonly used (17 of 25 cases), whereas 6-French sheaths were used in the rest of the cases (8 of 25 cases). 7-French sheaths were used in all cases of stent insertion (nine of ten cases), except for one case in which an 8-French sheath was used. In three cases of portal venography, 5- to 7-French sheaths were used; while in two cases of thrombolysis and thrombectomy, an 8-French sheath or a 9-French sheath was used. The amount of N-BCA and Lipiodol mixture injected ranged from 0.5 to 2.0 ml.

39 out of 40 patients underwent CT after a mean duration of 14.9 days (median, 11 days; range, 0–120 days) after the procedure. One patient did not undergo CT because he was lost to follow-up. Complete embolization of the tracts was confirmed in all of the 39 patients, and none of the follow-up images showed perihepatic haematoma or any other severe complications such as liver infarction. Unintentional, extensive portal

Figure 1. A 60-year-old male who underwent stent placement in the portal vein owing to long-segmental portal vein stenosis after cadaveric donor liver transplantation. (a) The transhepatic tract (arrowheads) that has been embolized with 1:1 mixture of *N*-butyl cyanoacrylate and Lipiodol® (Lipiodol Ultra Fluide; Laboratoire Guerbet, Aulnay-sous-Bois, France) is clearly demarcated under fluoroscopy (incidental bile duct puncture and opacification during portal vein puncture). (b) Post-procedural abdominal CT performed 8 days after tract embolization shows complete embolization of the tract (arrowheads) without evidence of complications such as haematoma or liver infarction.



vein embolization was not observed in any of the cases (Figure 1b).

Follow-up laboratory investigations performed 1–4 days after the procedure showed that seven patients had decreased haemoglobin and haematocrit levels compared with baseline levels before the procedure (mean haemoglobin level, $2.1 \pm 1.2\,g\,dl^{-1}$; range, 1.1–4.2 $g\,dl^{-1}$; and mean haematocrit level, $6.0 \pm 4.2\%$; range, 2.2–13.4%), three of whom showed a decrease in haemoglobin and haematocrit levels of $>2\,g\,dl^{-1}$ and 4%, respectively. However, none of these patients showed evidence of bleeding around the percutaneous access tract or the haemoperitoneum on CT. Three patients had underlying bleeding diathesis: two patients showed prolonged PT or aPTT (PT/aPTT of 6.29/85 and 1.87/50 s, respectively), whereas one had underlying haemophilia. However, none of these three patients showed evidence of bleeding or decreased haemoglobin or haematocrit levels after the procedure. 16 patients died during the follow-up period owing to the progression of underlying disease. The survival period ranged from 17 to 328 days (median, 140 days; mean, 141.0 ± 121.6 days). Nine patients complained of mild pain at the site of the embolization tract, which was easily controlled by analgesics. Three patients presented with mild fever after the procedure, which resolved within 4 days.

DISCUSSION

There are various routes for accessing the portal vein, including transjugular intrahepatic portosystemic shunt (TIPS), mesenteric vein, umbilical vein, percutaneous transhepatic access or percutaneous transsplenic access.[7–9,22–25] Among these routes, TIPS and percutaneous transhepatic access are the two most commonly used access routes. Compared with the TIPS access, the percutaneous transhepatic access offers direct access to the portal vein along the long axis of the portal vein and allows easier access to the peripheral intrahepatic portal vein branches. However, there is a higher risk of bleeding, especially when the patient has underlying conditions of bleeding diathesis, such as thrombocytopaenia or coagulopathies.[26] Furthermore, since patients undergoing portal vein interventions are more prone to have an underlying liver disease than the normal population, such a complication is potentially life threatening. Embolization of percutaneous transhepatic portal venous access tracts to prevent acute bleeding is not a new concept, and there are several reports that have been published in the past emphasizing the importance of such a procedure to prevent a potentially dangerous complication of intraperitoneal haemorrhage.[10,27] In addition, several reports have presented examples of bleeding complications that lead to life-threatening morbidity and mortality.[28,29]

Various materials are used for embolization of tracts in the liver parenchyma after portal vein manipulation, including gelatin sponge particles, biological tissue adhesives, coils and vascular plugs.[10–13,23–25] The most commonly used embolic materials for the closure of percutaneous portal vein access tracts are coils and gelatin sponge particles; however, they have their own drawbacks. With the use of gelatin sponge particles, incomplete tract embolization or delayed bleeding may occur owing to its soluble and impermanent nature.[14] The risk of delayed bleeding is increased in patients with underlying bleeding diathesis.[30] With respect to the use of coils, longer procedure times may be inevitable owing to the complex, multistep technique. Multiple coils may be required to achieve complete embolization. Longer procedure time may be related to an increased risk of accidental withdrawal of the introducer sheath, consequently leading to incomplete embolization of the tract. Other technical problems may be encountered when using coils, such as difficulty in packing coils appropriately if the tract is too short, and migration of the coils into the portal vein or peritoneal space, especially owing to inappropriate coil sizing. For using vascular plugs, a longer procedure time is necessary since a minimum of 5 min is necessary for adequate formation of thrombus. Similar to that with the use of coils, there is a risk of distal migration.[15] Furthermore, plugs are more expensive than other embolic materials.

N-BCA is a permanent, fast-acting and relatively inexpensive embolic material, which is associated with a very low possibility of rebleeding or migration. The technique for using this embolic material is very simple, can be performed in a relatively short time and also enables embolization of the skin tract. In accordance with previous studies that describe the use of N-BCA for the closure of percutaneous transhepatic access after biopsy or biliary intervention,[16–21] our study also showed excellent results with regard to haemostasis. Technical success rate of 100% was achieved, without evidence of early or delayed bleeding on immediate and follow-up imaging, and no major complications were observed. Although seven patients showed a decrease in haemoglobin and haematocrit levels, follow-up CT of these patients did not show any evidence of bleeding in the tract or haemoperitoneum, thus ruling out the possibility of failed embolization. Three patients had underlying bleeding diathesis, two with prolonged PT/aPTT and one with haemophilia. However, none of these patients showed evidence of early or delayed bleeding after tract embolization with N-BCA, and their haemoglobin and haematocrit levels were also stable.

There are some precautions to be taken when using N-BCA to prevent unintentional, extensive embolization of the portal vein or hepatic vein. To prevent such adverse events, the portal vein should be accessed as peripherally as possible so as to avoid puncturing the hepatic vein along the course. If a large communication between portal venous access tract and hepatic vein is detected upon injection of contrast media through the sheath before embolization, coil embolization of the communicating segment may be necessary before injecting N-BCA to prevent its propagation through the communication. In our study, after injection of contrast media through the sheath, none of the patients was found to have large communications between the tract and hepatic vein. As a result, unintended, extensive portal vein or hepatic vein embolization did not occur in any of the cases. In order to perform a safer procedure, N-BCA injection was administered after the tip of the sheath was withdrawn from the portal vein, and it was positioned in the parenchymal portion of the tract. For more accurate and controlled injection of N-BCA, a 1-ml syringe was used in all of the cases.

There are some limitations to this study. The study population was relatively small. A relatively large proportion of the population had serious underlying conditions, and many patients died during the follow-up period, and, hence, this did not allow for evaluation of long-term outcomes. In addition, N-BCA was the sole material of choice for embolization of percutaneous transhepatic portal venous access tract, and therefore, this study does not include a control group to demonstrate the superiority of N-BCA over the other embolic materials. However, to the best of our knowledge, this is the first study to investigate the efficacy of N-BCA as an embolic material for use in percutaneous transhepatic portal venous access tracts.

In conclusion, embolization of percutaneous transhepatic portal vein access tract with N-BCA is feasible and technically safe, even in patients with bleeding diathesis. With the appropriate technique, N-BCA can be used as an alternate embolic material since it is easy to use and inexpensive compared with the other embolic materials.

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