Transcatheter Arterial Embolization of Gastrointestinal Tract Bleeding with N-Butyl-2-Cyanoacrylate in 71 Patients at a Single Institution

Poster No.: C-2555
Congress: ECR 2012
Type: Scientific Exhibit
Keywords: Hemorrhage, Embolisation, Catheters, Catheter arteriography, Interventional vascular, Gastrointestinal tract
DOI: 10.1594/ecr2012/C-2555

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Purpose

To evaluate the safety and effectiveness of transcatheter arterial embolization (TAE) with N-Butyl Cyanoacrylate (NBCA) for nonvariceal gastrointestinal (GI) bleeding, and to determine the factors associated with clinical outcomes.

Transcatheter arterial embolization (TAE) is a crucial method to cease acute gastrointestinal (GI) bleeding. As an embolic material, the use of N-Butyl Cyanoacrylate (NBCA) has been rising with its various advantages. First of all, because NBCA is a liquid embolic material, it is convenient to handle and inject the NBCA to the target site, even to the distal small branches where access with a microcatheter is difficult [1-4]. In addition, NBCA is known to be effective in patients with coagulopathy because its mechanism to harden is not affected by coagulopathy [5, 6]. When other embolic materials such as coils do not always fit to the target site, using NBCA as an adjunctive for secure embolization is useful [1].

Although there have been several reports regarding the TAE of acute GI bleeding with use of NBCA, most of them involved fewer than 32 patients [1-4, 7]. Studies in larger patient populations are warranted in order to determine its safety and effectiveness of NBCA in the settings of acute GI bleeding.

In this regard, the purpose of this study was to evaluate the safety and effectiveness of TAE with NBCA for acute GI bleeding of various etiologies from a large, single-center group. The second most important purpose of this study was to analyze clinical factors to affect the outcome of patients who underwent TAE with NBCA.

Methods and Materials

Patient Selection

We retrospectively analyzed our database of patients who underwent TAE using NBCA from January 2001 to July 2011 revealing a total of 192 patients. Among them, NBCA embolization for nonvariceal GI bleeding was performed in 77 sessions in 71 patients (56 male and 15 female; mean age 61.9 years, range 6-90). NBCA was used exclusively on its own in 55 cases (71%) in a single procedure, while NBCA was used as an adjunct to the use of other embolic materials such as coils and gelatin sponge particles (Gelfoam) in 22 cases (19%). Endoscopic hemostasis was failed in 45 patients and 2 of them also had previous TAE without NBCA for the bleeding site. Medical records and computed tomography (CT) images were reviewed to analyze various factors
including underlying diseases and etiologies of bleeding, laboratory data associated with hemostasis, transfusion amount, and previous hemostasis trials including endoscopic bleeding control or history of TAE which may affect clinical outcomes.

The use of clinical data for this study was approved by our institutional review board and informed consent to use the data was waved due to the retrospective study. The informed consents of all cases for emergent TAE were obtained from the patients or their family members.

**Embolization Technique**

TAE was performed by four interventional radiologists with 5 - 26 years of clinical experience in endovascular intervention. After a common femoral artery was accessed, a standard 5-F angiographic catheter was advanced and angiography was performed to reveal the bleeding site based on a location depicted on CT scans, previous hemostatic trials such as endoscopy and previous angiographic images if available. 2 - 3-F microcatheter was used to select branches of artery to identify the specific location of target vessels.

NBCA (Histoacryl) was mixed with iodized oil (Lipiodol) at ratios varying from 1:2 to 1:4, regarding the distance from the tip of the microcatheter to the target lesion, blood flow rate or extent of bleeding site. Before injecting the NBCA mixture, Dextrose 5% in water (D5W) solution was used to flush the microcatheter to prevent premature polymerization of the mixture with residual blood or saline inside of the microcatheter. The NBCA mixture was injected by a 1 mL syringe guided with fluoroscopic monitoring to check to avoid reflux into non-target vessels. If the mixture filled in a pseudoaneurysm or extravasation of the mixture from the bleeding site was detected, injection was ended. In several cases with bleeding sites such as gastroduodenal artery where had more than two parent arteries, "sandwich technique" was used to block the backflow from another parent artery that can cause recanalization. Then, the microcatheter was removed promptly to prevent adherence of the catheter tip to the vessel wall. The inner lumen of the guiding catheter was aspirated and post-embolic angiography was performed to confirm successful occlusion of the target lesion.

**Definitions and Study Endpoints**

A thorough review of the medical charts was done in order to collect the data regarding underlying diseases with etiologies of bleeding, bleeding sites, previous hemostasis history, laboratory findings representing coagulopathy, amount of transfusion before and after TAE, technical and clinical success rate, recurrent bleeding rate, procedure-related complications, and 30-day mortality with final outcome.
Coagulopathy was confirmed when patients had one or more of the following conditions: 1) prothrombin ratio >1.3 2) partial thromboplastin time greater than 40 seconds, or 3) platelet count less than 80,000 per microliter [3, 8]. Amount of transfusion was calculated as the amount used during 1 day before and after TAE.

Types of embolization were subdivided into three according to the embolization extent; localized, proximal and segmental (Figure 1). Localized embolization was defined as superselective embolization of the bleeding point without embolization of adjacent branching arteries. Proximal embolization was defined as embolization of only proximal portion of the bleeding point with or without embolization of adjacent branching arteries. Segmental embolization was defined as embolization of both proximal and distal portions of the bleeding point with simultaneous embolization of adjacent branching arteries.

Technical success was achieved by complete occlusion of bleeding site on immediate post-embolization angiogram. Clinical success was defined as the cessation of bleeding after TAE without the need for repeat TAE or additional surgery within 24 hours and the resolution of the patients' symptoms and signs to suspect bleeding. Recurrent bleeding was defined as another bleeding episode, such as presenting hematemesis or melena with changes in vital signs, revealing bleeding on the second-look endoscopy after 24 hours following TAE within one month in patients with initial clinical success.

The outcome of the procedure was evaluated by 30-day mortality after TAE, and any complications related to embolization.

Statistical Methods

The outcome was compared between successful and failed TAE with NBCA for unvariceal acute GI bleeding. Univariate and multivariate analyses were performed to determine factors associated with clinical success. Univariate analysis of data was assessed using Fisher's exact test and ANOVA for analysing independent variables including age, sex, coagulopathy, transfusion amount before and after TAE, types of embolization, and previous trials such as endoscopy for hemostasis.

Logistic regression test was used to compare the independent predictive value of each variable; analytic factors with p-value of 0.2 or less were included to the multivariate analysis. All statistical analysis were performed using standard statistical software SPSS for Windows, version 12.0; SPSS, Chicago, Illinois.

Images for this section:
Fig. 1: Types of embolization that were categorized by access routes of microcatheter. (a, b) Microcatheter delivered the direct bleeding artery and localized embolization was done. (c, d) Proximal embolization was done when distal bleeding artery was not specifically selected and NBCA was used in the parent artery of the bleeding point. (e, f) Segmental embolization was defined when the microcatheter delivered to near the bleeding site and pull through the microcatheter to cover the bleeding site, and other branch arteries also embolized.
Results

Patient characteristics

A total of 71 patients received 77 sessions of TAE with NBCA at our institution for managing nonvariceal acute GI bleeding. Four patients underwent secondary TAE with NBCA for recurrent bleeding within one month after initial successful bleeding cessation. The most common bleeding etiology was cancer bleeding; 30 sessions of TAE were performed in 27 patients while 44 patients with non-cancer bleeding had 47 sessions of TAE. Their bleeding etiologies were ulcer bleeding (n = 30), postoperative bleeding (10), and other etiologies (4). The detailed disease entities were listed in Table 1. Overall bleeding sites were most commonly duodenal (40), followed by gastric (16), jejunal (13), ileal (3), ileocecal (2), rectal (2) and colic (1). Bleeding sites of the cancer group (n=30) were most commonly duodenal (16), followed by gastric (8), jejuna (4), ileal (1) and rectal (1). Bleeding sites of 47 sessions of TAE in the non-cancer group (44) were most commonly duodenal (24), followed by jejunal (9), gastric (8), ileal or ileocecal (4), colic (1) and rectal (1).

Outcome of TAE

Detailed outcomes of TAE between the two groups with the clinical success and failure are summarized in Table 2.

The overall technical success rate and overall clinical success rate of all sessions of TAE were 100% and 85.7% (66/77), respectively. Three patients (4%) failed to achieve primary clinical success after the first session of TAE, and they underwent repeat TAE successfully.

Microcoils and gelatin sponge particles were used as embolic materials complementary to NBCA in 23 sessions and were delivered through the microcatheter before administration of NBCA. The clinical success rates were not statistically different regarding whether NBCA was used only or in combination with other embolic materials (p = 1.0).

Twenty nine patients (40.8 %) presented with coagulopathy at the time of procedure, and there was no statistical difference of clinical and technical success rates between the patients with and without coagulopathy (p = 0.33).

Recurrent bleeding was noted in 4 patients, and a mean interval day in each of the two sessions of the patients was 4.75 days (range: 2 - 9 days). The etiologies of the recurrent bleeding in the patients were cancer (n = 2), ulcer (1) and EST site bleeding (1). Those four patients with recurrent bleeding underwent secondary TAE, and the bleeding points were successfully embolized. Among them, 1 patient used NBCA only, 2 patients used
NBCA with coil or gelatin sponge particles, and 1 patient used coils and gelatin sponge particles without NBCA for secondary TAE. One patient died 7 days after secondary TAE due to lymphoma presenting with unceased bleeding.

As complications, two patients showed bowel infarction after TAE even though successful bleeding control was achieved and clinical symptoms were resolved. One of them showed duodenal perforation detected on abdominal CT scans 4 days following segmental embolization of anterior pancreaticoduodenal artery with NBCA (Figure 3). His duodenal perforation led to septic shock despite conservative management for six weeks. Another patient (56-year-old woman) with duodenal bleeding from duodenal cancer developed abdominal pain 14 hours after segmental embolization of two jejunal branches of superior mesenteric artery with NBCA. Ischemic enteritis and transmural infraction were detected by follow-up CT scans. Although she survived this complication, she died of extensive metastasis 11 weeks after TAE.

Thirty-day mortality rate was 18% (13 out of 71 patients); six patients with cancer bleeding and seven patients with non-cancer bleeding. Twelve patients expired after the first session of TAE, and one patient died after unsuccessful repeat TAE. Causes of death in cancer bleeding patients was most commonly hypovolemic shock due to massive bleeding (n = 5) and acute myocardial infarction (1), while that in non-cancer bleeding patients was most commonly underlying disease progression such as hepatic failure or infection (5), hypovolemic shock due to massive bleeding (1), and DIC secondary to massive transfusion (1).

Univariate analysis showed that the clinical success of TAE with NBCA was related to the transfusion amount before TAE ($p = 0.14$) and etiologies of bleeding ($p = 0.016$). Higher demand of transfusion amount before TAE and cancer bleeding as bleeding etiology were related with higher risk of clinical failure. Clinical success was not associated with history of previous hemostasis, coagulopathy, transfusion amount after TAE, types of embolization.

Multivariate analysis showed that the cancer bleeding was independently related to the clinical failure of TAE with NBCA ($p = 0.029$).

**Images for this section:**
**Fig. 1:** Types of embolization that were categorized by access routes of microcatheter. (a, b) Microcatheter delivered the direct bleeding artery and localized embolization was done. (c, d) Proximal embolization was done when distal bleeding artery was not specifically selected and NBCA was used in the parent artery of the bleeding point. (e, f) Segmental embolization was defined when the microcatheter delivered to near the bleeding site and pull through the microcatheter to cover the bleeding site, and other branch arteries also embolized.

<table>
<thead>
<tr>
<th>Etiologies of bleeding (No. of pts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer bleeding (27)</td>
</tr>
<tr>
<td>Bile duct ca. (6); duodenal ca. (5); pancreatic ca. (4); gastric ca. (3); lymphoma (3); rectal metastasis (1); esophageal ca. (1); gall bladder ca. (1); ampulla of Vater ca. (1); multiple myeloma (1) and neuroblastoma (1)</td>
</tr>
<tr>
<td>Ulcer bleeding (30)</td>
</tr>
<tr>
<td>Gastric (6); duodenal (18); jejunal (3); ileal (1); ileocecal (1) and rectal (1)</td>
</tr>
<tr>
<td>Postoperative bleeding (10)</td>
</tr>
<tr>
<td>Small bowel anastomosis (3); ileosomy (2); repair of duodenal stump leakage (1); hemicolecotomy (1); proctocolectomy (1); LDLT (1) and pancreatectomy (1)</td>
</tr>
<tr>
<td>Others (4)</td>
</tr>
<tr>
<td>Trauma (1); EST site bleeding (1); shock bowel syndrome (1) and anticoagulation therapy-related bleeding (1)</td>
</tr>
</tbody>
</table>

**Table 1:** Etiologies of bleeding and bleeding sites in four categorized groups.
Table 2: Patient characteristics and comparison of clinical outcomes of TAE between clinical success and failure groups

<table>
<thead>
<tr>
<th></th>
<th>Total No.</th>
<th>Clinical success (case = 66)</th>
<th>Clinical failure (case = 11)</th>
<th>$P$ value univariate</th>
<th>$P$ value multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD (yrs)</td>
<td></td>
<td>62.7 ± 12.2</td>
<td>55.7 ± 17.9</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>Sex (M : F)</td>
<td></td>
<td>53 : 13</td>
<td>8 : 3</td>
<td>0.69</td>
<td></td>
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<tr>
<td>Hx. of previous hemostasis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Endoscopy</td>
<td>45</td>
<td>36</td>
<td>9</td>
<td></td>
<td></td>
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<tr>
<td>TAE without NBCA</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulopathy</td>
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<td>0.33</td>
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<td>Yes</td>
<td>36</td>
<td>29</td>
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</tr>
<tr>
<td>No</td>
<td>41</td>
<td>37</td>
<td>4</td>
<td></td>
<td></td>
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<tr>
<td>Cause of bleeding</td>
<td></td>
<td></td>
<td></td>
<td>0.016</td>
<td>0.029</td>
</tr>
<tr>
<td>Cancer</td>
<td>29</td>
<td>21</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-cancer</td>
<td>48</td>
<td>45</td>
<td>3</td>
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<tr>
<td>Amount of pRBCs</td>
<td></td>
<td></td>
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<td>0.44</td>
<td></td>
</tr>
<tr>
<td>(mean no. of packs)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before TAE</td>
<td>7.7</td>
<td>11</td>
<td>0.14</td>
<td></td>
<td></td>
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<tr>
<td>After TAE</td>
<td>5.1</td>
<td>8.5</td>
<td>0.40</td>
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<tr>
<td>Embolic materials</td>
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<td></td>
<td></td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>NBCA only</td>
<td>54</td>
<td>46</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With other materials</td>
<td>23</td>
<td>20</td>
<td>3</td>
<td></td>
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<tr>
<td>Types of embolization</td>
<td></td>
<td></td>
<td></td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>Localized</td>
<td>23</td>
<td>4</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Segmental</td>
<td>38</td>
<td>6</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Technical success (no. of cases)</td>
<td>66 (100%)</td>
<td>11 (100 %)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Fig. 2: Examples of (a) localized and (b) segmental embolizations.

Fig. 3: A 65-year-old male underlying B-cell lymphoma had duodenal ulcer bleeding presented with melena. (a) Celiac arteriography shows active bleeding in anterior pancreaticoduodenal artery (arrow). (b) Radiography obtained after injecting NBCA. Post-embolic celiac arteriography show successful embolization of the bleeding site including proximal and distal portion after segmental embolization with NBCA mixture (not shown). (c) Follow up CT scans obtained 4 days later show perforation of 2nd to 3rd duodenum with air density surrounding embolic material.
Conclusion

This study shows that TAE with the use of NBCA as the sole or complementary embolic agent with coils or gelatin sponge particles is an effective and feasible method for the treatment of acute GI bleeding related to various etiologies. The overall clinical success rate was 85.7% (66/77). Multivariate analysis showed that cancer bleeding was the only independent factor to increase the risk of clinical failure.

In terms of technical success based upon complete occlusion of bleeding site on immediate post-embolization angiogram, our success rate was 100%. No technical failure in this series supports that TAE with NBCA is feasible and effective. In previous case studies with 16 - 32 patients, the clinical success rates of TAE with NBCA for GI bleeding ranged from 88 to 91%. In agreement with the earlier studies, our study involving a larger sample size demonstrated that the success rate relatively lower (85.7 %) [3, 7]. Moreover, the cancer bleeding was the only significant factor affecting clinical failure in the multivariate analysis. It seems that the number of cancer patients is increased; the clinical success rate is lower [2, 3]. There is another evidence converging to support this, Jae et al showed 91% of clinical success rate with 25% of the underlying cancer patients in 32 patients (8 patients with cancer and 24 patients with non-cancer including benign ulcer) with nonvariceal upper GI bleeding. Nevertheless, regardless of the various etiologies of bleeding and patients' clinical condition, patients who had a clinically successful TAE procedure were 13.3 times more likely to survive than those who had a failure to cease the bleeding [9].

When the group with NBCA only and the group with NBCA with other embolic materials were compared, there was no significant difference in clinical success rate between the two groups. This finding is compatible with other previous studies that did not demonstrate any variation in outcome when differing embolic materials were used [9, 12, 13, 15]. Although the reason of this result is uncertain due to lack of randomized studies have been performed, appropriate methods for each cases could be varied with interventional radiologists' experiences, the types of hemorrhage, and the availability of embolic materials.

There have been several reports that the patients who needed transfused a lot before TAE developed higher chance of organ failure, and it could result in worse clinical outcome [9-11, 16]. Although transfusion amount was not a significant factor affecting clinical outcome in multivariate analysis, transfusion in itself could be a consequence of DIC or be associated with vital instability. Moreover, bowel infarctions following TAE have been detected as main complications with use of NBCA [7, 10, 18]. In this study, two patients with bowel infarction after TAE were given excessive segmental embolization.
Thirty-day mortality was not significantly different between the two groups; however, bleeding related mortality could be higher in the cancer bleeding group. Among the 6 patients expired within 1 month in the cancer bleeding group, 4 patients died due to intractable cancer bleeding and 1 patient died during TAE procedure, and 1 patient died due to cardiovascular shock following massive transfusion. On the other hand, in the non-cancer group, the bleeding-related deaths were only two, including indirect complications, hypoxic multiorgan failure and DIC.

This study shows several limitations. First of all, the study is retrospective and the patients were not randomly selected because our hospital is tertiary referral hospital where the patients with advanced disease usually admit. Second, there have not been established the criteria for using NBCA, so that the use of NBCA is operator dependent and case selection was not randomized.

In conclusion, in our 7 years experiences, TAE with NBCA was effective and feasible method for managing acute nonvariceal upper GI tract bleeding with various bleeding causes. Although cancer bleeding showed lower clinical success rates than the other cause of bleeding, the role of NBCA as an embolic material is considerable. NBCA has definite advantages of rapid embolization, easy delivery to the distal small branches or tortuous vessels where access with the microcatheter is difficult, and being useful for the patients with coagulopathy [3]. Although dealing with NBCA is challenging and needs more experience than other embolic materials, the advantages of NBCA support the use of it.

References


**Personal Information**