



EVALUATION OF THE SAFETY AND EFFICACY OF TRANSCATHETER CYANOACRYLATE GLUE EMBOLIZATION IN ACUTE ARTERIAL BLEEDING

AKUT ARTERİYEL KANAMALARDA TRANSKATATER SİYANOAKRİLAT GLUE EMBOLİZASYONUN GÜVENLİĞİNİN VE ETKİNLİĞİNİN DEĞERLENDİRİLMESİ

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Abstract

Aim: To demonstrate the safety and efficacy of endovascular embolization with N-butyl cyanoacrylate glue in acute bleeding.

Methods: The data of 31 patients who underwent endovascular embolization using N-butyl cyanoacrylate glue due to acute visceral hemorrhage were retrospectively evaluated. In order to detect the bleeding focus before the procedure, computed tomography with contrast-enhanced and non-contrast phases was routinely performed on the suspected bleeding site. Technical success was accepted as the closure of the targeted artery in control angiography, and clinical success was defined as the absence of bleeding that would require reoperation within one month postoperatively.

Results: Eleven patients with gastrointestinal tract or vaginal bleeding or hematuria due to malignancy, nine with hemoptysis due to infection sequelae or bronchiectasis, four with bleeding secondary to percutaneous medical procedures, three with trauma-related hemorrhage, and four with hemorrhage due to peptic ulcers were treated with endovascular embolization. Embolization was undertaken using a glue-lipiodol mixture of 5% in 17 patients and 10% in 14 patients. The targeted artery was closed in all patients, and the technical success rate was 100%. No technical and clinical complications developed during and after the procedure.

Conclusions: N-butyl cyanoacrylate is a safe embolizing material with high technical and clinical success in patients with active bleeding.

Keywords: N-butyl cyanoacrylate glue, embolization, hemorrhage, endovascular treatment

Öz

Amaç: Akut kanamalarda N-butyl cyanoacrylate glue ile yapılan endovasküler embolizasyonun güvenliğini ve etkinliğini göstermek.

Yöntemler: Akut visseral kanama nedeni ile tarafımızca glue ile endovasküler embolizasyon uygulanan toplam 31 hastanın verileri retrospektif olarak değerlendirildi. Hastalara işlem öncesi kanama odağını saptama amacıyla rutin olarak kontrastsız ve kontrastlı fazlardan oluşan şüphe edilen kanama bölgesine yönelik bilgisayarlı tomografi çekildi. Teknik başarı kontrol anjiyografide hedeflenen damarın kapatılması, klinik başarı ise post-op 1 aylık sürede tekrar işlem gerektirecek kanama olmaması şeklinde kabul edildi.

Bulgular: Maligniteye bağlı gastrointestinal sistem (GIS), vajinal kanama ya da hematürisi olan 11 hasta, enfeksiyon sekeli ya da bronşektaziye bağlı hemoptizisi olan 9 hasta, perkütan tıbbi işlemler sonrası kanaması olan 4 hasta, travmaya bağlı kanaması olan 3 hasta, peptik ülser nedeni ile kanaması olan 4 hasta endovasküler embolizasyon ile tedavi edildi. 17 hastada %5'lik, 14 hastada ise %10'luk glue-lipiodol karışımı embolizasyon için kullanıldı. Hedeflenen arter tüm hastalarda kapatıldı ve teknik başarı oranı %100 idi. İşlem sırasında ve sonrasında herhangi bir teknik ve klinik komplikasyon gelişmedi.

Sonuç: N-butyl siyanoakrilat aktif kanaması olan hastalarda teknik ve klinik başarıları yüksek güvenilir bir embolizan materyeldir.

Anahtar Kelimeler: N-butyl siyanoakrilat glue, embolizasyon, hemoraji, endovasküler tedavi



Introduction

Acute bleeding has high mortality and morbidity, therefore it is an emergency that requires rapid and effective treatment¹. Transcatheter arterial embolization using gelatin sponge, coils, polyvinyl alcohol (PVA), N-butyl cyanoacrylate (NBCA) glue, or a combination of these agents is widely used in the treatment of acute visceral hemorrhage or tumor hemorrhage^{2,3}. Although these methods are successful in most cases, adequate hemostasis may not be achieved in some patients due to reasons such as insufficient access to the bleeding site, formation of collateral circulation after embolization, and recanalization of embolized arteries^{3,4}. NBCA glue is an embolizing liquid material that undergoes rapid polymerization upon contact with blood and also causes rapid and permanent embolization. NBCA glue can also provide the simultaneous embolization of collateral arteries connected to the bleeding focus, which can prevent reverse bleeding from retrograde collateral flow. However, complications such as catheter sticking and reflux scare the operators and are seen as the main obstacle to the widespread use of NBCA glue. The current study aimed to evaluate the safety, efficacy and complication rates of NBCA glue in acute arterial bleeding.

Materials and Methods

This retrospective study was approved by the Ethical Committee and conducted in full accordance with the guidelines of the Declaration of Helsinki. The Ethics Committee approval was obtained from Clinical Research Ethics Committee. Informed consent was obtained from both patients and their relatives before the embolization procedure. The data of 31 patients, who presented to our center with acute visceral hemorrhage between September 2019 and February 2022, continued to have persistent hemorrhage despite attempts with endoscopy or bronchoscopy, and therefore, patients who

underwent endovascular embolization using a mixture of 5% or 10% N-butyl cyanoacrylate glue and lipiodol were evaluated retrospectively. Embolization was performed on the patients included in the study by 3 operators. This study is single-center. Before the procedure, the patients routinely underwent hemogram and biochemistry tests, and computed tomography (CT) comprising non-contrast and contrast-enhanced phases was performed for the suspected bleeding site to detect the bleeding focus. In addition, cone beam CT was used to map and clarify the bleeding focus during the procedure and to confirm whether intraoperative bleeding persists after embolization of the targeted focus. Technical success was accepted as the closure of the targeted artery in follow-up angiography, and clinical success was defined as the absence of bleeding that would require reoperation within one month postoperatively. Embolization results were evaluated separately in terms of technical and clinical success.

- *Technique*

Lipiodol (iodophendylate oil) was mixed with 5% (distal embolization) or 10% (proximal embolization) to increase the visibility of the glue under angiography and dilute it. The preferred microcatheter diameter for embolization was selected in the range of 1.9 F- 2.4 F according to the lumen width of the artery to be catheterized (Fig 1). Artery with signs of bleeding was mapped with cone beam CT at every step of the embolization procedure. The mixture was prepared in a small sterile ceramic cup immediately before embolization. Care was taken in the preparation of the glue mix to avoid contamination with ionic solutions that could cause polymerization, such as blood and normal saline. The microcatheter was washed with 5% dextrose solution before injection. During this procedure, the most common technical problem is that the glue polymerizes proximally before penetrating to the desired depth. 5%

dextrose was attached to the guide catheter and continuous flushing of the periphery of the microcatheter aimed to avoid this problem. It was thought that this technique could prevent complications, which are thought to be more common, while embolizing the distal artery, which is difficult to reach, especially with current generation micro-catheters.

The mixture was drawn into a 5 ml syringe and connected directly to the superselective catheterized microcatheter. Injection was performed in a slow controlled manner to prevent the reflux and adherence of the catheter. After the injection was completed, the microcatheter was quickly withdrawn.

Results

There were 25 male and 6 female patients, with a mean age of 58.1 (34-75) years. Eleven patients had malignancy-related hemorrhage (Fig 2,3), including five patients with gastrointestinal bleeding, three with cervical cancer causing vaginal bleeding, three with causing hematuria;

nine patients had hemoptysis due to infection sequelae or bronchiectasis (Fig 1) ; four patients had iatrogenic hemorrhage following percutaneous procedures; three had trauma-related hemorrhage; and four had hemorrhage due to peptic ulcers (Table 1). For the embolization procedure, a glue-lipiodol mixture of 5% was used in 17 patients and 10% in 14 patients. The targeted artery was closed in all patients, and the technical success rate was 100%.

No technical and clinical complications developed during and after the procedure. However, clinical success was not achieved in eight patients (25.8%). In seven (87.5%) of these eight patients, the cause of hemorrhage was mass bleeding due to malignancy. The mean duration of admission with re-hemorrhage was 22 (15-30) days. Nineteen patients had at least one of the angiography findings indicating the bleeding site (active extravasation, pseudoaneurysm, or hypervascularity), and the technical and clinical success rate of treatment was 100% in these patients.

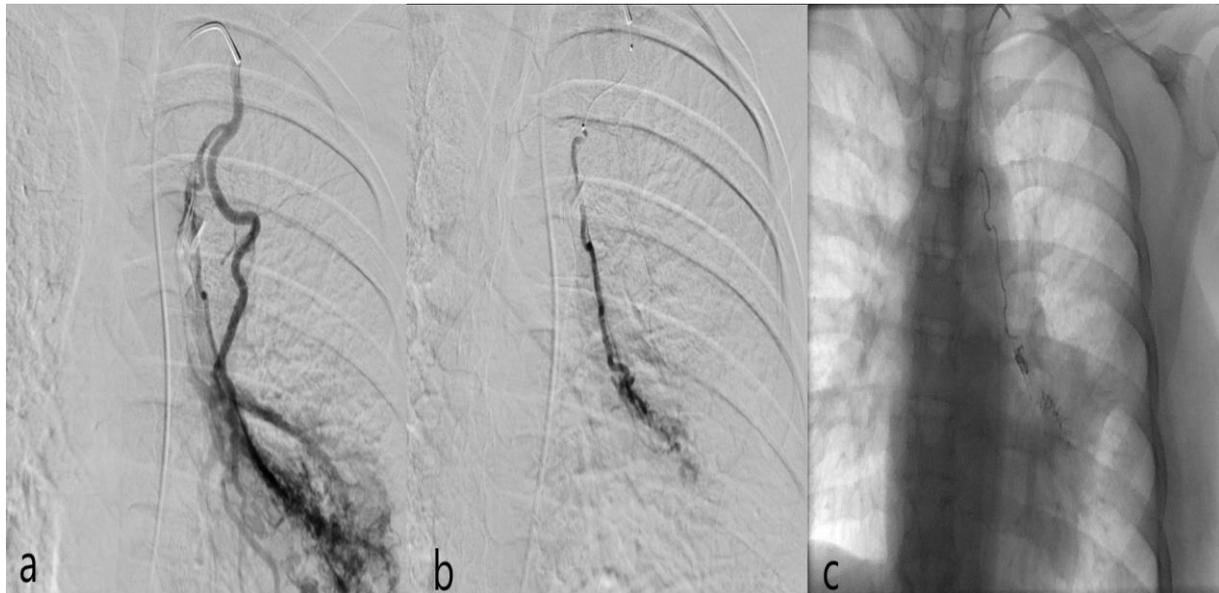


Figure 1. After left bronchial artery catheterization, DSA examination with microcatheter superselective catheterization reveals prominent tortuous arteries and hypervascularity. (a) After the injection of glue-lipiodol, the absence of contrast filling (b) and the mixture of glue-lipiodol (c) are confirmed in the control imaging.



Figure 2. Hepatocellular carcinoma metastasis in the posterior left shoulder. After left subclavian artery catheterization, arteries responsible for mass feeding are observed in DSA. (a) In the control DSA taken after the glue injection, it is seen that the mass does not show contrast filling and the glue completely occludes the arteries. (b)

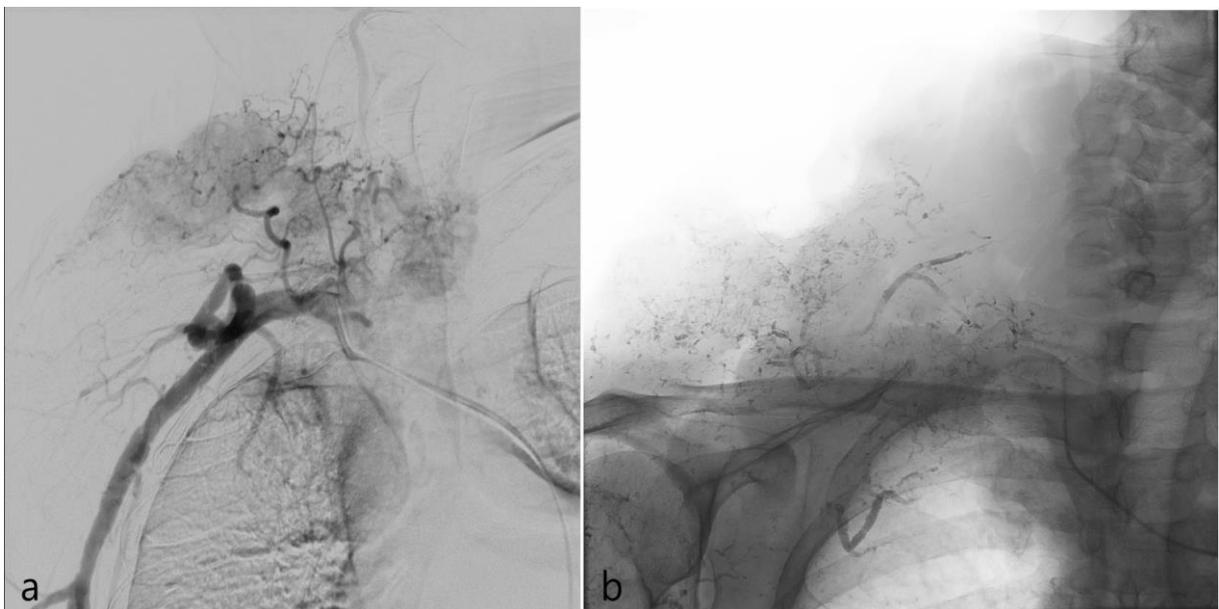


Figure 3. Giant RCC metastasis located adjacent to the right scapula. In DSA images taken after subclavian artery catheterization, it is seen that the mass is significantly enhanced. (a) After the glue-lipiodol injection, it was observed that the mass did not enhance and the glue-lipiodol mixture was distributed up to the distal part of the mass. (b)

Table 1. Explaining the causes of bleeding in patients undergoing embolization

	Total
Arterial bleeding due to malignancy	11
GI bleeding	0
Stomach adeno cancer	2
Gastric non-Hodgkin lymphoma (NHL)	1
Plasmocytoma with duodenal invasion	1
Hepatocellular cancer with gastric invasion (HCC)	1
Vaginal bleeding (cervical cancer)	3
Hematuria	
Renal cell cancer (RCC)	2
Bladder cancer	1
Hemoptysis due to infection sequela or bronchiectasis	9
Iatrogenic bleeding after percutaneous procedures	0
Lithotripsy	2
Percutaneous kidney parenchyma biopsy	1
After percutaneous transhepatic cholangiography (PTC)	1
Bleeding after trauma	3
Bleeding due to peptic ulcer	4

Discussion

Although endoscopic treatment methods are the first choice in the treatment of arterial bleeding, they are often insufficient⁵. Endovascular embolization is a suitable option for patients with surgical risk, especially in cases of acute bleeding or where endoscopy has failed^{5,6}. In coil or PVA particle embolization, the occlusion of arteries or pseudoaneurysms is due to thrombosis rather than the embolic material itself, and the patient's coagulation function is critical for the final success of the embolization procedure for hemorrhage⁷.

Considering the speed and efficiency of hemostasis, liquid embolic materials, such as NBCA should be used more frequently, especially in the presence of coagulation disorders^{1,6,8}.

Several factors affect the depth of glue penetration, with the most important being the velocity of the flow passing through the catheter tip, the ratio of NBCA to lipiodol, and the injection technique^{1,8}. Therefore, in cases where proximal embolization is desired, more diluted mixtures should be preferred if more intense and distal embolization is desired. When the literature is reviewed, 50%-70% dense mixtures have been preferred for proximal embolization and 25-50% mixtures for distal embolization^{2,8,9}. Complications such as catheter adhesion at certain rates, glue reflux, and non-target embolization have been described in these cases^{10,11}. Due to these glue-related complications, operators avoid the use of this material^{12,13}. However, in our study, a 10% mixture was preferred when proximal embolization was to be performed, and a 5% mixture for distal embolization. The technical success rate of 100% and the absence of complications in our case series suggest that these mixing ratios can be used safely.

In addition, the use of cone-beam computed tomography during the use of NBCA, as in all endovascular procedures, increases both technical and clinical success^{14,15}. Conical CT is known to be superior to DSA in providing microcatheter-guided navigation in order to embolize the correct vessel and showing the presence of other vessels causing bleeding. Cone beam CT was used during all embolization procedures included in this study.

Major complication rates in the use of NBCA have been defined as 3-5%. The primary concerns regarding the use of glue-lipiodol mixture are reflux and catheter adhesion^{15,16}. Other common complications include non-target embolization and ischemia-necrosis after over-embolization¹⁷. Arterial embolization in the upper gastrointestinal tract above the ligament of Treitz is

generally considered safe due to the rich collateral supply. It is considered that the risk of ischemic complications is higher in the lower gastrointestinal tract^{18,19}. These major complications are seen more frequently in patients with vascular malformation, tortuosity, and previous surgery or radiotherapy^{20,21}. However, when careful attention is paid to the technique, the probability of these complications is very low. In our study, no complication was encountered in any of the patients that underwent embolization. In recent studies, the frequency of NBCA use in gastrointestinal bleeding is increasing. In our study, we achieved complete technical and clinical success in patients with hemorrhage caused by peptic ulcer.

Technical success was confirmed by a follow-up angiography examination in all patients embolized with Glue-lipiodol mixture. Re-hemorrhage was detected in a total of eight patients, who were accepted to be clinically unsuccessful cases. Seven of these eight patients with re-hemorrhage had undergone embolization due to malignant mass bleeding. This suggests that the reason for recurrence was not due to the inadequacy of our technique or glue, but it was associated with the nature of malignant bleeding. When the literature is reviewed, the number of studies on the effect of glue-lipiodol mixture on malignant mass bleeding is limited, and there is a need for large case series on this subject. There may be several reasons for recurrent hemorrhage. As the main reason, we hypothesize that the malignant mass forms new feeding vessels or collaterals during the follow-up period. Another possible reason is that the glue-lipiodol mixture may not have provided sufficient distal embolization. Further studies with larger case series are needed to clarify this.

- *Limitations*

There were major limitations of our study, the main ones being; the reasons were that the study was retrospective and single-cen-

tered, the number of cases was low, unknown comorbidities, the anatomical localizations embolized, that is, the vessels were different, and therefore the diameters of the catheters used were not standard.

Conclusion

NBCA is a highly effective and safe liquid embolizing material in patients with active bleeding, who are planned to undergo endovascular embolization. A mixture of 5% and 10% NBCA-lipiodol can be safely used in acute bleeding.

Author contributions

All authors contributed to the study conception and design. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

Ethical approval was taken from the Cukurova University School of Medicine local Ethics Committee, and the principles of the Declaration of Helsinki had carried out (Document No.2022/08/04-121).

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