

# Safety and efficacy of modified endoscopic ultrasound-guided selective N-butyl-2-cyanoacrylate injections for gastric variceal hemorrhage in left-sided portal hypertension

by JY

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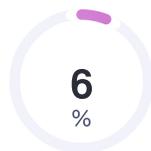
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# Safety and efficacy of modified endoscopic ultrasound-guided selective N-butyl-2-cyanoacrylate injections for gastric variceal hemorrhage in left-sided portal hypertension

## Abstract

### BACKGROUND

Gastric variceal hemorrhage is one of the primary manifestations of left-sided portal hypertension (LSPH). The hemorrhage is fatal and requires safe and effective interventions.

### AIM

- <sup>1</sup> To evaluate the clinical safety and efficacy of modified endoscopic ultrasound (EUS)-guided selective N-butyl-2-cyanoacrylate (NBC) injections for gastric variceal hemorrhage in LSPH.

### METHODS

A retrospective observational study of patients with LSPH-induced gastric variceal hemorrhage was conducted. Preoperative EUS evaluations were performed. Enrolled patients were divided into 2 groups (modified and conventional groups) according to the NBC injection technique. The final selection of NBC injection technique types depended on the patient's preferences and clinical status. The technical and clinical success rates, operation time, NBC doses, perioperative complications, postoperative hospital stay, and recurrent bleeding rates were analyzed, respectively.

## 2 RESULTS

3 A total of 27 patients were enrolled in this study. No statistically significant differences were observed between the two groups regarding baseline characteristics. In comparison to patients in the conventional group, patients in the modified group demonstrated significantly reduced NBC doses ( $2.0 \pm 0.6$  mL vs.  $3.1 \pm 1.0$  mL;  $P=0.004$ ) and increased endoscopic operation time ( $71.9 \pm 11.9$  minutes vs.  $22.5 \pm 6.7$  minutes;  $P < 0.001$ ). Meanwhile, the two groups had no significant difference in the technical and clinical success rates, perioperative complications, postoperative hospital stay, and recurrent bleeding rates.

## CONCLUSION

Modified EUS-guided selective NBC injections demonstrated safety and efficacy for LSPH-induced gastric variceal hemorrhage, with advantages mainly in reducing injection dose and having no radiation risk. However, the inadequacies are time-consuming and challenging to perform.

**Key Words:** Endoscopic ultrasound, Selective, N-butyl-2-cyanoacrylate, Gastric varices, hemorrhage, Left-sided portal hypertension

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**Core Tip:** Gastric variceal hemorrhage is a severe and critical complication of left-sided portal hypertension (LSPH). Endoscopic ultrasound (EUS)-guided interventions are emerging endoscopic treatments with massive potential in

4 the diagnostic and therapeutic fields. Our study revealed that EUS-guided selective N-butyl-2-cyanoacrylate injection is a safe and effective treatment alternative for patients with LSPH-induced gastric variceal hemorrhage, with reduced NBC doses and satisfactory technical and clinical success rates.

## **INTRODUCTION**

5 Left-sided portal hypertension (LSPH) is caused by splenic vein stenosis, thrombosis, or obstruction, with pancreatic diseases as the most common etiology[1, 2], among which pancreatitis and pancreatic tumors account for the leading causes of LSPH[3, 4]. Clinical symptoms of LSPH are attributed to an increase in the pressure gradient between the portal vein and the inferior vena cava[5]. Gastric variceal hemorrhage is one of the primary manifestations and the foremost cause of emergency department visits in LSPH patients[6], first described in 1969[7]. Given normal liver function and no obvious clinical symptoms in LSPH patients, gastric varices (G.V.) have received little attention, and their hemorrhage can be unexpected and fatal[8]. Thus, safe and effective interventions are required.

In recent years, the widespread use of digestive endoscopy in clinical practice has led to a gradual shift in patient preference towards minimally invasive endoscopic techniques, especially in the field of EUS[9, 10]. EUS has demonstrated convenience and promise in diagnostic procedures and hemostatic interventions for G.V. due to the combined function of endoscopy and ultrasound[11]. Moreover, EUS-guided GV therapies offer a safer and more practical alternative than the conventional therapy of endoscopic N-butyl-2-cyanoacrylate (NBC) injection[12, 13].

Based on previous studies, we reported a modified EUS-guided selective NBC injection procedure in a patient with LSPH-induced GV hemorrhage[6]. The

preliminary advantages of this modified procedure included reduced NBC doses, radiation avoidance, and a firmer obliteration effect with fewer rebleedings caused by glue ulcers[6]. We conducted this retrospective study in our single center to verify these clinical values and provide more basis for future research on EUS-guided GV treatment.

## **MATERIALS AND METHODS**

### ***Study design and study population***

6 This retrospective study received approval from the Ethics Committee of The  
First Affiliated Hospital of Chongqing Medical University. We retrospectively  
7 reviewed qualified LSPH patients from the First Affiliated Hospital of  
Chongqing Medical University from October 2019 to September 2023. All  
enrolled patients were diagnosed with LSPH-induced gastric variceal  
8 hemorrhage and received endoscopic NBC injections. Written informed consent  
was obtained from all the patients before each endoscopic procedure.  
Exclusion criteria included previous endoscopic hemostasis, severe organ  
dysfunction, or other conditions unsuitable for endoscopic procedures.

### ***Endoscopic interventions***

The final selection of NBC injection technique types (modified EUS-guided selective NBC injection or conventional endoscopic NBC injection) depended on the patient's preferences and clinical status. Patients electing conventional endoscopic NBC injection constituted the "conventional" group and received conventional "sandwich" injection[14], while patients electing modified EUS-guided selective NBC injection formed the "modified" group and received selective NBC injection under EUS guidance (Linear Pentax echoendoscope, Hoya Co., Tokyo, Japan) (Figure 1)[6].

### ***Postoperative follow-up and data collection***

The technical and clinical success rates, operation time, NBC doses, perioperative complications, and postoperative hospital stay were collected from inpatient medical records and analyzed, respectively. The follow-up records were reviewed 1 month, 3 months, and 6 months after the NBC injections. Recurrent upper gastrointestinal hemorrhage rates were derived from the routine outpatient follow-up at the Gastroenterology Department. Only patients with complete medical records were included.

### ***Data analysis***

Continuous variables and categorical were expressed as means  $\pm$  S.D. and n (%), respectively. Unpaired Student t-test and Mann-Whitney U-test were used for continuous variables, while the chi-square and Fisher's exact tests were performed for categorical variables. Statistical analyses were performed using the SPSS statistical software (version 23.0), and statistical significance was defined as a *P* value  $< 0.05$ .

## **RESULTS**

### ***Patient characteristics***

This study preliminarily enrolled 30 patients. However, some participants underwent splenectomy or had both modified EUS-guided selective NBC injection procedures and conventional endoscopic NBC injection procedures during the follow-up period and, therefore, were excluded. Thus, the final number of qualified participants in the conventional and modified groups was 16 and 11, respectively (Figure 2). Statistically significant differences regarding baseline characteristics were not observed between the two groups (Table 1). The median age was 46.6 years (range 24.0-68.0) for the modified group and 47.9 years (range 29.0-68.0) for the conventional group. Seven patients in the

modified group (63.6%) and eleven in the conventional group (68.8%) were male ( $P = 0.78$ ). In all enrolled patients, the three most common causes for LSPH-induced gastric variceal hemorrhage were, in order, walled-off necrosis (12/27, 44.4%), pancreatic pseudocyst (8/27, 29.6%) and pancreatitis (5/27, 18.5%). Eight patients in the modified group (72.8%) and twelve in the conventional group (75.0%) were diagnosed with walled-off necrosis or pancreatic pseudocyst ( $P = 0.93$ ) (Table 1).

### ***Safety and efficacy of endoscopic procedures in two groups***

12 | Technical success was defined as successful injection and absolute occlusion of the targeted gastric varices, while clinical success was defined as the resolution or improvement of gastric variceal hemorrhage. The technical success rate was 100% for both types of injection procedures, and clinical success rates were 90.9% and 100% in the modified and conventional groups, respectively ( $P=0.41$ ). The technical and clinical success rates were not significantly different in both groups (Table 2).

Perioperative complications included ectopic embolization, local venous thrombosis, extravascular injection, severe new-onset bleeding following the needle removal, and the early appearance of glue ulcers[15, 16]. In comparison to patients in the conventional group, patients in the modified group demonstrated significantly reduced NBC doses ( $2.0\pm 0.6$  mL vs.  $3.1\pm 1.0$  mL;  $P=0.004$ ) and increased endoscopic operation time ( $71.9\pm 11.9$  minutes vs.  $22.5\pm 6.7$  minutes;  $P < 0.001$ ). Meanwhile, the perioperative complications, postoperative hospital stay, and recurrent bleeding rates for patients in the modified group were 0%,  $4.4\pm 1.6$  days, and 9.1%, respectively, vs 6.3%,  $5.8\pm 2.2$  days, and 18.8% for those in the conventional group; nevertheless, the two

groups had no significant difference in the perioperative complications, postoperative hospital stay, and recurrent bleeding rates (Table 2).

## **DISCUSSION**

This present study built on our prior research and compared the safety and efficacy of a modified EUS-guided selective NBC injection procedure for gastric variceal hemorrhage in LSPH with conventional endoscopic NBC injection procedures. To the best of the authors' knowledge, no similar studies had previously been reported in the literature.

Our result revealed consistency with previous research that LSPH was most common in patients with pancreatic disease, especially those with walled-off necrosis and pancreatic pseudocyst[17, 18], which occurred because of the anatomical proximity between the splenic vein and the pancreas[6]. Therefore, regular follow-ups should be scheduled for LSPH patients to reduce unexpected and fatal bleeding. Moreover, when considering endoscopic minimally invasive procedures, sufficient attention to intraoperative and postoperative bleeding should be paid to patients with pancreatic pseudocysts or walled-off necrosis[2, 19].

Although endoscopic NBC injection was recommended with great clinical value in achieving hemostasis in LSPH patients[20], conventional injection procedures have striking defects in identifying varices below the gastric mucosal layer, locating culprit vessels during massive gastric hemorrhage, and reducing possible operation-related complications, including ectopic embolization, extravascular injection[21-23]. These deficiencies also place new demands on further developments of endoscopic procedures. EUS is quite a productive and promising approach to perform real-time ultrasonic scanning

and interventions for gastric varices, perforating feeding veins, portal vein and its tributaries, and collateral circulations[11, 24]. EUS-guided NBC injection in G.V. patients revealed superior clinical outcomes than conventional endoscopic injection dual to properties of NBC dosage reduction, better obliteration, and fewer recurrences and rebleedings[13, 25].

We applied this modified EUS-guided selective NBC injection in LSPH-induced GV hemorrhage patients, and we found that it was, first and foremost, safe and effective in this retrospective study in our single center. Safety is the primary premise and final goal of exploring technical development. Compared with conventional endoscopic injection, this modified procedure did not increase the incidence of perioperative complications, nor would it prolong the patient's hospital stay. Meanwhile, more cases were included in this study to verify our previous research and testify to the benefits of NBC dosage reduction and its consequent reduced medical cost and complications[6]. Reducing glue-related complications focuses on effectively minimizing the injection dose, including endoscopic clips-assisted injection, balloon-occluded retrograde transvenous obliteration (BRO), combined deployment of embolization coils and cyanoacrylate, and our modified procedure[26-28]. Each of these above procedures has its own advantages and applicable population. The modified procedure in our study can not only locate the puncture site more accurately in real-time, but the injection depth and angle can be precisely controlled, the injection can be timely terminated through observing the real-time flow blocking effect, and it can also help avoid the extravascular injection and reduce the total injection dose, avoid the radiation exposure during the combined coil deployment or the BRO, and reduce the related medical costs. It is also worth noting that the operation time was significantly longer in the modified group than in the conventional group. We considered that was

relevant to time consumption in confirming the ideal puncture site during the EUS procedure. Therefore, this method is currently unsuitable for endoscopic centers lacking relevant experience, nor is it applicable for critically ill patients with unstable vital signs who need urgent endoscopic hemostasis.

Moreover, EUS technology and equipment have not been satisfactorily popularized in many Asian regions, and there is still a significant training demand for many endoscopic interventional operations, including EUS-guided GV procedures[29]. Compared to these more difficult and time-consuming EUS-guided GV procedures, the technique and equipment required for conventional injection are more accessible to acquire and, therefore, cannot be discarded[30]. In the inclusion phase of this study, it was also noticed that two patients shifted from the original modified procedure to the conventional method in their follow-up endoscopic treatment. We presume that the reason lies in the advantages of the conventional operation in reducing difficulties and operational time. Consequently, a multidisciplinary discussion team (MDT) is a widely recommended approach to selecting the most appropriate individual treatment.

## LIMITATIONS

There are three main limitations. First of all, this is a retrospective observational study. Our findings are limited by the study design, and future prospective randomized controlled studies are needed. Secondly, this is a single-center study, and EUS-guided operation is noticeably affected by technical conditions and experience levels. In the future, multicenter studies involving more endoscopy centers in multiple tertiary hospitals are needed. Last but not least, the sample size of this study is relatively small and has a specific regional characteristic. On the one hand, the modest number of

enrolled patients is because LSPH is a rare cause of gastric varices and consequent hemorrhage[31, 32]. On the other hand, since the author's endoscopic center is a regional center for treating severe pancreatitis, most patients included in this study had complications such as pancreatic pseudocyst or walled-off necrosis, which may have an unavoidable impact on the results. Therefore, future studies need to include more LSPH patients with varied causes.

### **CONCLUSION**

In conclusion, modified EUS-guided selective NBC injections demonstrated safety and efficacy for LSPH-induced GV hemorrhage, with advantages mainly in reducing injection dose and having no radiation risk. Still, the inadequacies are time-consuming and technically challenging to perform. Therefore, this procedure is recommended for complicated patients in experienced endoscopy centers.

1.	<i>To evaluate the clinical safety and efficacy of</i>	Safety and Efficacy Studies of Vertebroplasty, Kyphoplasty, and Mesh-Container-Plasty for the Treatment of Vertebral Compression Fractures: Preliminary Report	Originality
2.	<i>RESULTS A total of 27 patients were enrolled in this study.</i>	What is the better surgical treatment option for recurrent common bile duct stones?	Originality
3.	<i>No statistically significant differences were observed between the two groups</i>	Clinical Study Prognostic Significance of DR-70 Levels in	Originality
4.	<i>is a safe and effective treatment alternative for patients with</i>	Laparoscopic versus conventional appendectomy - a meta-analysis of randomized controlled trials	Originality
5.	<i>an increase in the pressure gradient between the portal vein and the inferior vena cava</i>	Portal Hypertension: Nonsurgical and Surgical Management	Originality
6.	<i>from the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University.</i>	Hematoma Ventricle Distance on Computed Tomography Predicts Poor Outcome in Intracerebral Hemorrhage	Originality
7.	<i>the First Affiliated Hospital of Chongqing Medical University from</i>	The Relationship of Anti-Mullerian Hormone in Polycystic Ovary Syndrome Patients with Different Subgroups	Originality
8.	<i>Written informed consent was obtained from all the patients</i>	Exclusion Criteria	Originality
9.	<i>Only patients with complete medical records were included.</i>	<a href="https://austinpublishinggroup.com/urology/fulltext/aju-v1-id1006.php">https://austinpublishinggroup.com/urology/fulltext/aju-v1-id1006.php</a>	Originality
10.	<i>Unpaired Student t-test and Mann-Whitney U-test were used</i>	Polytrauma Defined by the New Berlin Definition: A Validation Test Based on Propensity-Score Matching Approach	Originality

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11.	<i>Statistical analyses were performed using the SPSS statistical software (version</i>	Association of C-Reactive Protein with the Extent of Angiographically Verified Coronary Artery Disease	Originality
12.	<i>clinical success was defined as the resolution or improvement of</i>	New External Hacks 2023   VAC Bypass, Stealth Injection, Updated   Mikedetimmerman.nl <a href="https://www.mikedetimmerman.nl/new-external-hacks-2023-vac-bypass-stealth-injection-updated/">https://www.mikedetimmerman.nl/new-external-hacks-2023-vac-bypass-stealth-injection-updated/</a>	Originality

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