

A study on EUS guided coil plus N butyl cyanoacrylate therapy (without lipiodol) in the treatment of fundal varices

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Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background and Aims: Gastric varices can affect approximately 20% of patients with portal hypertension. Cyanoacrylate injection is the conventional treatment method. Various complications with systemic embolism being the most severe are reported with this method. EUS-guided imaging with coil and glue injection is a new option for the treatment of gastric varices. The aim of this study was to evaluate the outcomes of EUS guided coil plus N butyl cyanoacrylate therapy (without lipiodol) in the treatment of gastric fundal varices.

Material & Methods: This study was conducted in NH Multispeciality Hospital, Mysuru after obtaining approval from Hospital Ethical committee. Retrospective data-based analysis of 22 patients who had undergone EUS guided glue and coil injection therapy between May 2017 and June 2019 was done. The main outcomes measured were hemostasis, obliteration on follow-up EUS and post treatment bleeding rate. The characteristics of the patients are reported with descriptive statistics.

Results: 2 coils were placed in 20 [91%] and 3 coils in 2 [9%] patients. Mean amount of dye was 1.5ml. None had pulmonary embolism or rebleeding. Abdominal pain [18%] was the predominant adverse event within 24 hours. At 1-month follow up; varix obliteration was documented in 20[91%] patients. On 6 month follow-up, 5[22.7%]

presented with bleeding. Gastric varix was the etiology in only 1[4.5%] patient.

Conclusion: EUS guided coil and glue injection is safe method for controlling fundal variceal bleed. Since the amount of glue required is less due to coils scaffold, embolization is nil.

Keywords: Gastric varices, EUS, Coil and glue, Lipiodol, Re-bleeding, Pulmonary embolism

Introduction

Gastric varices though less common than esophageal varices, can affect approximately 20% of patients with portal hypertension. Gastric varices can lead to more severe bleeding, which can be difficult to control, and have higher re-bleeding rates, which can range from 34%–89%.^[1,2] The mortality rate from first variceal bleeding within 6 weeks is as high as 20%.^[3] Within 1 year of diagnosis, the risk of gastric variceal bleeding has been reported to be 10%–16%, necessitating a meticulous evidence-driven approach. While previous literature has clearly demonstrated risk factors and independent predictors of bleeding (e.g., size of GV, the presence of red signs, and the degree of liver dysfunction), there remains a paucity of the literature regarding treatment efficacy and how endoscopic options fit into the treatment continuum.^[4]

While various endoscopic and radiologic treatment techniques have been previously described in the

literature, cyanoacrylate injection, first published by Soehendra in 1986, remains the conventional treatment method [5,6]. Various complications have been described related to the use of this technique, with systemic embolism being the most severe. In the majority of cases, these emboli are asymptomatic, and thus the actual incidence of systemic embolism remains unknown. However, symptomatic embolism was reported to occur in approximately 0.7% of cases by Cheng et al [7]. Band ligation or sclerotherapy of GV has inferior hemostasis and higher rebleeding rates than endoscopic injection of cyanoacrylate. [8,9]

However, the endoscopic technique is associated with severe adverse events, mainly pulmonary or systemic embolisms, bleeding ulcers from the injection site, peritonitis, needle impaction, and even death. Also, the injection of cyanoacrylate done by direct visualization using standard gastroscopes has been related to damage of the working channel of the endoscope. [10-15]

Endoscopic ultrasound (EUS) can assist in the diagnosis of these gastric varices, and, through the use of EUS-guided imaging, coil injection has become a new option for the treatment of gastric varices. Since coils were first used to treat ectopic varices by Levy in 2008 [16], this technique has been increasingly implemented into clinical practice. However, its higher cost has been a limiting factor in more widespread use. Binmoeller and colleagues first described treatment combining EUS-guided coil and cyanoacrylate for managing gastric varices. They reported an obliteration rate of 96% in a single treatment session and no symptoms or signs of cyanoacrylate embolization, suggesting a reducing in the risk of embolism using this technique. EUS-guided coil combined with cyanoacrylate in order to reduce the risk of embolism in the treatment of gastric varices was thus first described in 2011. [17]

Aims

To evaluate the outcomes of EUS guided coil plus N butyl cyanoacrylate therapy (without lipiodol) in the treatment of gastric fundal varices.

Material & Methods

Study design: Retrospective observational

Study population: 22 patients

Study period: 2 years (May 2017- April 2019)

Inclusion criteria

1. Patients above 18 years age
2. Patients of both sexes
3. Patients with gastro-esophageal varices type II (GOV II) (fundal varices communicating with esophageal varices), isolated gastric varices type I (IGV I) (fundal varices within a few centimeters of the gastric cardia), patients with active bleeding and history of recent bleeding due to GV (secondary prophylaxis).

Exclusion criteria

1. Patients below 18 years age
2. Gastro-esophageal varices type I (GOV I)
3. Patients with gastric varices of diameter under 10 mm in endosonographic view
4. Pregnant women
5. Patients with prior surgery of the upper gastrointestinal (GI) tract
6. Patients who had multi-organ failure

This study was conducted in Narayana Multispeciality Hospital, Mysuru after obtaining approval from Hospital Ethical committee. Retrospective data-based analysis of 22 patients who had undergone EUS guided glue and coil injection therapy between May 2017 and June 2019 was done. The main outcomes measured were hemostasis, obliteration on follow-up EUS, post treatment bleeding rate and other adverse effects.

Procedural steps: All procedures were performed under deep sedation in the endoscopy room by single

endoscopist. All patients received prophylactic intravenous broad-spectrum antibiotics. Upper GI diagnostic endoscopy was performed in all patients and esophageal and fundal varices were assessed. Fundal varices were classified using the classification of Sarin and Kumar.^[18]

Gastroesophageal varices type 2[GOV2] and Isolated gastric varices type 1[IGV1] were only enrolled . EUS was performed using a oblique-viewing linear echoendoscope[EU- ME2, from Olympus corp].Using doppler, flow was confirmed.

EUS-guided coil and cyanoacrylate glue injection was performed as follows. First, 50 ml of water was filled inside gastric lumen to improve the visualisation of gastric varices. Next , echoendoscope was positioned at distal esophagus (transesophageal-transcural approach) to visualize the gastric varices and feeder vessels. Varices were measured in short axis diameter.

After good positioning, puncture of gastric varices done using standard 19G [Olympus] FNA needle . Intravariceal position of needle was confirmed by aspiration of blood. Then needle was flushed using normal saline. Embolisation coils[Nester, embolisation coils, Cook Medical] were delivered into the varix using stylet as pusher. Coils of diameter 8mm to 16 mm were selected according to the short axis diameter of the varix. Complete deployment of coil inside varix was confirmed by aspiration of blood, which was flushed later. Finally, injection of 1-2 ml N- Butyl cyanoacrylate (Endocryl, Samarth Life Sciences, Mumbai) glue was injected into the varix without mixing with the lipiodol. 5 ml of distilled water was immediatly injected and during injection of distil water needle was withdrawn from the varix.

Color Doppler was applied 10 minutes after treatment to confirm absence of flow in the varix. If persistant flow

was present, additional glue was injected using same technique.

The presence of concomitant esophageal varices was assessed. Patients with grades 2 or 3 esophageal varices underwent conventional band ligation after successful obliteration of GFV with coil and CYA treatment (performed during subsequent endoscopic sessions).

Repeat upper endoscopy and EUS was performed at the end of 1 month, followed by 6-month surveillance examinations. Any clinical suspicion of recurrent GI bleeding was immediately investigated by upper GI endoscopy.

Statistical analysis: The characteristics of the patients are reported with the use of descriptive statistics.

Results

The median age of the patients was 48 years (20–65 years). All patients had liver cirrhosis except 1 who had EHPVO. Patient characteristics are as shown in Table 1.

Two coils were placed in 20 [91%] and 3 coils were placed in 2[9%] patients. Mean amount of dye needed was 1.5ml.None of them had pulmonary embolism or rebleeding. Abdominal pain[18%] was the predominant adverse event reported within 24 hours.(Table 2)

22 patients had EUS at 1-month follow up; varix obliteration was documented in 20[91%] patients . 2 patients had persistant flow in EUS . This was managed by injection of glue alone.

All 22 patients were followed upto 6 months . During this period, five[22.7%] of them presented with bleeding episodes. Gastric varix was the etiology in only 1[4.5%] of these patients which was managed with only glue injection. (This patient had persistent flow in varix at 1 month follow up also). Esophageal varix was confirmed to cause bleed in remaining 4[18.18%] patients.

Mean age	48[20-65]
No of men	18[82%]
Portal hypertension etiology	
Alcohol	14[63%]
Hepatitis B	2[9.09%]
Hepatitis C	1[4.5%]
NAFLD	3[13.6%]
EHPVO	2[9.09%]
Bleeding during presentation	
Active	1[4.5%]
History of recent bleeding	21[95.5%]
Never Bled	0

Table 1: Patient characteristics

Varix type[GOV2/IGV1]	20/2[90.9/9.1%]
Mean varix size	18[15- 22mm]
Mean coil number	2[1-3]
Mean glue volume	1.5[1-2ml]
Technical success	100%
Adverse events	
Abdominal Pain	4[18.2%]
Embolisation	0
Bleeding from coil extrusion	1[5%]

Table 2 ; Procedure and adverse events

Procedure steps



Fig. 1: Large fundal varix on upper GI endoscopy

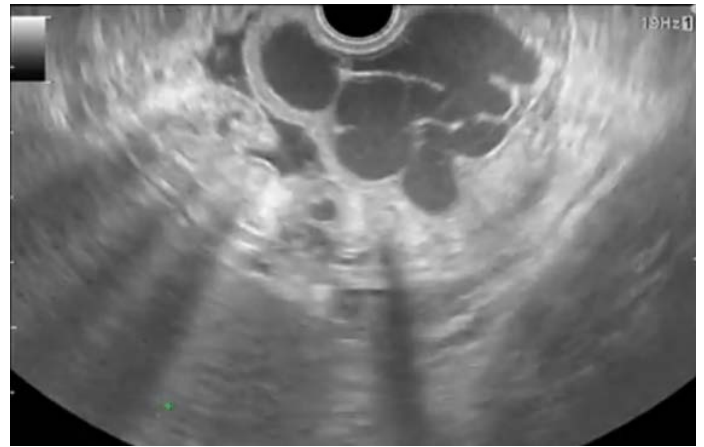


Fig. 2: Linear EUS showing the varix



Fig. 3: Deployment of coils through 19 gauge FNA needle

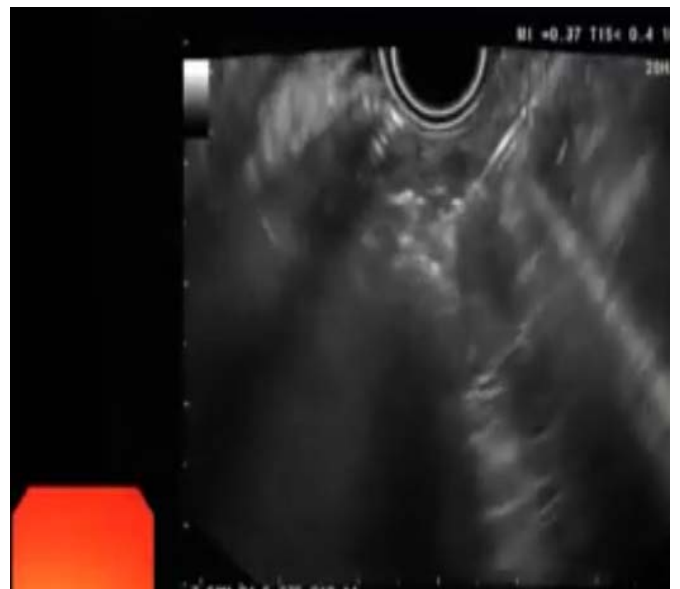


Fig 4-Injection of N-Butyl Cyanoacrylate glue



Fig. 5: Appearance of varix after one month follow up

Discussion

According to current practice guidelines, endoscopic band ligation and glue injection are the recommended conventional endoscopy-guided treatment modalities for Esophageal varices[EV] and Gastric varices[GV], respectively.^[19] Endoscopic therapy with tissue adhesives like cyanoacrylate glue is considered the first-line treatment for acute bleeding from IGV1 and GOV2 type Gastric varices and TIPS as the second alternative after failed cyanoacrylate injection in accordance with the International Consensus in Portal Hypertension Workshop held in 2015 (Baveno VI). An early TIPS with PTFE-covered stents within 72 h (ideally <24 h) must be considered in patients bleeding from gastric varices who are at high risk of treatment failure (Child-Pugh class B with active bleed or Child-Pugh class C) after initial pharmacological and endoscopic therapy. Also it states that, to prevent rebleeding from treated gastric varices, consideration should be given to additional glue injection (after two to four weeks), beta-blocker treatment or both combined or TIPS.^[20]

Endoscopic ultrasound-guided glue injection and EUS-guided coil application have been described in the literature where either only glue or both coil and glue were used for therapy of Gastric varices.

Primary prevention for GV bleeding has not been established in current guidelines, but there are studies in which GV with a high risk of first bleeding (a gastric varix diameter >20 mm, an MELD (Model for End-Stage Liver Disease) score >17, and presence of portal hypertensive gastropathy) were obliterated with EUS-guided endovascular procedures^[21,22,23].

Despite the controversy and lack of consensus about the role of GV primary prophylaxis, Mishra and colleagues described a 2-year probability of bleeding of 13% in those patients with IGV1 and GOV2 treated with endoscopic injection of cyanoacrylate compared with 45% in those patients in whom no intervention was instituted and 28% in those taking beta-blockers.^[24]

EUS-guided coil application is an emerging treatment modality of bleeding gastric varices. EUS-guided coil application with cyanoacrylate under EUS guidance also has the potential to reduce the risk of embolization, as the volume of glue used is small^[17]. The synthetic fibers (“wool coils”) covering the coils promote thrombosis and function as a scaffold to retain n-butyl-2-cyanoacrylate (Histoacryl blue) within the varix and may decrease the amount of glue injection needed to achieve obliteration^[25]

In our present study, secondary prophylaxis for gastric variceal bleeding was the aim and we used both coil and glue injection for large fundal varix[>10mm] who came with active bleed or recent bleed.

The mean age of patients in this study was 48 years and majority were males(82%). Alcohol(63%) was the major etiology of portal hypertension followed by NAFLD [13.6%], Hepatitis B[9.09%], Hepatitis C & EHPVO 4.5% each. 21 (95.5%) had history of recent bleeding & 1(4.5%) had active bleeding.

Yasser Bhat et al in their study also had majority males(64%), but Hepatitis C was the major etiology of

portal hypertension.^[26] In a study by Taufic Khoury et al, NAFLD was the major cause.^[27]

In this study we used a standardized protocol to treat the patients with GFV. Our aim was to achieve complete varix obliteration. This was achieved in a single procedure in most patients (20/22, 90.9%), whereas 9% of patients required 2 procedures due to persistent flow in the varices. This study found that once obliteration was achieved, rebleeding due to gastric varices is very low [1/22 patients, 4.5%] on six month follow up period. Salvage therapy, in the form of glue injection was required in only 2 [9.09%] patients suggest that single session of coil and glue injection is sufficient to obliterate the large gastric varix. Procedure related adverse events reported in 5/22 [22.7%]. Self-limited abdominal pain was the predominant adverse event occurred in 4 [18.2%] patients. It was managed with only analgesics. Coil extrusion from varix occurred in 1 [4.5%] patient which required re-puncture and procedure. None of them had pulmonary embolism.

In study by Yasir Bhat et al^[26], complete obliteration of varix was seen in 79% of patients and post treatment bleeding occurred in 3%, on follow up. Procedure-related adverse events occurred in 9 of 125 patients (7%), which included self-limited abdominal pain and one patient had symptomatic pulmonary embolism. In 4 patients, minor post-treatment bleeding was attributed to the extrusion of the coil and glue complex (3%) from the previously treated varix. However, in their study they have used N-Octyl cyanoacrylate instead of N-Butyl cyanoacrylate. In the present study, N-Butyl cyanoacrylate was used and the results were comparable to the study of Yasir Bhat et al. Also in present study, amount of glue injected was less compared to Bhat et al. Binmoeller K et al reported excellent clinical utility and safety in 30 patients with combined coil and glue deployment with no clinical adverse events.^[27] Romero-

Castro et al^[28] reported a retrospective comparative cohort (30 patients) comparing N-butyl-CYA injection alone to coil embolization. Overall obliteration rate achieved was 96.7%; however, 47.4% required repeat therapy in the CYA group, whereas 36.4% in the coil group either required additional coil or CYA placement. A recent case series of 14 patients who underwent EUS-guided coil with (n = 4) or without (n = 10) concomitant glue injection in a variety of varices also demonstrated excellent clinical effect.^[29]

We found that coils with small amount of glue is sufficient to completely obliterate the varix because of synthetic fibers in coils with glue causes complete obliteration of varices. Number of coils required were also less, due to careful selection varices on Endoscopic ultrasound. It is comparable to study by Mukkada et al^[30]

Recent study by Robles-Medranda et al. demonstrated that EUS-guided therapy for GV using CYA or coils is effective; however, coil therapy had higher clinical and technical success and was associated with fewer adverse events compared with EUS-CYA injection. The technical success rate was 100%. On endosonographic varicealography technical success was observed in 26/30 patients. Complete variceal obliteration was observed in 96.6% of patients, and the immediate disappearance of the varix was observed in 24 (80%) patients.^[21]

In our study, glue used was N-Butyl cyanoacrylate, which was not mixed with lipoidal. Lipiodol is commonly used to prevent the polymerisation of glue in endoscopy channel and also to enable slow injection of glue to prevent embolism. We used distilled water to flush the glue with simultaneous withdrawal of needle from the varix. We found that in spite of not using lipiodol, adverse events like blocking of endoscopy channel, sticking of needle to varix or pulmonary embolism were

nil. It is because the amount of glue required is less due to usage of multiple coils.

The localization and approach of the feeder vessel are difficult, time-consuming, and require additional training; however, it has shown several benefits, mainly in the safety of the procedure due to the fewer amount of glue needed for obliteration.^[22,26]

To the best of our knowledge, there are very few studies reporting the use N- Butyl cyanoacrylate without lipiodol to treat gastric varices with coil. Also post procedural complications and embolism are low, suggesting that it can be used to treat large gastric varices safely.

Conclusion

EUS guided coil and glue injection is safe method for controlling fundal variceal bleed. Since the amount of glue required is less due to coils scaffold, embolization is nil. The fatty contrast agent lipiodol ultra-fluid usually used to avoid occlusion in the endoscopy channel during the procedure and reduce the risk of embolization was not used in this study. We found that N butyl cyanoacrylate glue, though has fast polymerization time can be safely used even without lipiodol. Also it is a better method to achieve hemostasis in large gastric varices as the rebleed rate is low.

Limitation: Sample size is small and this is a single center study.

References

1. Weilert F, Binmoeller KF. Endoscopic management of gastric variceal bleeding. *Gastroenterol Clin North Am.* 2014;43:807-18.
2. Martins FP, Macedo EP, Paulo GA, Nakao FS, Ardengh JC, Ferrari AP. Endoscopic follow-up of cyanoacrylate obliteration of gastric varices. *Arq Gastroenterol.* 2009;46:81-4.
3. Carbonell N, Pauwels A, Serfaty L, et al. Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. *Hepatology* 2000; 40: 652–659
4. Garcia-Pagán JC, Barrufet M, Cardenas A, et al. Management of gastric varices. *Clin Gastroenterol Hepatol* 2014;12:919-280.
5. Soehendra N, Grimm H, Nam Ch. V, Berger B. N-butyl-2-cyanoacrylate: A supplement to endoscopic sclerotherapy. *Endoscopy.* 1987;19:221-4.
6. Greenwald BD, Caldwell SH, Hespenheide EE, Patrie JT, Williams J, Binmoeller KF, et al. N-2-butyl-cyanoacrylate for bleeding gastric varices: a United States pilot study and cost analysis. *Am J Gastroenterol.* 2003;98:1982-8.
7. Cheng LF, Wang ZQ, Li CZ, Lin W, Yeo AET, Jin B. Low incidence of complications from endoscopic gastric variceal obturation with butyl cyanoacrylate. *Clin Gastroenterol Hepatol.* 2010;8:760-6.
8. Hashizume M, Akahoshi T and Tomikawa M. Management of gastric varices. *J Gastroenterol Hepatol* 2011; 26: 102–108.
9. Irani S, Kowdley K and Kozarek R. Gastric varices: an updated review of management. *J Clin Gastroenterol* 2011; 45: 133–148.
10. Kok K, Bond R, Duncan I, et al. Distal embolization and local vessel wall ulceration after gastric variceal obliteration with N-butyl2-cyanoacrylate: a case report and review of the literature. *Endoscopy* 2004; 36: 442–446.
11. Hwang S, Kim H, Park S, et al. N-butyl2-cyanoacrylate pulmonary embolism after endoscopic injection sclerotherapy for gastric variceal bleeding. *J Comput Assist Tomogr* 2001; 25: 16–22.
12. Noophun P, Kongkam P, Gonlachanvit S, et al. Bleeding gastric varices: results of endoscopic injection with cyanoacrylate at King Chulalongkorn

- Memorial Hospital. *World J Gastroenterol* 2005; 11: 7531–7535.
13. Bhasin D, Sharma B, Prasad H, et al. Endoscopic removal of sclerotherapy needle from gastric varix after N-butyl-2-cyanoacrylate injection. *Gastrointest Endosc* 2000; 51: 497–498.
14. Saracco G, Giordanino C, Roberto N, et al. Fatal multiple systemic embolisms after injection of cyanoacrylate in bleeding gastric varices of a patient who was noncirrhotic but with idiopathic portal hypertension. *Gastrointest Endosc* 2007; 65: 345–347.
15. Rickman O, Utz J, Aughenbaugh G, et al. Pulmonary embolization of 2-octyl cyanoacrylate after endoscopic injection therapy for gastric variceal bleeding. *Mayo Clin Proc* 2004; 79: 1455–1458.
16. Levy MJ, Wong Kee Song LM, Kendrick ML, Misra S, Gostout CJ. EUS-guided coil embolization for refractory ectopic variceal bleeding (with videos). *Gastrointest Endosc*. 2008;67:572-4.
17. Binmoeller KF, Weilert F, Shah JN, Kim J. EUS-guided transesophageal treatment of gastric fundal varices with combined coiling and cyanoacrylate glue injection (with videos). *Gastrointest Endosc*. 2011;74:1019-25.
18. Sarin S, Kumar A. Gastric varices: profile, classification, and management. *Am J Gastroenterol* 1989;84:1244-9.
19. Garcia-Tsao G, Sanyal AJ, Grace ND et al. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology (Baltimore, Md)* 2007; 46: 922 – 938
20. De Franchis R and Baveno VIF. Expanding consensus in portal hypertension: report of the Baveno VI Consensus Workshop: stratifying risk and individualizing care for portal hypertension. *J Hepatol* 2015; 63: 743–752.
21. Robles-Medrand C, Valero M, Nebel JA, et al. Endoscopic-ultrasound-guided coil and cyanoacrylate embolization for gastric varices and the roles of endoscopic doppler and endosonographic varicealography in vascular targeting. *Dig Endosc* 2019;31:283-90.
22. Bick B, Al-Haddad M, Liangpunsakul S, et al. EUS-guided fine needle injection is superior to direct endoscopic injection of 2-octyl cyanoacrylate for the treatment of gastric variceal bleeding. *Surg Endosc* 2019; 33: 1837–1845.
23. Bhat YM, Weilert F, Fredrick RT, et al. EUS-guided treatment of gastric fundal varices with combined injection of coils and cyanoacrylate glue: a large U.S. *Gastrointest Endosc* 2016; 83: 1164–1172.
24. Mishra SR, Sharma BC, Kumar A, et al. Primary prophylaxis of gastric variceal bleeding comparing cyanoacrylate injection and beta-blockers: a randomized controlled trial. *J Hepatol* 2011; 54: 1161–1167.
25. Rose SC. Mechanical devices for arterial occlusion and therapeutic vascular occlusion utilizing steel coil technique: clinical applications. *AJF Am J Roentgenol* 2009; 192: 321 – 324
26. Romero-Castro R, Pellicer-Bautista FJ, Jimenez-Saenz M, et al. EUS-guided injection of cyanoacrylate in perforating feeding veins in gastric varices: results in 5 cases. *Gastrointest Endosc*. 2007;66: 402–7.
27. Tawfik Khoury, * Muhammad Massarwa, 1 * Saleh Daher, Ariel A. Benson, Wadi Hazou, Eran Israeli, Harold Jacob, Julia Epstein, and Rifaat Safad . *HEPATOLOGY COMMUNICATIONS, VOL. 3, NO. 2, 2019*
28. Romero-Castro R, Ellrichmann M, Ortiz-Moyano C, et al. EUS-guided coil versus cyanoacrylate therapy

for the treatment of gastric varices: a multicenter study. *Gastrointest Endosc* 2013;78:711-21.

29. Fujii-Lau LL, Law R, Wong Kee Song LM, et al. Endoscopic ultrasound (EUS)-guided coil injection therapy of esophagogastric and ectopic varices. *Surg Endosc Epub* 2015 Jul 3.
30. Roy J Mukkada, Rajesh Antony, et al , Endoscopic ultrasound-guided coil or glue injection in post-cyanoacrylate gastric variceal re-bleed . *Indian Journal of Gastroenterology*; 2018, 37, 153–159

How to citation this article: Dr. Satheesh Rao A K, “A study on EUS guided coil plus N butyl cyanoacrylate therapy (without lipiodol) in the treatment of fundal varices”, *IJMACR*- November - December - 2020, Vol – 3, Issue -6, P. No. 107 – 115

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