

# **A State of the Art Approach to the Management of Gastric Varices**

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# Conflict of Interest Disclosure

(Over the past 24 months)

Name: Mayur Brahmania & Tasha Kulai

No relevant relationships with any commercial or non-profit organizations

# Objectives

- Describe the pathophysiology and anatomy of gastric varices
- Describe the evidence for primary prophylaxis of gastric varices
- Describe the optimal treatment for bleeding gastric varices

# Case 1

- 60 year old male with compensated HCV (untreated) cirrhosis. Screening EGD showed an isolated fundal gastric varix (2cm) with no high risk stigmata. There were no esophageal varices. MELD score is 20. He is awaiting transplant. What is your next step?
- A. Non-selective beta-blocker
  - B. Cyanoacrylate glue
  - C. TIPS
  - D. BRTO
  - E. EUS coiling
  - F. Repeat EGD in one year



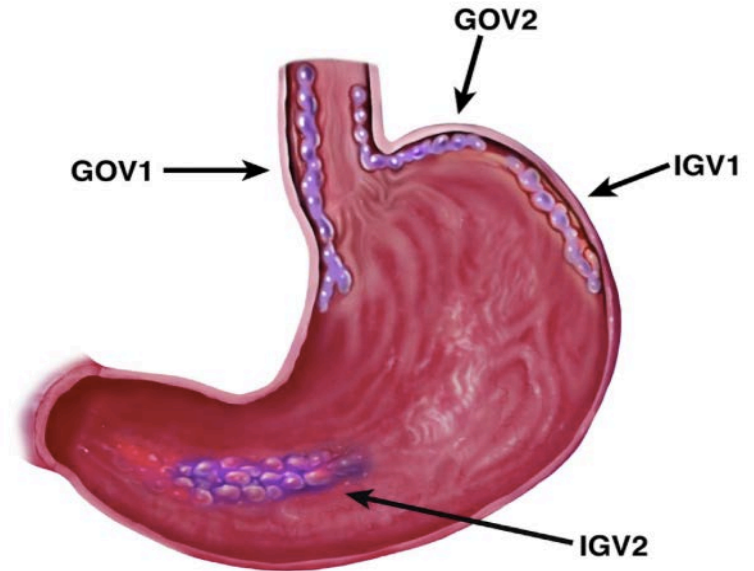
- Gastric varices (GV) are present in **20%** of patients with cirrhosis
- Bleeding from gastric varices is less common than from esophageal varices (**30%** vs **70%**)
- Associated with more severe blood loss, higher rates of re-bleeding and higher mortality (**20%**)
- Risk of bleeding from incidentally discovered gastric varices is: **16%, 36%, and 44%** at **1, 3, and 5 years**

# Classification of Gastric Varices

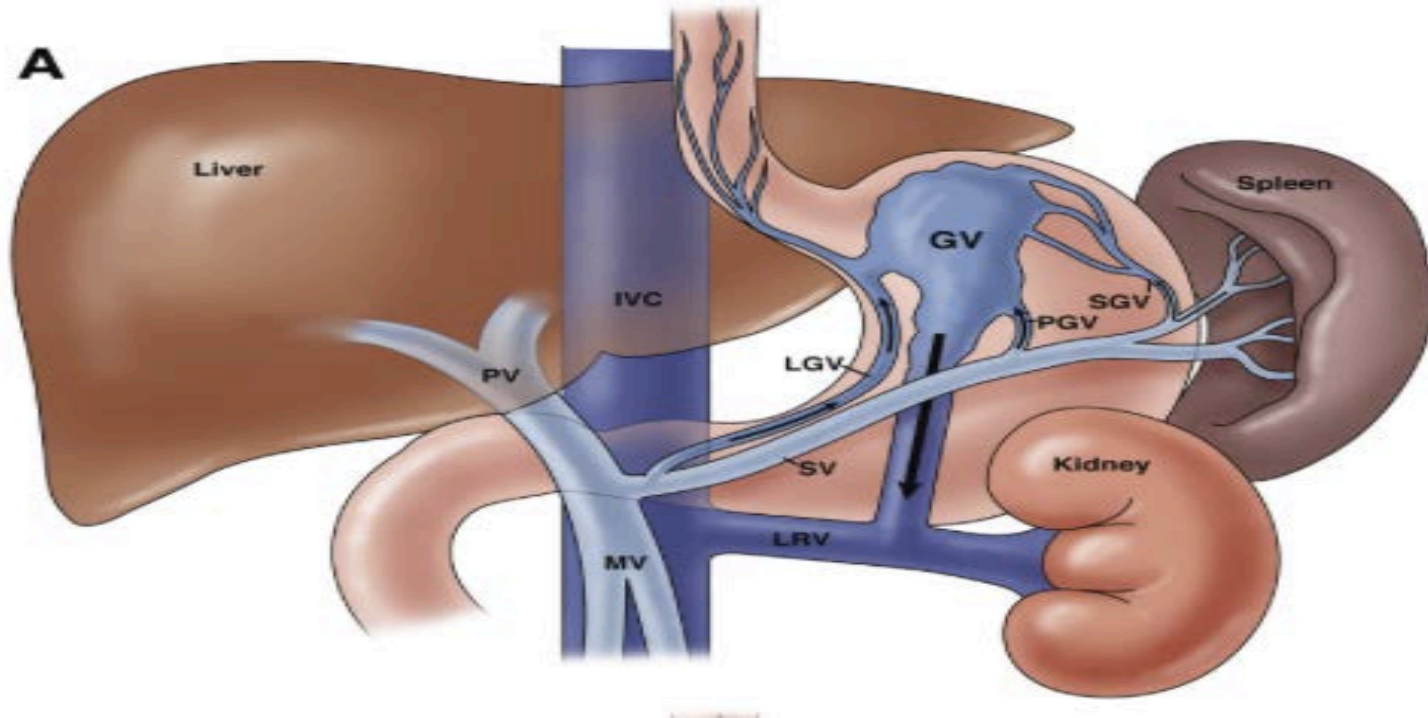
**Table 6. Classification, prevalence and risk of bleeding of gastric varices.**

Type	Definition	Relative frequency	Overall bleeding risk without treatment
GOV 1	OV extending below cardia into lesser curvature	70%	28%
GOV 2	OV extending below cardia into fundus	21%	55%
IGV 1	Isolated varices in the fundus	7%	78%
IGV 2	Isolated varices else in the stomach	2%	9%

GOV, gastro-oesophageal varices; IGV, isolated gastric varices; OV, oesophageal varices.



**Figure 1.** Sarin's classification of GV. Modified with permission from the American Gastroenterological Association (AGA) Institute Gastroslides – Cirrhosis and Portal Hypertension.





# Why do Varices Bleed?

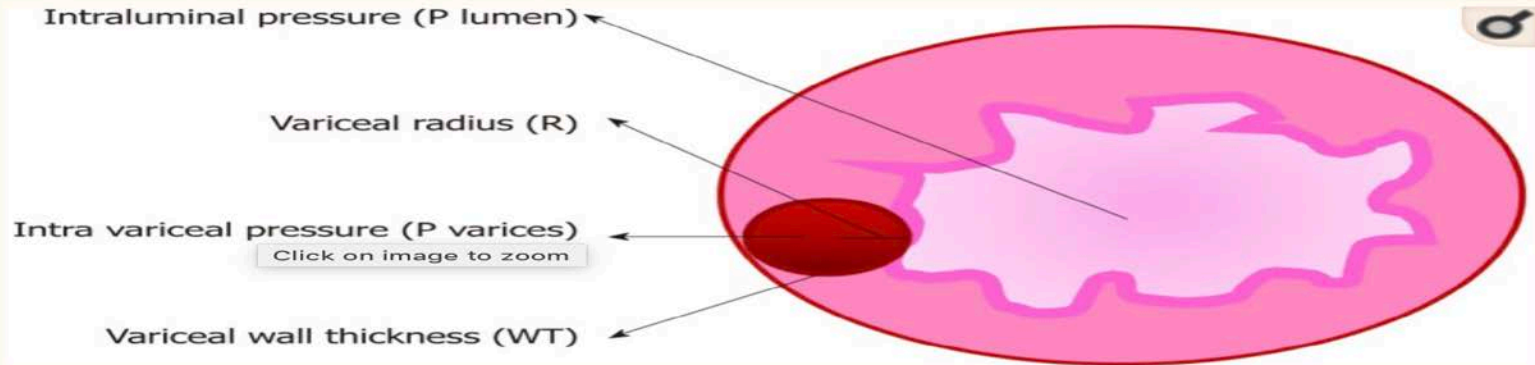


Figure 2

Mechanism of variceal bleeding. P: Pressure; R: Radius; WT: Wall thickness.

Wall tension (T) = [Transmural pressure (Pvarices-Plumen) × variceal radius (R)]/[Variceal wall thickness (WT)].

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[June 2011](#) Volume 54, Issue 6, Pages 1161–1167

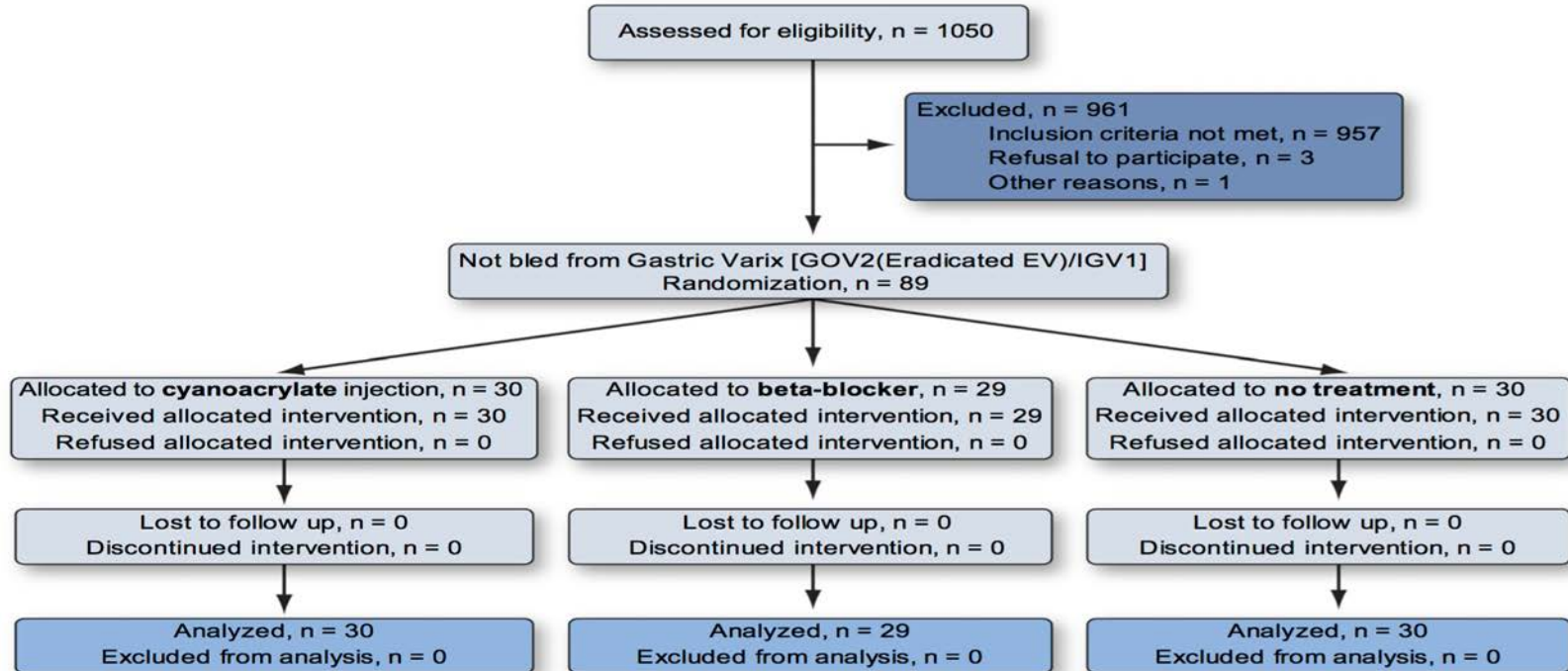
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## Primary prophylaxis of gastric variceal bleeding comparing cyanoacrylate injection and beta-blockers: A randomized controlled trial

[Smruti Ranjan Mishra](#)<sup>1</sup>, [Barjesh Chander Sharma](#)<sup>1</sup>, [Ashish Kumar](#)<sup>2</sup>, [Shiv Kumar Sarin](#)<sup>1,2,\*</sup>,  

# Primary Prophylaxis – Cyanoacrylate Glue



# Primary Prophylaxis – Cyanoacrylate Glue

**Table 1. Baseline characteristics of patients.**

Parameters	Cyanoacrylate Group I (n = 30)	Beta-blocker Group II (n = 29)	No treatment Group III (n = 30)	p value
Age (Median,range) yrs	40 (10-71)	40 (10-65)	38 (11-60)	0.850
Sex (Male:Female)	20:10	21:8	23:7	0.356
Etiology of Cirrhosis (Alcohol/cryptogenic/others)	16/9/5	14/8/7	15/9/6	0.4378
Ascites	12/30	11/30	13/30	0.870
HE (Grade I/II)	0	0	1	1
Serum Bilirubin (Median,range) mg/dl	1.8 (0.6-9.5)	2.0 (0.8-6.3)	1.8 (0.5-6.6)	0.952
Serum Albumin (Median,range) g/dl	3.2 (1.8-3.8)	3.1 (2.2-3.6)	3.2 (2.2-3.7)	0.976
INR (Median,range)	1.3 (1.1-2.1)	1.3 (1.1-2.3)	1.3 (1.2-2.1)	0.555
Platelet (Median,range)10 <sup>5</sup> /ml	1.2 (0.7-3.2)	1.0 (0.7-2.3)	1.1 (0.4-2.1)	0.372
Serum Creatinine (Median,range) mg/dl	0.6 (0.3-1.5)	0.6 (0.4-1.4)	0.7 (0.3-1.5)	0.706
Child Score (Median,range)	8 (5-12)	8 (5-12)	8 (6-12)	0.782
Child A/B/C	10/12/8	9/11/9	10/12/8	0.561
MELD Score (Median,range)	13 (7-26)	13 (7-30)	13 (8-25)	0.883
HVPG (Median,range) mmHg	14 (8-26)	14 (11-26)	14 (8-24)	0.815
Follow Up (Median,range) mo	26 (3-34)	26 (3-34)	26 (3-34)	0.989
Gastroesophageal varix type 2	26/30	25/29	25/30	0.927
Isolated gastric varix type 1	4/30	4/30	5/30	0.927
Size of GV (Median,range) mm	20 (10-35)	20 (10-30)	20 (10-30)	0.162
Portal Hypertensive Gastropathy	7/30	9/30	9/30	0.211
Color of GV (Red/Blue)	15/15	16/13	15/15	0.854
Spontaneous shunt	13/30	10/29	11/30	0.885

HE. hepatic encephalopathy; INR. international normalized ratio; MELD. model for end-stage liver disease; HVPG. hepatic venous pressure gradient.

# Primary Prophylaxis – Cyanoacrylate Glue

**Table 1** Risk of bleeding, mortality and complication rate according to treatment group[11].

Characteristics	Cyanoacrylate Group I(n = 30)	Propranolol Group II(n = 29)	No treatment Group III(n = 30)	P value
GV bleed	10%	38%	53%	0.003
Bleed-related mortality	0	10%	24%	0.034
Overall mortality	7%	17%	26%	0.113
Complications	3%	3%	7%	1

# Primary Prophylaxis – Cyanoacrylate Glue

- Predictors of high risk of first bleeding from gastric varices:
  1. Size of gastric varix >20 mm
  2. MELD score  $\geq 17$
  3. Presence of PHG
- Primary prophylaxis with gluing was recommended in patients with large and high risk gastric varices in this study

# Primary Prophylaxis – Cyanoacrylate Glue

- Cons:
  - Glue injection requires expertise, which is not always available
  - Highly skilled endoscopists who conducted the study
  - Data suggesting that carvedilol is more effective in reducing the hepatic venous pressure gradient (HVPG) may reduce the gap in efficacy between NSBB and cyanoacrylate injection
  - The number of patients with IGV1 was small (15%)
- Pro
  - Bleeding from GV does not depend only on the HVPG, but also on the wall tension and size of the varix

# Glubran 2 – The new glue

- No studies in GV bleeding
- Authorized for surgical use and endovascular radiology
- Glubran 2 is not the same as other cyanoacrylate glues
  - Co-monomer (N butyl 2 cyanoacrylate and MS (a monomer owned by GEM Srl) vs monomer)
  - Addition of MS allows for faster polymerization
  - Also has anti-inflammatory effect

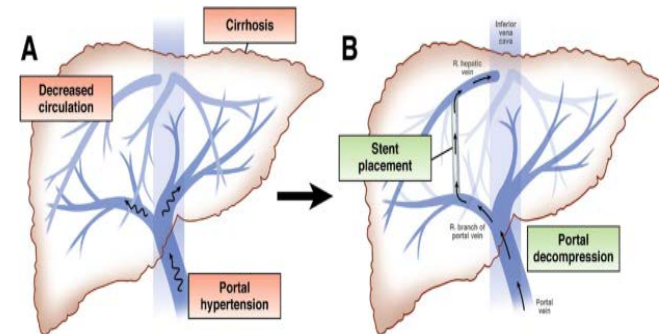


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# Primary Prophylaxis - TIPS

- Compared to EV (high portal pressures), GV have a low mean portal pressure because fundal varices drain through a natural shunt, i.e., gastroduodenal shunt
- Gastric varices travel thru the wall of the stomach, the overlying muscularis mucosa and lamina propria becomes thinner – the likely point of rupture
- TIPS may not decrease the diameter and thickness of the markedly engorged fundal varices
- TIPS may not reverse this already thin wall



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**[November 2013](#)** Volume 78, Issue 5, Pages 711–721

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## EUS-guided coil versus cyanoacrylate therapy for the treatment of gastric varices: a multicenter study (with videos)

Presented at Digestive Disease Week, May 19-22, 2012, San Diego, California (Gastrointest Endosc 2012;75:AB129).

[Rafael Romero-Castro](#), MD, PhD<sup>\*,1,\*</sup>, [Mark Ellrichmann](#), MD<sup>\*,2</sup>, [Carlos Ortiz-Moyano](#), MD, PhD<sup>3</sup>, [Jose Carlos Subtil-Inigo](#), MD, PhD<sup>4</sup>, [Felix Junquera-Florez](#), MD<sup>5</sup>, [Joan B. Gornals](#), MD<sup>6</sup>, [Alejandro Repiso-Ortega](#), MD<sup>7</sup>, [Juan Vila-Costas](#), MD, PhD<sup>8</sup>, [Francisco Marcos-Sanchez](#), MD<sup>9</sup>, [Miguel Muñoz-Navas](#), MD, PhD<sup>4</sup>, [Manuel Romero-Gomez](#), MD, Prof, PhD<sup>3</sup>, [Enric Brullet-Benedi](#), MD<sup>5</sup>, [Javier Romero-Vazquez](#), MD<sup>1</sup>, [Angel Caunedo-Alvarez](#), MD<sup>1</sup>, [Francisco Pellicer-Bautista](#), MD, PhD<sup>1</sup>, [Juan M. Herrerias-Gutierrez](#), MD, Prof, PhD<sup>1</sup>, [Annette Fritscher-Ravens](#), MD, Prof, PhD<sup>2</sup>



# Primary Prophylaxis – EUS coiling

**TABLE 1. Patient characteristics**

	CYA	Coil	Total	P value
No. of patients	19	11	30	
Age ± SD, y	60.8 ± 8.2	59.0 ± 10.0	60.6 ± 8.7	.59
Sex, M/F, no.	14/5	8/3	22/8	.64
Child-Pugh class, no.				
A	6	4	10	.55
B	6	7	13	.09
C	7	0	7	.02*
Etiology of cirrhosis/portal hypertension, no.				
Alcohol	8	2	10	.18
Viral hepatitis	7	6	13	.47
Unknown origin	3	3	6	.38
Hepatocellular carcinoma	2	1	3	.70
Nonalcoholic steatohepatitis	1	0	1	.63

CYA, Cyanoacrylates; SD, standard deviation; M, male; F, female.

\*Significant difference.

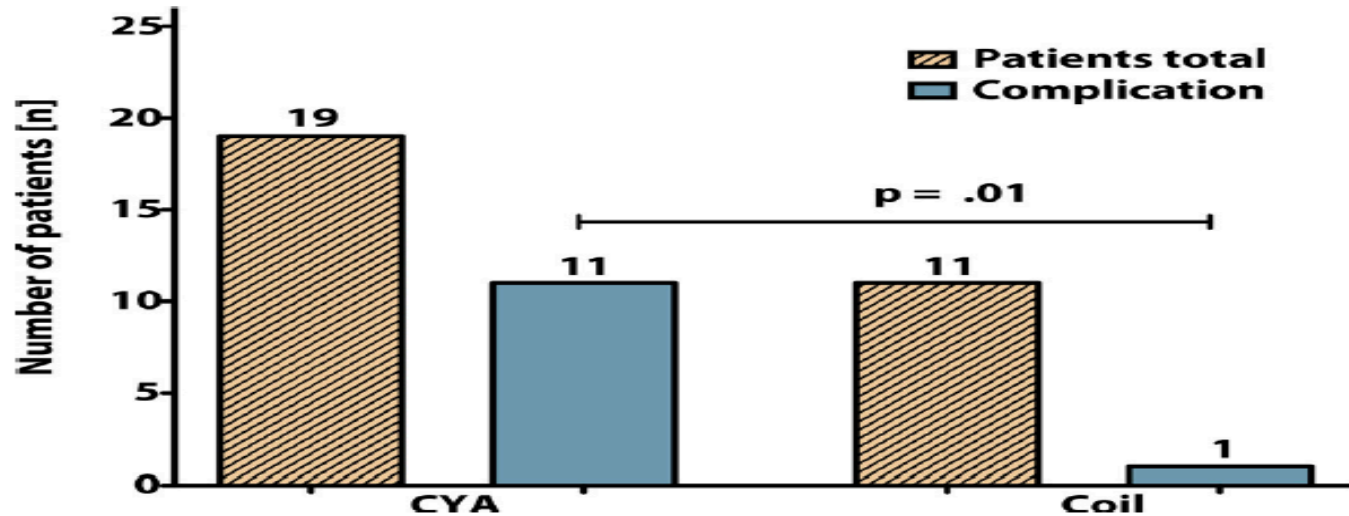
**TABLE 3. Sarin classification**

	CYA	Coil	Total	P value
Isolated gastric varices I, no.	9	6	15	.50
Gastroesophageal varices type II, no.	9	5	14	.61
Gastroesophageal varices type I, no.	1	0	1	.63
Active bleeding of previous EUS-guided therapy, no. (%)				
Yes	10	0	10 (33.3)	.003*
No	9	11	20 (66.7)	

CYA, Cyanoacrylate.

\*Significant difference.

# Primary Prophylaxis – EUS coiling



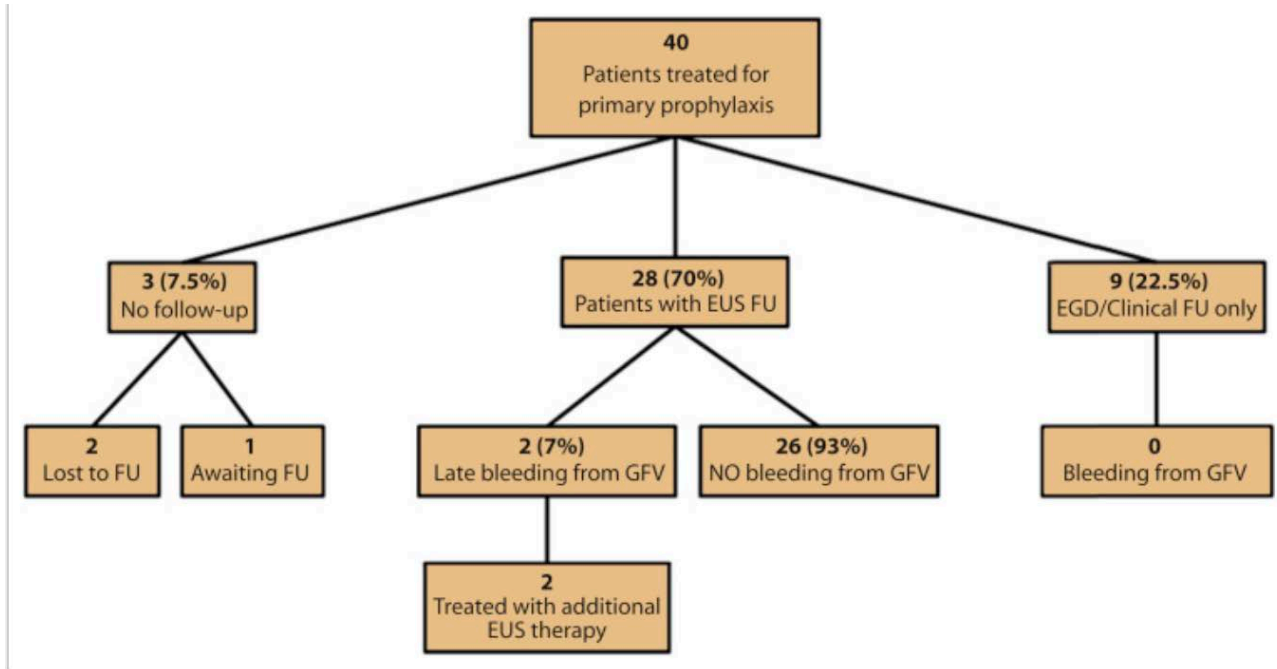
**Figure 7.** Rate of overall adverse events between the cyanoacrylate (CYA) and the coil group. Data are presented as mean  $\pm$  standard error of the mean.

## EUS-guided treatment of gastric fundal varices with combined injection of coils and cyanoacrylate glue: a large U.S. experience over 6 years (with video)

[Yasser M. Bhat](#), MD, [Frank Weilert](#), MD, [R. Todd Fredrick](#), MD, [Steven D. Kane](#), BS, [Janak N. Shah](#), MD, [Chris M. Hamerski](#), MD, [Kenneth F. Binmoeller](#), MD\* 

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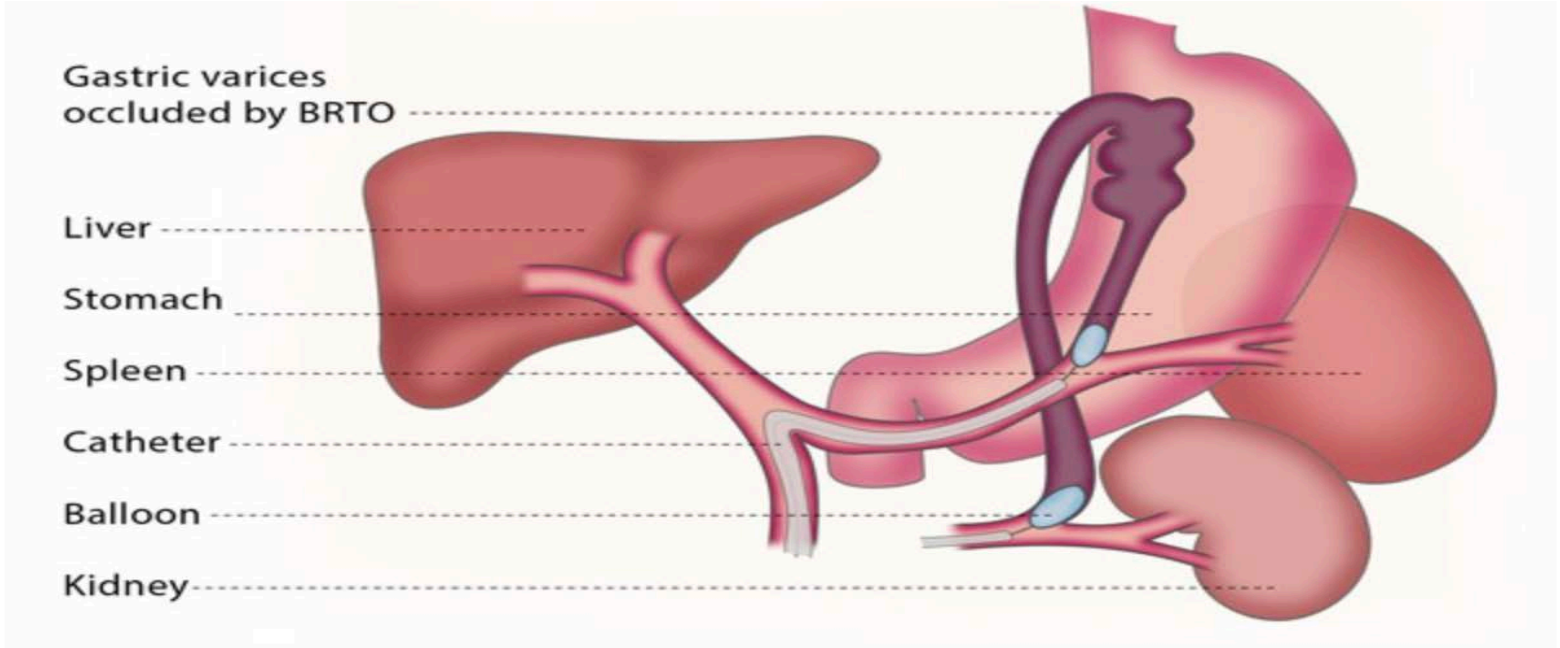
# Primary Prophylaxis – EUS coiling



# Primary Prophylaxis – BRTO

- Balloon-occluded Retrograde Transvenous Obliteration was first described in 1984
- It has been the primary endovascular treatment for bleeding gastric varices in Japan and South Korea. Also can be used to treat refractory HE
- BRTO procedure fell into disuse in the Western world due to the possibility of worsening portal HTN
- The shunt closure by BRTO has a positive counter effect increasing hepatic blood flow and improving hepatic function

# Primary Prophylaxis – BERTO





- **There are some relative contraindications to BROTO:**
- Gastric varices formed by chronic portal or splenic vein thrombosis
- Severe uncorrected coagulopathy
- Uncontrolled esophageal variceal bleeding
- Large volume intractable ascites
- The presence of hepatocellular carcinoma greater than 5 cm

# Primary Prophylaxis – BRTO

- **2 modifications of BRTO:**
- Plug-assisted retrograde transvenous obliteration (PARTO)
- Coil-assisted retrograde transvenous obliteration (CARTO)



## Clinical Gastroenterology and Hepatology

Volume 3, Issue 12, December 2005, Pages 1245-1252

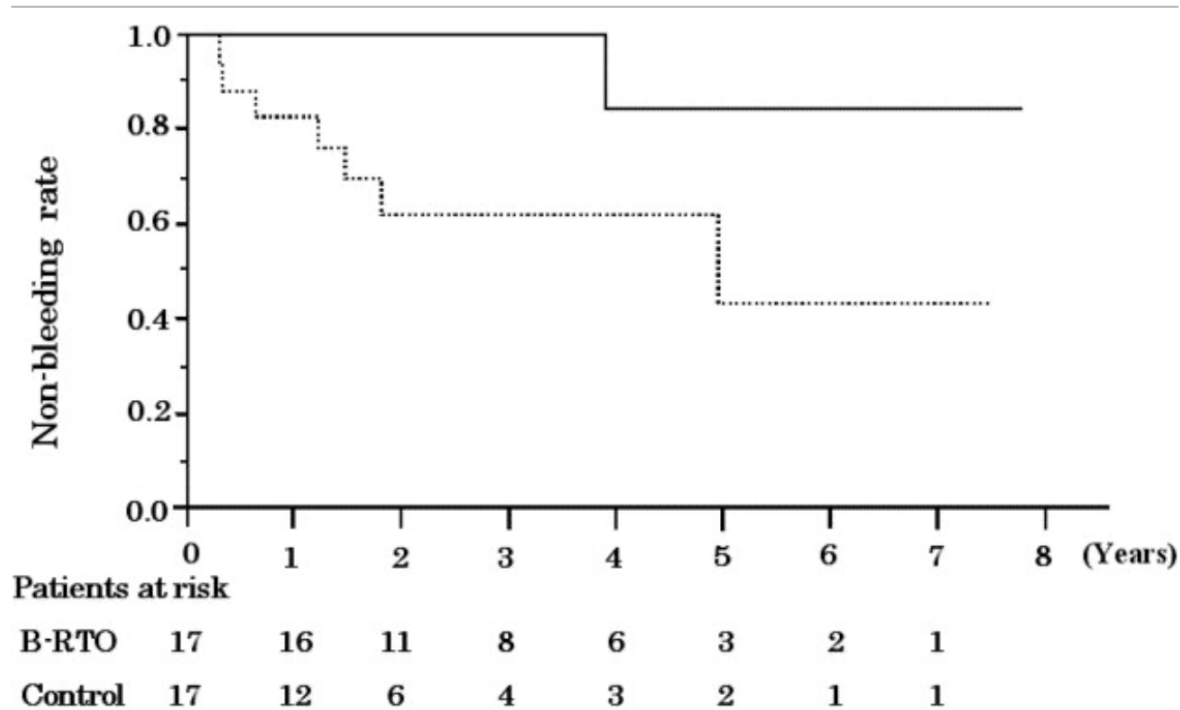


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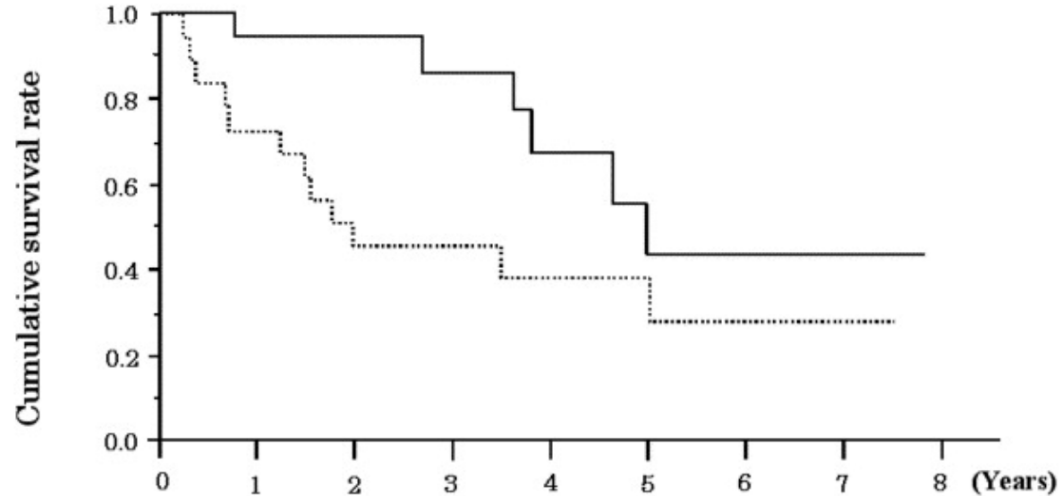
# Prophylactic Balloon-Occluded Retrograde Transvenous Obliteration for Gastric Varices in Compensated Cirrhosis

Yoshitaka Takuma \*  , Kazuhiro Nouso †, Yasuhiro Makino \*, Syunsuke Saito \*, Yasushi Shiratori 

# Primary Prophylaxis – BRT0



# Primary Prophylaxis – BRT0



**Patients at risk**

<b>B-RTO</b>	17	16	11	8	6	3	2	1
<b>Control</b>	17	12	7	5	3	2	1	1

## *Guidance statements*

- For prevention of first VH from GOV2 or IGV1, NSBBs can be used, although the data are not as strong as for EV.
- Prevention of first bleeding from GOV1 varices may follow the recommendations for EV.
- Neither TIPS nor BRTO are recommended to prevent first hemorrhage in patients with fundal varices that have not bled.

## **Recommendations**

- NSBBs are suggested for primary prevention of VH from gastro-oesophageal varices type 2 or isolated gastric varices type 1 (III;2).
- Primary prevention for gastro-oesophageal varices type 1 follow the recommendations of oesophageal varices (III;2).

#### 4. Is there a role for primary prophylaxis of gastric variceal bleeding?

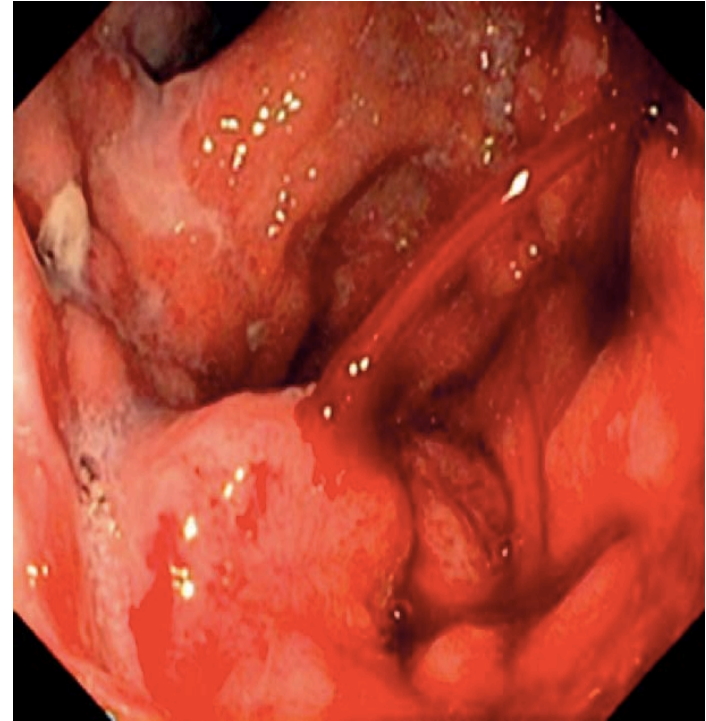
- NSBB (level 2a, grade B) can be considered in selected high-risk patients with large GOV-2 after taking into account the patient's preferences and clinical judgement.
- Cyanoacrylate injection is not recommended outside clinical trials (level 2a, grade A).

# Case 1 Conclusion

- No large scale studies to make definite treatment plan (rare event, large numbers needed, etc.)
- Beta blockers safest but...
- If expertise available and high risk patient (Child B or C/High MELD/>2cm varix) then can challenge status quo:  
BRTO>EUS>Glue>TIPS with embolization

## Case 2

- What do you do?
  - A) Endoscopic band ligation
  - B) Cyanoacrylate glue
  - C) Hemospray
  - D) Code blue + Linton/Blakemore/Minnesota tube
  - E) BRTO





# Endoscopic Band Ligation

- Two studies with 49 patients treated with EBL showed a hemostasis rate of 89-100%, however re-bleeding rates were 20%
- Works very well for esophageal varices
- Can be only used in very small gastric varix in which both mucosal and contralateral wall can be suctioned in the ligator. Otherwise very high risk of band falling off and massive bleeding due post-band ulceration
- EBL could still be a useful treatment option but...

## HEPATOLOGY



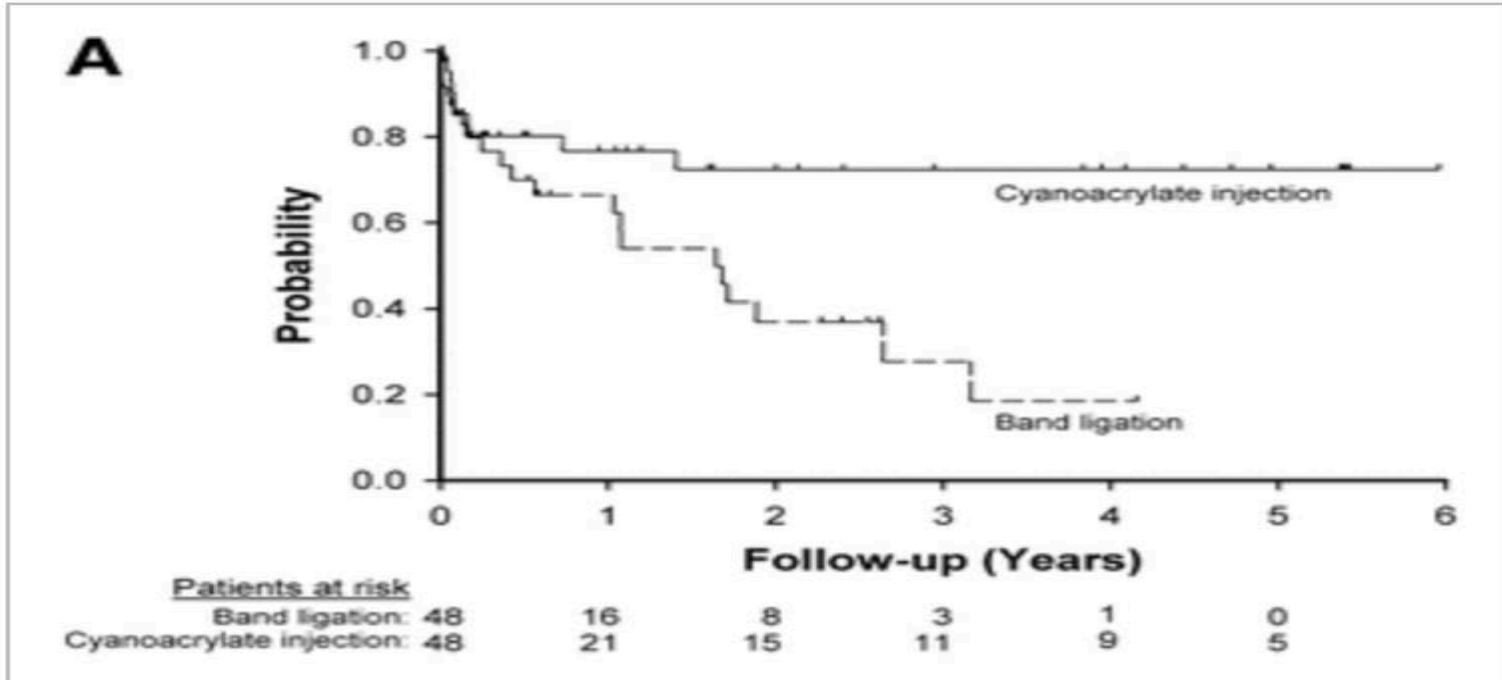
Liver Failure and Liver Disease |  [Free Access](#) |

## A randomized trial of endoscopic treatment of acute gastric variceal hemorrhage: N-Butyl-2-Cyanoacrylate injection versus band ligation<sup>†‡</sup>

Pen-Chung Tan, Ming-Chih Hou , Han-Chieh Lin, Tsu-Te Liu, Fa-Yauh Lee ... [See all authors](#) 

First published: 23 March 2006 | <https://doi.org/10.1002/hep.21145> | Citations: 173

# Cyanoacrylate glue



[Medicine \(Baltimore\)](#). 2015 Oct; 94(41): e1725.

PMCID: PMC4616775

Published online 2015 Oct 16. doi: [10.1097/MD.0000000000001725](https://doi.org/10.1097/MD.0000000000001725)

PMID: [26469912](https://pubmed.ncbi.nlm.nih.gov/26469912/)

## Cyanoacrylate Injection Versus Band Ligation in the Endoscopic Management of Acute Gastric Variceal Bleeding Meta-Analysis of Randomized, Controlled Studies Based on the PRISMA Statement

[Weiguang Qiao](#), MD, [Yutang Ren](#), MD, [Yang Bai](#), MD, [Side Liu](#), MD, [Qiang Zhang](#), MD, and [Fachao Zhi](#), MD

[Gut](#). 2019 May; 68(5): 844–853.

PMCID: PMC6580783

Published online 2018 May 5. doi: [10.1136/gutjnl-2017-314653](https://doi.org/10.1136/gutjnl-2017-314653)

PMID: [29730601](https://pubmed.ncbi.nlm.nih.gov/29730601/)

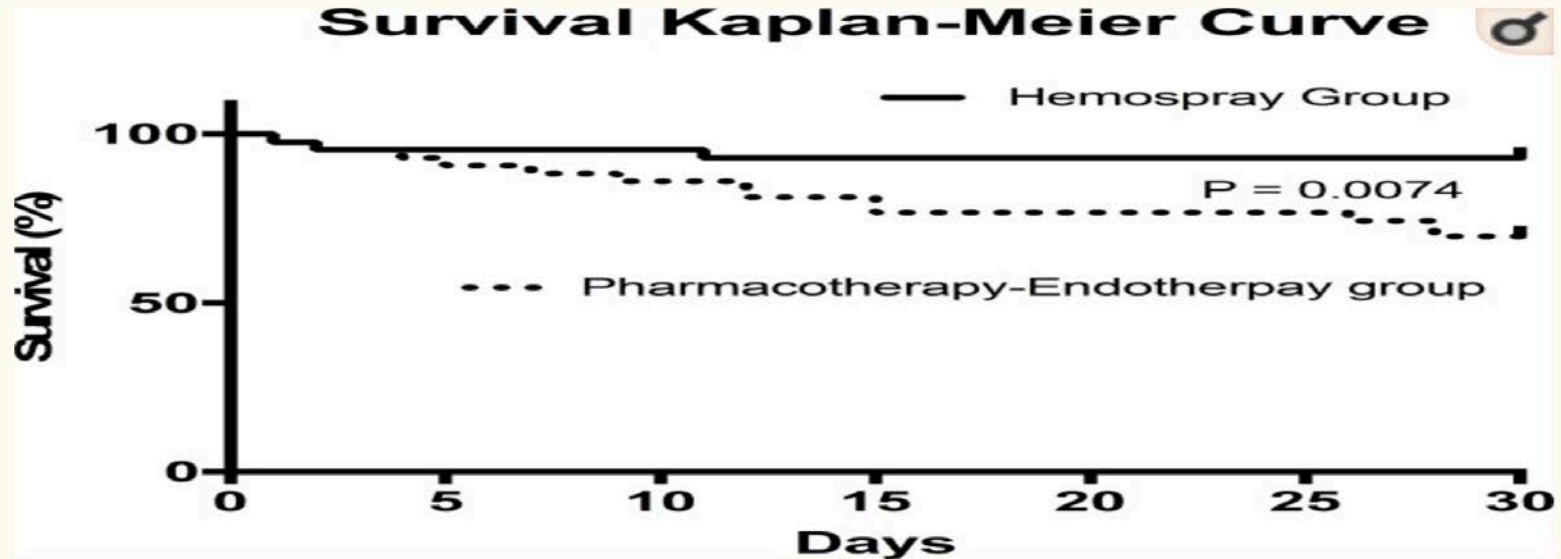
Original article

## Early application of haemostatic powder added to standard management for oesophagogastric variceal bleeding: a randomised trial

[Mostafa Ibrahim](#),<sup>1,2</sup> [Ahmed El-Mikkawy](#),<sup>2</sup> [Mohamed Abdel Hamid](#),<sup>2</sup> [Haitham Abdalla](#),<sup>2</sup> [Arnaud Lemmers](#),<sup>1</sup>  
[Ibrahim Mostafa](#),<sup>2</sup> and [Jacques Devière](#)<sup>1</sup>

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# Rescue Therapies - Hemospray



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Figure 3

[Gastroenterology](#), 1998 May;114(5):981-7.

## "Salvage" transjugular intrahepatic portosystemic shunts: gastric fundal compared with esophageal variceal bleeding.

[Chau TN](#)<sup>1</sup>, [Patch D](#), [Chan YW](#), [Nagral A](#), [Dick R](#), [Burroughs AK](#).

### [+ Author information](#)

#### Abstract

**BACKGROUND & AIMS:** The optimal emergency treatment for gastric fundal variceal bleeding is still unclear. In this study, the efficacy of transjugular intrahepatic portosystemic stent/shunt (TIPS) in patients with uncontrolled gastric fundal vs. esophageal variceal bleeding was compared.

**METHODS:** One hundred twelve consecutive patients with uncontrolled variceal bleeding required emergency TIPS, 84 with esophageal varices (EV group) unresponsive to endoscopic and vasoconstrictor therapy and 28 with gastric fundal varices (GV group) unresponsive to vasoconstrictor therapy. Clinical and biochemical data were retrieved, and the two groups were compared.

**RESULTS:** Variceal bleeding was controlled in all patients after TIPS except for 1 in each group. There were no significant differences between the two groups in terms of markers of disease severity, severity of bleeding, or portal hemodynamics. During a median follow-up period of 7 months, 20 in the EV group (24%) and 8 in the GV group (29%) developed clinical rebleeding. Most early rebleeding (within 7 days after TIPS) was related to esophageal ulceration secondary to previous sclerotherapy. Rates of mortality were similar in both groups.

**CONCLUSIONS:** These results suggest that emergency TIPS is equally effective in the immediate short-term control of gastric fundal variceal bleeding compared with esophageal variceal bleeding.

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**November 2009** Volume 70, Issue 5, Pages 881-887

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## Endoscopic cyanoacrylate versus transjugular intrahepatic portosystemic shunt for gastric variceal bleeding: a single-center U.S. analysis

[Nicholas J. Procaccini](#), MD, JD, MS , [Abdullah M.S. Al-Osaimi](#), MD, [Patrick Northup](#), MD, MS, [Stephen H. Caldwell](#), MD

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Published online 2015 Feb 2. doi: [10.1093/gastro/gou095](https://doi.org/10.1093/gastro/gou095)

Comparative study of endoscopy vs. transjugular intrahepatic portosystemic shunt in the management of gastric variceal bleeding  
[Gursimran Singh Kochhar](#),<sup>1</sup> [Udayakumar Navaneethan](#),<sup>1</sup> [Jason Hartman](#),<sup>2</sup> [Jose Mari Parungao](#),<sup>1</sup> [Rocio Lopez](#),<sup>1</sup>  
[Ranjan Gupta](#),<sup>1</sup> [Baljendra Kapoor](#),<sup>3</sup> [Paresh Mehta](#),<sup>1</sup> and [Madhu Sanaka](#),<sup>1</sup>

PMCID: PMC4324874  
PMID: [25673803](https://pubmed.ncbi.nlm.nih.gov/25673803/)



# Rescue Therapies - TIPS

- Both studies noted that patients treated with glue had significantly less long-term morbidity than the TIPS patients along with re-bleeding and recurrent hospitalizations but there was no difference in mortality
- Same limitations apply to previous

META ANALYSIS AND SYSTEMATIC REVIEW

## **Balloon-occluded retrograde transvenous obliteration versus transjugular intrahepatic portosystemic shunt for treatment of gastric varices due to portal hypertension: A meta-analysis**

Yun-Bing Wang,<sup>\*,†</sup> Jian-Ying Zhang,<sup>‡</sup> Jian-Ping Gong,<sup>†</sup> Fan Zhang<sup>§</sup> and Yong Zhao<sup>§</sup>

\*Graduate School, Chongqing Medical University, <sup>†</sup>Department of Hepatobiliary Surgery, The Second Affiliated Hospital of Chongqing Medical University, <sup>‡</sup>Department of Radiology, The Second Affiliated Hospital of Chongqing Medical University, and <sup>§</sup>School of Public Health and Management, Chongqing Medical University, Chongqing, China

# Rescue Therapies - BRTO

- Meta-analysis of 5 comparison studies ( $n = 210$  in BRTO versus  $n = 143$  in TIPS) showed no differences between BRTO and TIPS in terms of technical success, immediate hemostasis, and postprocedure complications
- BRTO has advantages over TIPS regarding incidence of rebleeding (OR, 0.27; 95% CI: 0.09–0.81;  $p = 0.02$ ) and encephalopathy (OR, 0.05; 95% CI: 0.02–0.13,  $P < 0.001$ )
- Complications reflective of increased portal hypertension following BRTO include: Ascites, Hydrothorax, Splenomegaly, PHG, and development of EV (33%)

## *Guidance statements*

- Patients with acute bleeding from GV should be initially managed in a similar fashion to those bleeding from EV (using a restrictive transfusion policy, vasoactive drug infusion, and antibiotic prophylaxis).
- In patients bleeding from GOV1 varices, either EVL (if technically feasible) or cyanoacrylate glue injection, if available, are the recommended endoscopic treatments.
- TIPS is the treatment of choice in the control of bleeding from cardiofundal varices (GOV2 or IGV1).
- Cyanoacrylate glue injection is an option for cases in which TIPS is not technically feasible, but it is not approved for treatment of GV in the United States and should be performed only in centers where the expertise is available.

- Acute gastric VH should be treated medically, like oesophageal VH (I;1). Cyanoacrylate is the recommended endoscopic haemostatic treatment for cardiofundal varices (gastro-oesophageal varices type 2 or isolated gastric varices type 1) (I;2).
- TIPS with potential embolisation efficiently controls bleeding and prevents rebleeding in fundal VH (gastro-oesophageal varices type 2 or isolated gastric varices type 1) and should be considered in appropriate candidates (II-2;1).
- Selective embolisation (BRTO/BATO) may also be used to treat bleeding from fundal varices associated with large gastro/splenorenal collaterals, although more data is required (III;2).

## Case 2 Conclusion

- Cyanoacrylate glue is the treatment of choice for bleeding gastric varices
- However, if not able to use cyanoacrylate glue, rescue with EBL, Hemospray or Linton/Blakemore/Minnesota tube acceptable with plan for BRTO>TIPS with embolization

- There is little literature regarding management of GV compared with the abundant quantity published on EV
- Probably, cyanoacrylate injection has a role in primary prophylaxis, but NSBB in primary prophylaxis is less invasive and easily accessible. Can consider BRTO if expertise available
- In bleeding fundal varices (*i.e.*, GOV2 and IGV1) management with cyanoacrylate injections is the preferred option leaving BRTO (>TIPS) as rescue therapy once patient stabilized
- There is still a wide area for research in GV therapy