

MÁSTER EN HEPATOLOGÍA



“Endoscopia en la cirrosis: tratamiento de las varices fúndicas y la gastropatía de la hipertensión portal”.

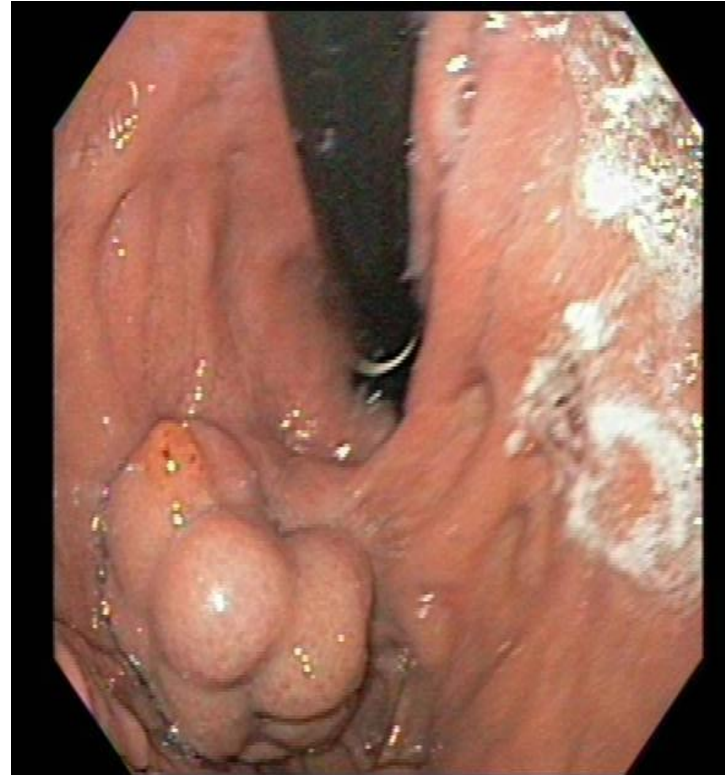
Andrés Cárdenas

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Gastric Varices

- Present in 5-30% of patients with cirrhosis
- Account for 10-15% of variceal bleeding episodes
- Risk factors: location, size, Child class, presence of red spots, HCC
- Bleed less but more severe
- Therapy can be challenging



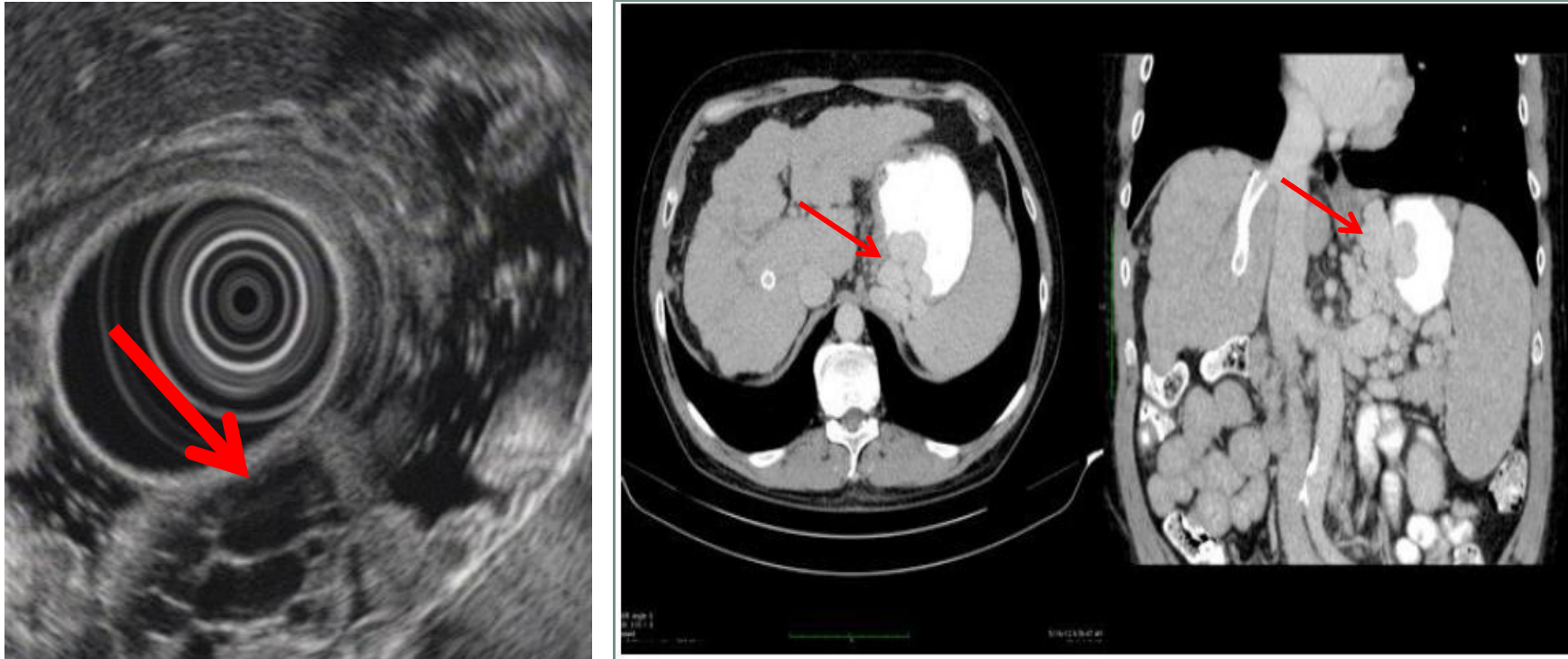
Tripathi D, Aliment Pharmacol Ther. 2006

Irani S, J Clin Gastroenterol, 2011

Bazarbashi AN, Ryou M. Curr Opin Gastroenterol. 2019

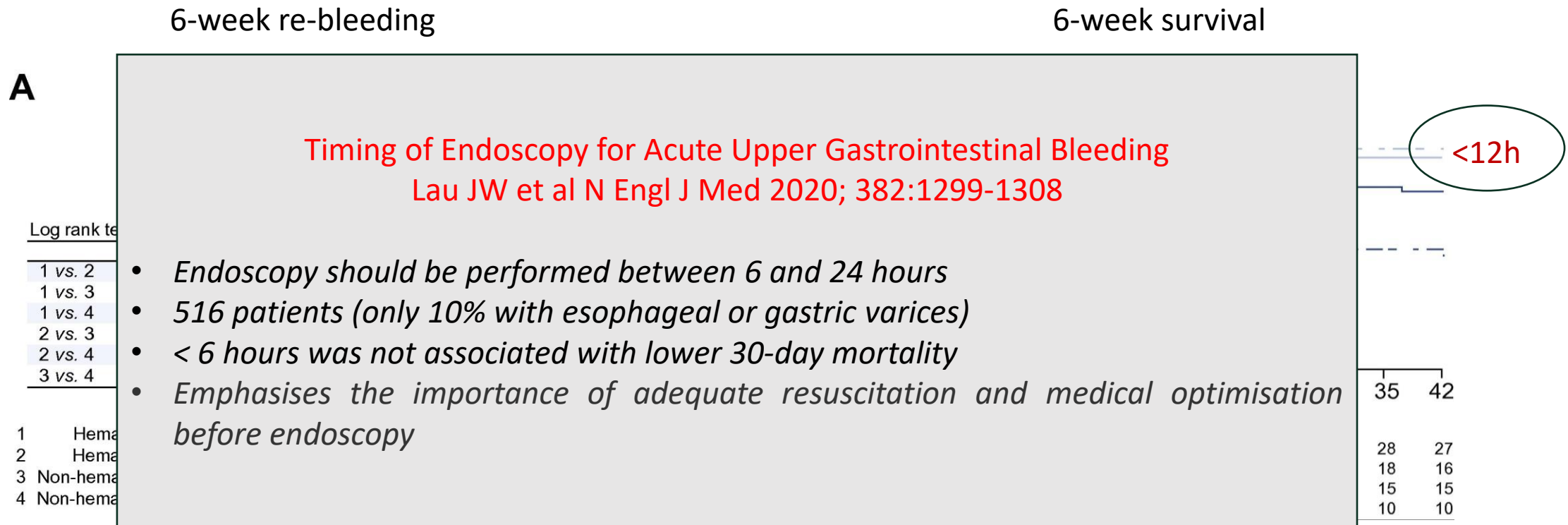
Diagnosis

- Diagnosis: endoscopy, CT scan or EUS
- Maybe difficult to detect by endoscopy in some cases (small and isolated).
- Endoscopic ultrasound may help confirm diagnosis and direct therapy

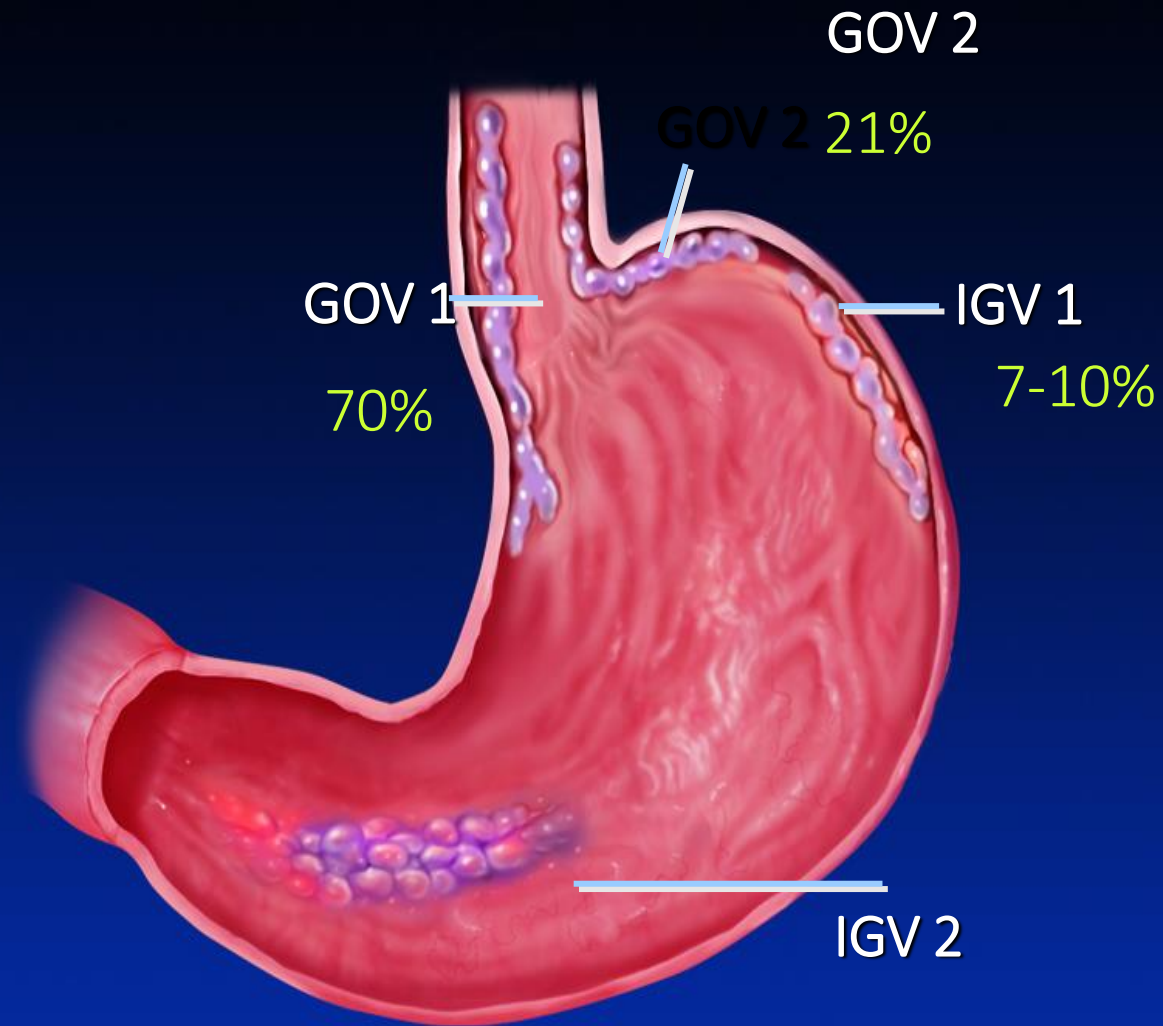


*Romero- Castro, GIE 2007,2014
Binmoeller , Endoscopy 2011*

6-week re-bleeding and survival stratified by hematemesis and door-to-endoscopy time (hrs).



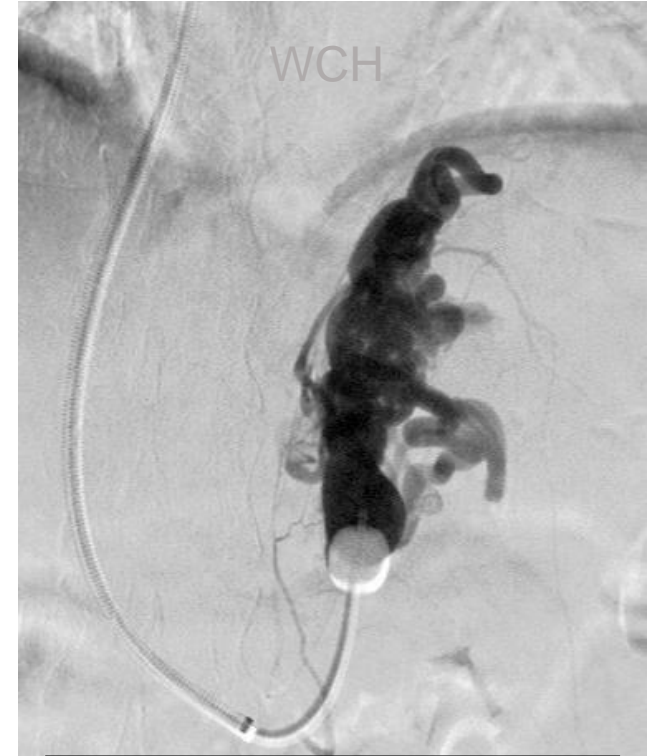
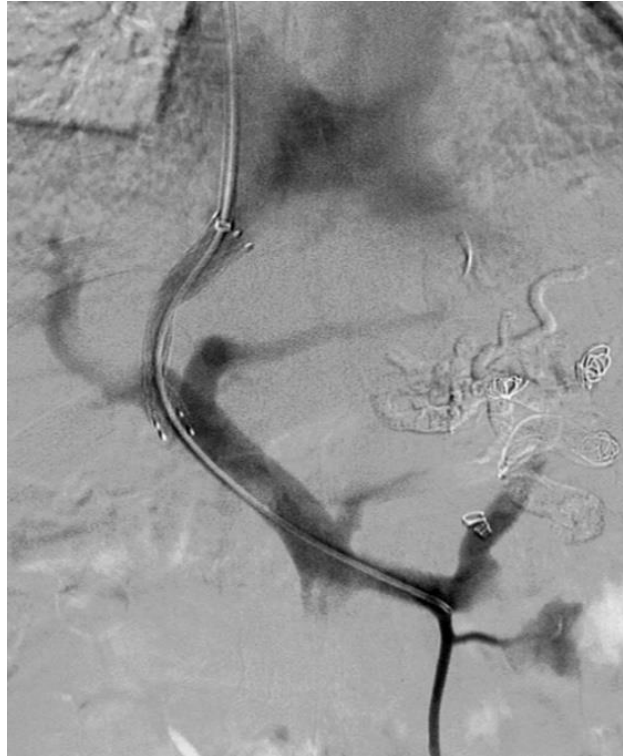
Classification of Gastric Varices



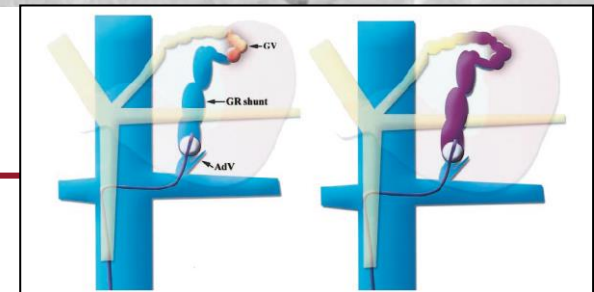
GOV1 (some GOV2) can be treated in the same way as esophageal varices

Sarin et al, Am J Gastro 1989; 84:1244

Treatment Options GV bleeding



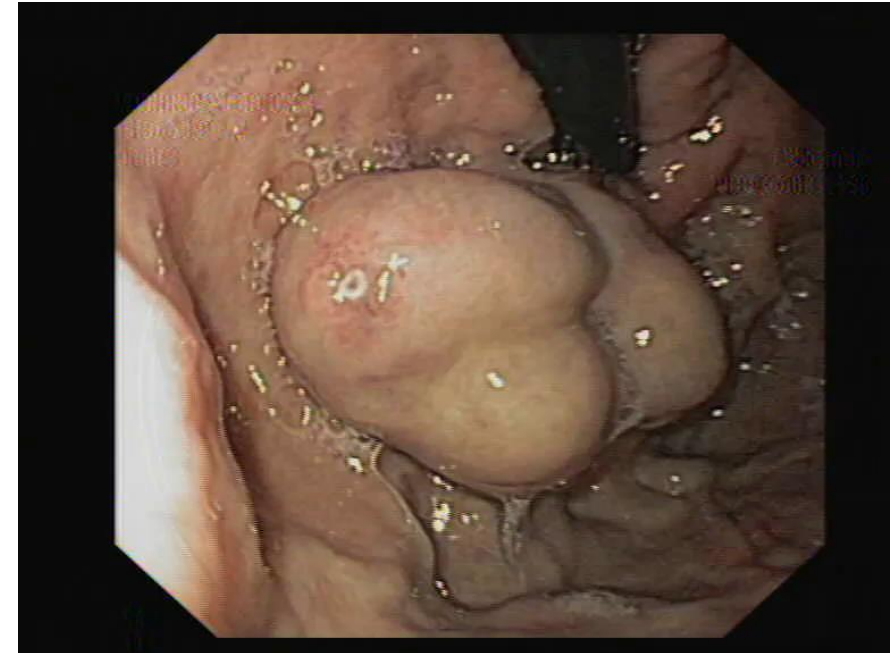
Treatment options of GV



Treatment of acute GV bleeding

Endoscopy – first choice

- Cyanoacrylate injection (free hand):
 - 90-98% control of bleeding
- Thrombin injection:
 - 92-100% control of bleeding
- EUS – Guided glue +/- coils
 - Promising, rates similar to endo-glue therapy
- BRTO & TIPS:
 - 95% control of bleeding



*Rios-Castellanos. Cochrane Database Syst Rev. 2015 May 12;(5):CD010180.
Bhurwal A et al. Dig Dis Sci. 2021 Mar 17. doi: 10.1007/s10620-021-06915-5.
Lo GH et al Endoscopy. 2020 Jul;52(7):548-555.
Mohan BP et al . Endoscopy. 2020 Apr;52(4):259-267
Sallout D. Frontline Gastroenterol. 2022 Jun 17;13(6):535-542.
Luo X, Hernández-Gea V. Liver Int. 2022 Jun;42(6):1250-1258.*

Cyanoacrylate

• A variety of cyanoacrylate - they are not the same.

	 <p>n-Butyl-2 cyanoacrylate</p>		 <p>2-Octyl cyanoacrylate</p>
Trade name	Histoacryl, Indermil, Glueon, Liquiband, Skin Link		DermaBond, SurgiSeal
Setting time	Fast		Slower

References on straight glue injection: Mishra S, Sarin SK et al. Gut 2010; 59:729-35.
 Mishra, Sarin et al. J of Hepatology (2011); 54: 1161-1167
 Sarin -- Personal communication 1/2012
 Reddy -- Personal communication 1/2012

Cyanoacrylate

- Rapidly undergoes polymerization upon contact with any type of tissue.
- Hardens into a solid mass within the varix
- Occludes flow
- Varix hardens after injection
- *Europe / Asia: N-butyl 2 cyanoacrylate (Histoacryl / Glubran)*
- *USA: 2-octyl cyanoacrylate (Dermabond)*



Cyanoacrylate / Histoacryl®

- Used with / without lipiodol
- Mix 0.5 ml : 0.5 ml (prepare 3-4 ml)
- Use distilled water
- Limit 1 ml per injection
- Use 5 ml luer-lock syringes
- Gloves and eye protection for preparation



1. Prime Sclero needle (21 gauge) with distilled water, and coat tip needle and gastroscope with lipiodol.



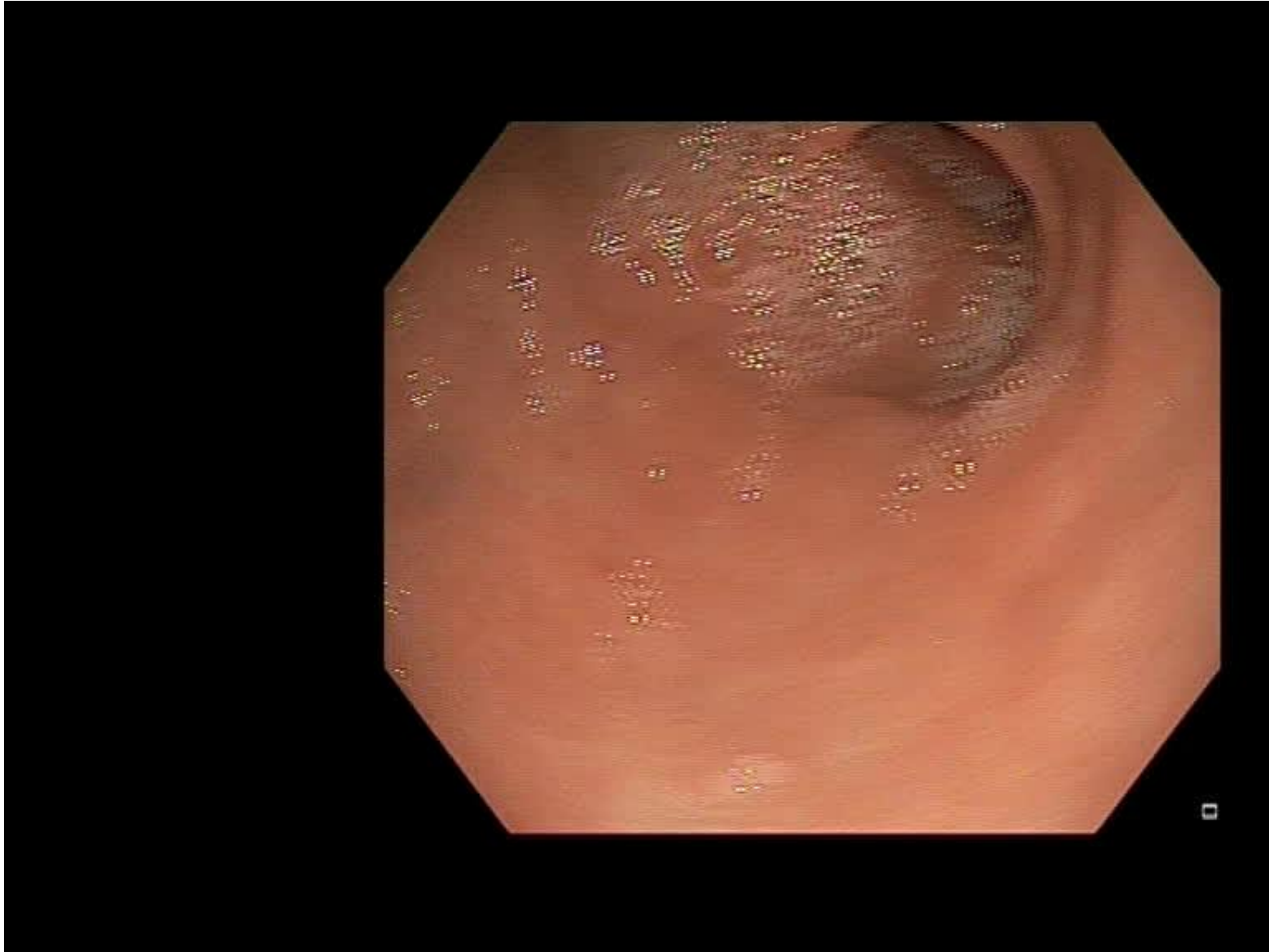
2. Prime the mix [lipiodol/cyanoacrylate] into needle / aprox 1ml



3. Puncture varix and push the mix with distilled water.



4. Repeat as needed finally flush needle with water. Limit injection to 1 or 2 ml per site.



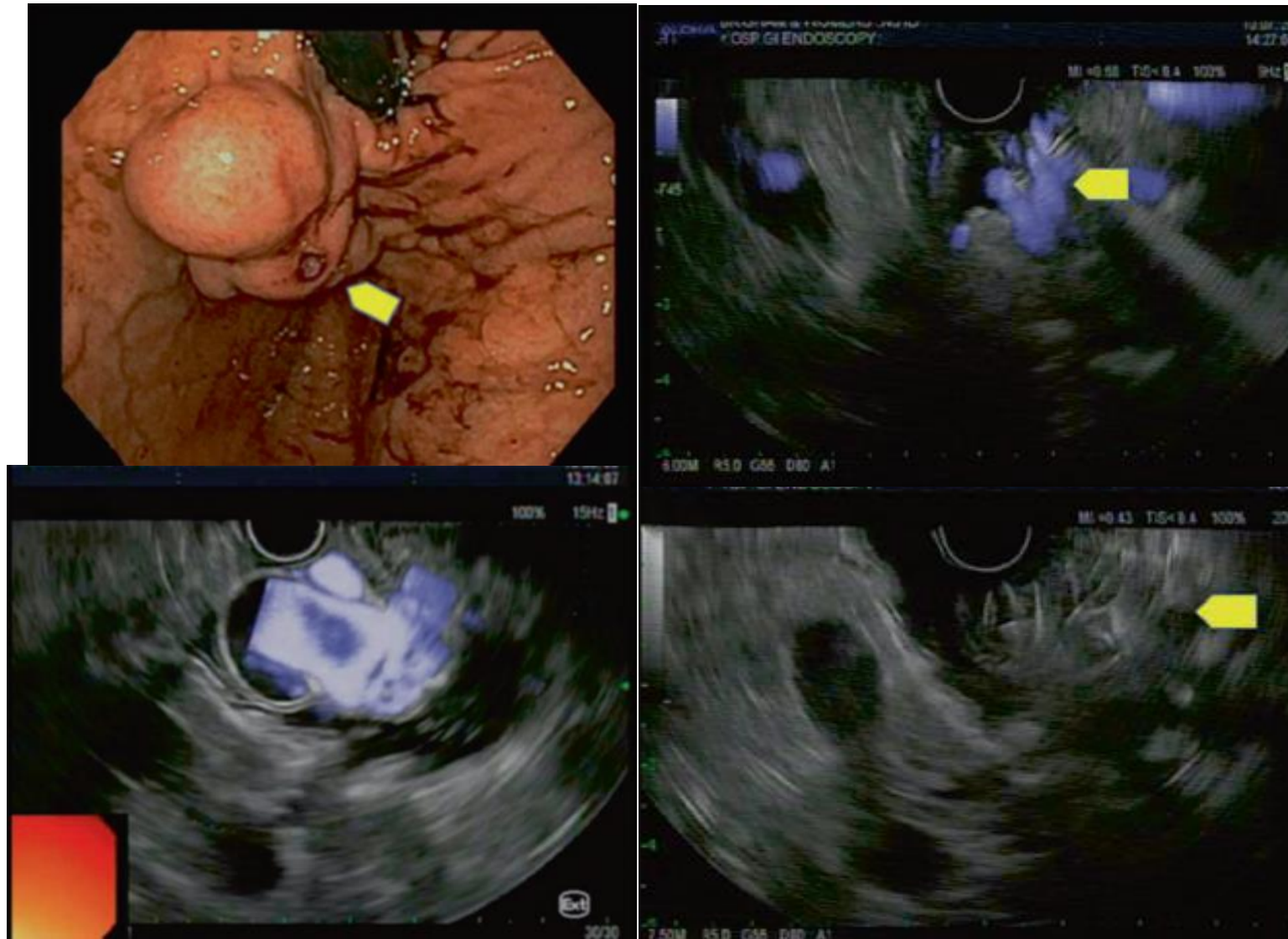
Studies (last 15 yrs) evaluating endoscopic cyanoacrylate injection for acute gastric (cardiofundal) variceal (GOV2, IGV1) hemorrhage

Author	N	Hemostasis (%)	Rebleeding (%)	Mortality (%)
Lo GH 2020	35	97.1%	5.7	2.9
Chandra 2018	57	100%	3.5	NA
Singh 2016	30	100%	6.7	none
Mc				
Ka				
Ra				
Hc				
Seewald 2008	131	100	11.1	6.1
Belletrutti 2008	34	94	12	18
Fry 2008	33	88	15	18
Marques 2008	48	87	20.5	NA
Cheng 2007	635	95	8.0	7

Guidelines recommend endoscopic cyanoacrylate injection for acute gastric (cardiofundal) variceal (GOV2, IGV1) hemorrhage.

1. Henry Z. AGA Clinical Practice Update on Management of Bleeding Gastric Varices: Expert Review. *Clin Gastroenterol Hepatol.* 2021 Jun;19(6):1098-1107.e1.
2. Baveno VII. *J Hepatol.* 2022 Apr;76(4):959-974. doi: 10.1016/j.jhep.2021.12.022
3. European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy.* 2022 Sep 29. doi: 10.1055/a-1939-4887

Endoscopic Ultrasound (EUS)-Guided Injection (Glue and coils)



Efficacy and safety of endoscopic ultrasound-guided therapy versus direct endoscopic glue injection therapy for gastric varices: systematic review and meta-analysis

23 studies (851 patients) evaluating EUS-guided therapy were included

► Table 1 Pooled results of outcomes.

Intervention/comparators, pooled % (95%CI, P)	EUS-guided therapy	EUS-guided therapy	EUS-guided therapy	EUS-guided therapy	END-glue (comparator group)
Treatment efficacy					91.4 (82.8–95.9, 97) 28 cohorts; P=0.4
Obliteration of varices					62.6 (42.6–79.1, 97); 13 cohorts; P=0.02
Recurrence of gastric varices	5.1 (3.2–13.7, 32) 16 cohorts	15 (0.8–24.5, 6) 5 cohorts	N/C	5.2 (2.6–9.6, 6) 6 cohorts; P=0.01	18 (11.4–27.2, 89) 8 cohorts; P=0.06
Early rebleeding	7 (4.6–10.7, 0) 20 cohorts	6 (3.1–11.1, 0) 8 cohorts	N/C	7.7 (3.9–14.9, 46) 7 cohorts	5 (3.3–7.4, 72) 23 cohorts; P=0.7
Late rebleeding	11.6 (8.8–15.1, 22) 26 cohorts	16.3 (9.7–26.1, 65) 8 cohorts	16.8 (7.3–34.1, 0) 3 cohorts	9.2 (6.4–13, 0) 12 cohorts	17 (12.3–22.9, 92) 27 cohorts; P=0.1

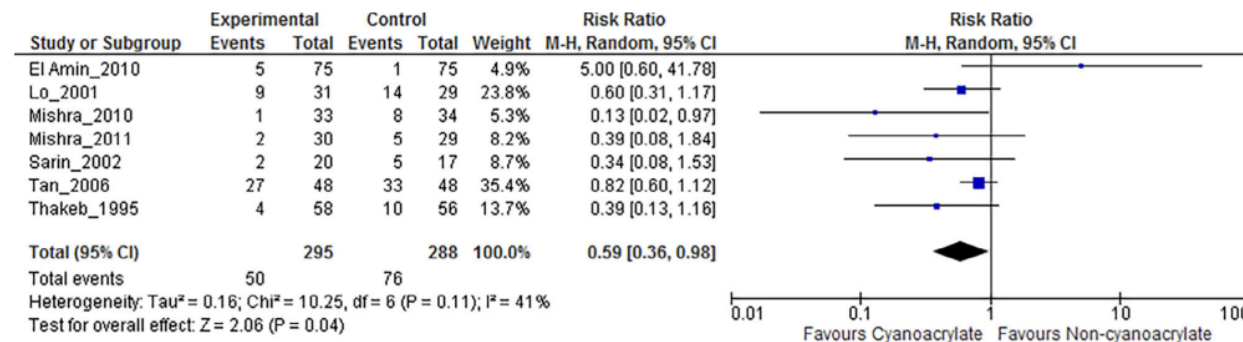
EUS-guided management of bleeding gastric varices combining injection of coils and cyanoacrylate may be used in centers with expertise and familiarity with this technique

Safety and efficacy of endoscopic cyanoacrylate injection in the management of gastric varices: A systematic review and meta-analysis

Seven RCT (six for secondary prophylaxis and one for primary prophylaxis)

Studies	Primary endpoint	Comparison	Characteristic of studied patients		
			Type of GOV (n)	Etiology of PTN	Duration of follow up
Mishra (2011)	Primary prophylaxis	Propranolol	GOV2 (51) IGV1 (8)	Cirrhosis	26 months (3–34)
Lo (2001)	Secondary prophylaxis	Band ligation	GOV1 (37) GOV2 (13) IGV1 (5)	Cirrhosis	14 months (GVO) 9 months (GVL)
Tan (2006)	Secondary prophylaxis	Band ligation	GOV1 (53) GOV2 (25) IGV1 (19)	Cirrhosis	610 ± 603.04 days (GVL) 680.67 ± 710.54 days (GVO)
El Amin (2010)	Secondary prophylaxis	Band ligation	GOV1 (150)	Cirrhosis and non-cirrhotic	6 months
Mishra (2010)	Secondary prophylaxis	Propranolol	GOV2 (54) IGV1 (10)	Cirrhosis	26 months (3–34)
Thakeb (1995)	Secondary prophylaxis	Ethanolamine	GOV1 (14) GOV2 (10) IGV1 (3)	Cirrhosis	1 year
Sarin (2002)	Secondary prophylaxis	Alcohol	GOV2 (28) IGV1 (9)	Cirrhosis and non-cirrhotic	15.4 ± 3.7 months

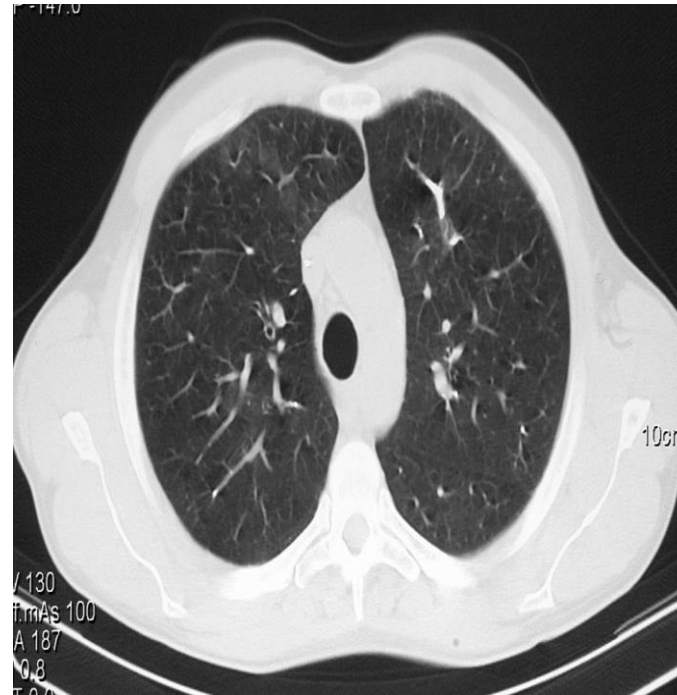
GOV, gastroesophageal varices; GVL, gastric varices ligation; GVO, gastric varices obliteration; IGV, isolated gastric varices; n/a, not available; PTN, portal hypertension.



Mortality between the cyanoacrylate injection and non-cyanoacrylate therapy

Complications

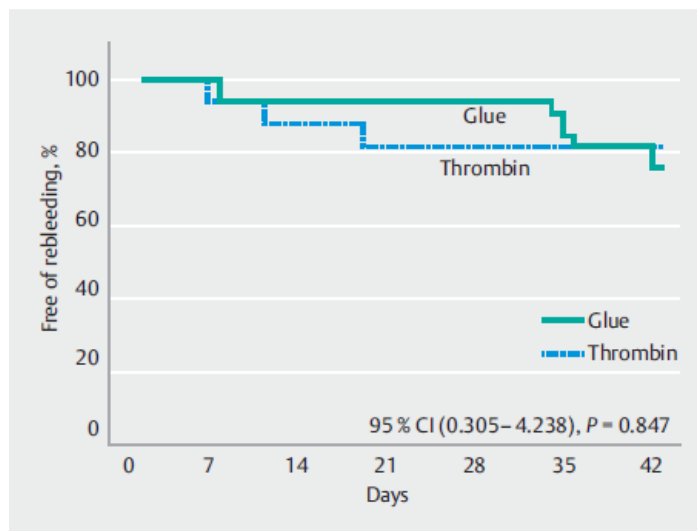
- Retrospective analysis in 753 patients
- Total rate (51/753) 6.7%
- Ulcer and bleeding 4.4%
- Sepsis (1.3%)
- 5 distant embolisms (0.7%)
 - 1 pulmonary, 1 brain, and 3 splenic
- Mesenteric /portal vein embolism
- Stroke
- Splenic infarction



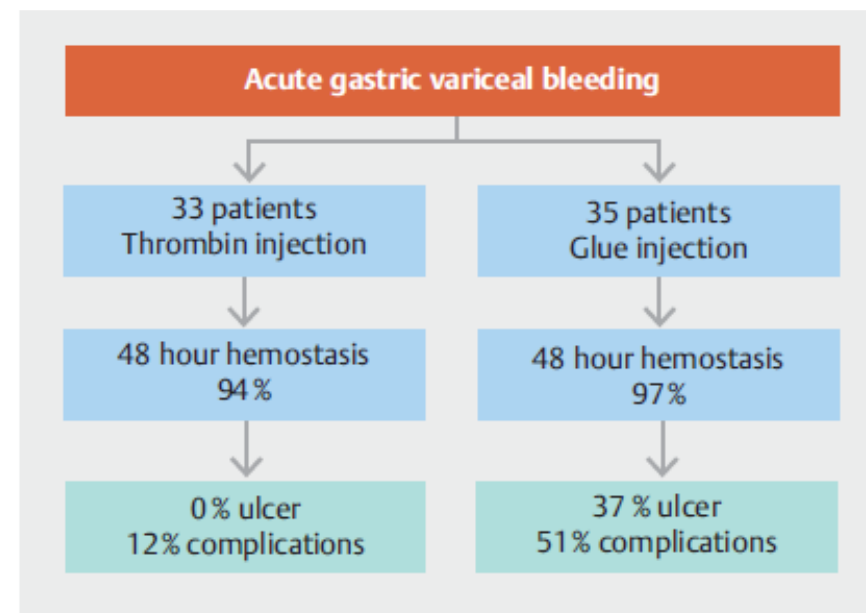
A prospective, randomized trial of thrombin versus cyanoacrylate injection in the control of acute gastric variceal hemorrhage

► **Table 2** Main outcomes in the two treatment groups.

	Thrombin (n=33)	Glue (n=35)	P
Volume, mL			
▪ Mean (SD)	5.1 (0.5)	1.8 (0.2)	
▪ Range	5.0–10.0	1.5–3.0	
Hemostasis of active bleeding, n/N (%)	9/10 (90.0)	10/11 (90.9)	0.58
▪ GOV1	2/2	3/3	
▪ GOV2	6/6	5/6	
▪ IGV1	1/2	2/2	
Initial hemostasis for 48 hours, n (%)	31 (93.9)	34 (97.1)	0.60
Very early rebleeding (3–5 days), n	0	1	> 0.99
Treatment failure (5 days), n (%)	2 (6.0)	2 (5.7)	> 0.99
▪ GOV1	0/15 (0)	0/17 (0)	
▪ GOV2	2/12 (16.7)	1/14 (7.1)	
▪ IGV1	0/6 (0)	1/4 (25)	
Rebleeding between 6–42 days, n	3	4	0.67

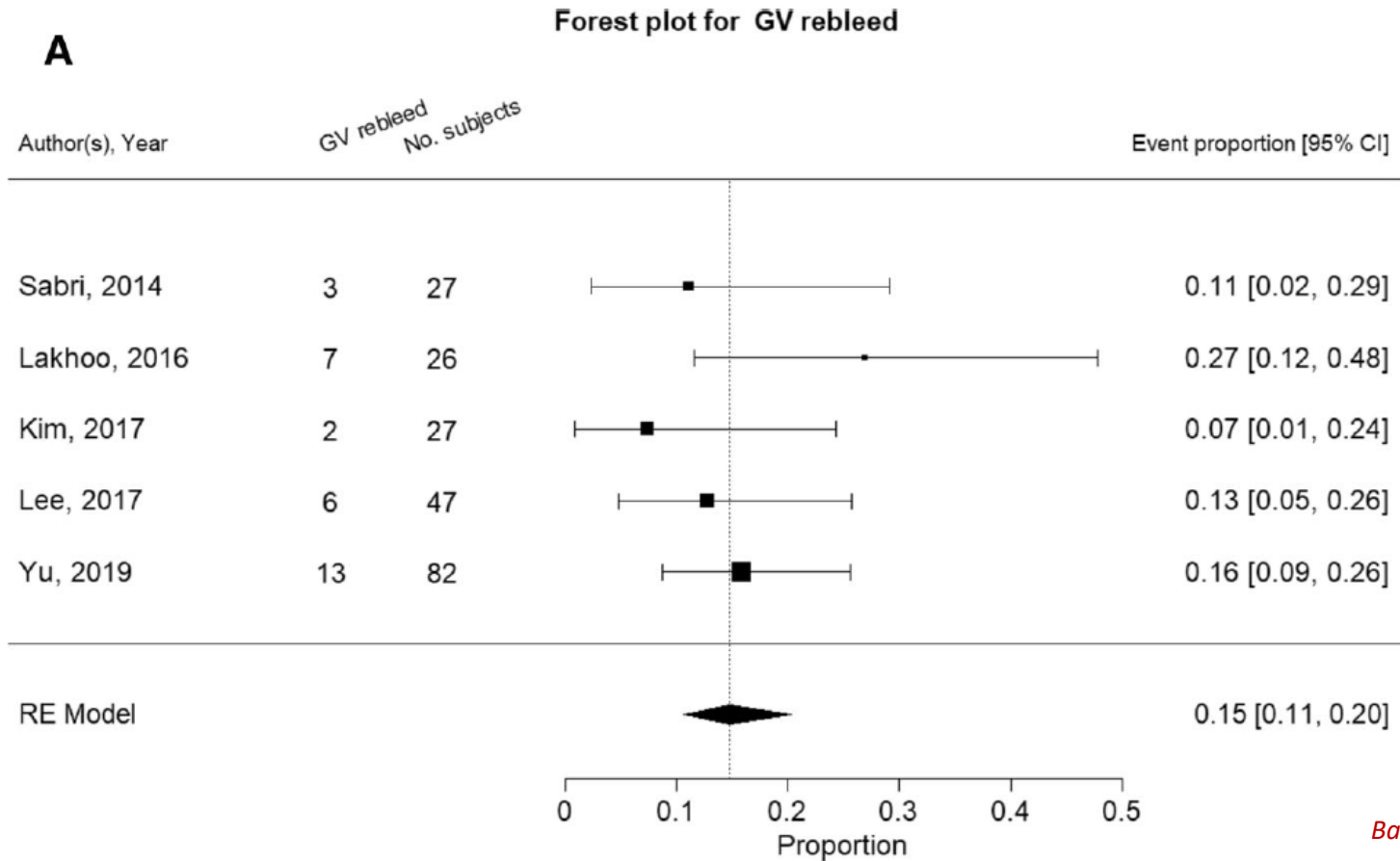


► **Fig. 2** Probability of being free of rebleeding from gastric varices.



TIPS for Gastric Varices

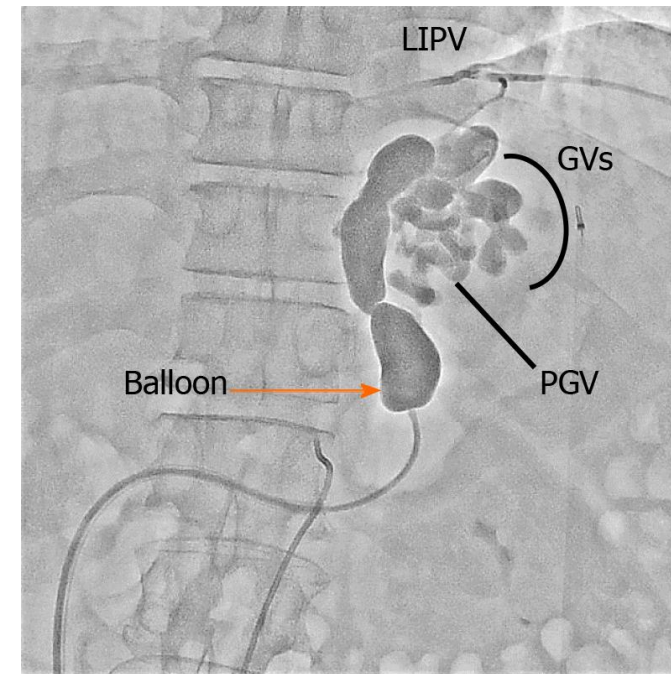
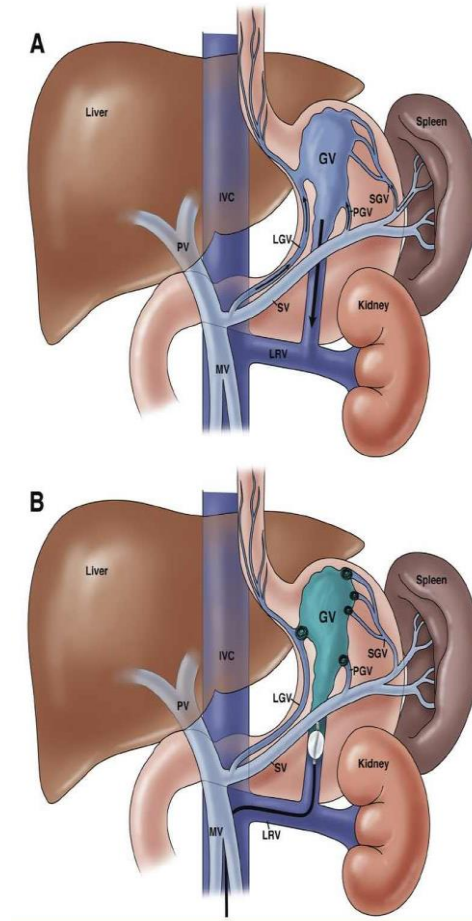
- 1st line (USA)
- Recombinant
 - If g
- Hemostatic
- Few studies or IGVs
- Rebleeding
 - Me



Barange et al Hepatology. 1999; 30: 1139-1143
Lo G et al. Endoscopy. 2007; 39: 679-685
Procaccini et al. Gastrointest Endosc. 2009; 70: 881-887
Henry Z et al. Clin Gastroenterol Hepatol. 2021 Jun;19(6):1098-1107.e1
Alqadi M et al. Cardiovasc Intervent Radiol (2021) 44:1231-1239

Balloon-occluded retrograde transvenous obliteration (BRTO) for Gastric Varices

- BRTO could be considered as an alternative to endoscopic treatment or TIPS
- Occlusion of blood flow with balloon catheter with instillation of a sclerosant proximal to the site of balloon occlusion.
- In the case of gastric varices, there frequently is a spontaneous gastrorenal shunt
- Hemostasis 95%, comparable to TIPS
- Very limited high-level data (e. g. RCTs) comparing TIPS and BRTO for cases where endoscopic hemostasis has failed and/or early recurrent gastric variceal bleeding occurs



J Clin Gastroenterol 2020; 54: 655-660

Yu Q, et al. J Clin Gastroenterol. 2021 Feb 1;55(2):147-158.

Balloon-occluded Retrograde Transvenous Obliteration Versus Transjugular Intrahepatic Portosystemic Shunt for Gastric Varices A Meta-Analysis

5 RCT and retrospective cohort studies. BRTO (n: 308) and TIPS (n:127)

TABLE 10 - Pooled Immediate Bleeding Control Rate of BRTO Versus TIPS

References	IBC of BRTO	Total BRTO	IBC of TIPS	Total TIPS
Choi et al ⁷	8	8	7	7
Lee et al ⁹	95	95	47	47
Gimm et al ¹¹	153	159	16	19
Total	256	262	70	73
Success rate	256/262	97.7%	70/73	95.9%

BRTO indicates balloon-occluded retrograde transvenous obliteration; IBC, immediate bleeding control; TIPS, transjugular intrahepatic portosystemic shunt.

1. *Similar technical success rates (91.4% vs. 89.7%, P=0.995)*
2. *BRTO -> lower likelihood of rebleeding (10.6% vs. 18.7%, P=0.027) and HE (0.00% vs. 23.1%, P<0.001)*
3. *BRTO more likely to aggravate ascites (22.4% vs. 4.3%, P=0.009).*

BRTO and Gastric Varices

- In patients with GOV2 or IGV1, BRTO could be considered first-line (alternative to endoscopic treatment or TIPS), in centers with significant expertise, as it has been shown to be safe and effective
- Urgent rescue TIPS or BRTO are the best options for acute GV bleeding when there is a failure of endoscopic hemostasis or early recurrent bleeding.
- BRTO and TIPS have similar technical success rates and AE rates.
- Patient selection is important; however, given the limited quality of comparative data, specific selection criteria are not currently available

J Clin Gastroenterol 2020; 54: 655-660

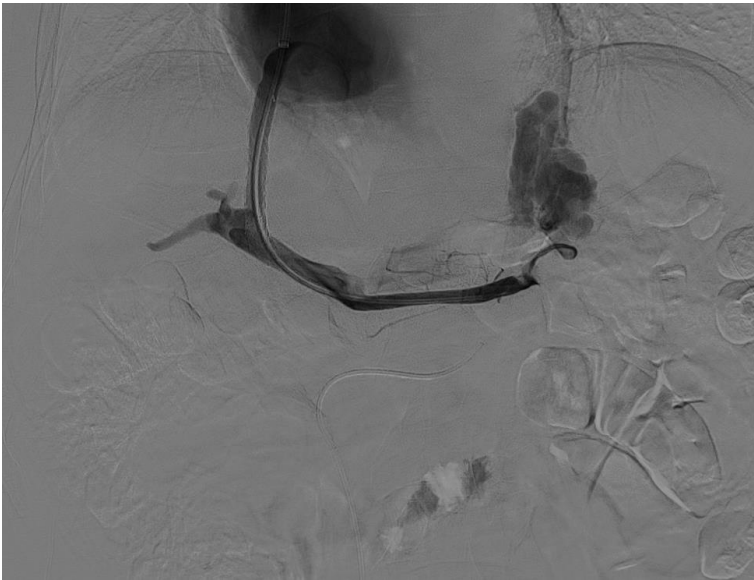
Yu Q, et al. J Clin Gastroenterol. 2021 Feb 1;55(2):147-158

Baveno VII. J Hepatol. 2022 Apr;76(4):959-974. doi: 10.1016/j.jhep.2021.12.022

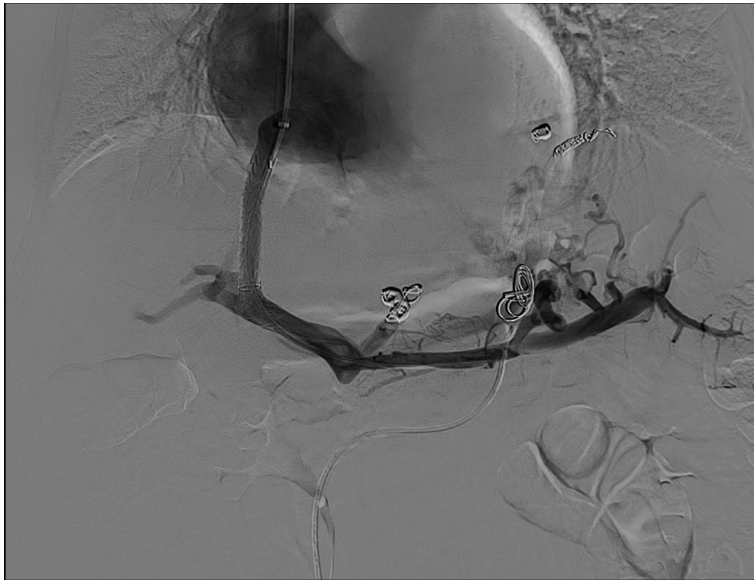
Combined TIPS & BRTO versus TIPS Alone for the Management of Gastric Varices



Pre-TIPS



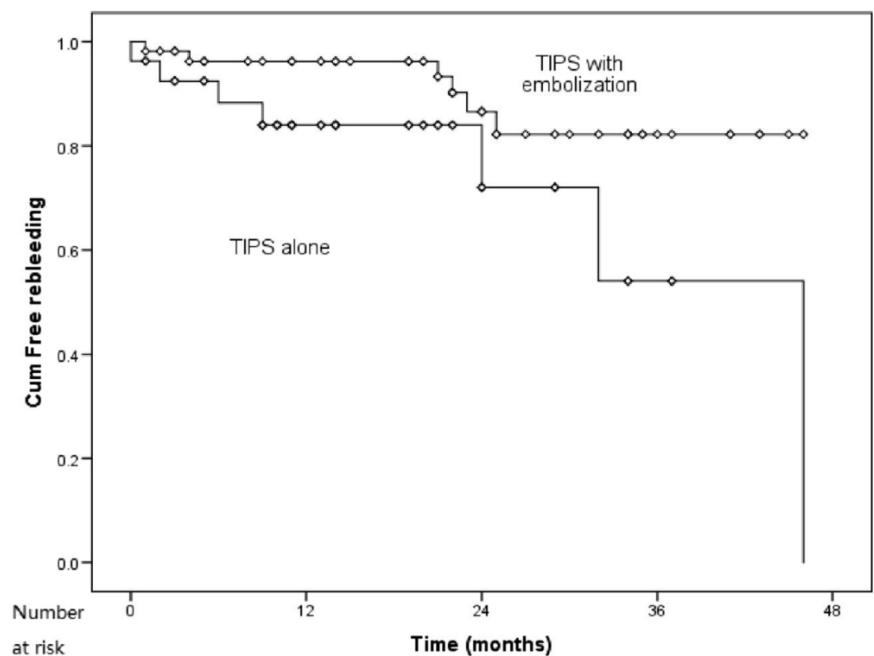
Post-TIPS



Post-TIPS+embolization

Combined TIPS & Obliteration versus TIPS Alone for the Management of Gastric Varices

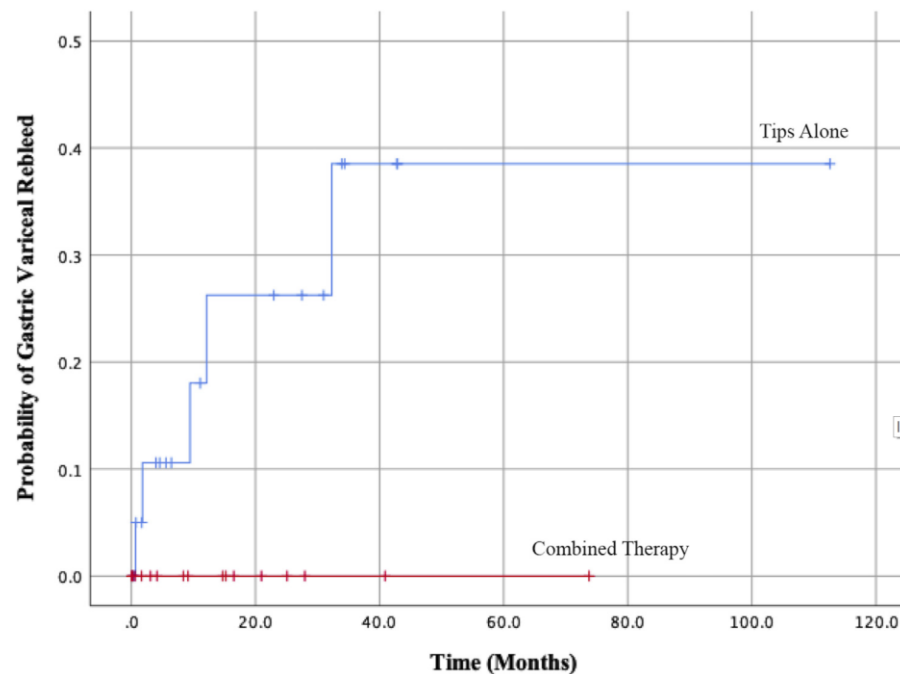
TIPS+ Emb (n=55) vs TIPS (n=26)



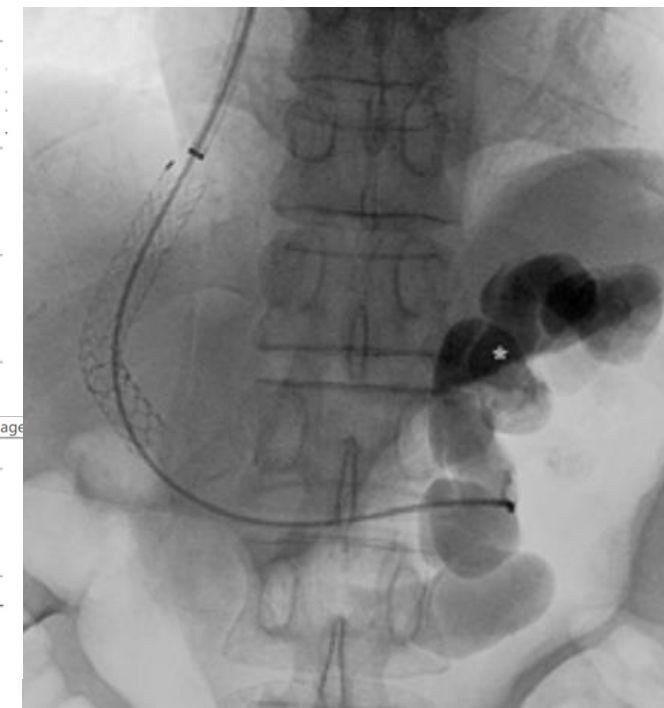
1 yr re-bleeding rate

3.8% vs 13%, P =.041

TIPS+ BRTO (n=18) vs TIPS (n=22)



0% vs 23%, P =.056



Combined TIPS & Embolization

Management of Gastric Varices

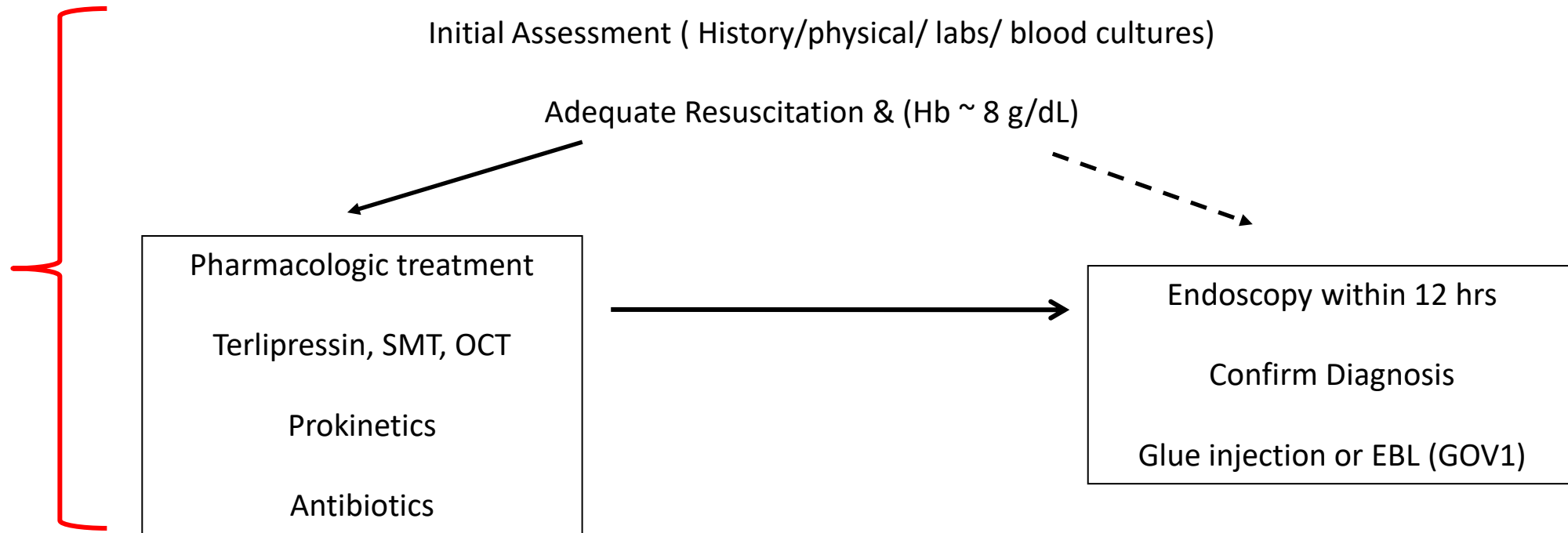
TIPS may be combined with embolization to control bleeding or to reduce the risk of recurrent variceal bleeding from gastric or ectopic varices (mainly large IGV's), particularly in cases when, despite a decrease in portosystemic pressure gradient, portal flow remains diverted to collaterals.

Lv Y. Lancet Gastroenterol Hepatol. 2022 Aug;7(8):736-746
Shah K et al J Vasc Interv Radiol. 2021 Feb;32(2):282-291.e1
Baveno VII. J Hepatol. 2022 Apr;76(4):959-974. doi: 10.1016/j.jhep.2021.12.022
Yu et al. Eur Radiol. 2019 Feb;29(2):699-706.

Treatment of Acute GV Bleeding

Baveno VII (2022), AASLD Guidance (2017)

FIRST STEP

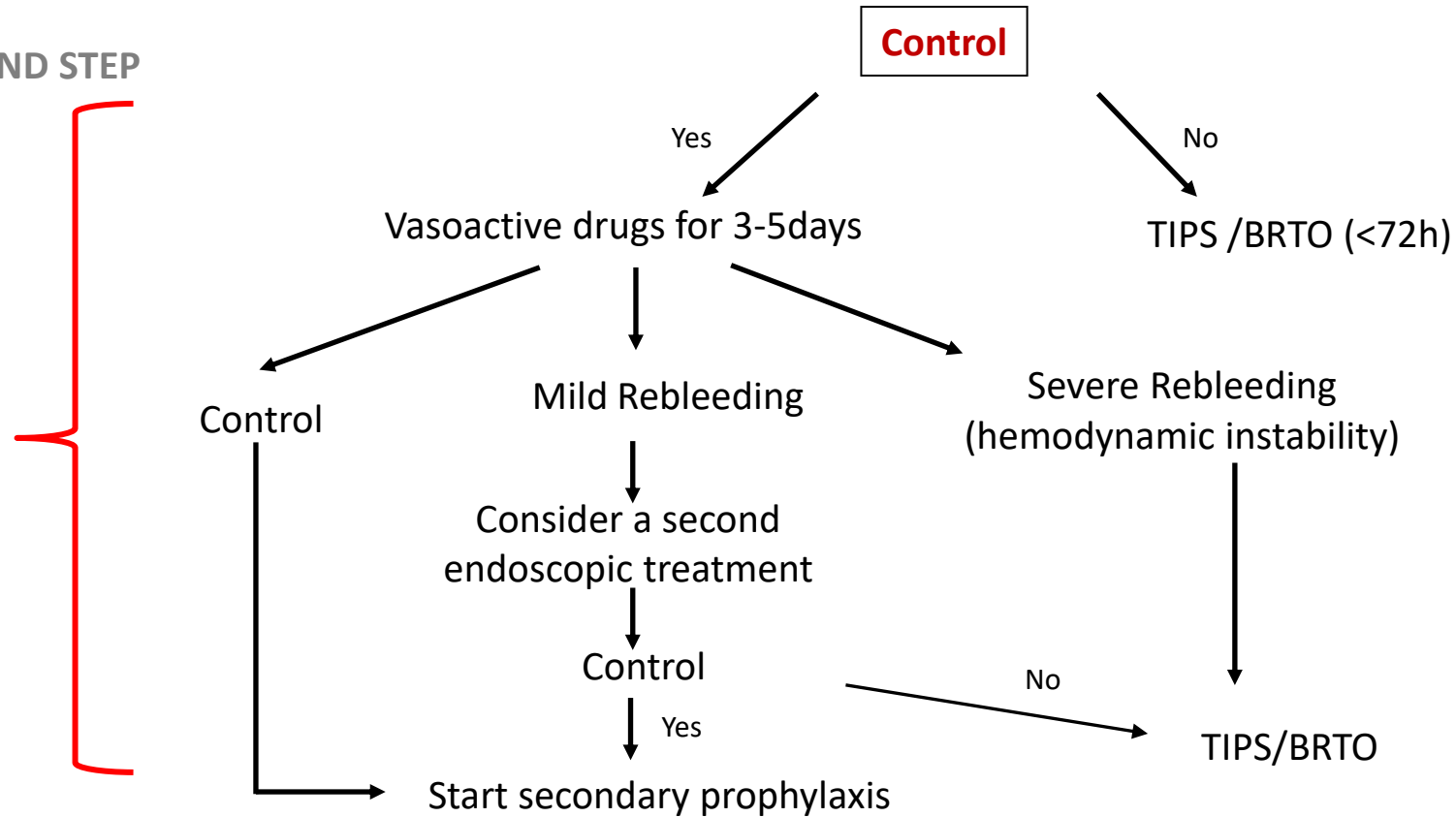


*Baveno VII. J Hepatol. 2022 Apr;76(4):959-974. doi:
10.1016/j.jhep.2021.12.022*

Treatment of Acute GV Bleeding

Baveno VII (2022), AASLD Guidance (2017)

SECOND STEP



Baveno VII. J Hepatol. 2022 Apr;76(4):959-974. doi: 10.1016/j.jhep.2021.12.022

Portal Hypertensive Gastropathy (PHG) Characteristics

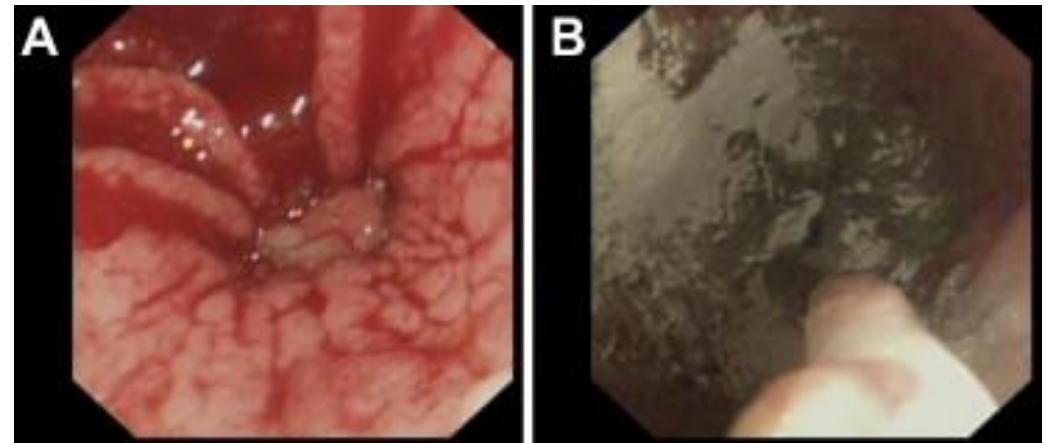
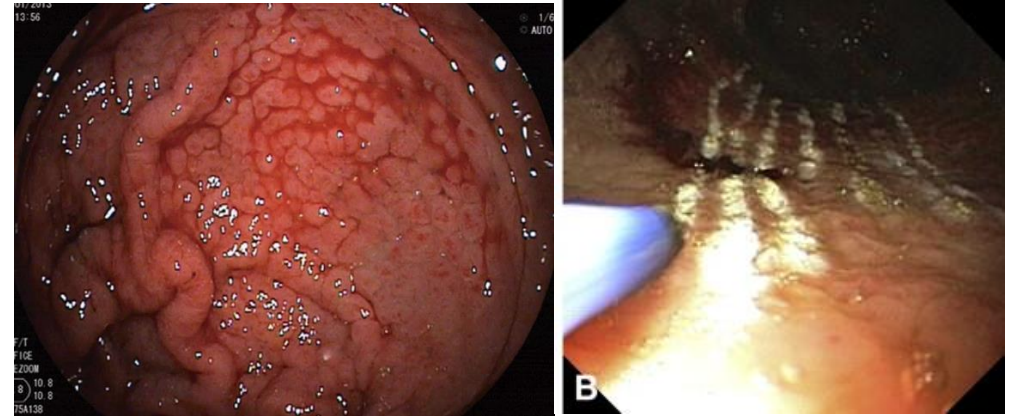
- Present in up to 90% of patients with cirrhosis
- Mild or severe
- Characterized by a cobblestone / snakeskin appearance
- Distribution – fundus and body
- Bleeding responds to measures that reduce portal hypertension



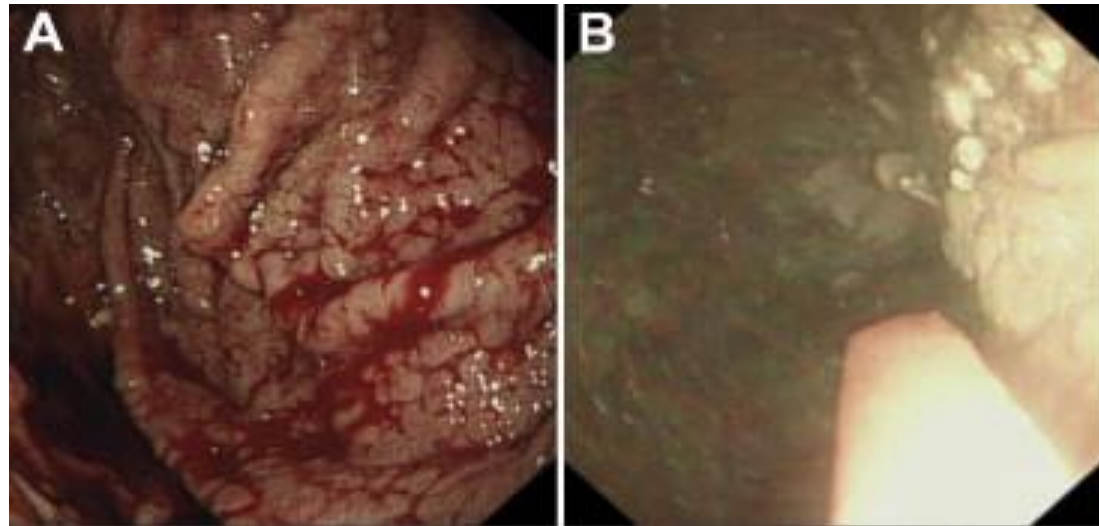
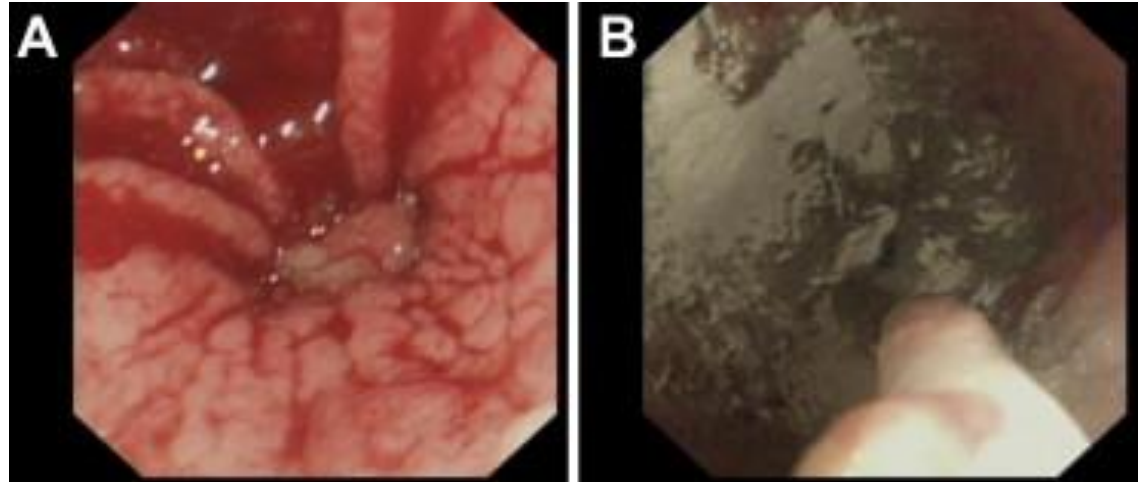
Treatment of Portal Hypertensive Gastropathy

Indicated for active/acute bleeding

- Acute bleeding – occurs in 2-12% of cases
- Severe PHG and advanced liver disease
- Therapy –
 1. IV vasoconstrictors & antibiotics
 2. Consider TIPS
 3. Endoscopic therapy- scarce data.
 1. Argon plasma coagulation
 2. Hemostatic powder



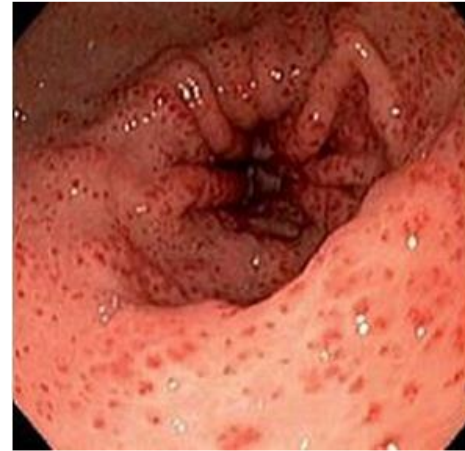
The use of hemospray in portal hypertensive bleeding; a case series (n=4)



J Hepatol. 2014 Feb;60(2):457-60

Gastric Antral Vascular Ectasia Therapies

- Indicated for bleeding
- **Endoscopy**
 - APC (effective)
 - Band ligation (effective)
 - RFA (refractory cases)
- Effective in 85-90%
- Reduces transfusion requirements
- Increases Hb levels (mean 2-3g/L)
- Safe , easily applied,
- Recurrence varies-



*Kwan Am J Gastroenterol 2006
Fuccio Digestion 2008
Wells, Gastrointest Endosc 2008
Sato Digest Endosc 2012*

Gastric Antral Vascular Ectasia

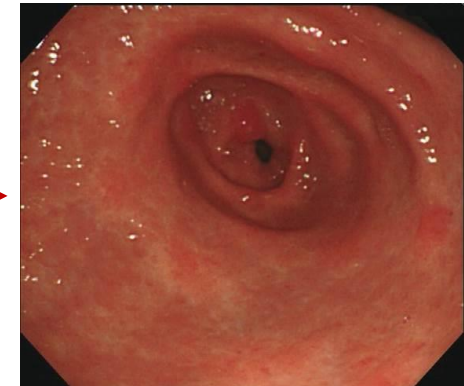
APC for GAVE

Author	N.	Study type	F-up (month)	Efficacy	N° of sessions	Complications
Probst et al. 2001	17	Prospective	30,4	Hb levels increase.	2	Asymptomatic antrum scarring
Yusoff et al. 2002	5	Retrospective	20	Hb levels increase; transfusion dependence ceased in all patients	2,6	Minor bleeding
Roman et al. 2003	21	Retrospective	15	Hb levels increase.	2,8	2 hematemesis, 1 sepsis
Sebastian et al. 2004	12	Retrospective	24	Hb levels increase; decrease transfusion need.	2	1 minor bleeding
Kwan et al. 2006	26	Prospective	16	Hb levels increase; decrease transfusion need.	2	None
Chaves et al. 2006	14	Prospective	9,9	70 % response;	3,2	35 % bleeding
Herrera et al. 2008	8	Prospective	24	87 % treatment success.	2,3	None
Lecleire et al. 2008	30	Retrospective	22	80 % treatment success.	2,18	None
Batthi et al. 2009	50	Prospective	8,5	Hb levels increase; decrease transfusion need.	5	None
Fuccio et al. 2009	20	Prospective	25	90 % treatment success.	3	Abdominal pain and bloating in 80 % of the cases
Chiu et al. 2012	19	Retrospective	NR	78,9 % recurrent bleeding	2,4	None
Garg et al. 2017	20	Retrospective	20,6	40 % treatment success	2-2,5	None
St. Romain et al. 2017	25	Retrospective	18	100 % treatment success	2,4	None

Gastric Antral Vascular Ectasia - Banding

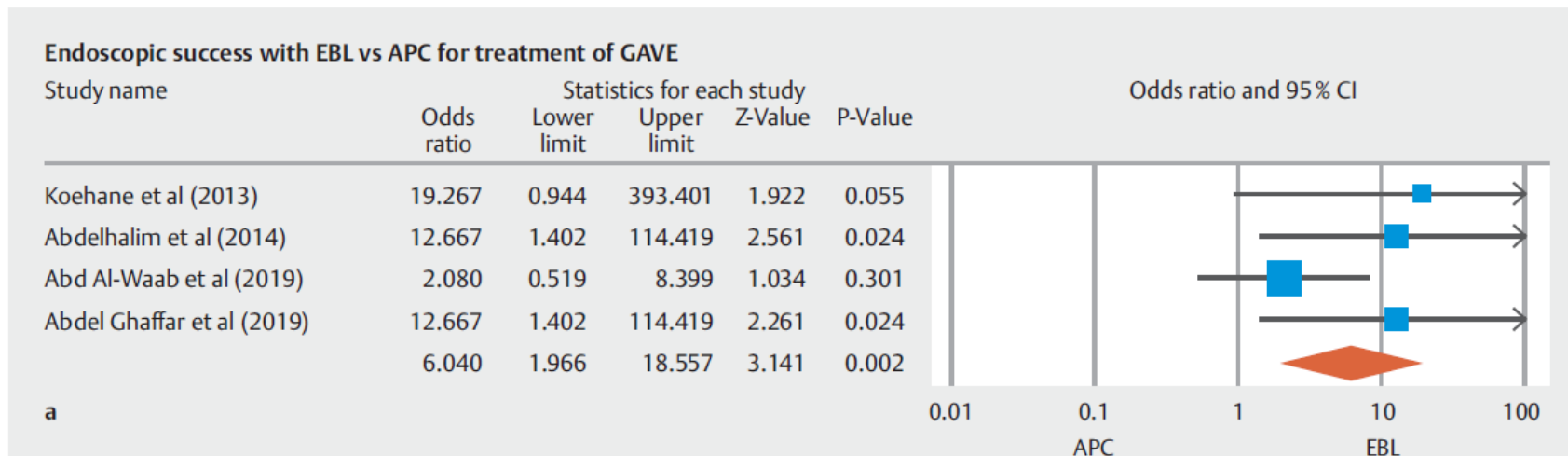
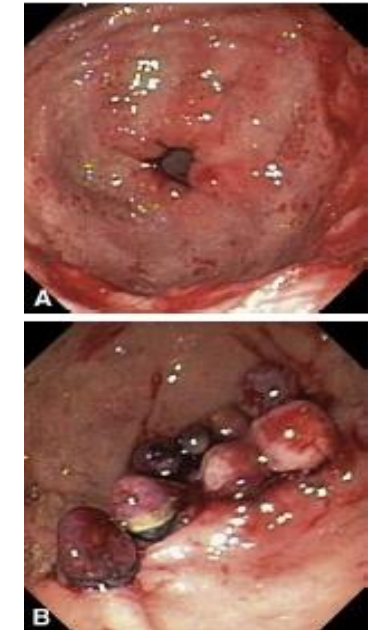
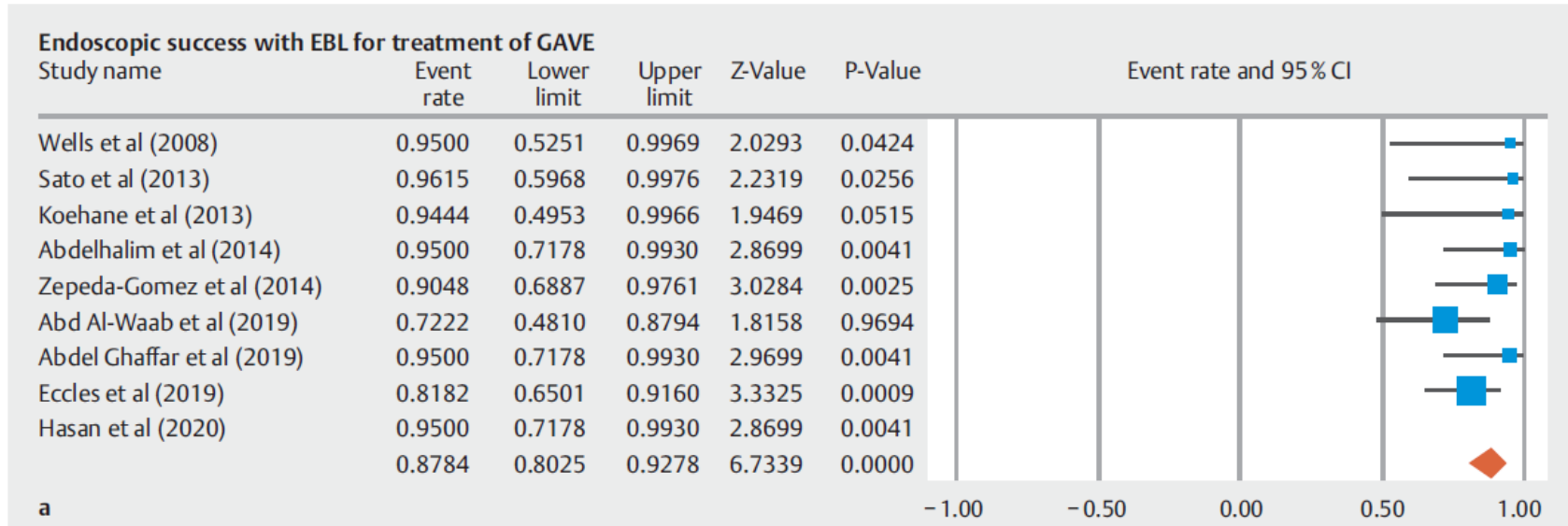
- Used given safety and efficacy of EBL in obliterating submucosal vascular plexus
- Involves banding a large area of antrum
- Maximum amount of bands placed (mean 7-12)

Author	N.	F-up (month)	Efficacy	Sessions	Complications
Wells et al. 2008	9	12.7	Higher rate of bleeding cessation, post-treatment transfusion and hospitalization with EBL.	1.9	None
Sato et al. 2012	12	15.6	8.3 % recurrence with EBL.	3	1 bleeding in EBL group
Keohane et al. 2013	8	26	100 % endoscopic improvement in EBL	2.5	None
Zepeda-Gomez et al. 2019	33	35.9	81,8 % responder	2.9	None
Fabián et al. 2020	18	/	Increased Hb levels	2.2	Two polyps after EBL procedure
O'Morain et al. 2021	12	19.9	Increased Hb levels	2.9	None



New approaches for GAVE in cirrhosis

Endoscopic band ligation in the treatment of gastric antral vascular ectasia: a systematic review and meta-analysis



Thank you



