Especialización en **Ultrasonografía Endoscópica Avanzada**

Universidad de Alcalá

5ª Edición
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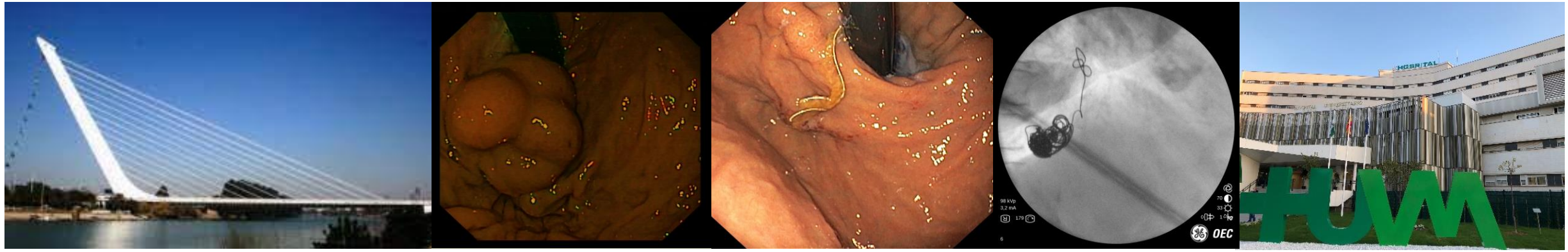
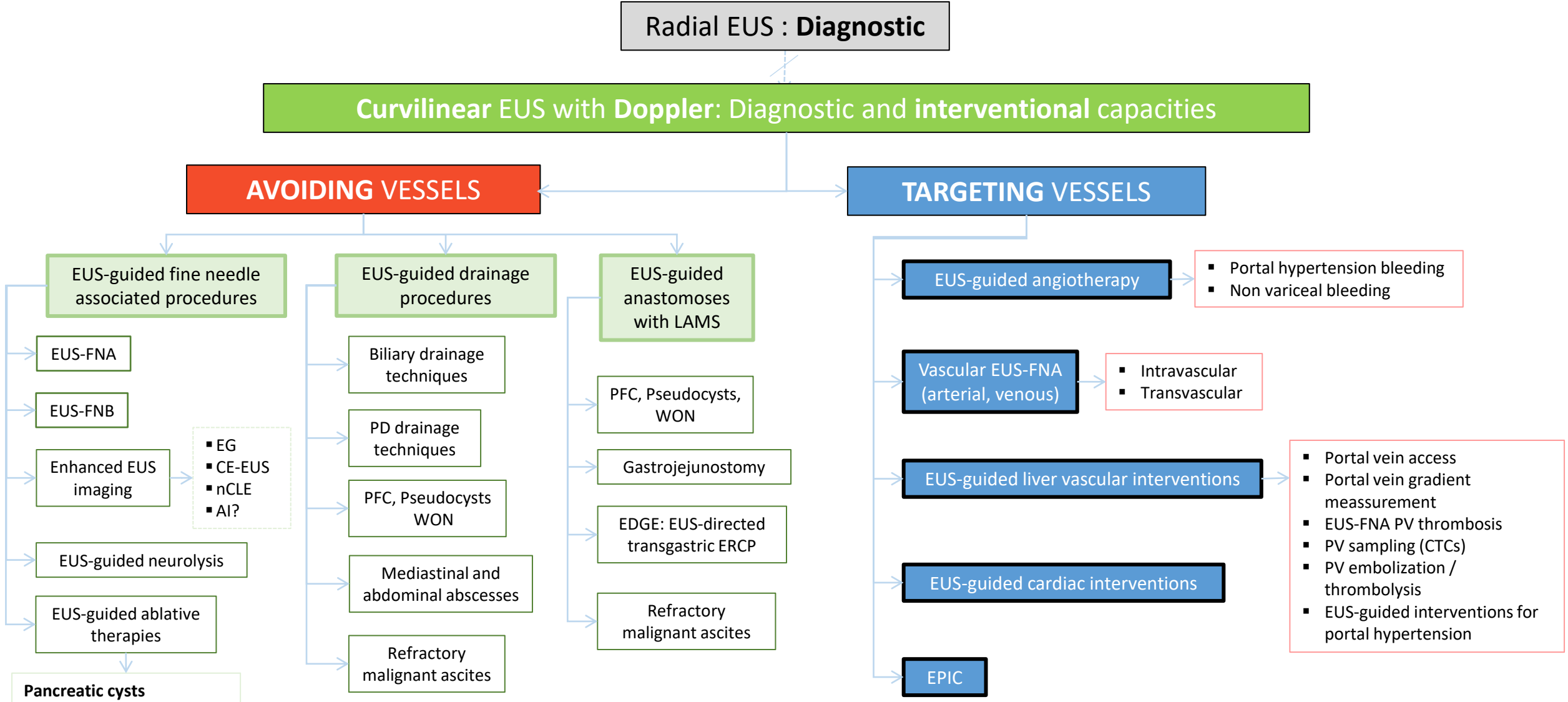
Prof. José Ramón Foruny Olcina, Prof. Enrique Vázquez Sequeiros, Prof. Agustín Albillos Martínez

Tratamiento de las Varices Gástricas: Cianoacrilato y Endocoils

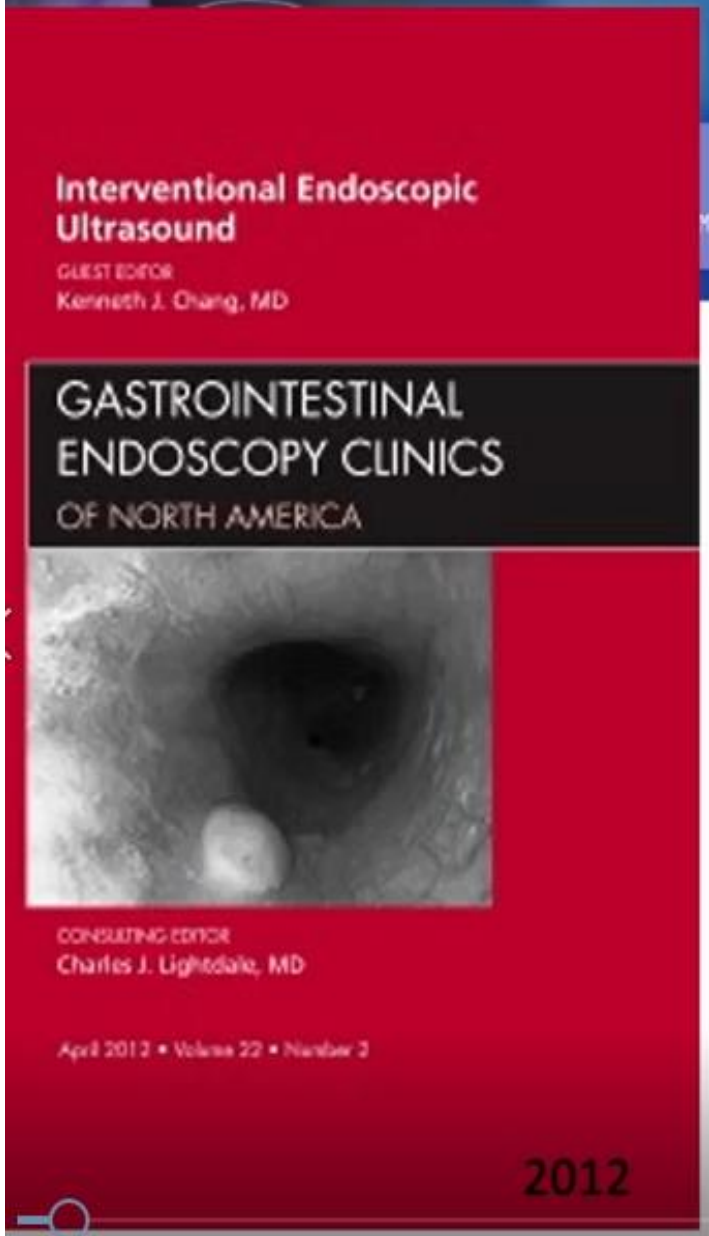
Dr. Rafael Romero Castro. Hospital Universitario Virgen Macarena. Sevilla.





"New and established applications of EUS-guided techniques: An overview and insight into new trends"

Dr. Victoria Alejandra Jiménez García



Preface

Interventional Endoscopic Ultrasound

Kenneth J. Chang, MD
Guest Editor

Organised by:

SEPD

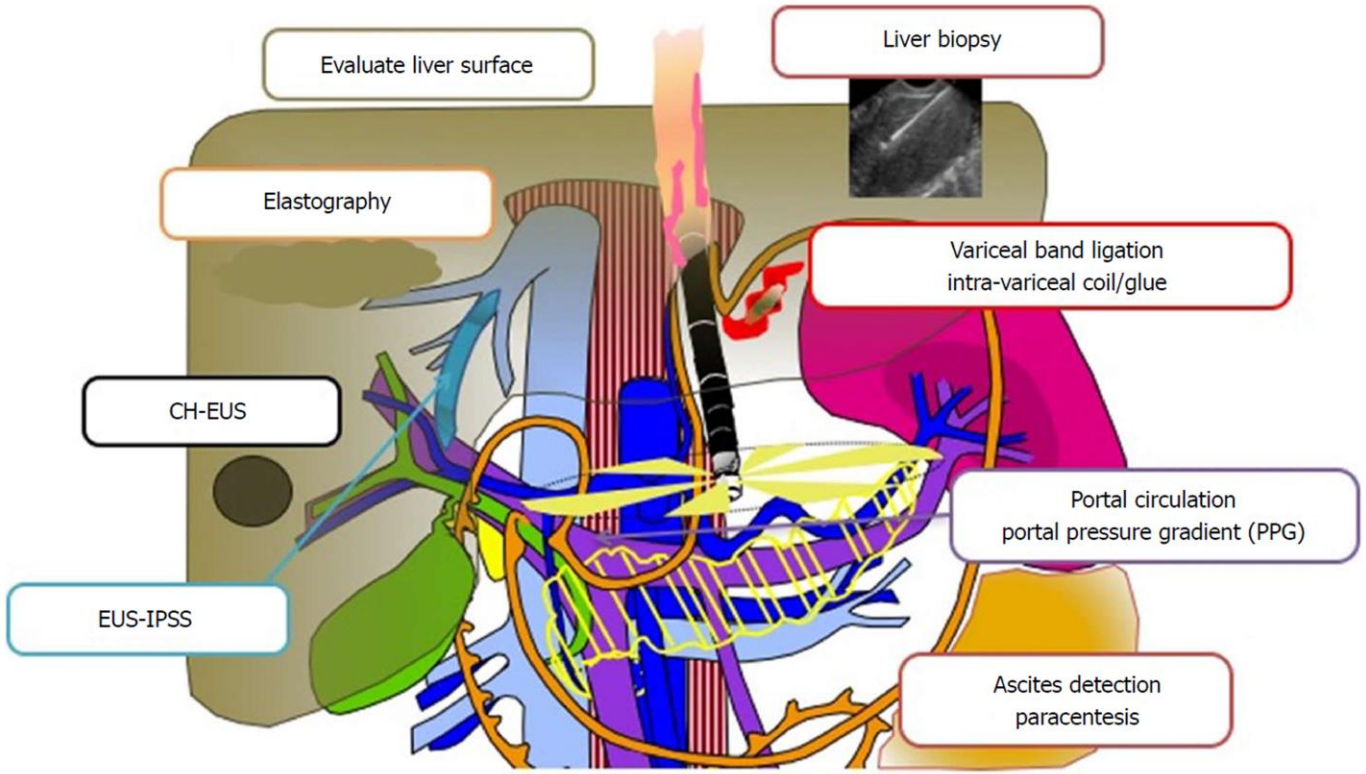
Endo-Hepatology: A New Paradigm

Kenneth J. Chang, MD[a,*], Jason B. Samarasena, MD[a], Takuji Iwashita, MD, PhD[b,c], Yosuke Nakai, MD, PhD[a,d], John G. Lee, MD[a]

0:00:21

EUS-Hepatology

- Intervention procedures for liver disease has predominantly been performed through the percutaneous approach (US or CT).
- However, as EUS applications have expanded, there have emerged various EUS-guided interventions for liver disease (Endo-Hepatology).



CH-EUS = contrast enhanced harmonic EUS
EUS-IPSS = intrahepatic porto-systemic shunt

Chang K. WJG 2019

Table 1 Endoscopic ultrasound (EUS) hepatic interventions

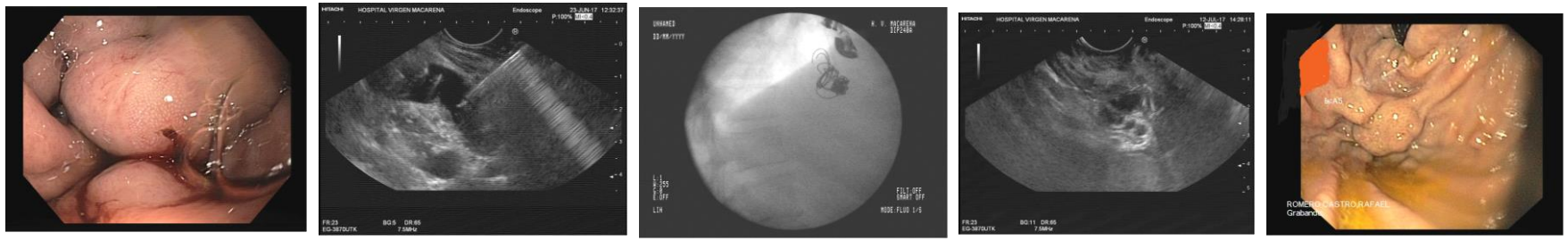
1. EUS-guided liver biopsy (EUS-LB)
2. EUS-guided vascular intervention
   - EUS-guided PV access
   - EUS-guided PV pressure measurement
   - EUS-FNA of PV thrombosis
   - EUS-guided PV blood sampling
   - EUS-guided PV embolization/thrombolysis
   - EUS-guided intervention for portal hypertension
3. EUS for the diagnosis and staging of liver lesions
4. EUS-guided treatments of liver tumors
   - Fine-needle injection
   - Thermal therapy
   - Photodynamic therapy
   - Brachytherapy and fiducial markers placement
5. EUS-guided drainage of the liver cyst and abscess/biloma

PV, portal vein.

Hashimoto R, Chang K. DEN 2021

Clinical ussefulnes of EUS-guided portal pressure gradient measurement in two patients

Therapy of Gastric Varices



- Esophageal varices account for more than 80% in cirrhotic patients. However bleeding from gastric varices is more severe with higher rates of rebleeding (up to 90% after initial hemostasis), significant transfusion requirements and higher mortality.

Wani ZA, et al. J Res Med Sci 2015

- Gastric varices account for up to 20% of all types of varices and carry a 1-year risk of bleeding as high as 16%.
- Risk factors associated to gastric variceal bleeding :
  - ✓ **Location of fundic varices** (IGV1>GOV2>GOV1)
  - ✓ Gastric varices measuring more than 5 mm
  - ✓ Presence of red spots
  - ✓ **Advanced liver disease** (Child-Pugh B-C)

Kim T, et al. Hepatology 1997

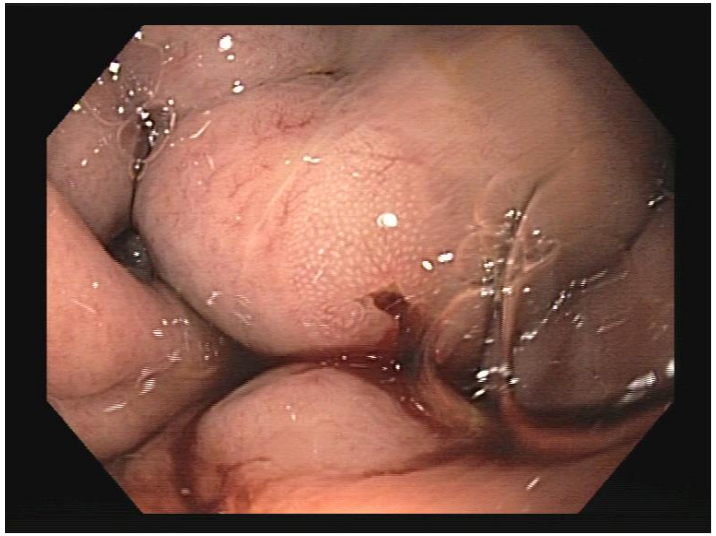
- The reported 6-week mortality rate related to gastric variceal bleeding is 17%-45%.

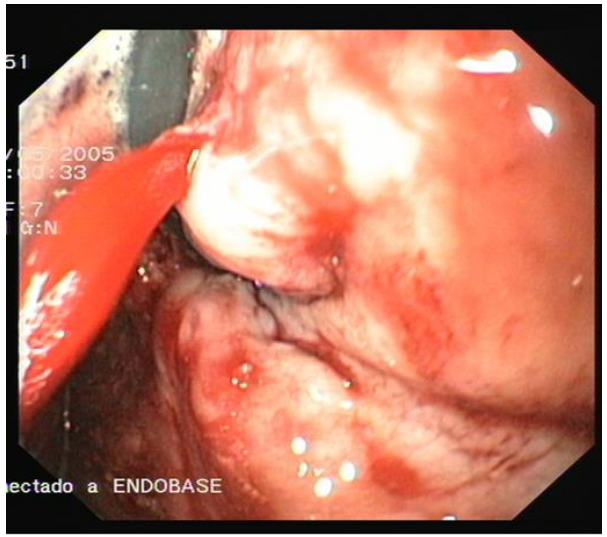
Teng W, et al. Medicine (Baltimore) 2014

Therapy of Gastric Varices

- It is still challenging.
- There is no a worldwide consensus.
- Lack of well-designed comparative studies.
- Lack of understanding of anatomical vascular structure and hemodynamics of gastric varices.

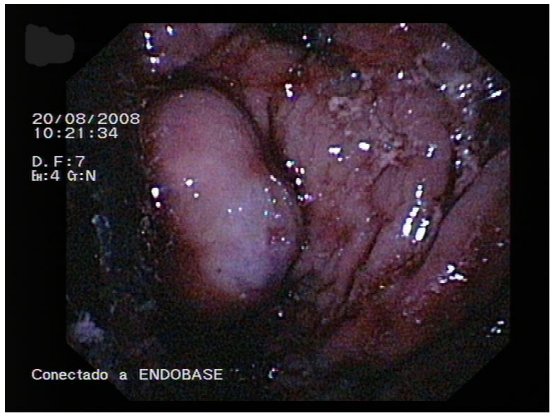
Hashizume, J Gastroenterol Hepatol 2011





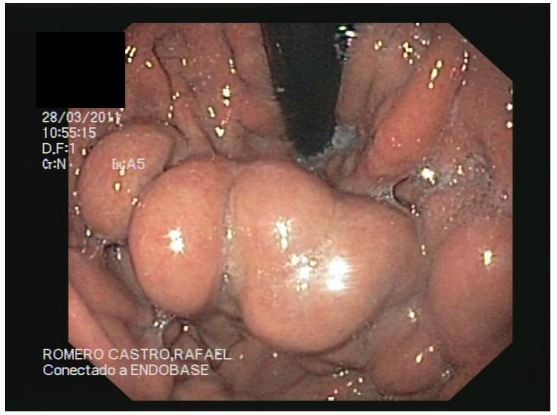
Management of Gastric Varices : Clinical Settings

- Acute variceal bleeding



- Secondary prophylaxis

- Primary prophylaxis



Guidelines

Journal Pre-proof

BAVENO VII - RENEWING CONSENSUS IN PORTAL HYPERTENSION

Roberto de Franchis, Jaime Bosch, Guadalupe Garcia-Tsao, Thomas Reiberger, Cristina Ripoll, on behalf of the Baveno VII Faculty

6.22 Endoscopic therapy with tissue adhesives (e. g. N-butyl-cyanoacrylate/thrombin) is recommended for acute bleeding from isolated gastric varices (IGV) (A.1), gastroesophageal varices type 2 (GOV2) that extend beyond the cardia (D.2)

(Unchanged)

6.23 EVL or tissue adhesive can be used in bleeding from gastroesophageal varices type 1 (GOV1) (D.1)
(Unchanged)

6.27 Pre-emptive TIPS with PTFE-covered stents within 72 hours (ideally <24hours) is indicated in patients bleeding from EV, GOV1 and GOV2 who meet any of the following criteria: Child Pugh class C<14 points or Child class B >7 with active bleeding at initial endoscopy or HVPG >20 mmHg at time of hemorrhage (A.1)
(Changed)

Journal Pre-proof

BAVENO VII - RENEWING CONSENSUS IN PORTAL HYPERTENSION

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Research Agenda

o Management of high risk in patients not fulfilling the high-risk criteria used for preemptive TIPS
o Cost effectiveness data regarding the use of SEMSs
o Alternatives other than Blakemore/Linton should be developed as they are in shortage
o The role of global hemostasis tests, such as viscoelastic tests and thrombin generation assays, to assess and correct hemostasis abnormalities in decompensated cirrhosis and acute variceal bleeding (using clinical endpoints).
o The potential role of prothrombin complex concentrates, fibrinogen, or cryoprecipitate in bleeding patients with cirrhosis.
o Is there any relation between low platelet count (up to which level?) or fibrinogen and the risk of variceal bleeding, failure to control bleeding, or bleeding after endoscopic band ligation?
o Identification of patients that will benefit from variceal embolization during TIPS
o Role of EUS-guided therapy with tissue adhesive with or without coils
o The impact of PVT on the prognosis of cirrhotic patients with AVB
o The optimal duration of vasoactive therapy in cirrhotic patients with PVT and AVB
o Role of pre-emptive TIPS in cirrhotic patients with PVT presenting with AVB
o Management of AVB in patients with cirrhosis and PVT, including management of anticoagulation and timing of endoscopic/invasive procedures.
o Role of vasoactive drugs and antibiotics in Child-Pugh A patients
o Optimal shorter time frame limit for vasoactive drug therapy?
o Definition of active bleeding at endoscopy, assessment of its subjectivity, and prognostic value
o Identifying the clinical role of non-invasive markers of portal pressure
o Role of hemostatic powder in acute and refractory variceal bleeding
o Role of thrombin in gastric variceal bleeding
o Pre-emptive TIPS in patients with gastric varices

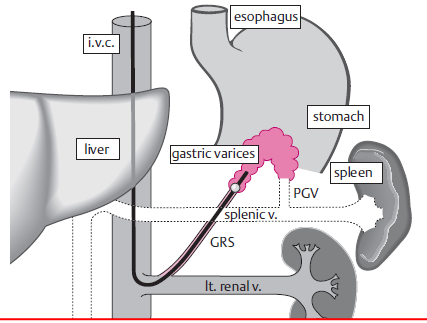
Management of Acute Gastric Variceal Bleeding and Secondary Prophylaxis

- Balloon tamponade
- Vasoactive drug therapy
- **Endoscopic therapy:**
  - ✓ **Endoscopic direct injection of cyanoacrylate**
  - ✓ **EUS-guided therapeutic procedures**
- **Vascular invasive radiology:**
  - ✓ **TIPS**
  - ✓ **B-RTO**
- Surgery: Shunts and other surgical procedures

Management of Acute Gastric Variceal Bleeding and Secondary Prophylaxis

Vascular invasive radiology

- **TIPS**
- B-RTO



6.27 Pre-emptive TIPS with PTFE-covered stents within 72 hours (ideally <24hours) is indicated in patients bleeding from EV, GOV1 and GOV2 who meet any of the following criteria: Child Pugh class C<14 points or Child class B >7 with active bleeding at initial endoscopy or HVPG >20 mmHg at time of hemorrhage (A.1) (Changed)

6.28 In patients fulfilling pre-emptive TIPS criteria, ACLF, HE at admission and hyperbilirubinemia at admission should not be considered as contra-indications to pTIPS (B.1) (New)

Journal Pre-proof

BAVENO VII - RENEWING CONSENSUS IN PORTAL HYPERTENSION

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Management of Acute Gastric Variceal Bleeding and Secondary Prophylaxis

Vascular invasive radiology

- TIPS
- **B-RTO**

6.40 In patients with GOV2, IGV1, and ectopic varices, BRTO could be considered as an alternative to endoscopic treatment or TIPS, provided it is feasible (type and diameter of shunt) and local expertise is available, as it has demonstrated to be safe and effective (D.2) (New)

6.41 Either endovascular or endoscopic treatment should be considered in patients with ectopic varices (D.1) (New)

- TIPS and B-RTO are time-consuming interventional radiology procedures which may be not widely and readily available.

Management of Acute Gastric Variceal Bleeding and Secondary Prophylaxis

Endoscopic therapy:

- **Endoscopic direct injection of cyanoacrylate (CYA)**
- EUS-guided therapeutic procedures

Since the 80's, endoscopic direct injection with CYA was a step forward in the treatment of gastric varices.

NEW METHODS

Endoscopy 18 (1986) 25–26
© Georg Thieme Verlag Stuttgart · New York

Endoscopic Obliteration of Large Esophagogastric Varices with Bucrylate

N. Soehendra, V.Ch. Nam, H. Grimm, and I. Kempeneers

Department of Surgery, University Hospital of Hamburg

Mr. Coover, chemist inventor of CYA (superglue)

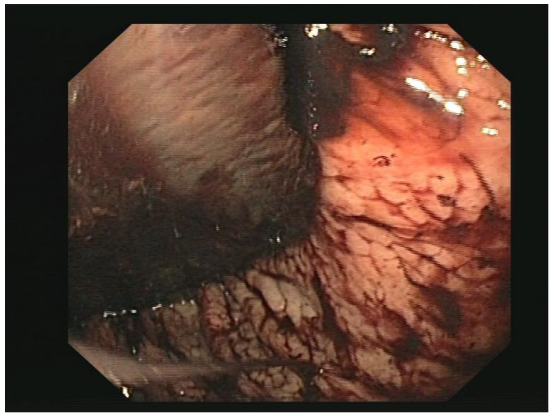
Drawbacks of Direct Endoscopic Injection with CYA

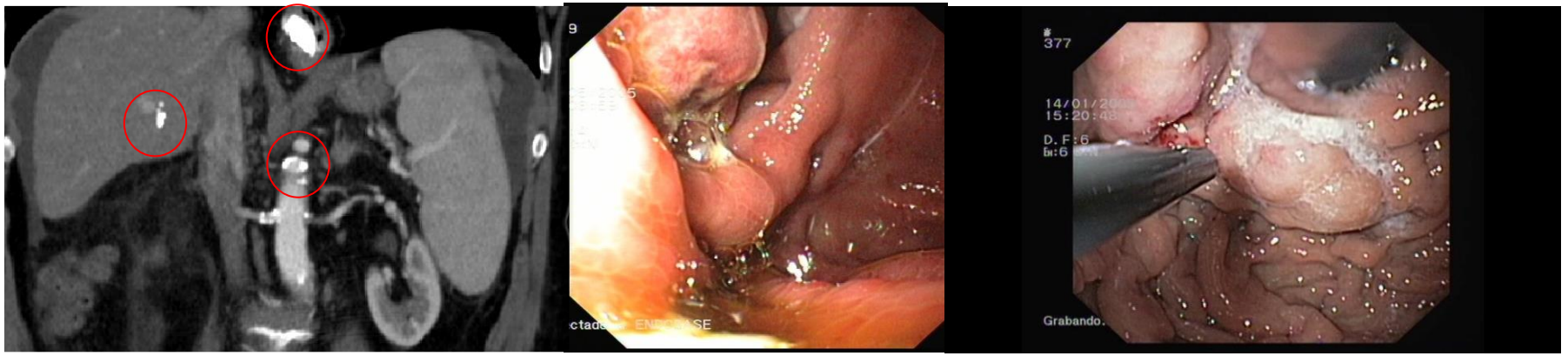
Adverse events

Systemic: glue embolism, infection

Local: ulcers, massive refractory bleeding, leakege and visceral fistulas

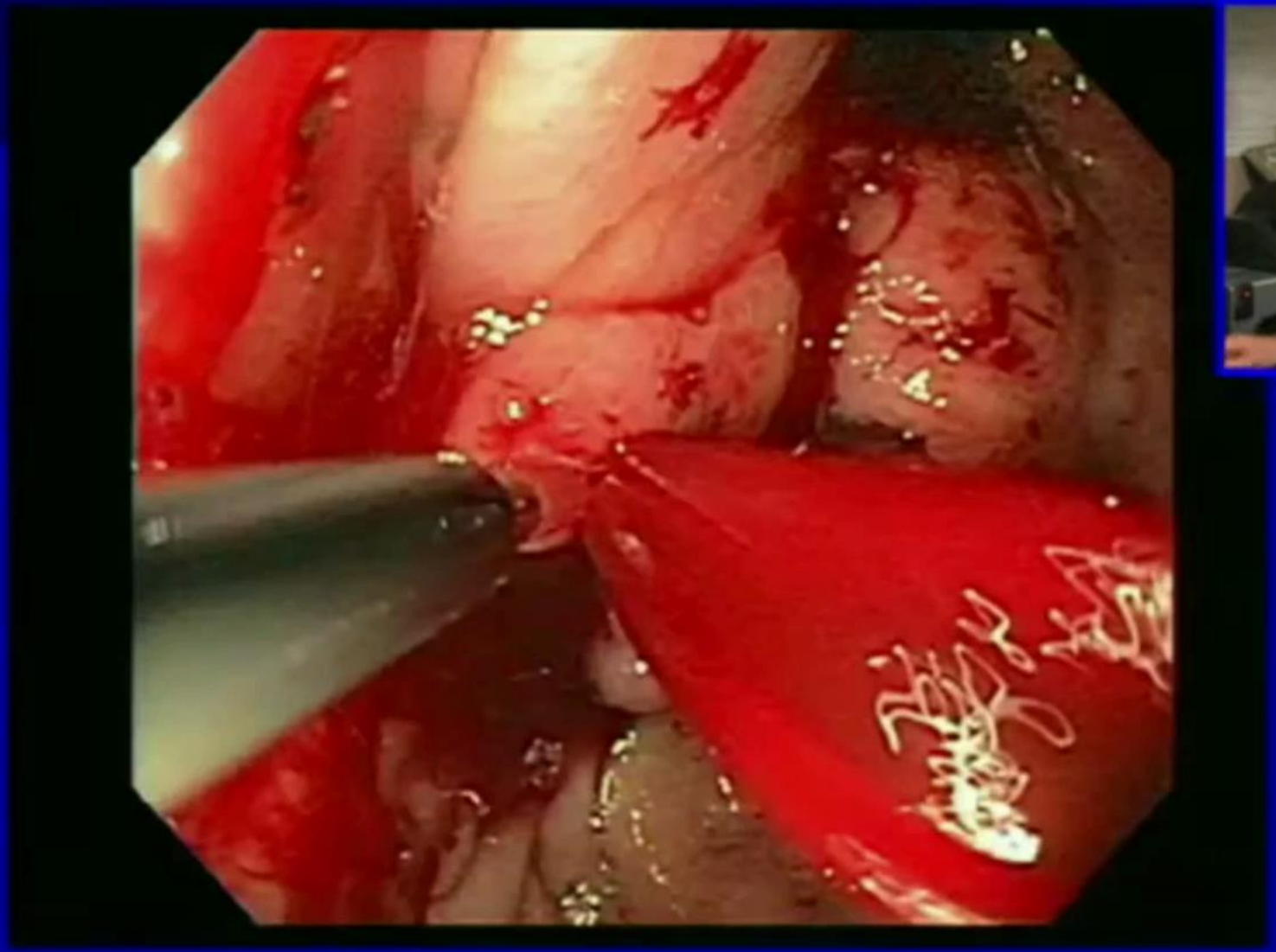
- Rebleeding for incomplete obliteration.
- Poor endoscopic field of vision of the fundus in case of massive bleeding.
- Problematic choice of the point of injection in case of former endoscopic therapy.
- The more CYA injected the more probability for complications.
- EUS-guided procedures use less or no amount of CYA and lower its risks.





Courtesy of Dr. Ortiz-Moyano

2015 Live Endoscopy Course. CPMC. Courtesy of Dr. Kenneth Binmoeller



2015 Live Endoscopy Course. Dr. Kenneth Binmoeller

Management of Acute Gastric Variceal Bleeding and Secondary Prophylaxis

Endoscopic therapy:

- Endoscopic direct injection of CYA
- **EUS-guided therapeutic procedures**

Anatomic classifications of gastric varices

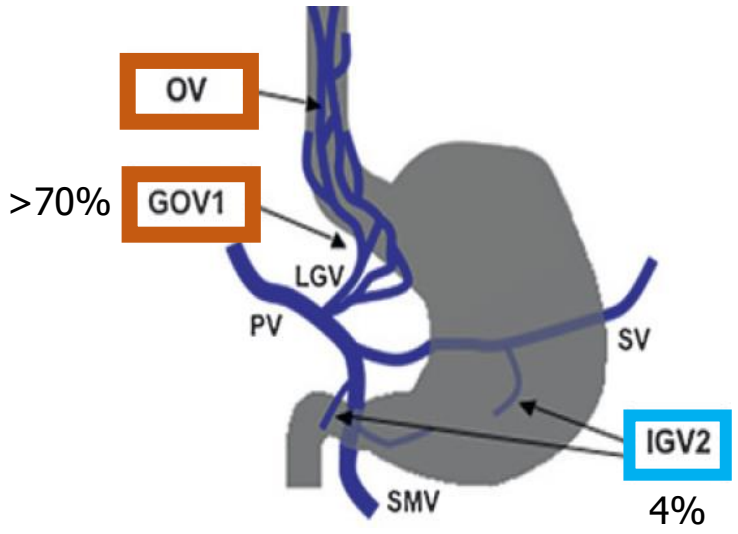
- Endoscopic Band Ligation

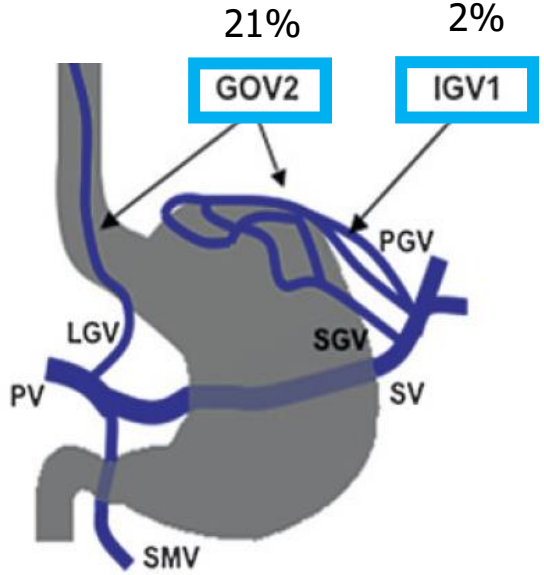
- Invasive vascular radiology
- Endoscopic direct injection of CYA
- EUS-guided Therapy

DEDICATED THERAPY

Sarin

Localization





Sarin SK. et al, Hepatology 1992

Management of Acute Gastric Variceal Bleeding

Endoscopic therapy:

- Endoscopic direct injection of CYA
- **EUS-guided therapeutic procedures**

DEDICATED THERAPY

- Endoscopic direct injection of CYA
- EUS-guided Therapy

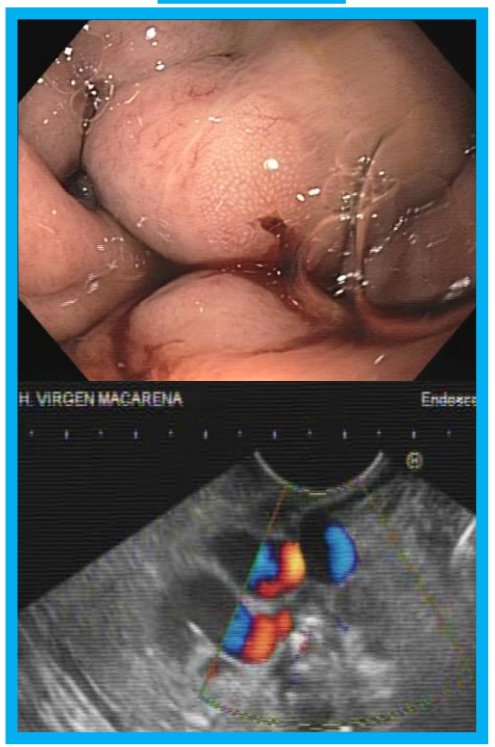
- Invasive vascular radiology

Anatomic classifications of gastric varices

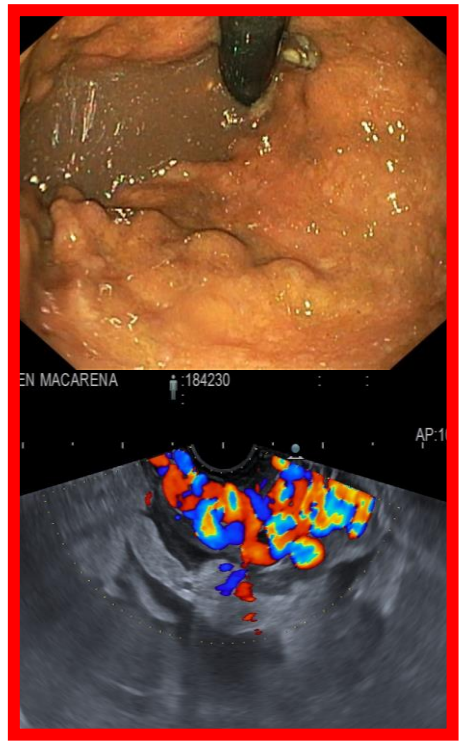
Arakawa

Morphological

Type I
Localyzed

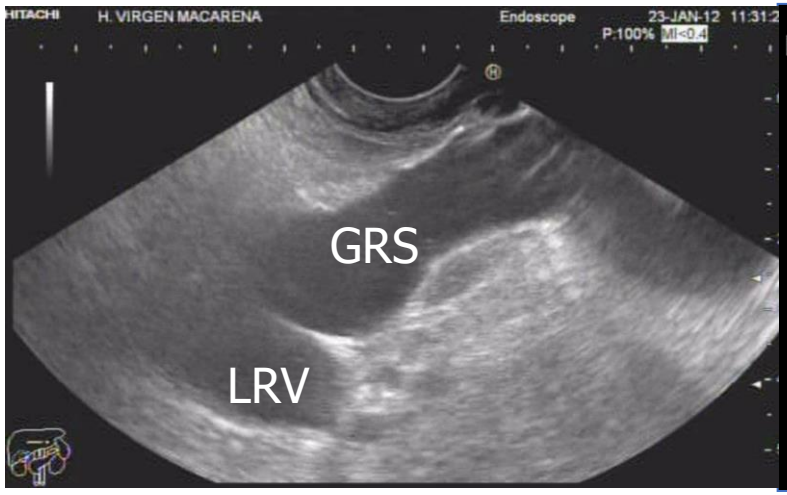


Type II
Diffuse

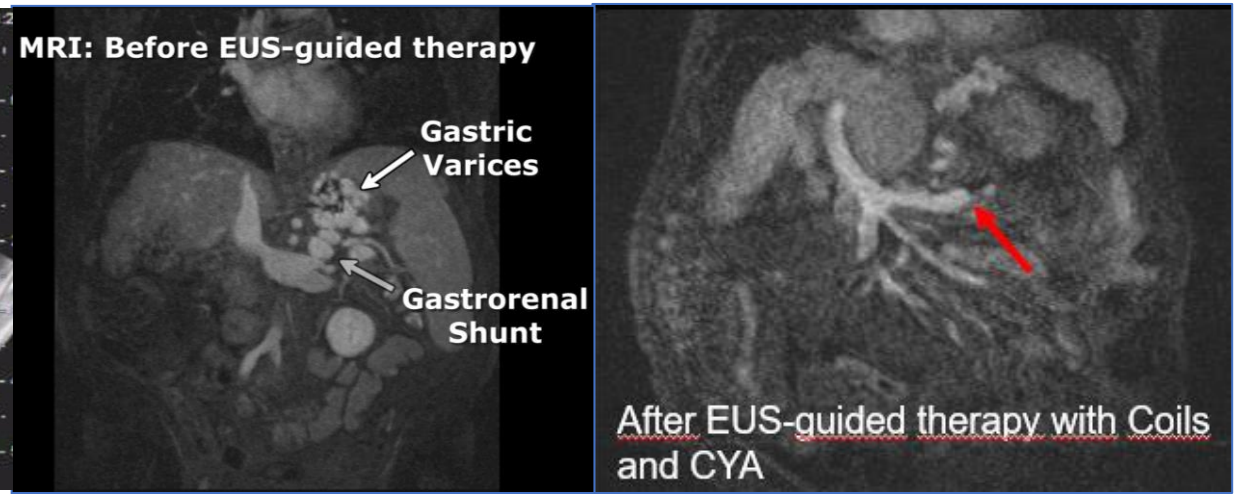


Anatomy of gastric varices : Gastrorenal shunts

- Gastrorenal shunt (GRS) occur in 80%-85% of cirrhotic patients with gastric varices.
- Gastric variceal bleeding is the most frequent complication of GRS.
- The best imaging procedure to assess GRS is angio-CT scan. Angio-MRI can also displays GRS. *Nardelli S et al. World J Gastroenterol 2020*
- GRS has also been displayed by EUS in 26/40 patients. *Kakutani H, et al. Endoscopy 2004*



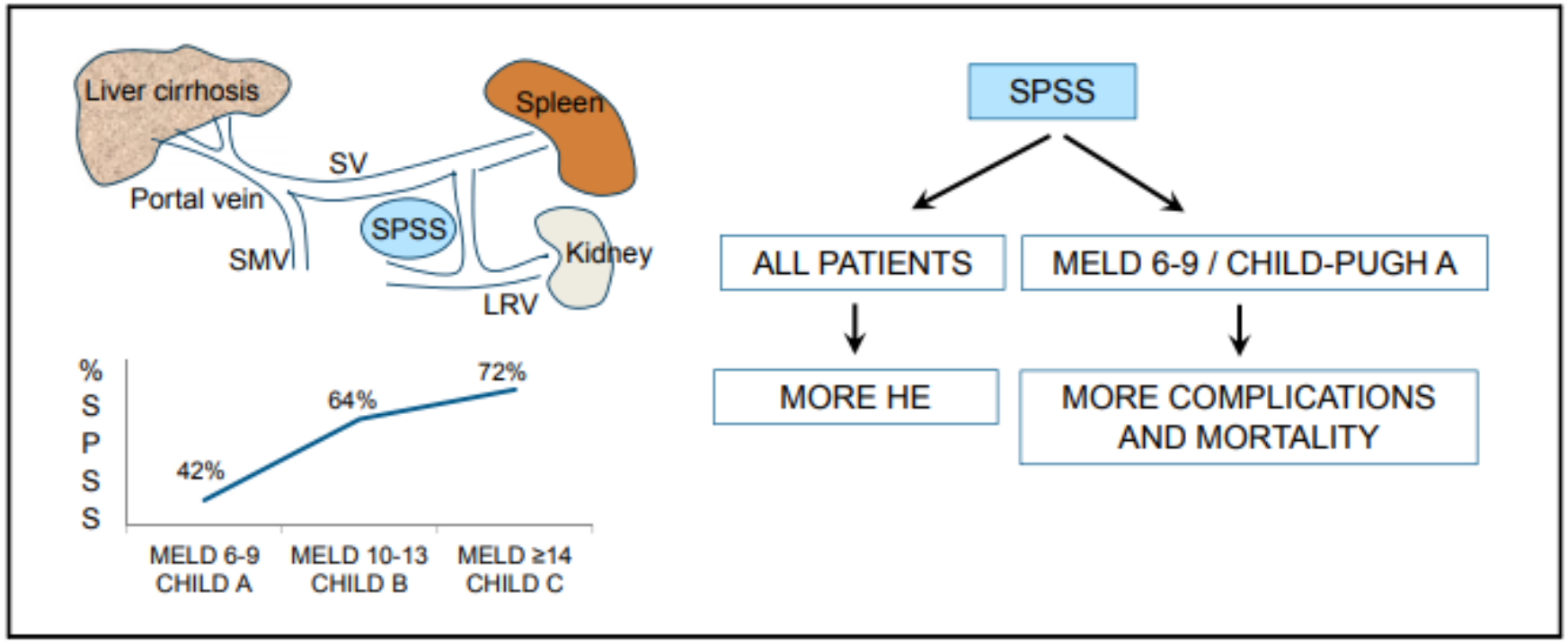
Romero-Castro R et al, GIE 2013



Romero-Castro R et al, Endoscopy 2010

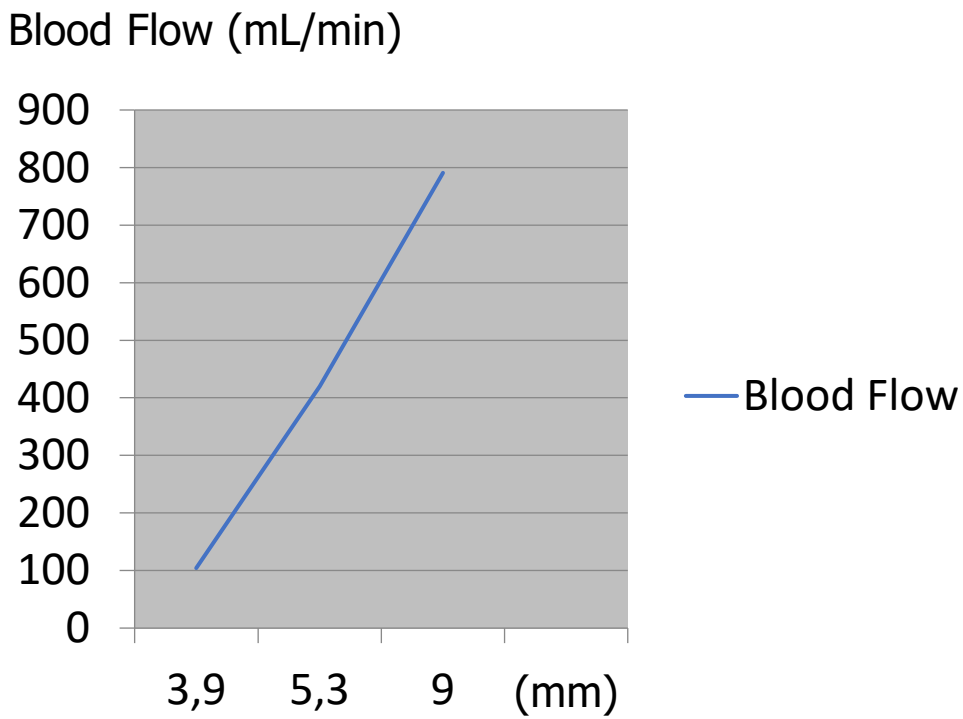
Anatomy of gastric varices : Gastrorenal shunts

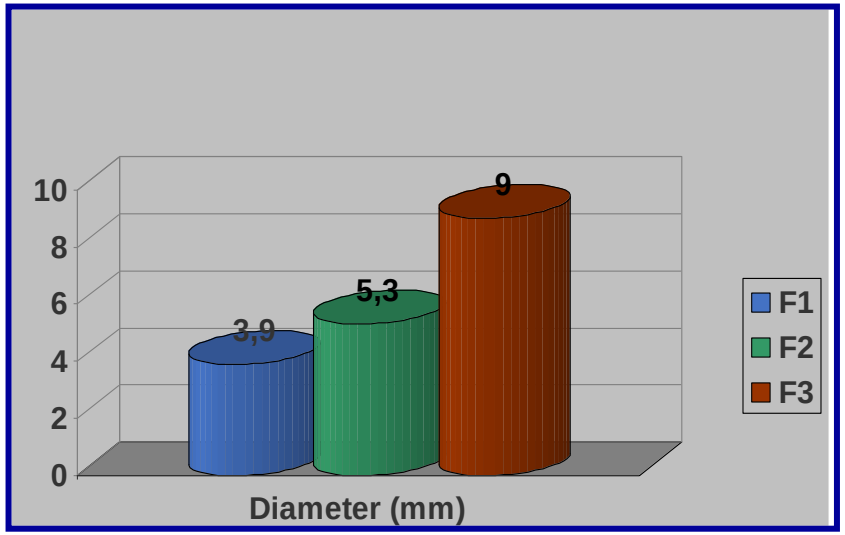
- The prevalence of spontaneous portosystemic shunts increases with the impairment of liver function.
- The detection of SPSS allows identify patients at risk of worse clinical outcomes.



Simón-Talero M, et al. Gastroenterology 2018

Hemodynamics of gastric varices

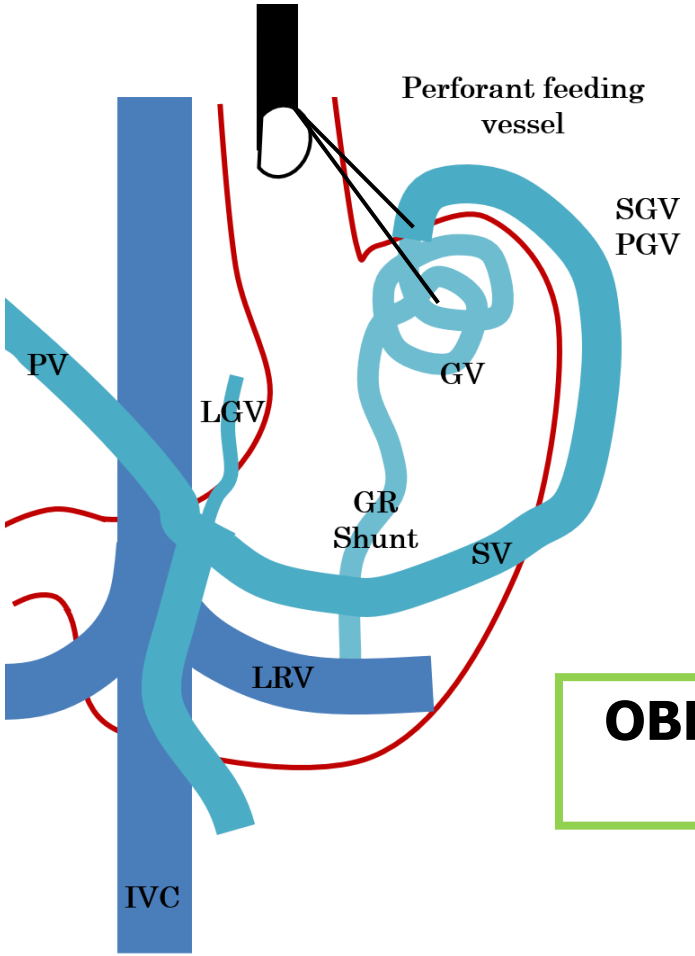




The blood flow is directly related to the diameter of the isolated gastric varices, increasing with its diameter.

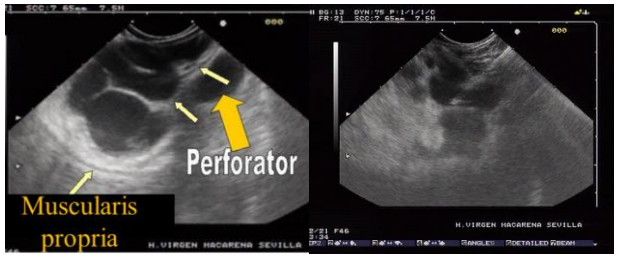
Imamura H et al, GIE 2006

EUS-guided therapeutic approaches of gastric varices



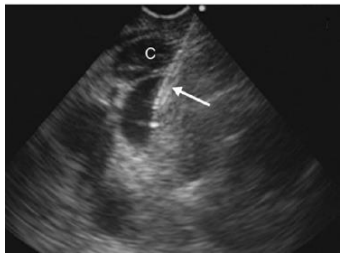
TARGET

PERFORANT
feeding vein punction



Romero-Castro R , GIE 2007
Romero-Castro R , Endoscopy 2010
Romero-Castro R , GIE 2013
Robles-Medranda C, Endoscopy 2020

GASTRIC
varices punction



Binmoeller K, GIE 2011
Bhat Y, GIE 2015

OBLITERATION METHOD

Injection of CYA
Romero-Castro R , GIE 2007
Gubler C, Scan J Gastroenterol 2014
Bick BL, Surgical Endosc 2018

Coil deployment
Romero-Castro R , Endoscopy 2010
Romero-Castro R, GIE 2013

Combined: Coils + CYA
Binmoeller K, GIE 2011
Bath Y, GIE 2015
Robles-Medranda C, DEN 2019
Robles-Medranda C, Endoscopy 2020

EUS-Guided Therapy of gastric varices: Experience

Author	Patients	Devices Used	Eradication	Adverse Events
Romero-Castro R, GIE 2007	5	22G CYA + **with lipiodol**	5/5: 100% 1.6 sessions (1-2)	None
Levy MJ, GIE 2008	1	22G Microcoils	100% 2 sessions	One rebleeding
Romero-Castro R, Endoscopy 2010	4	19G Coils	3/4: 75% 1.5 sessions (1-3)	None
Binmoeller K, GIE 2011	30	19G 1 coil + 1 mL CYA **without lipiodol**	30/30: 100% 1.3 sessions (1-3)	▪ Recurrent gastric variceal bleending: 14% ▪ Esophageal varices bleeding: 16%
Gonzalez JM, Endoscopy 2012	3	19G CYA + lipiodol	3/3: 100%	None

Author	Patients	Devices Used	Eradication	Adverse Events
Romero Castro R, GIE 2013 Multicenter Study	30	19 patients 22G: CYA + lipiodol	29/30: 97% 1.4 session (1-3)	9 asymptomatic pulmonary glue embolism
		11 patients 19G: Coils		1 bleeding from esophageal varices
Gubler C, Scand J Gastroenterol 2014	40	22G CYA + lipiodol	Not Reported 1.4 sessions (1-7)	▪ 1 transient bacteriemia ▪ 1 self limited bleeding
Law R, CGH 2015	14	22G Coils With/without CYA	Hemostasis in all cases.	One coil migration to the liver
Bhat Y, GIE 2015	152	19G Coils + CYA **without lipiodol**	Obliteration in 93%	▪ Abdominal pain (3%) ▪ Bledding from coil/glue extrusion (3%) ▪ Rebleeding (3%) ▪ 1 symptomatic pulmonary embolism
Bick BL, Surg Endosc 2018	104	40 patients 22G: CYA by endoscopy	30/40: 75% 1.3 sessions (1-3)	▪ Mild/moderate bleeding 7/40 (17.5%)
		64 patients 22G: CYA by EUS	49/64: 79% 1.1 sessions (1-2)	▪ Abdominal pain (7.8%) ▪ Fever (4.6%) ▪ Hepatic encephalopathy (1.5%) ▪ Pulmonary embolism (1.5%) ▪ Bacteriemia (1.5%)

Author	Patients	Devices Used	Eradication	Adverse Events
Khouri T, Hepatol Commun 2019	10	6 patients 19G Coils 4 patients Coils+CYA	2/10: 20%	▪ Persistent bleeding (10%) ▪ Self-limited bleeding (50%)
Lobo MRA, Arq Gastroentol 2019 Controlled study	32	16 patients 19G EUS: Coils+CYA **With lipiodol**	12/13 (93%)	▪ **Pulmonary embolism (25%)** ▪ Epigastric pain (48%) ▪ Mild bleeding (12.5%)
		16 patients 23G Direct endoscopic injection CYA **with lipiodol**	12/16 (75%)	▪ **Pulmonary embolism (50%)** ▪ Epigastric pain (6%) ▪ Mild bleeding (6%) ▪ Mental confusion (6%) ▪ Exitus (1 bleeding & 1 sepsis): (12.5%)
Robles-Medranda, C Dig Endosc 2019	30	19G Coils + CYA **without lipiodol**	29/30: 96.7%	▪ Abdominal pain (3%) ▪ Fever (3%)
Robles-Medranda C Endoscopy 2020 Controlled Study	60	19G 30 patients Coils (median 2) + CYA (median 1.8 mL)	30: 100%	▪ Abdominal pain 1 (3.3%) ▪ Fever 1 (3.3 %) ▪ Rebleeding 1 (3.3%)
		30 patients Coils alone (median 3)	27: 90%	▪ Abdominal pain 1 (3.3%) ▪ Rebleeding 6 (20%)

Bleeding ectopic varices

EUS-guided injection of CYA, coil deployment or combination therapy

- **Anastomotic varices**

Levy MJ et al , GIE 2008

- **Duodenal varices**

Rana SS et al, Indian J Gastroenterol 2011

Kinzel J et al, J Clin Gastroenterol 2014

- **Rectal varices**

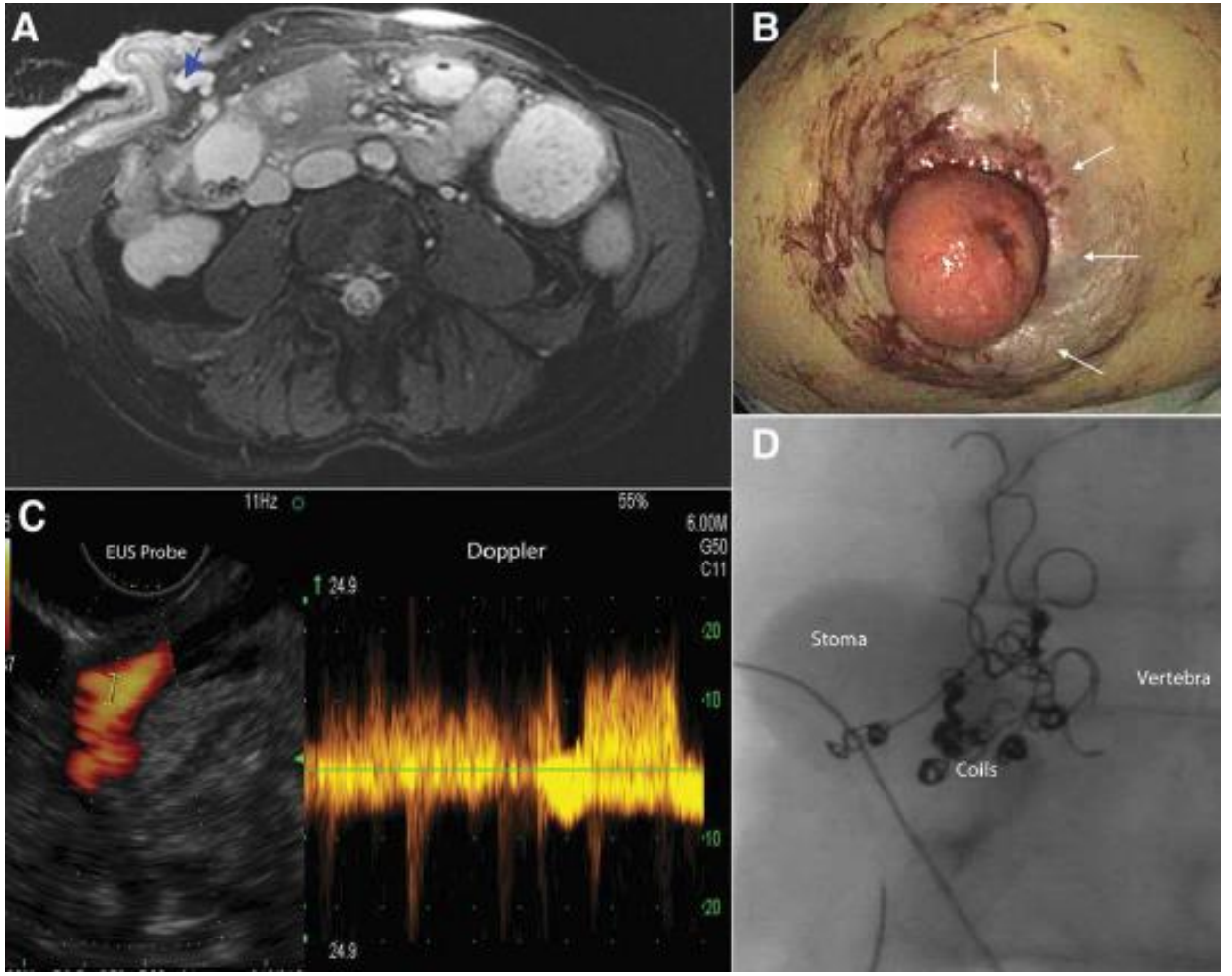
Weilert F et al, GIE 2012

Connor EK et al, GIE 2014

Storm AC et al, GIE 2014

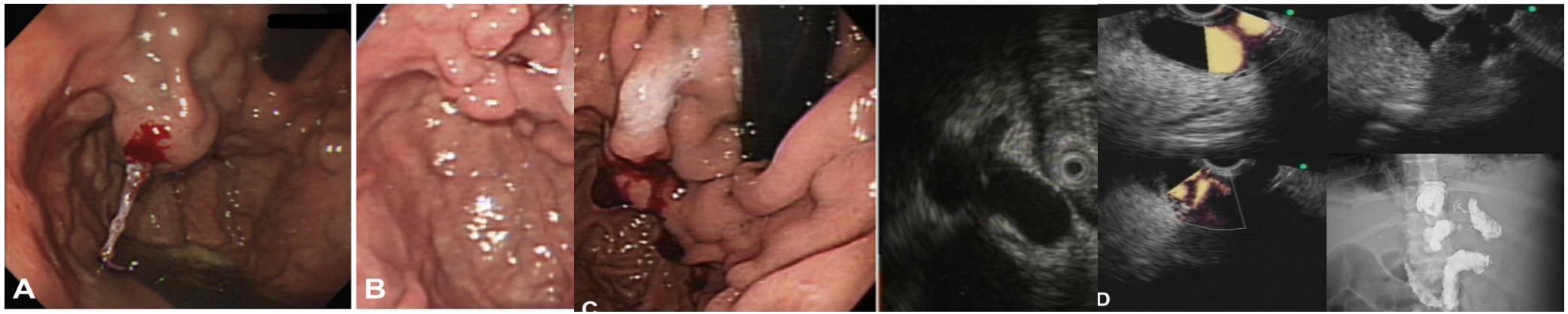
- **Peristomal varices**

Tsynman DN et al, GIE 2014



EUS-guided rescue therapy

Hemostasis is achieved with EUS-guided salvage therapy after intramural direct endoscopic injection of CYA and further refractory rebleeding from incomplete variceal thrombosis



Sharma M, Goyal A. Gastroenterology 2012

Lin M-S et al. GIE 2014

Tang RS et al. GIE 2016

Mazzawi T et al. EIO 2019

Other EUS-guided approaches for gastric variceal therapy

EUS-guided thrombin injection
(8 patients)

Frost JW et al, EIO, 2018

EUS-guided coil deployment plus sclerosant injection
(8 patients)

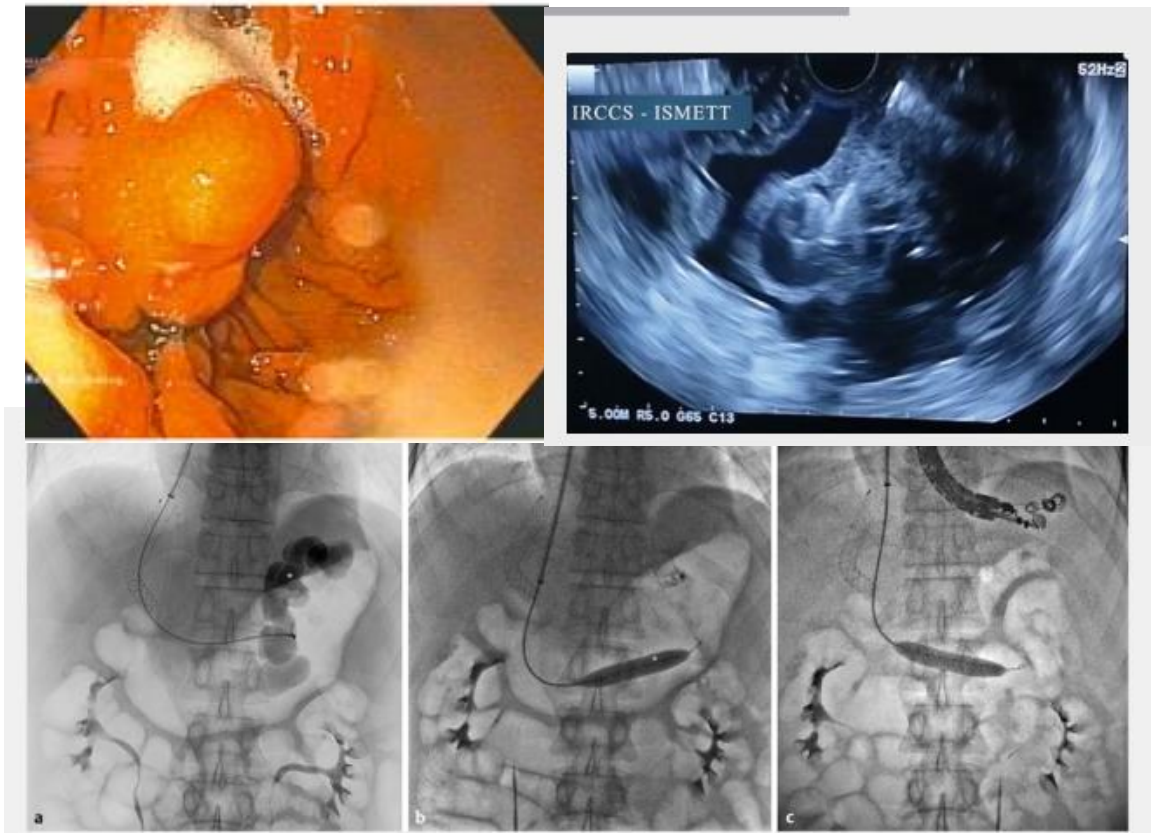
Irisawa A et al, Dig Endosc 2020

EUS-guided coil deployment combined with B-RTO
(1 patient)

Tarantino I et al, Endoscopy 2018

EUS-guided coil deployment and absorbable gelatin sponge
(10 patients)

Bazarbashi AN, et al. Endosc Int Open. 2020



Tarantino I et al, Endoscopy 2018

EUS-guided therapeutic approaches: Pros and Cons

TARGET

PERFORANT feeding vein punction	GASTRIC varices punction
Place of maximum blood flow blockade	Easy targeting
Time consuming	Less time consuming
Lesser amount of CYA/Coils?	Lesser amount of CYA/Coils?

OBLITERATION METHOD

Injection of CYA

- ✓ Easy to perform
- X Adverse events due to the glue

Coils deployment

- ✓ Avoids the possible drawbacks of CYA
- X More demanding technically

Combined: Coils + CYA

- ✓ Less amount of coils and CYA needed
- X When CYA is used without lipiodol, asymptomatic glue embolisms cannot be carried out

EUS-guided therapeutic approaches

- EUS-guided injection of CYA compared to direct endoscopic injection has the following advantages in a retrospective study in 104 patients:
  - ✓ Significantly lower mean volumen of CYA required to GV obliteration.
  - ✓ With a significant higher number of varices treated by EUS-guidance.
  - ✓ Significantly lower rates of rebleeding.

Bick BL et al, Surg Endosc 2018

- A retrospective multicenter study in 30 patients compared EUS-guided coil vs. EUS-guided injection of CYA plus lipiodol and further thoracic CT-scans found:
  - ✓ Similar obliteration rates.
  - ✓ Significantly higher rates of adverse events 9% vs. 58% ($p<0.001$), mainly asymptomatic glue embolism (9/19 patients, 47%) and longer hospital-stay.

Romero-Castro R et al, GIE 2013

- A controlled study of 62 patients compared EUS-guided therapy with coil deployment + injection of CYA vs direct endoscopic injection of CYA plus lipiodol with further thoracic CT-scans found asymptomatic glue embolism in 25% and 50% of patients in each group, respectively.

Lobo MRA et al, Arq Gastroentol 2019

EUS-guided therapeutic approaches

- The most extensive study reported combined coils plus CYA injection in 152 patients obtained GV obliteration in 93% with 3% of rebleeding. Neither lipiodol nor thoracic CT-scans were performed.

Bhat YM. et al. GIE 2016

- A randomized study of 60 patients comparing EUS-guided therapy with coils vs. EUS-guided combined method, there were not found differences in overall technical success and GV obliteration. However, there were significantly higher rates of rebleeding in patients treated only with coils (20% vs. 3%) and reinterventions.

Robles Medranda C et al. Endoscopy 2020

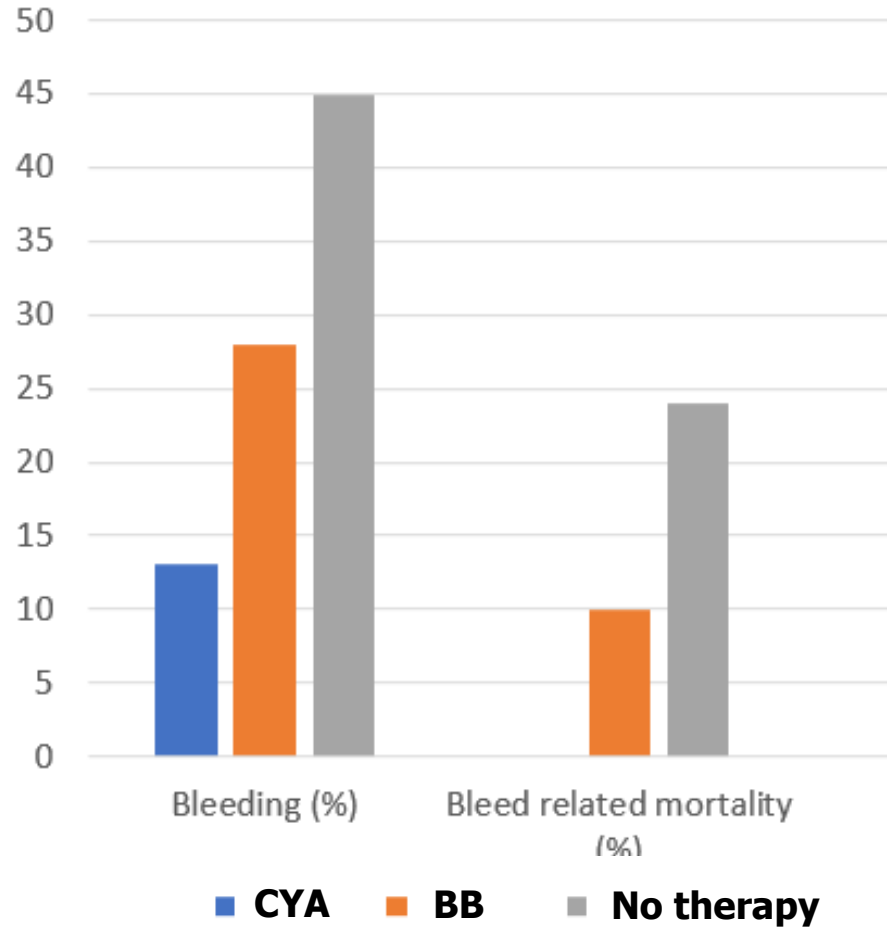
- In the study by Robles-Medranda et al there were employed a median number of 2 coils (range 1-3) and injected a median volume of 1.8 mL (range 1.2-2.4 mL) of CYA in the EUS combined group and a median of 3 coils (range 1-7), probably leading to undertreatment in the coil alone group. Besides, 2/7 patients whom rebled from the coil-alone group needed more than one session with combined therapy, probably reflecting a more severe portal hypertension stage.

Romero-Castro R et al. Endoscopy 2021

Primary Prophylaxis of Gastric Variceal Bleeding

Direct endoscopic injection of CYA

- Patients with GOV2 and IGV1 who never bled were randomised to:
  - ✓ Direct endoscopic injection of CYA (Group I: n=30),
  - ✓ Beta-blockers (Group II: n=29) or
  - ✓ No treatment (Group III: n=30).
- Median follow-up of 26 months
- There were a statistically significant difference of bleeding in groups II and III and in the probability of survival was higher in group I compared to group III.

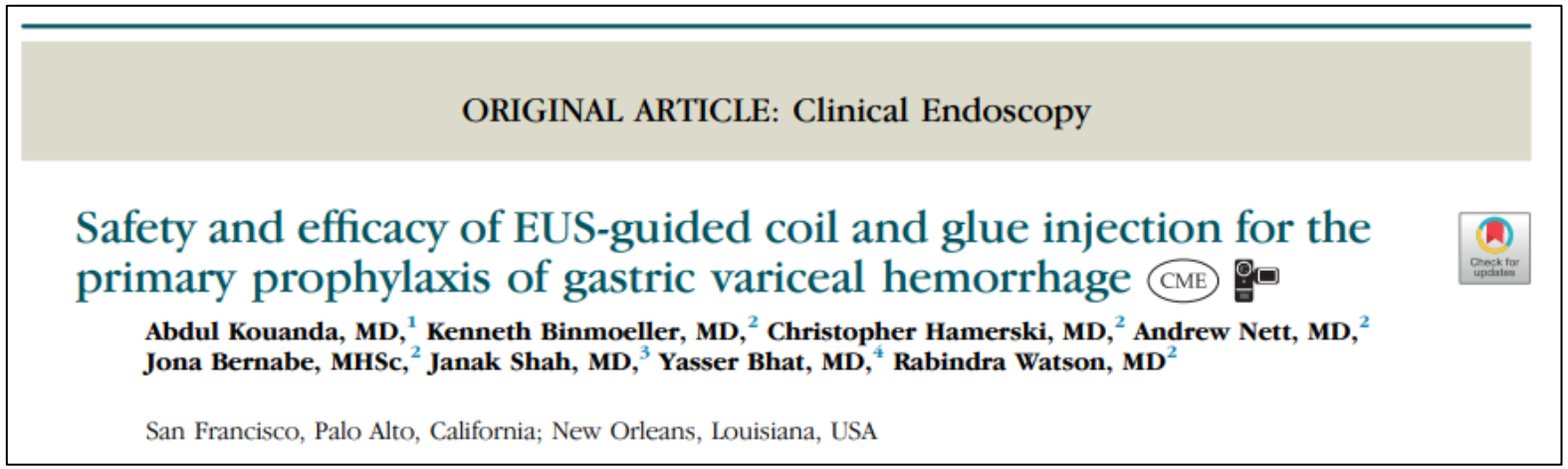


Misra SR et al. J Hepatol 2011

Primary Prophylaxis of Gastric Variceal Bleeding

EUS-guided combined therapy (coil + CYA)

- 80 patients who never bled with high risk GV: size >10 mm or cherry red spots and mean MELD 12.3±3.7
- Mean follow-up: 3±2.4 years
- Mean coil number 1.5 (range 1-3) and mean volume of CYA injected 2 mL (range 0.5-5)
- Technical success 100%
- GV obliteration confirmed by EUS in 96.7%
- Post-treatment GV hemorrhage was observed in 2 patients (2.5%) and adverse events in 4 patients (5%)
- There were observed neither deaths related to GV bleeding nor need for TIPS therapy



ORIGINAL ARTICLE: Clinical Endoscopy

Safety and efficacy of EUS-guided coil and glue injection for the primary prophylaxis of gastric variceal hemorrhage CME

Abdul Kouanda, MD,[1] Kenneth Binmoeller, MD,[2] Christopher Hamerski, MD,[2] Andrew Nett, MD,[2] Jona Bernabe, MHSc,[2] Janak Shah, MD,[3] Yasser Bhat, MD,[4] Rabindra Watson, MD[2]

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EUS-guided therapeutic approaches: getting evidence-based data

- A systematic review and meta-analyses of 11 studies with 536 patients evaluated the comparative effectiveness of EUS-guided therapy of gastric varices analyzed by three treatment cohorts: EUS-guided CYA injection alone, EUS-guided coil embolization plus CYA injection and EUS-guided coil embolization alone.

  - ✓ Overall technical success 100%
  - ✓ Clinical success 97%
  - ✓ Adverse events 14%

Table 3. Subgroup analyses comparing different treatment strategies for gastric varices

Comparison of treatments	Technical success	Clinical success	Rate of adverse events	Rate of reintervention	Rate of re-bleeding
EUS CYA alone *versus* EUS CYA + Coil (*P*)	97% *versus* 100% (<0.001)	96% *versus* 98% (<0.001)	21% *versus* 10% (<0.001)	26% *versus* 15% (<0.001)	30% *versus* 14% (<0.001)
EUS CYA alone *versus* EUS Coil alone (*P*)	97% *versus* 99% (0.005)	96% *versus* 90% (0.146)	21% *versus* 3% (<0.001)	26% *versus* 25% (0.846)	30% *versus* 17% (<0.001)
EUS CYA + coil *versus* EUS Coil alone (*P*)	100% *versus* 99% (<0.001)	98% *versus* 90% (<0.001)	10% *versus* 3% (0.057)	15% *versus* 25% (0.047)	14% *versus* 17% (1.00)

CYA: Cyanoacrylate, Coil: Coil embolization

McCarty TR. et al, Endosc Ultrasound 2020

EUS-guided therapeutic approaches: getting evidence-based data

- Another meta-analyses compared efficacy and safety of EUS-guided therapy of GV in 851 patients in 23 studies vs. endoscopic direct injection of CYA in 3467 patients in 28 studies. The pooled results for the different EUS-guided approaches were:
  - ✓ 94% treatment efficacy, GV obliteration 84%, GV recurrence 9%, early rebleeding 7% and late rebleeding 12%.
  - ✓ When compared to direct endoscopic injection, there were observed no differences between all the previously mentioned parameters except for ***a significantly highly rate of GV obliteration in the EUS-guided groups***.
  - ✓ On subgroup analyses the ***EUS-guided combined method was superior in terms of less recurrence rates***.

▶ **Table 1** Pooled results of outcomes.

Intervention/outcomes, pooled rate, % (95%CI, I^2)	All EUS modalities	EUS-glue	EUS-coil	EUS-coil/glue	END-glue (comparator group)
Treatment efficacy	93.7 (89.5–96.3, 53.7) 29 cohorts	91 (80–96.2, 40) 9 cohorts	84.2 (54.5–96, 6.5) 3 cohorts	96.7 (93–98.5, 55) 14 cohorts	91.4 (82.8–95.9, 97) 28 cohorts; $P=0.4$
Obliteration of gastric varices	84.4 (74.8–90.9, 77) 21 cohorts	90 (71.3–97, 0) 5 cohorts	N/C	86.2 (75.5–92.7, 74) 12 cohorts	62.6 (42.6–79.1, 97); 13 cohorts; $P=0.02$
Recurrence of gastric varices	9.1 (5.2–15.7, 32) 16 cohorts	15 (8.8–24.5, 0) 5 cohorts	N/C	5.2 (2.6–9.8, 0) 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; $P=0.1$
Adverse events					
Embolism	5.6 (3.1–9.8, 56) 28 cohorts	8.4 (3–21.3, 66) 9 cohorts	4 (0.5–25.7, 0) 3 cohorts	4.3 (1.8–9.8, 59) 13 cohorts; $P=0.3$	–
Mild adverse events	5.9 (4.1–8.3, 0) 28 cohorts	4.7 (2.1–10.6, 0) 9 cohorts	3.9 (0.8–18.1, 0) 3 cohorts	5.3 (3.2–8.6, 35) 13 cohorts	–
Moderate adverse events	5.7 (3.2–9.8, 53) 28 cohorts	9 (3.5–21.6, 66) 9 cohorts	4 (0.5–25.1, 0) 3 cohorts	4 (1.7–9.2, 57) 13 cohorts	
Mortality (all-cause)	13.1 (8.3–20.2, 68); 19 cohorts	27.9 (16.3–43.5, 75); 5 cohorts	N/C	9 (5.1–15.2, 0); 9 cohorts; $P=0.00$	
Mortality due to gastric varices rebleed	7.7 (4.9–11.9, 29) 18 cohorts	12 (5.2–25.6, 58) 5 cohorts	N/C	4.5 (2–9.8, 21) 8 cohorts; $P=0.09$	

EUS, endoscopic ultrasound; END, direct endoscopic glue injection; CI, confidence interval; N/C, not calculated due to limited studies.

Mohan BP. et al. Endoscopy 2020

EUS-guided therapeutic approaches: getting evidence-based data

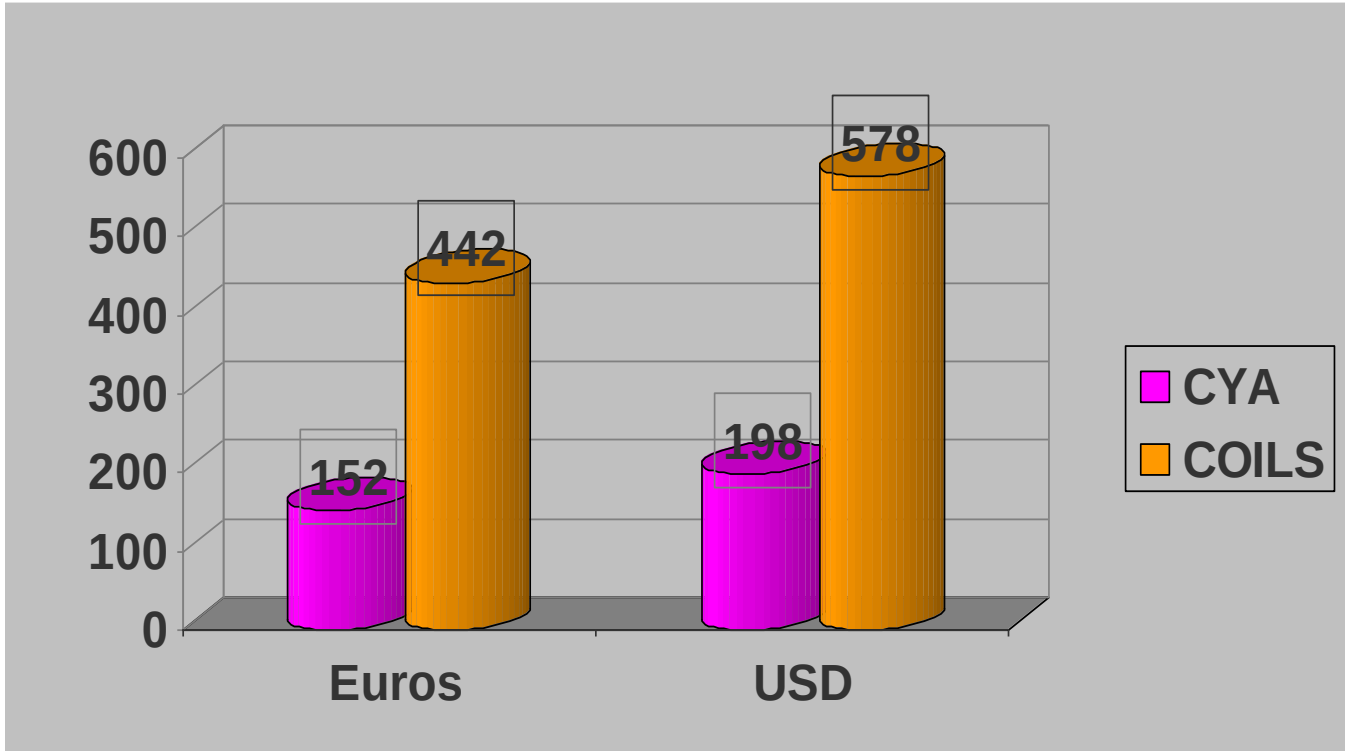
- EUS-guided therapy overall seems an effective and safe modality.
- Among the three EUS-therapies available, EUS combination therapy with coil embolization plus CYA injection appears as the preferred procedure over EUS-based monotherapy.

McCarty TR. et al. Endosc Ultrasound 2020

Mohan BP. et al. Endoscopy 2020

Comparative costs CYA vs coils

		€	USD
CYA	1 mL Histoacryl plus Lipiodol	55	72
	1 mL Glubran plus Lipiodol	143	188
1 COIL		76	99

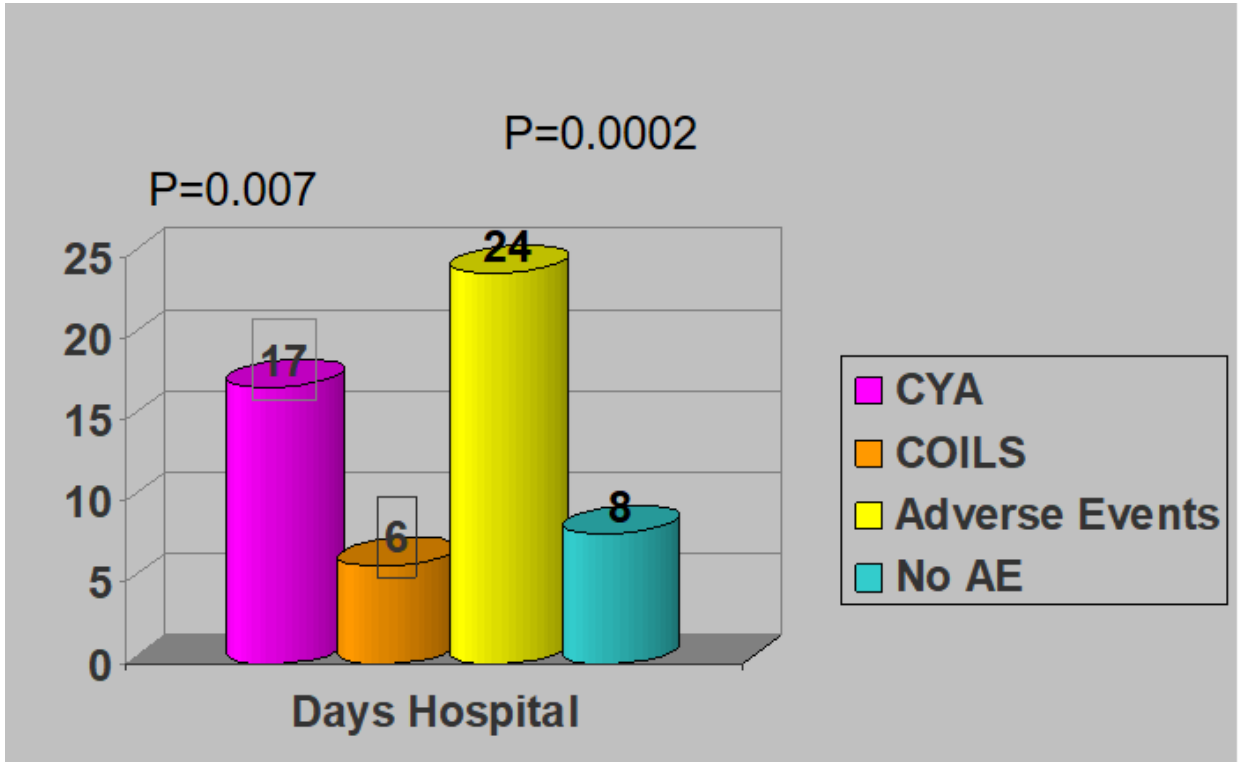


Romero-Castro R et al. GIE 2013

Comparative costs CYA vs coils

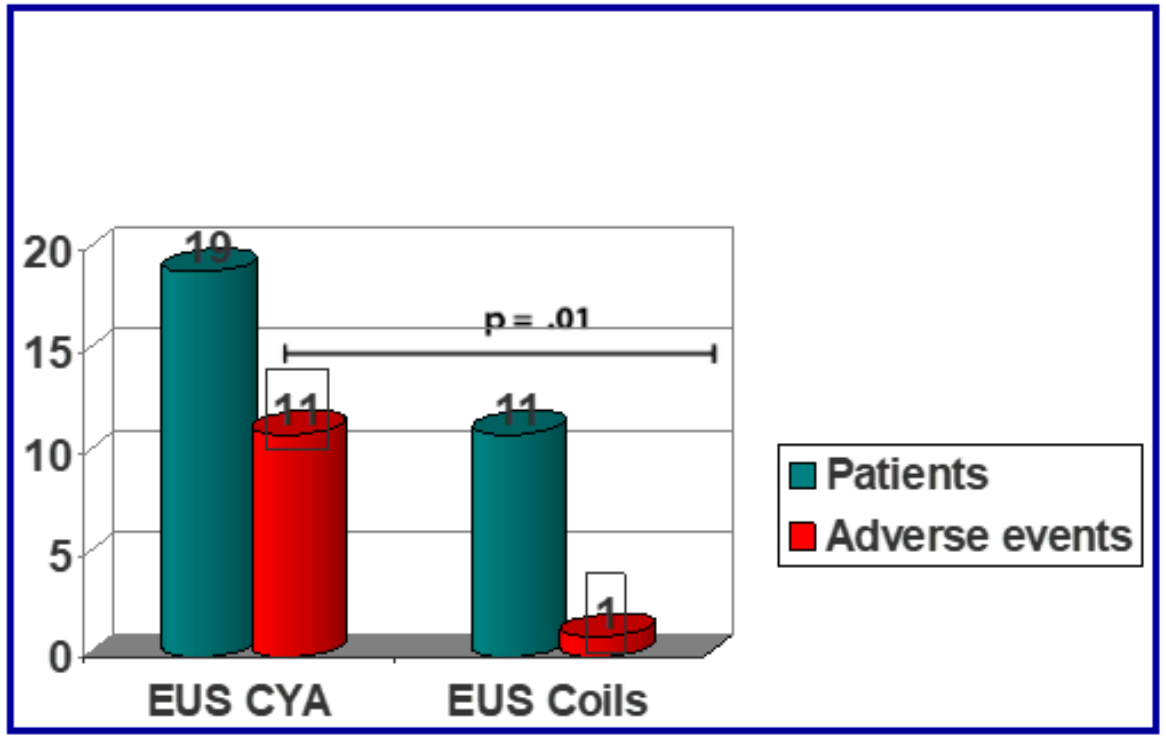
HOSPITAL STAY (in days)

Comparison between CYA and Coils groups and between patients with or without adverse events.



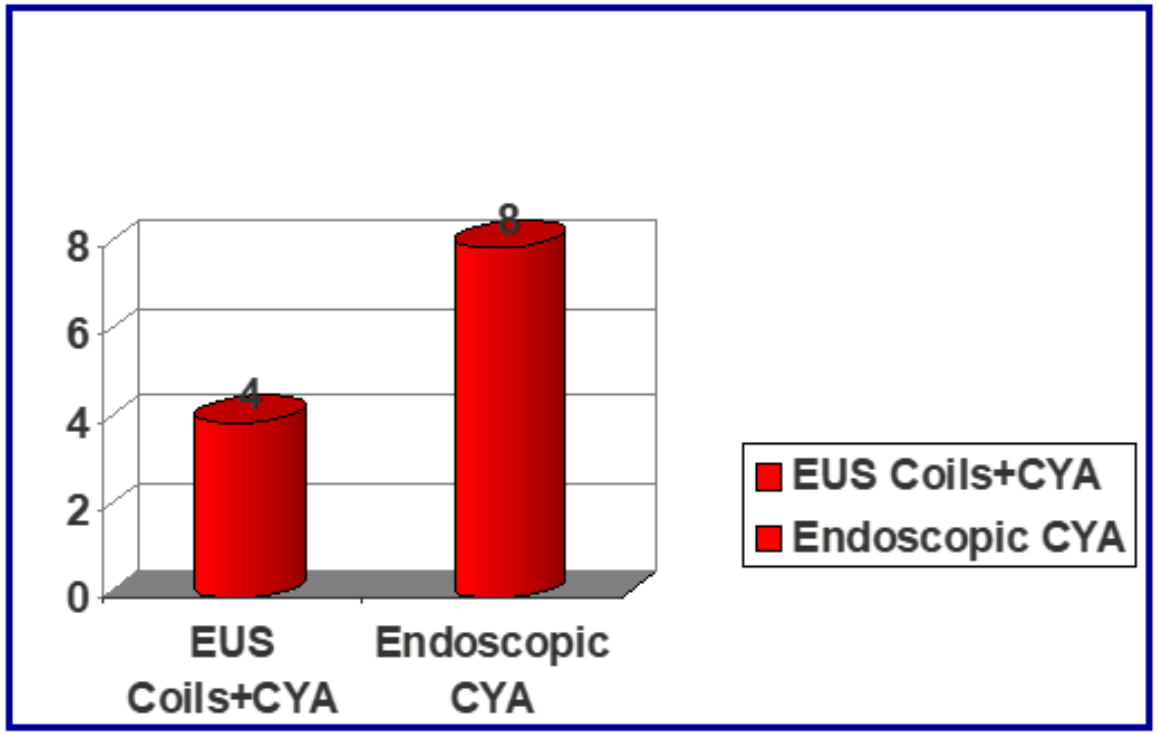
Romero-Castro R et al. GIE 2013

Rates of adverse events observed when lipiodol is mixed with CYA and CT-scans are performed later



Significantly higher rates of adverse events 9% vs. 58% (p<0.001), mainly asymptomatic glue embolism (9/19 patients, 47%)

Romero-Castro R et al. GIE 2013



Asymptomatic glue embolisms in 4/16 (25%) and 8/16 patients (50%) were observed, although no statistically significant difference was found.

Lobo MRA et al. Arq Gastroenterol 2019

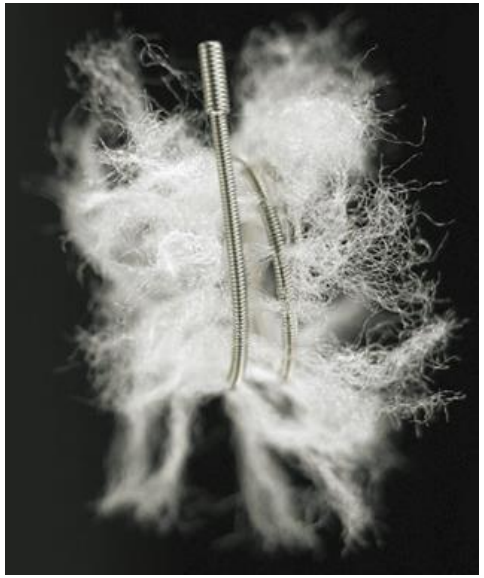
Coil before glue injection?

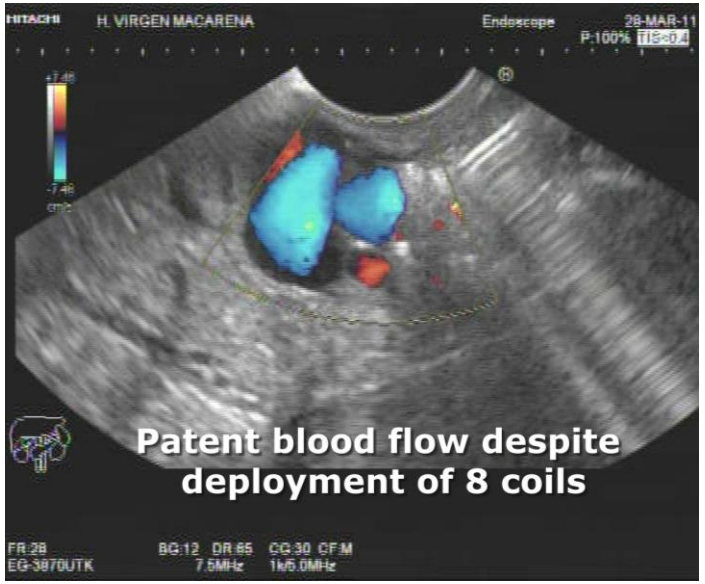
- Fibers serve as scaffold to retain glue on site
- Coil contributes to varix obliteration
- Reduced flow -> thrombosis

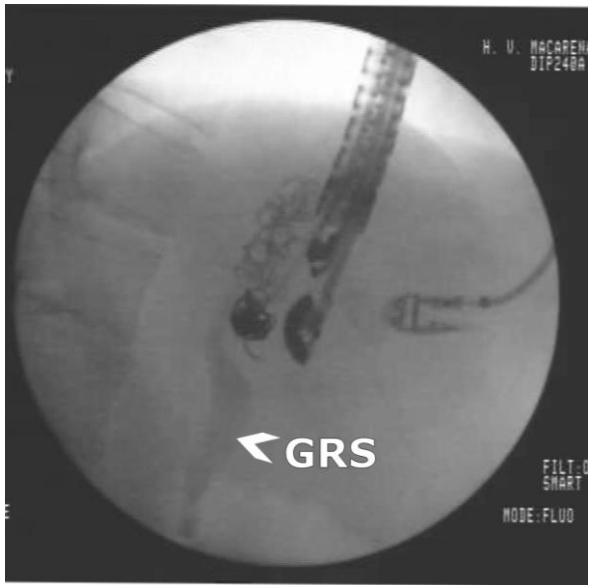
2015 Endoscopy Course. Courtesy Dr. Kenneth Binmoeller

EUS-guided combined therapy with coil + CYA: a note of caution

- It has been hypothesized that 1-2 haired-fiber coils serve as scaldfolds for the glue to prevent its embolization.
- However, we will show in the following videos the hemodynamic and anatomic backgroung in the setting of GV.
- Although we used contrast and no glue, concerns of glue embolism are reasonably raised.







GASTRIC VARICES

HEMODYNAMICS

Romero-Castro R, Jimenez-Garcia VA. EUS-guided angiography in gastric varices: anatomic and hemodinamic aspects. In: Atlas of Interventional EUS: Case-based Strategies. Teoh A, Itoi T, Giovannini M, Khashab M (eds). Singapore: Springer; in press. ISBN: 978-981-16-9339-7.

A:
Clearance of pure contrast injected with a 19G needle in the perforant feeding vein of gastric varices

Romero-Castro R, et al. EUS-guided angiography in gastric varices: anatomic and hemodynamic aspects. A note of caution. Endoscopy (under review)

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

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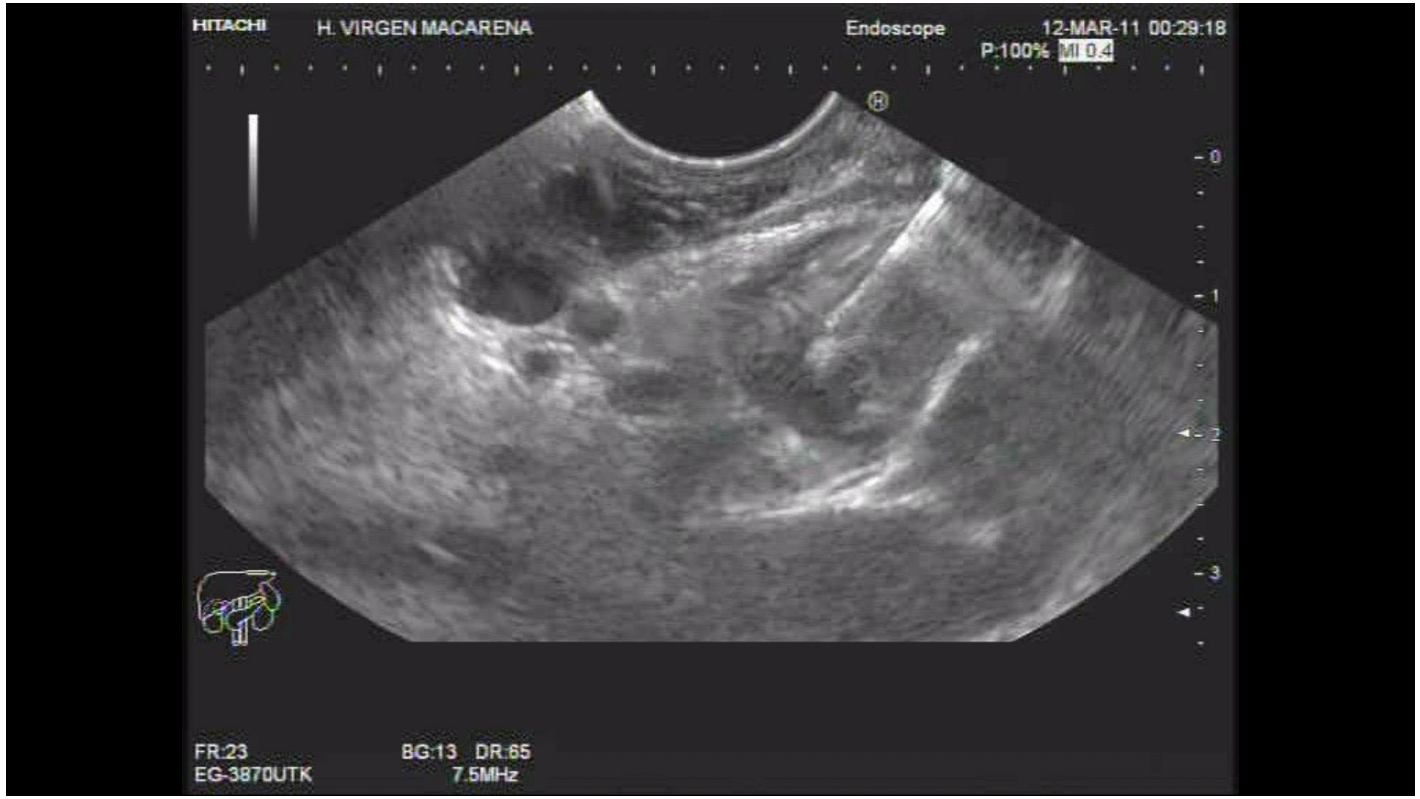

Advantages of EUS-guided therapy of gastric varices

- Accurate visualization of collaterals and perforants.
- Assess the risk of rebleeding in case of patent perforants.
- Lower risk of adverse events of CYA using less amount of glue.
- Therapy independent of endoscopic vision no matter the amount of blood.
- The risk of injection of CYA in the wall of the gastric varices with further ulceration and refractory bleeding is prevented.
- Minimizes the risk of damage to the endoscope.
- Accurate assessment of gastric varices thrombosis at follow-up allowing further therapy reducing the risk of rebleeding.
- The EUS-guided therapy with only coils nulifies the risks associated to CYA.

Tips and tricks in EUS-guided therapy

- **ECHOENDOSCOPE IN A STRAIGHTENED POSITION !!!!! NEVER IN RETROFLEXION !!!!!!!!**
- Flush povidone iodine in the working channel before the punction and prophylactic antibiotherapy.
- Punction in a perpendicular angle avoiding movements of torque or up and down, withdrawing 2-3 mm the stylet.
- Assess the proper position of the needle tip into the vessel by aspiring with the siringe and flushing the needle with saline.
- If an EUS-guided angiography is performed flush the needle with saline after.
- When coils are deployed, the caliber should be approximately a 20% more than the targeted vessel and the longer the better.
- In coil alone therapy, deploy as many coils are needed to obtain a thick mesh.
- When injecting CYA : Add lipiodol ???
- Do not spare in any that could be useful: fluoroscopy, colleagues, trained assistants, devices, etc.

TAKE-HOME MESSEGES

- EUS-guided therapy is placing in the pole position of the armamentarium of gastric varices and increasingly performed worldwide due to its accuracy and safety profile with growing evidence-based data.
- The flawness of EUS-guided therapy (availability and readiness) are rapidly being overcome thanks to the enthusiasm and skillness of the new generations of endosonographers.
- Among their different approaches, the combination therapy (coils plus CYA) is the most used method.
- However, although it is postulated that the injection of CYA without lipiodol is safe, there is no way to carry out asymptomatic but potential harmful glue embolisms if lipiodol and CT scans are not employed.
- EUS-guided coil deployment without CYA nullifies any risk associated to the glue injection in the setting of such high blood-flow vessels usually with gastrorenal shunts.
- New devices allowing even faster and safe EUS-guided procedures and well-designed controlled studies are still needed.

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On the shoulders of giants…

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Dr. F. Marcos
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