

TREATMENT OF GASTRIC VARICES

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GASTRIC VARICES

| Type [| Definition | Relative frequency | Overall bleeding risk without treatment |
|---|---|--------------------|---|
| Gastro-oes | ophageal varices (GOV) | | |
| GOV type 1 | OV extending below cardia into lesser curvature | 70% | 28% |
| GOV type 2 | OV extending below cardia into fundus | 21% | 55% |
| Isolated gas | stric varices (IGV) | | |
| IGV type 1 Isolated varices in the fundus | | 7% | 78% |
| IGV type 2 | Isolated varices else in the stomach | 2% | 9% |

Bleeding risk 1, 3 5 yrs 16%, 36%, e 44%

UPDATED ENDOSCOPIC CLASSIFICATIONS OF GASTRIC VARICES

| A. Sarin's classification of gastric varices ¹ | | | | | |
|---|--|--|--|--|--|
| Gastroesophageal varices GOV1 GOV2 | Varices in continuity with esophageal varices Along the lesser curvature Along the greater curvature extending toward the gastric fundus | | | | |
| Isolated gastric varices IGV1 IGV2 | Isolated cluster of gastric varices in the gastric fundus Isolated gastric varices in the other parts of the stomach | | | | |
| B. Hashizume classification of g | jastric varices ² | | | | |
| Form | F1 (tortuous), F2 (nodular) and F3 (tumorous) | | | | |
| Location | La (anterior), Lp (posterior), Ll (lesser curvature), Lg (greater curvature), Lf (fundus) | | | | |
| Color | Cw (white), Cr (red) | | | | |
| RCS | Glossy, thin-walled focal redness on the varix | | | | |
| C. Hoskins and Johnson's classification of gastric varices ³ | | | | | |
| Type 1 | Inferior extension of esophageal varices across the squamo-columnar junction | | | | |
| Type 2 | Gastric varices located in fundus, which appear to converge to cardia with esophageal varices | | | | |
| Type 3 | Gastric varices in fundus or body in the absence of esophageal varices | | | | |
| D. Arkawa classification of gast | ric varices ⁴ | | | | |
| Type I Ia Ib | A single supplying vessel forms a fundic varix Plural supplying vessels join and form a varix that drains into a single vessel | | | | |
| Type II | Gastric varices with multiple communications with vessels in stomach wall | | | | |
| E. Mathur's classification of gastric varices ⁵ | | | | | |
| Type 1 | Esophageal varices with lesser curvature varices | | | | |
| Type 2 | Esophageal varices with fundal varices (2a—subcardiac and 2b—diffuse fundal) | | | | |
| Type 3 | Isolated fundal varix (3a—due to splenic vein thrombosis, 3b—due to generalized portal hypertension) | | | | |
| Type 4 | Lesser curvature gastric varices with esophageal varices with fundal varices | | | | |
| Type 5 | Antral varices | | | | |

RISK OF BLEEDING OF GASTRIC VARICES

 Size of fundal varices (large>medium>small, defined as >10 mm, 5- 10 mm, and <5 mm, respectively)

• Child class (C>B>A)

• Endoscopic presence of variceal red spots (defined as localized reddish mucosal area or spots on the mucosal surface of a varix)

RISK FACTOR FOR BLEEDING IN GASTRIC VARICES

RCT primary prophylaxis GV: no treatment 45% bleeding
NSBB 28% bleeding
endoscopic treatment 13% bleeding

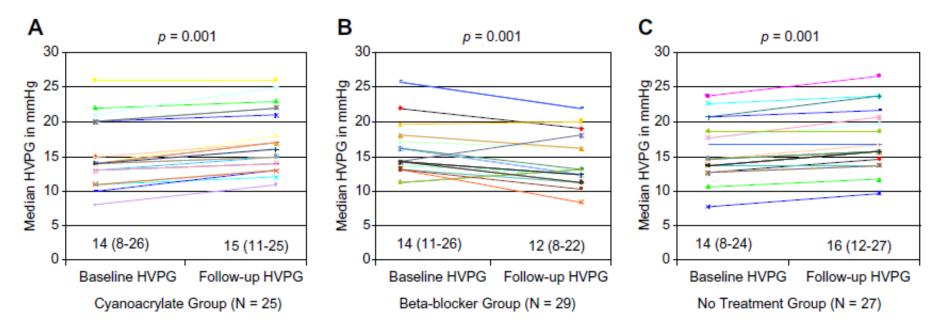
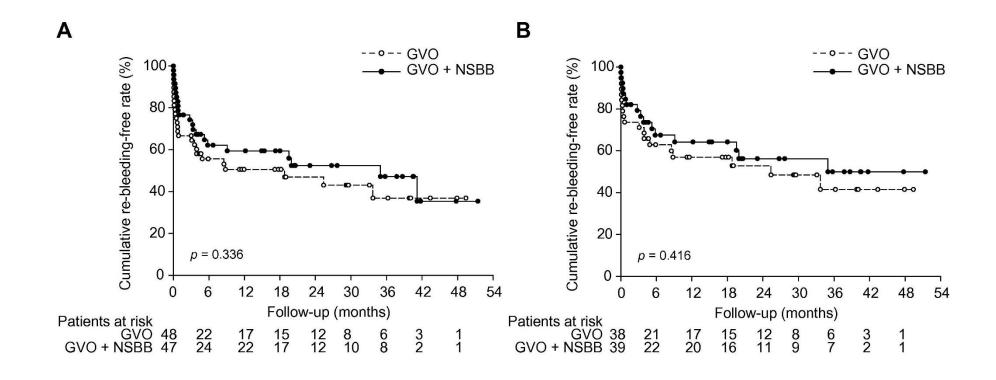


Fig. 2. Baseline and follow-up HVPG in cyanoacrylate group (A), beta-blockers group (B), and no-treatment group (C).

Efficacy of non-selective β-blockers as adjunct to endoscopic prophylactic treatment for gastric variceal bleeding: A randomized controlled trial

Hung-Hsu Hung^{1,2,3}, Chen-Jung Chang^{1,2,4}, Ming-Chih Hou^{1,2,3,*}, Wei-Chih Liao^{1,2,5}, Che-Chang Chan^{1,2}, Hui-Chun Huang^{1,2}, Han-Chieh Lin^{1,2}, Fa-Yauh Lee^{1,2}, Shou-Dong Lee^{1,6,7}



EFFICACY OF ENDOSCOPIC TREATMENT

SCLEROTHERAPY – GASTRIC VARICES

| Authors | Agent (%) | n | Success (%) | Rebleeding (%) | Complications |
|---------------------|-----------|----|-------------|----------------|------------------------|
| Gimson et al., 1991 | EO/glue | 41 | 40 | 16 | Ulcer 29%, perforation |
| Oho et al., 1995 | EO (5) | 24 | 67 | 25 | |
| Chang et al., 1996 | STD (1.5) | 25 | 80 | 70 | Ulcer 30% |
| Chang et al., 1996 | GW (50) | 26 | 92 | 30 | Ulcer 30% |
| Sarin et al., 1997 | AA (95) | 18 | 67 | 34 | Ulcer 100% |
| Ogawa et al., 1999 | EO (5) | 21 | 81 | 100 | - |
| Sarin et al., 2002 | AA (95) | 8 | 62 | 25 | - |

EO = Ethanolamine oleate; STD = Sodium tetradecyl; GW = Glucose water; AA = Acetic acid; GVS = Gastric variceal sclerotherapy

OBTURATION – GASTRIC VARICES

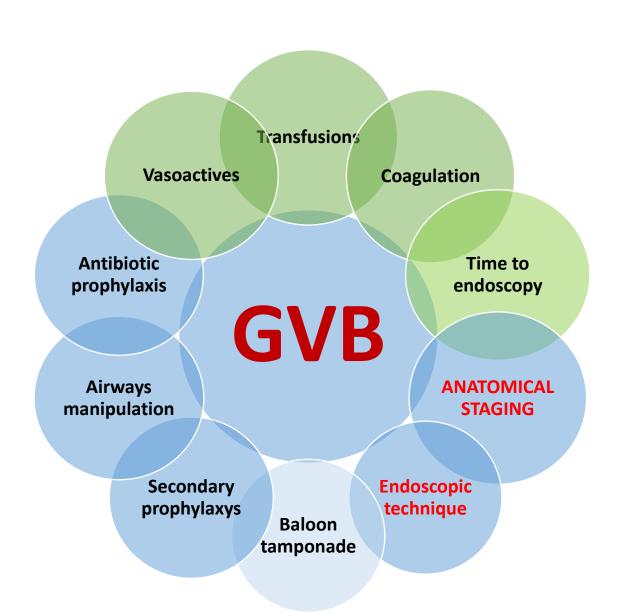
| Authors | Study design | n | Follow-up (month) | Hemostasis (%) | Rebleeding (%) | Mortality (%) |
|----------------------------|--------------|-----|-------------------|----------------|----------------|---------------|
| Seewald et al., 2008 | Retro | 131 | 60 | 100 | 17 | 47 |
| Fry et al., 2008 | Retro | 33 | 9 | 88 | 15 | 18 |
| Cheng et al., 2007 | Retro | 635 | 3-115 | 95 | 8 | 7 |
| Joo <i>et al.</i> , 2007 | Retro | 85 | 24 | 98 | 29 | 31 |
| Kim et al., 2006 | Pros | 86 | 11 | 93 | 16 | 45 |
| Noophun et al., 2005 | Retro | 24 | 8.3 | 71 | 10 | 6 |
| Mahadeva et al., 2003 | Retro | 23 | 6 | 96 | 35 | 24 |
| Greenwald et al., 2003 | Pilot | 44 | 12 | 95 | 20 | 23 |
| Sarin <i>et al.</i> , 2002 | RCT | 9 | 15.4 | 89 | 22 | 11 |
| Dhiman et al., 2002 | Retro | 18 | 31.6 | 100 | 10.3 | NA |
| Lo et al., 2001 | RCT | 31 | 14 | 87 | 31 | 9 |
| Huang et al., 2000 | Retro | 90 | 13.2 | 100 | 23 | 39 |

RCT = Randomized controlled trial; Retro = Retrospective; Pros = Prospective; NA = Not available; GVO = Gastric variceal obturation

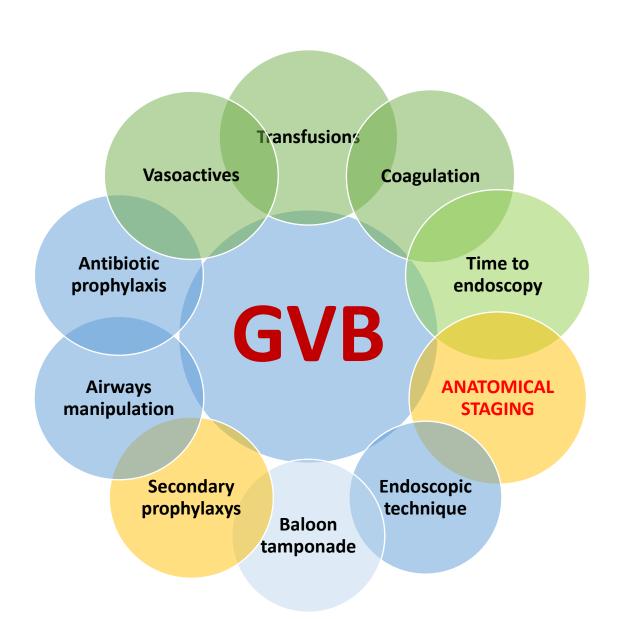
CURRENT GUIDELINES

Treat similarly to oesophageal varices, use glue for GOV2, BRTO if GRS

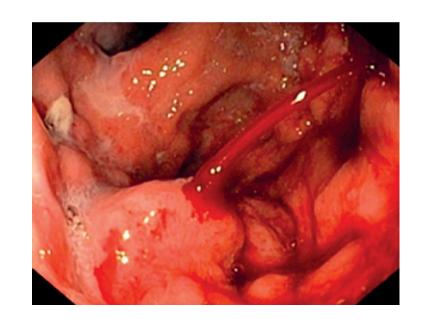
IMPROVE SURVIVAL IN GASTRIC VARICEAL BLEEDING



IMPROVE SURVIVAL IN GASTRIC VARICEAL BLEEDING



ENDOSCOPIC TREATMENT



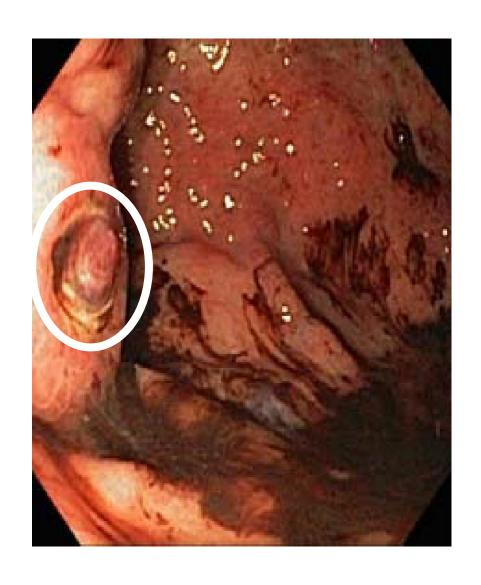


Prior to anatomical staging if:

-active bleeding

-endoscopic high risk signs

ENDOSCOPIC TREATMENT



DO NOT wash the fibrin clot

Prepare banding/looping only in GOV1

Glue injection....

N-BUTYL-2-CYANOACRYLATE TECHNIQUE

• Straight n-Butyl-2- Cyanoacrylate: to decrease ambolization

Not into the Fibrin Clot: it may dislodge it. Wall is thinnest,
 fragile, and may be removed when pulling the needle

Few mm away from clot

INTRAvariceal (stick needle inside the varix): submucosal injection causes ulcer formation

ENDOSCOPIC TREATMENT

Not very frequent: 1%

Extra GI embolization

Extravascular injection

Local venous thrombosis

Ulcerations

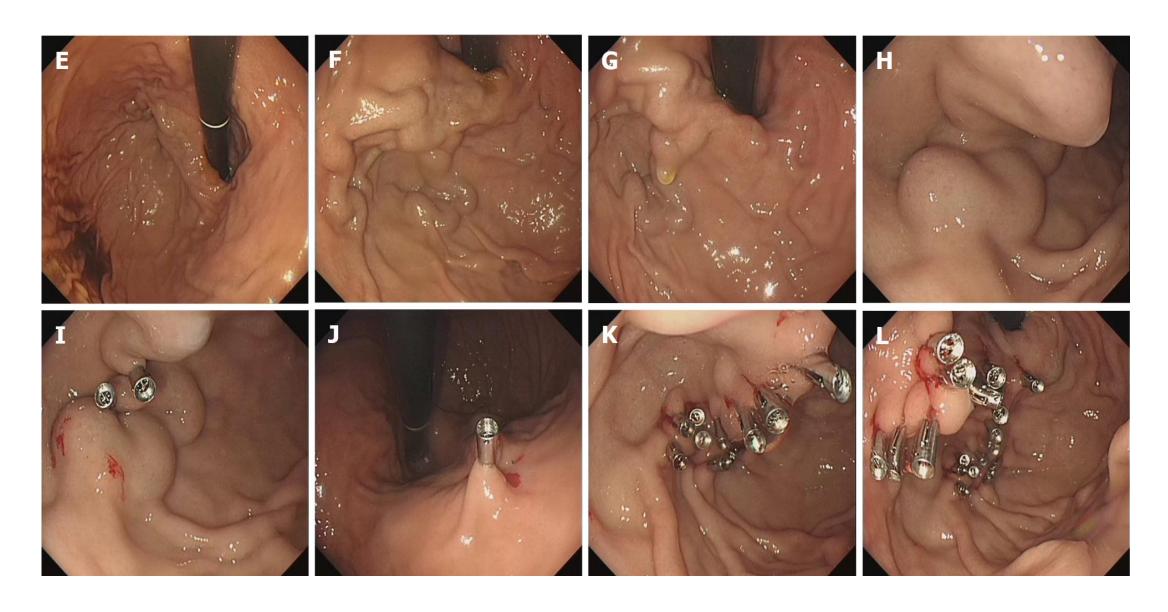
Stenosis

Sepsis



Risk factors for embolization are: excessive dilution, large volumes (> 1 mL/per injection), rapid injection.

CLIPPING OF GASTRIC VARICES



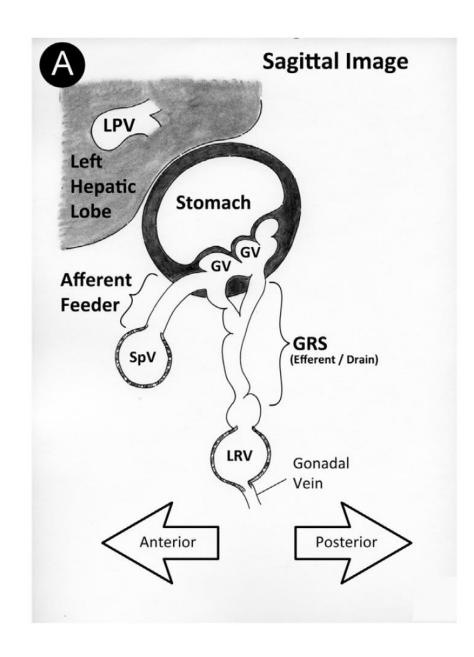
SPONTANEUS POSTO SYSTEMIC SHUNT AND GASTRIC VARICES

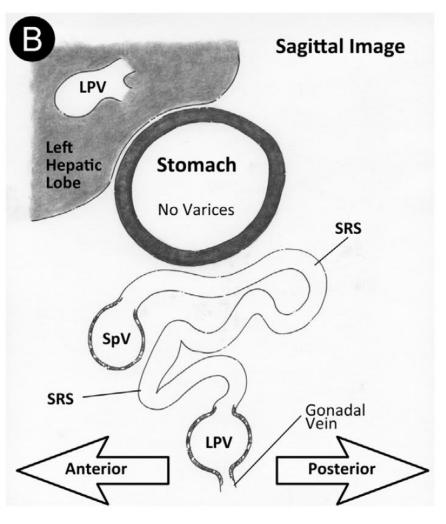
 Table 2 Spontaneous PortoSystemic Shunts (SPSS)

| SPSS | Portal Component | Systemic Component | Portal to Systemic | Systemic to Portal | Laterality |
|-------------------------|-------------------|---|-----------------------|-----------------------|------------------|
| Paraumbilical vein | Left portal vein | Anterior abdominal wall veins iliofemoral veins | Yes | Yes | Right |
| Subhepatic portoiliac | Main portal vein | lliac veins | Yes | | Right |
| Mesorenal | Mesentric vein | Left renal vein | Yes | | Central or right |
| Perisplenic splenoiliac | Splenic vein | lliac vein | Yes | | Left |
| Esophageal varices | Left gastric vein | Azygos-hemiazygos veins | Yes | Yes | Right |
| Gastrocaval | GVs or PGV | IVC | Yes | | Left |
| Indirect gastrocaval | GVs or PGV or SGV | Inferior phrenic vein | Yes | | Left |
| Gastrorenal | GVs or PGV or SGV | Left renal vein | Yes | | Left |
| Splenorenal shunt | Spleen | Left renal vein | Yes | | Left |
| Internal hemorrhoids | IMV | lliac vein | Yes | | Right |

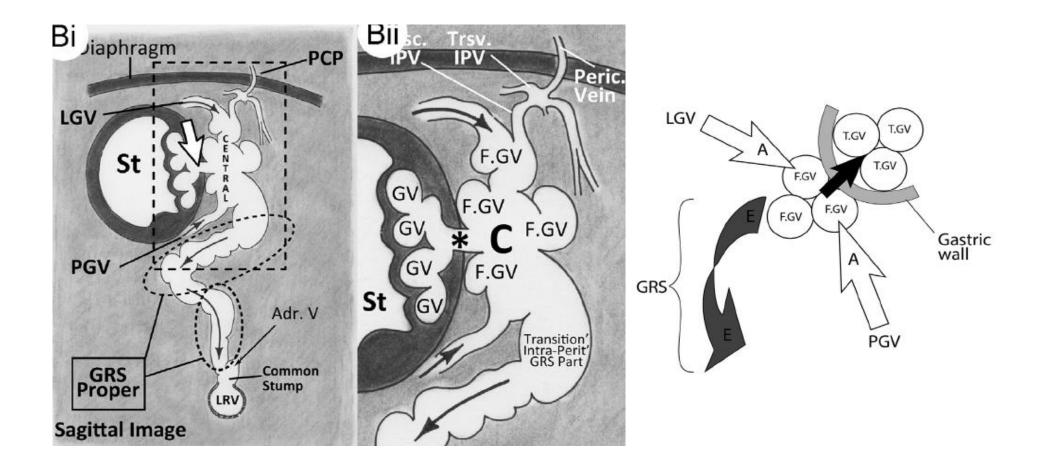
GVs, Gastric Varices; PGV, Posterior gastric vein; IMV, Inferior Mesenteric Vein; IVC, Inferior Vena Cava.

SPENORENAL VERSUS GASTRONENAL SHUNT



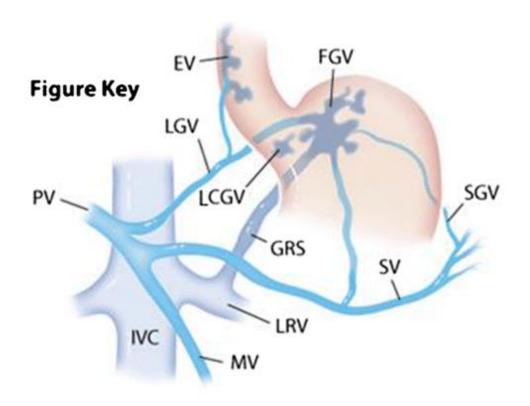


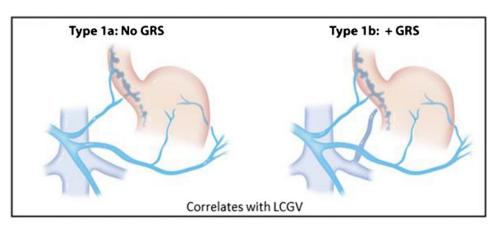
ANATOMICAL STAGING- SAAD CALDWELL CLASSIFICATION

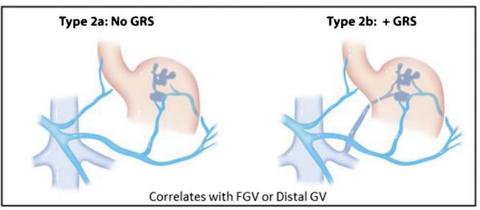


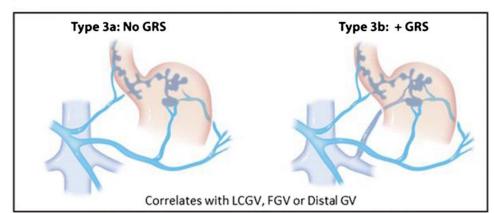
The gastric variceal system (GVS) is composed of the afferent portal venous feeders, the central variceal part, and the gastrorenal shunt (systemic venous drainer(s)).

ANATOMICAL STAGING- SAAD CALDWELL CLASSIFICATION



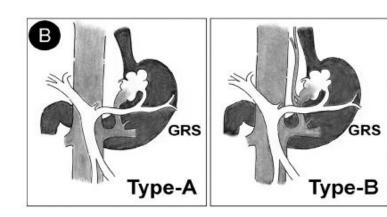


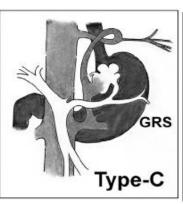


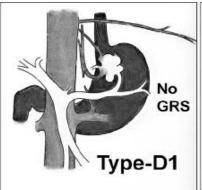


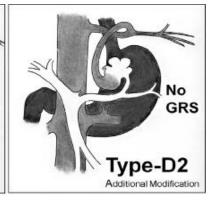
HEMODYNAMIC CLASSIFICATION

Kiyosue: systemic venous drenaige

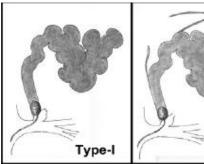


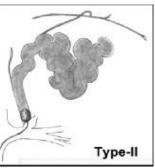


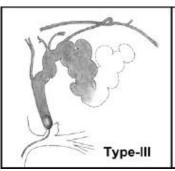


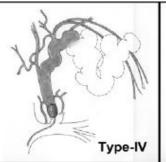


Hirota: BORV









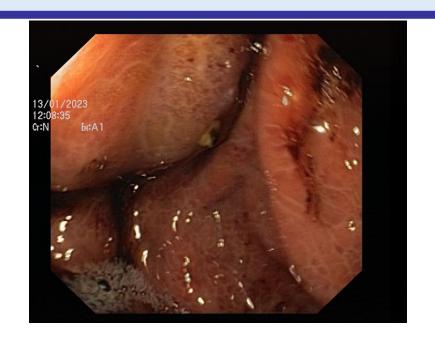


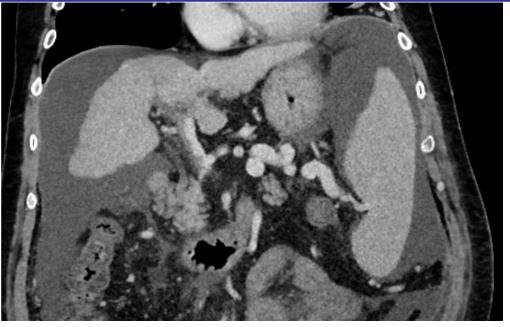


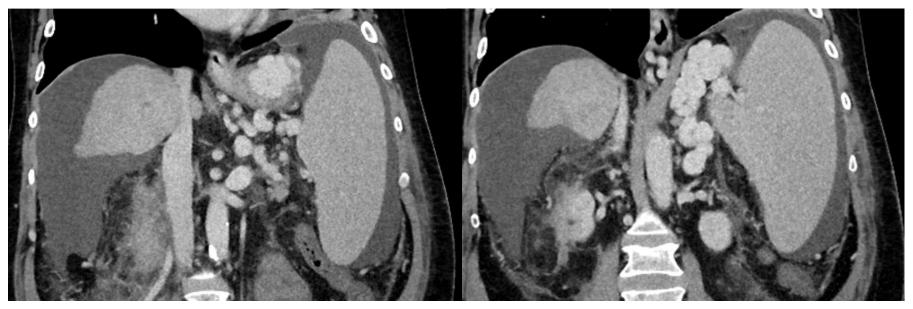
ANATOMICAL STAGING

WHY IS IMPORTANT?

CLINICAL CASE



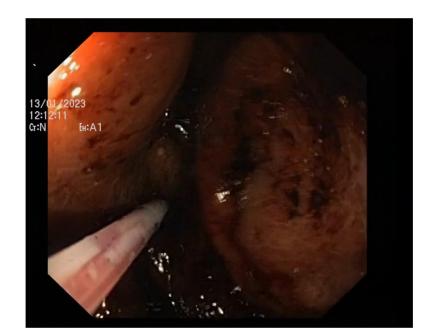




CLINICAL CASE

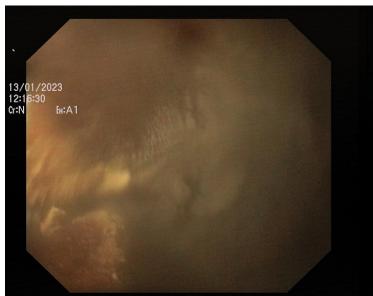






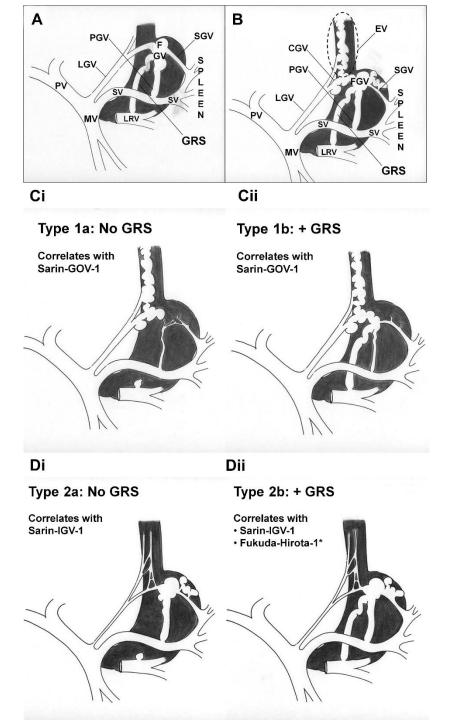
CLINICAL CASE

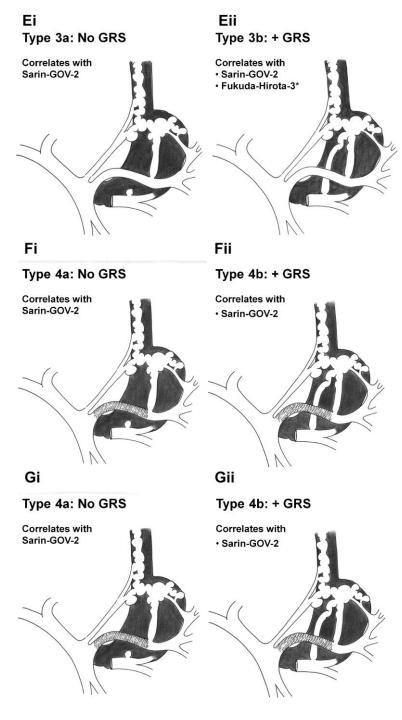


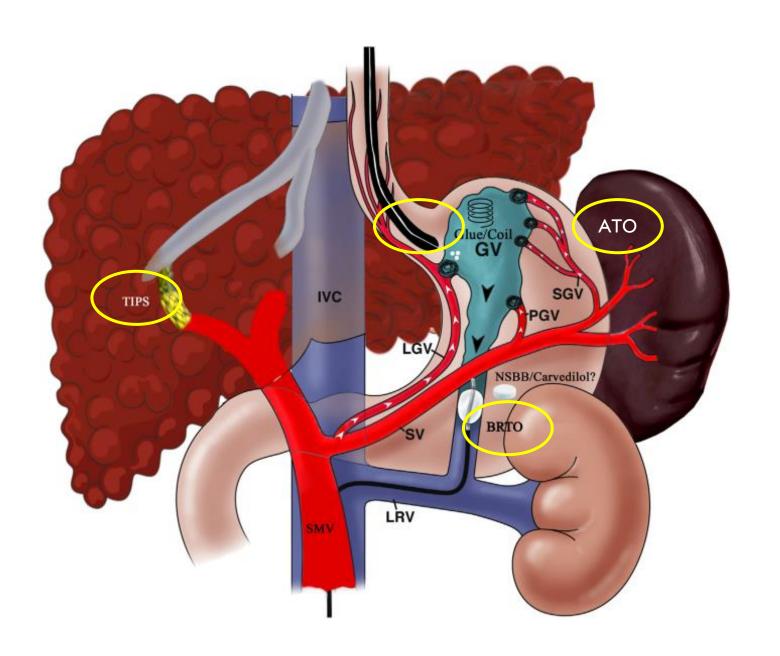


TEMPORARY HEMOSTASIS ACHIEVED WITH HEMOSTATIC POWDER AS RESCUE THERAPY









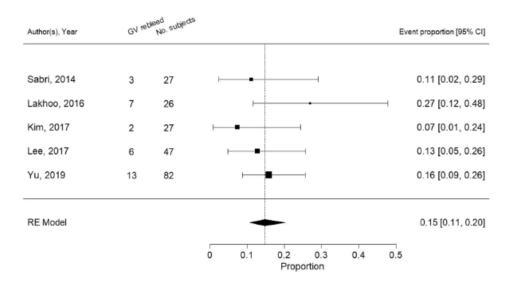
| Saad GV Classification Type | Management Opinion | | | | |
|--------------------------------|---|--|--|--|--|
| Type-1a | TIPS TIPS will probably decompress the EVs and the GVs in a similar way as if the EVs were solitary (please see the right vs left shunt discussion [Fig. 13].) | | | | |
| Type-1b | TIPS $+$ trans-TIPS BATO or BRTO \pm TIPS TIPS will possibly decompress these GVs $+$ EVs, however, its effectiveness depends on the size of the GRS or portosystemic gradient BRTO would be the primary treatment if the hepatic reserve is poor (MELD $>$ 18) (please see the Indications & Contraindications section of the article in this issue of Conventional-BRTO) | | | | |
| Type-2a | TIPS + trans-TIPS BATO or BATO alone If the portosystemic gradient is high and the hepatic reserve is adequate (MELD < 18) a TIPS + BATO sclerosis is appropriate If the gradient is low or the MELD is high or both, a BATO or unconventional BRTO (if feasible can be performed | | | | |
| Type-2b | BRTO TIPS will probably fail to decompress the GVs (please see the right vs left shunt discussion [Fig. 13], particularly in the presence of a large GRS.) | | | | |
| Туре-За | TIPS + BATO TIPS will decompress the EVs and partly decompress this complex (multifeeder) GV system (please see the right vs left shunt discussion [Fig. 13], particularly in the presence of a large GRS.). BATO will help obliterate the remainder of the GVs and eliminate the competing shun (GRS). This is providing that the hepatic reserve is adequate (MELD < 18) | | | | |
| Type-3b | BRTO $+$ TIPS BRTO alone will aggravate the already present EVs. TIPS will help decompress the EVs and par of the GVs This is providing that the hepatic reserve is adequate (MELD $<$ 18) | | | | |
| Туре-4а | Splenic embolization + TIPS The spleen is emptying via the gastroesophageal varices. The splenic embolization reduces the splenic outflow, which is the primary problem. The TIPS will help decompress the EVs. Obliterating the varices may close the outflow of the spleen and cause the development of ectopic varices | | | | |
| Type-4b | Splenic embolization $+$ BRTO \pm TIPS The spleen is emptying via the gastroesophageal varices. The splenic embolization reduces the splenic outflow, which is the primary problem. The TIPS will help decompress the EVs if they cannot be controlled endoscopically. Obliterating the varices may close the outflow of the spleen and cause the development of ectopic varices. If BRTO is to be performed a large part of the spleen needs to be embolized (this can be staged) | | | | |

MELD, model for end-stage liver disease (score).

Note: BATO or BRTO refers to "obliteration" that means sclerosis. Coil embolization of varices is not obliteration; it is embolization.

OBTURATION VS TIPS

TIPS +/- EMBOLIZATION vs ENDOSCOPIC THERAPY



TIPS: 16% rebleeding

TIPS FOR GASTRIC VARICES

- 6 TIPS studies, 147 patients
- Control of acute bleeding 95%
- Rebleeding rate 30% before 2000 and 11%-20% afterwards
- Gastric varices bleed at a lower hepatic-portal venous gradient (mean gradient
 11.2mmHg for gastric, 15.5mmHg for oesophagal) (Sanyal 1997)
- Moreover, four of the six unresolved gastric varices (75%) had a pre-TIPS portosystemic gradient of <12 mm mercury (Saad 2010).

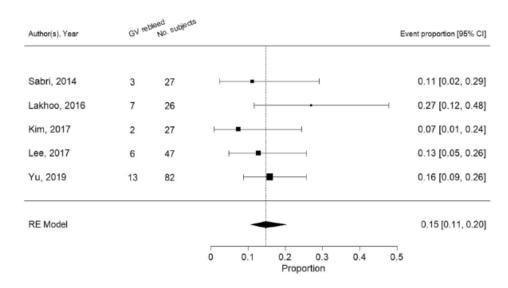
RCT CYANOACRYLATE VS BRTO

| Cause of rebleeding | Cyanoacrylate | BRTO |
|----------------------|---------------|------|
| Patients | 11/32 | 2/32 |
| Source of rebleeding | 5 | |
| GVs | 5 | 0 |
| GV ulcer | 1 | 0 |
| EVs | 3 | 2 |
| Undetermined | 2 | |
| Major | 10 | 2 |
| Minor | 1 | 0 |

NO DIFFERENCE IN SURVIVAL

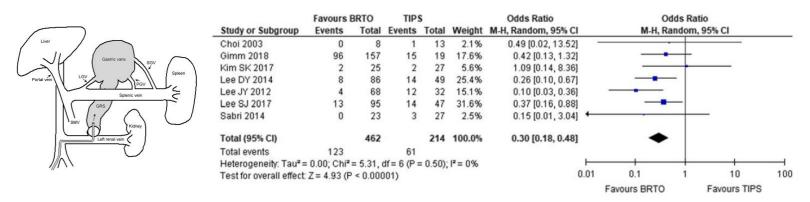
OBTURATION VS TIPS

TIPS +/- EMBOLIZATION vs ENDOSCOPIC THERAPY



TIPS: 16% rebleeding

TIPS VS BRTO



BALLOON-OCCLUDED RETROGRADE TRANSVENOUS OBLITERATION

1016 patients BRTO (24 uncontrolled studies: 23 retrospectives, 1 prospective)

Complete obliteration: 87%-100%

5 yrs survival at 5 yrs (10 studies) 39%-85 % (median 65.4 ± 13.5 %).

Rebleeding risk 1, 5, 8 years:

- secondary prophylaxis: 2.4%, 2.4%, 14.3%

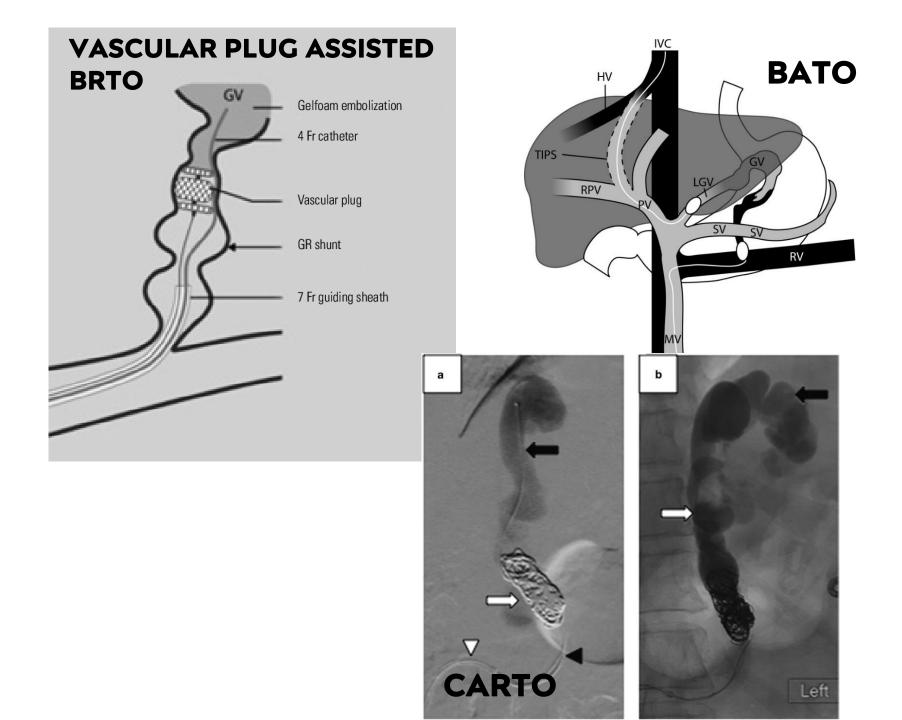
- primary prophylaxis: 0%, 0%, 0%,

(Akahoshi 2008)

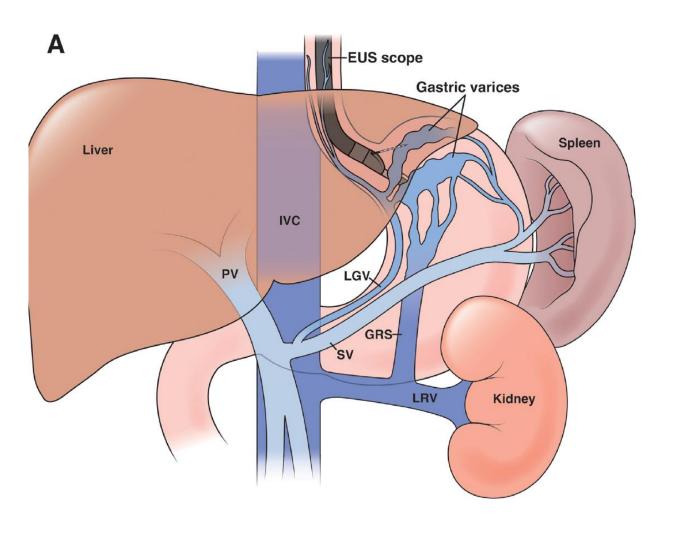
Possible worsening of portal hypertension!

Amongst 78 patients, 29 worsening EVs, 1, 3, e 5 yrs 27%, 58%, and 66%,

(Ninoi 2005)



EUS TREATMENT GASTRIC VARICES



- Cyanoacrilate
- Coils
- Combined Cya+Coils
- Gelfoam
- Tornado- and Nester-type coils

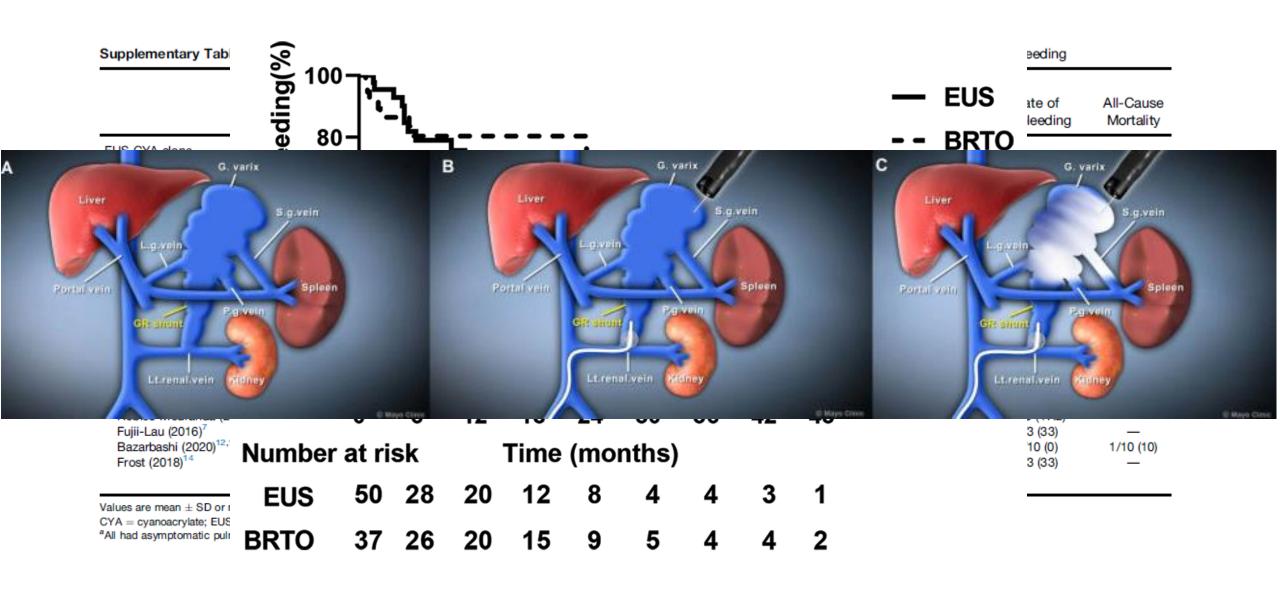


US GUIDED ENDOSCOPIC TREAMENT

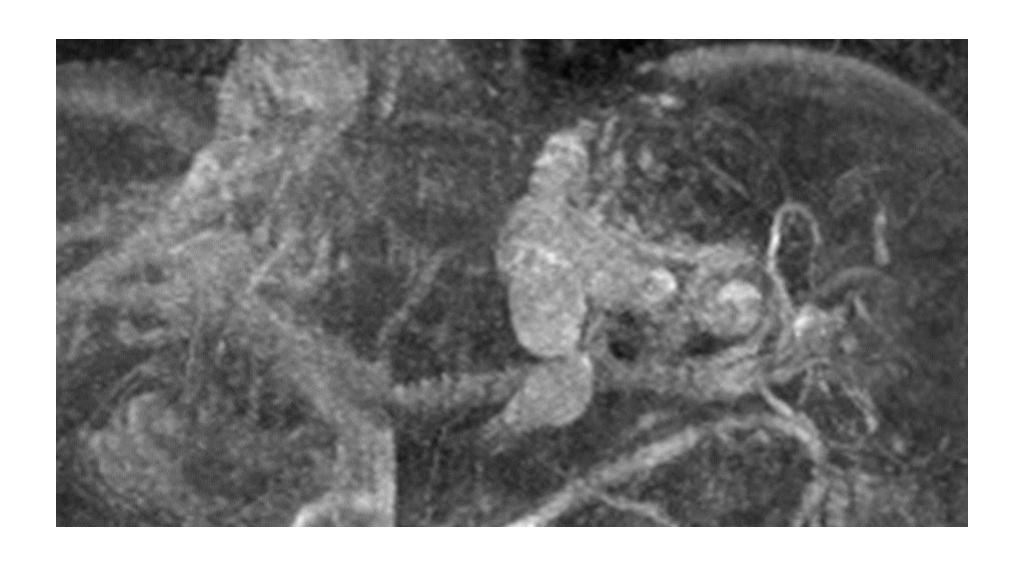


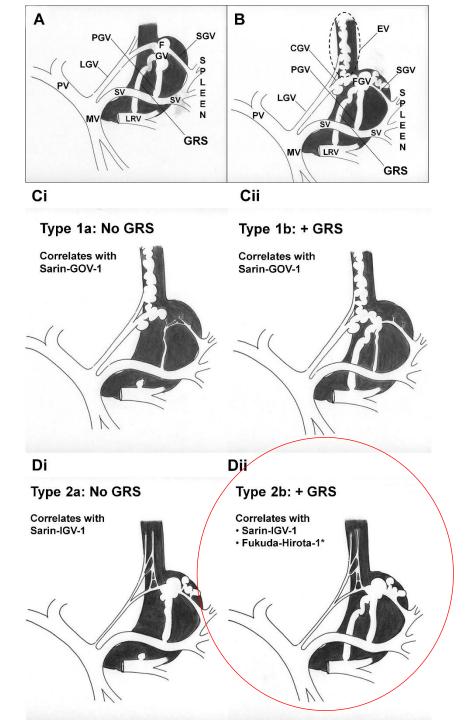
- Published literature involves small numbers of patients
- Meta-analysis comparing EUS-guided treatment of GV vs. direct endoscopic injection using data from 23 studies
 - No difference in pooled treatment efficacy
 - Pooled rate of GV obliteration significantly higher in the EUS group (84% vs 63%; P = 0.02)
 - No difference in early rebleeding
 - Lower rate of late rebleeding and GV recurrence in the EUS group

EUS TREATMENT OF GASTRIC VARICES



CLINICAL CASE - ATO





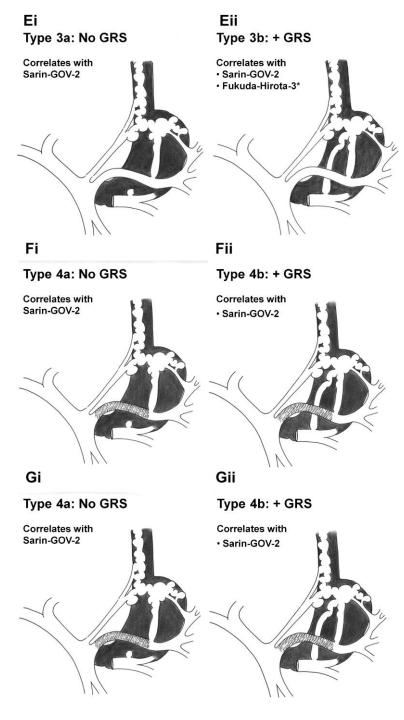
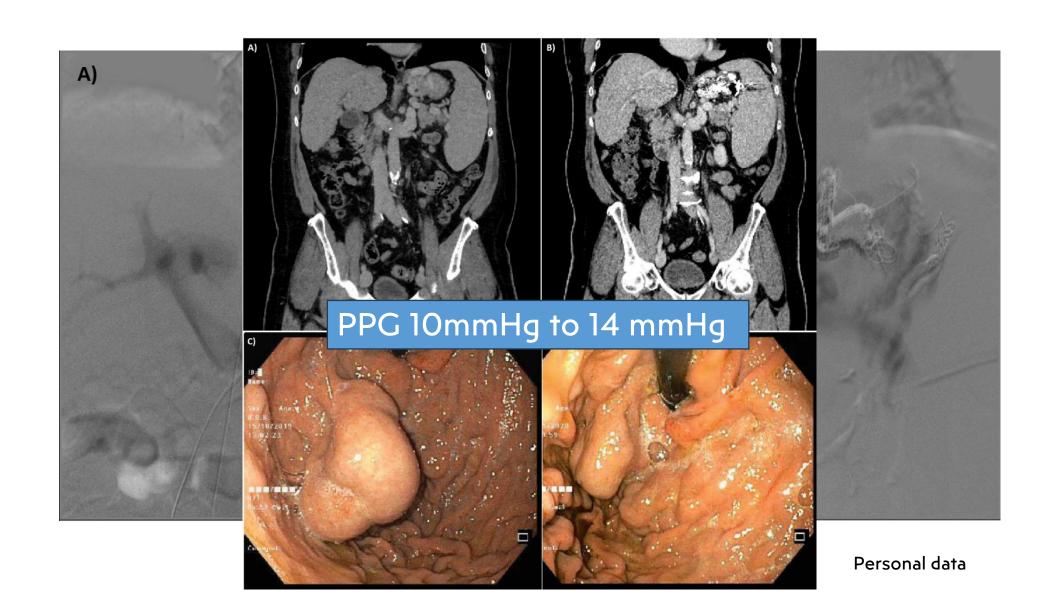


Table 6 Management Options for Variceal Types (Saad-Caldwell Classification)

| Saad GV Classification Type | Management Opinion | |
|---------------------------------------|--|--|
| Type-1a | TIPS TIPS will probably decompress the EVs and the GVs in a similar way as if the EVs were solitary (please see the right vs left shunt discussion [Fig. 13].) | |
| Type-1b | TIPS $+$ trans-TIPS BATO or BRTO \pm TIPS TIPS will possibly decompress these GVs $+$ EVs, however, its effectiveness depends on the size of the GRS or portosystemic gradient BRTO would be the primary treatment if the hepatic reserve is poor (MELD $>$ 18) (please see the Indications & Contraindications section of the article in this issue of Conventional-BRTO) | |
| Type-2a | TIPS $+$ trans-TIPS BATO or BATO alone If the portosystemic gradient is high and the hepatic reserve is adequate (MELD $<$ 18) a TIPS $+$ BATO sclerosis is appropriate If the gradient is low or the MELD is high or both, a BATO or unconventional BRTO (if feasible) can be performed | |
| Type-2b Correlates with IGV | BRTO TIPS will probably fail to decompress the GVs (please see the right vs left shunt discussion [Fig. 13], particularly in the presence of a large GRS.) | |
| Type-3a | TIPS + BATO TIPS will decompress the EVs and partly decompress this complex (multifeeder) GV system (please see the right vs left shunt discussion [Fig. 13], particularly in the presence of a large GRS.). BATO will help obliterate the remainder of the GVs and eliminate the competing shunt (GRS). This is providing that the hepatic reserve is adequate (MELD < 18) | |
| Type-3b | BRTO $+$ TIPS BRTO alone will aggravate the already present EVs. TIPS will help decompress the EVs and part of the GVs This is providing that the hepatic reserve is adequate (MELD $<$ 18) | |
| Type-4a | Splenic embolization + TIPS The spleen is emptying via the gastroesophageal varices. The splenic embolization reduces the splenic outflow, which is the primary problem. The TIPS will help decompress the EVs. Obliterating the varices may close the outflow of the spleen and cause the development of | |

TRANS-SPLENIC ANTEROGRADE COIL-ASSISTED TRANSVENOUS OCCLUSION (TACATO)



TRANS-SPLENIC ANTEROGRADE COIL-ASSISTED TRANSVENOUS OCCLUSION (TACATO) - PADUA EXPERIENCE

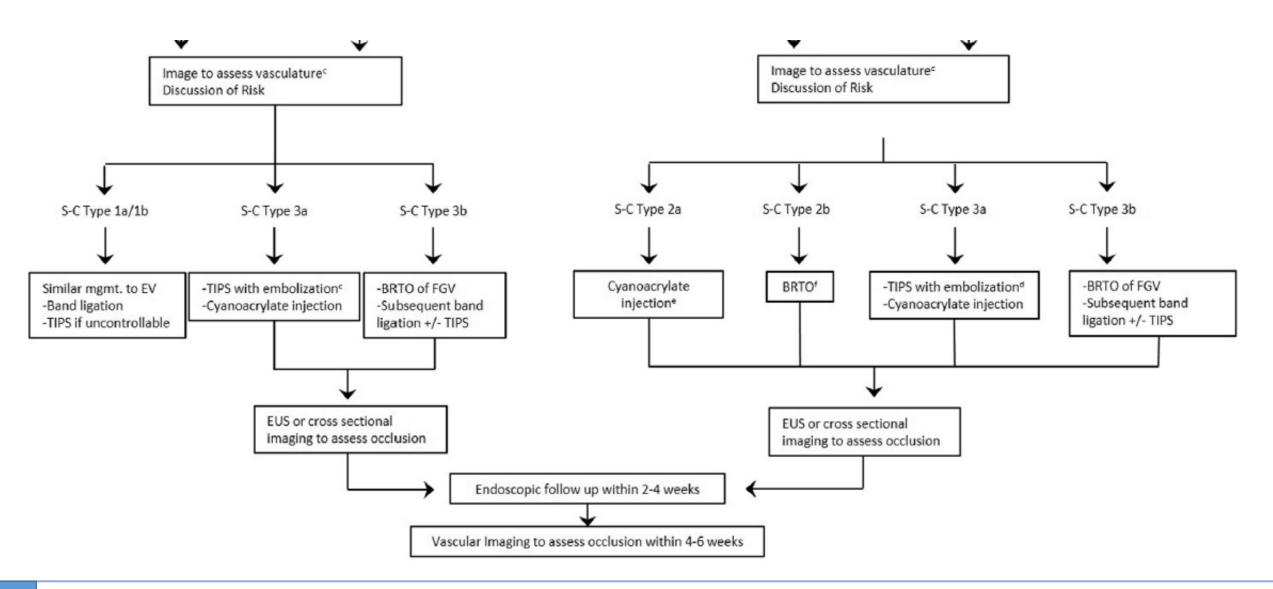
| Clinical characteristics | |
|---|------------|
| | |
| Sex - male, n of patients (%) | 16 (80) |
| Age, years, median (range) | 56 (48-74) |
| Etiology of cirrhosis | |
| Alcohol, n of patients (%) | 10 (50) |
| Viral, n of patients (%) | 4 (20) |
| Other, n of patients (%) | 6 (30) |
| Child-Pugh grade A/B/C, n of patients (%) | 12/8/0 |
| | (60/40) |
| MELD score, median (range) | 13 (11-15) |
| GOV2/IGV1, n of patients (%) | 17/6* |
| *Endoscopically 14 patients had only GOV2, 3 only IGV1 and 3 patients had combined GOV2 and IGV1. | (85/15) |
| Esophageal Varices (none/low risk), n of | 5/15 |
| patients (%) | (25/75) |
| Time interval between index | 5 ± 2 |
| bleed and TACATO, days, mean ± SD | |
| Saad-Caldwell classification, n of patients (%) | |
| 1ь | 2 (10.0%) |
| 2ъ | 10 (50%) |
| 3b | 8 (40%) |

- 3 yrs, 22 patients, secondary prophylaxis GVBs
 - 2 excluded from the analysis due to concomitant SVT
- Microcoils + NBCA+LUF 80%
- Complete radiological occlusion 75%

- No rebleeding, no worsening of EVs
- Amelioration of hepatic perfusion
- 1 minor bleeding after the procedure (concomitant AKI!)
- 2 partial PVT

ALGORITHM TREATMENT GVB

Eventual endoscopic urgent evaluation/treatment according to expertice/indication



CLINICAL STAGING IS ALSO ESSENTIAL

Severity of liver disease

Previous AD episodes

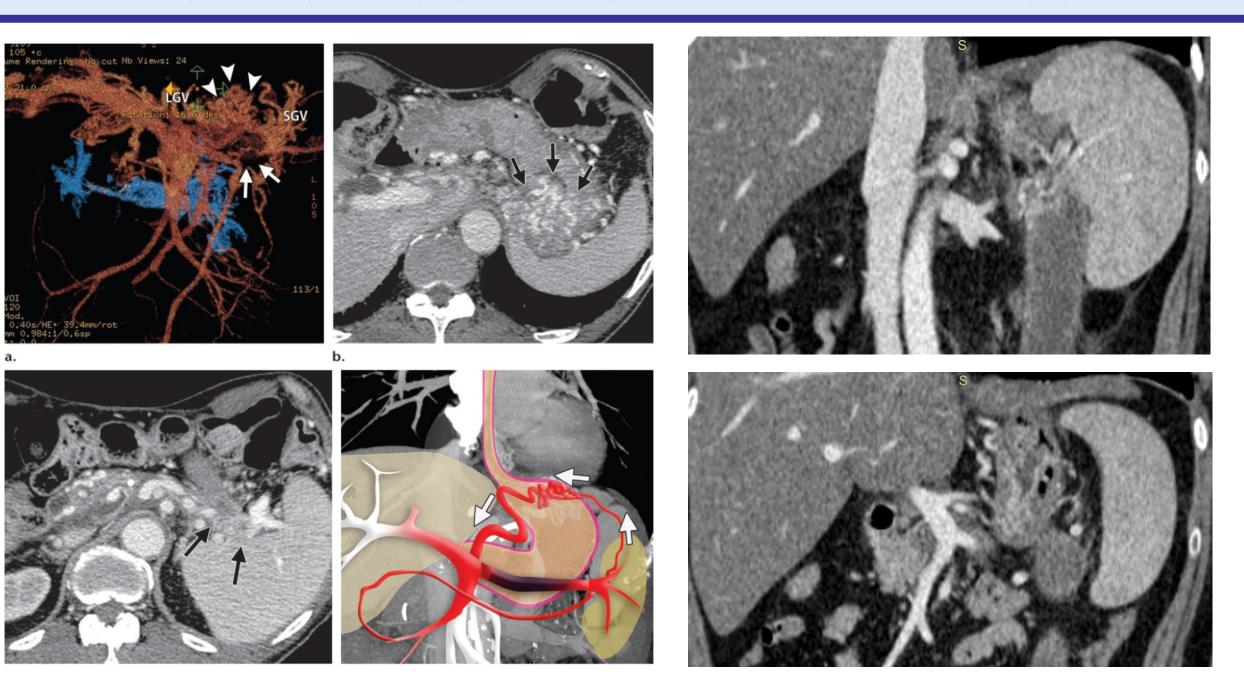
Clinical significant ascites

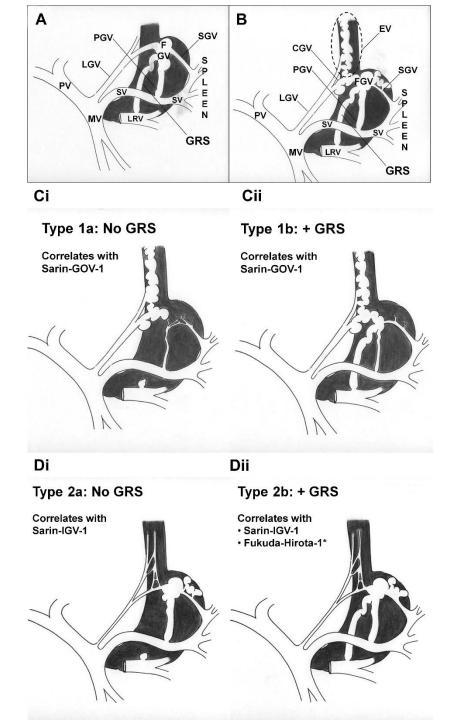
History of AVB

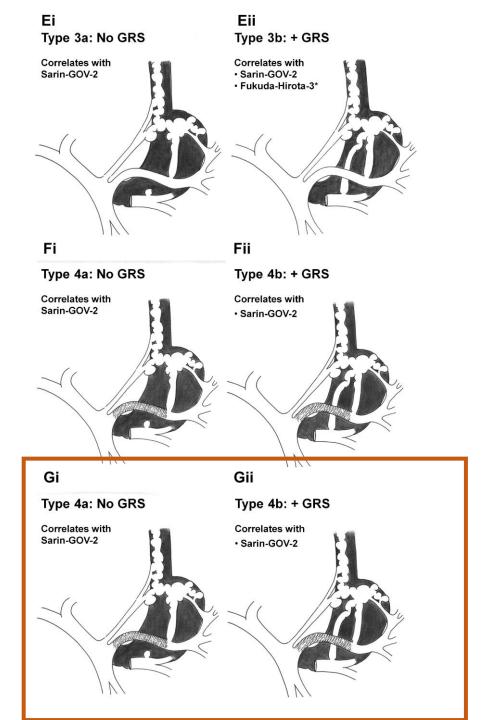
Multiple sessions of band ligations

(HVPG measurement)

GASTRIC VARICES IN LEFT SIDED PORTAL HYPERTENSION

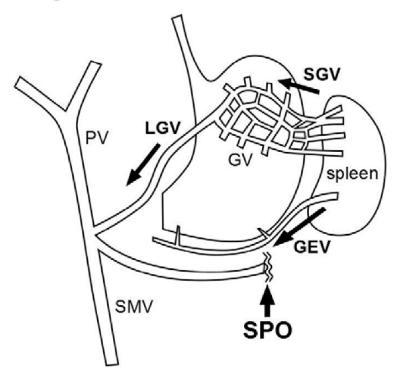






GASTRIC VARICES IN PVT WITH SVT

Splenic vein occlusion



In PVT, SVT and GV predictors of re-bleeding (5 folds)

(HR= 4.21 p=0.03 and HR= 5.07 p=0.01 respectively).

GV: gastric varices PV: portal vein SMV: superior mesenteric vein

SGV: short gastric vein LGV: left gastric vein

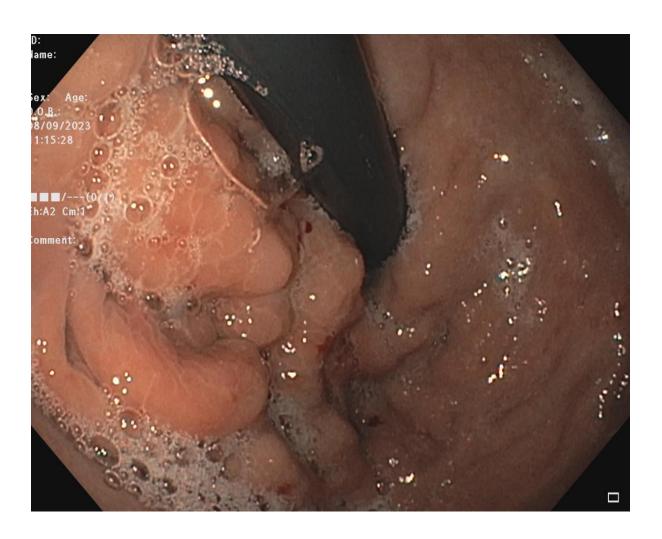
GEV: gastroepiploic vein SPO: splenic vein occlusion

GASTRIC VARICES IN PVT

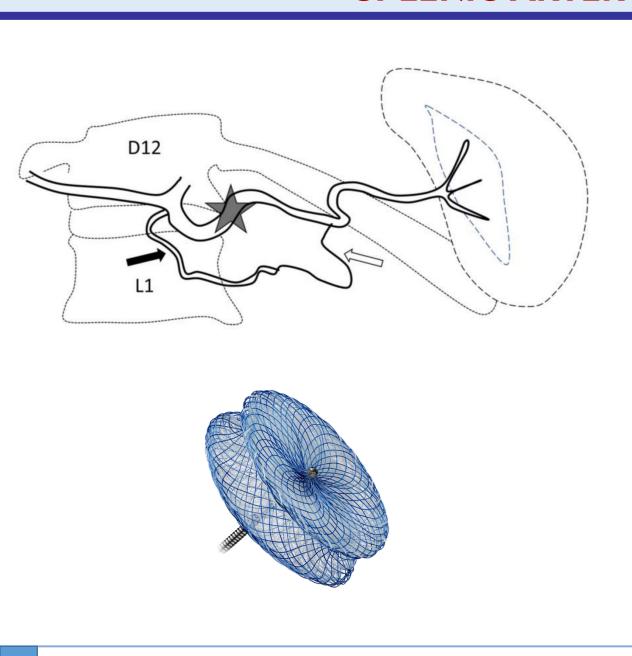
| | Cirrhosis (<i>n</i> = 56) | EHPVO (n = 30) | p Value |
|--|-------------------------------|---------------------------------|---------|
| Glue injection ≤2 ml at first session | 88% (n = 49) | 73% (n = 22) | 0.001 |
| >1 sessions of glue injection | 36% (n = 20) | 57% (n = 17) | 0.4 |
| >2 ml glue for GOV obturation | 57% (n = 32) | 60% (n = 12) | 0.4 |
| Total glue (ml) | $\textbf{3.2} \pm \textbf{2}$ | $\textbf{4.7} \pm \textbf{3.1}$ | 0.014 |
| Rebleeding | 9% (n = 5) | 10% (n = 3) | 0.87 |
| Rebleeding in <48 h | 3.6% (n = 2) | 6.7% (n = 2) | 0.4 |
| EVL for esophageal varices | 57% (n = 31) | 14% (n = 4) | 0.04 |
| Mean no. of sessions for obturation | 1.6 ± 1 | $\textbf{2.2} \pm \textbf{1.5}$ | 0.03 |
| Mortality | 11% (n = 6) | 3% (n = 1) | 0.4 |

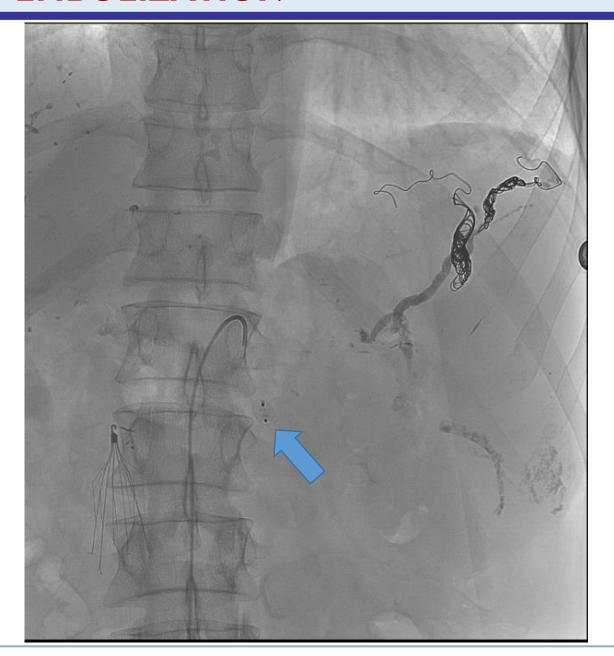
LEFT-SIDE PH WITH GVs





SPLENIC ARTERY EMBOLIZATION





TAKE HOME MESSAGES

| - GVs h | ave higher | risk of bleeding, | less response to | NSBB than EVs |
|---------|------------|-------------------|------------------|---------------|
|---------|------------|-------------------|------------------|---------------|

- Endoscopic technique/specific expertice in US obturation are important for optimal clinical

outcome

- Anatomical and clinical staging are definitively a part of the algorythm of treatment

- Early referral to centers with specific radiological or endoscopic experience should be timely

considered