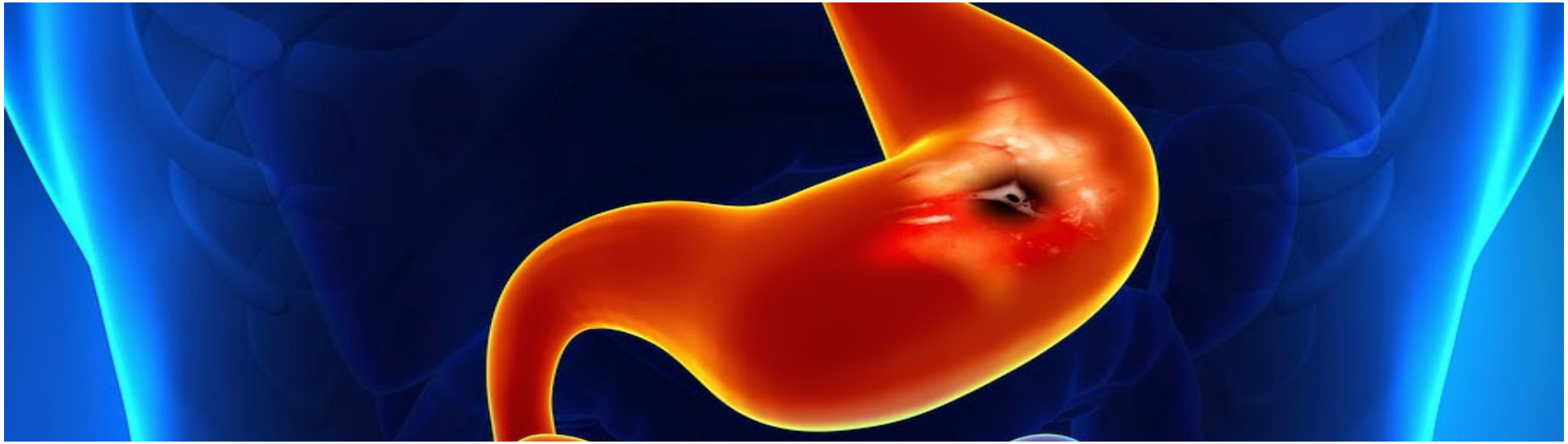
INSELGRUPPE

Acute Upper GI Bleeding

Bible Class 16.08.2023 - Gastroenterologie / F.Bravo



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European Society of Gastrointestinal Endoscopy - 2021
American College of Gastroenterology - 2021
British Society of Gastroenterology – 2019
BMJ Update 2022

Contents

- Epidemiology and clinical presentation
- Risk factors and risk stratification
- Early management
- Endoscopy
  - Ulcer classification
  - Techniques and settings
- Post-endoscopy management

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Epidemiology and clinical presentation

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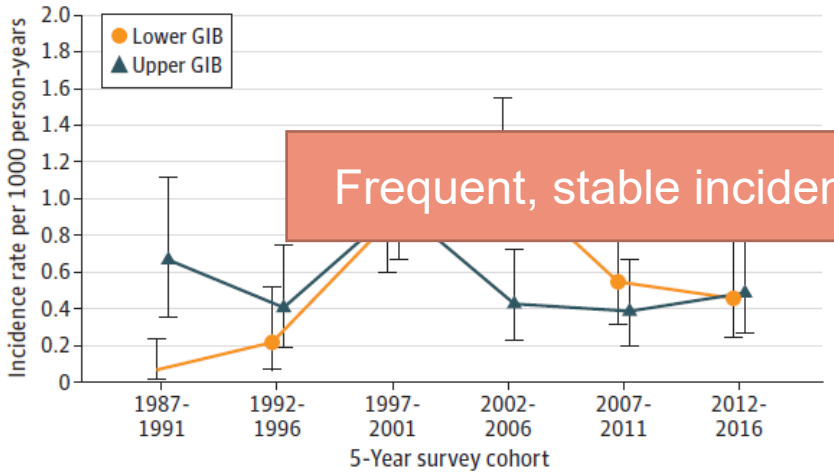
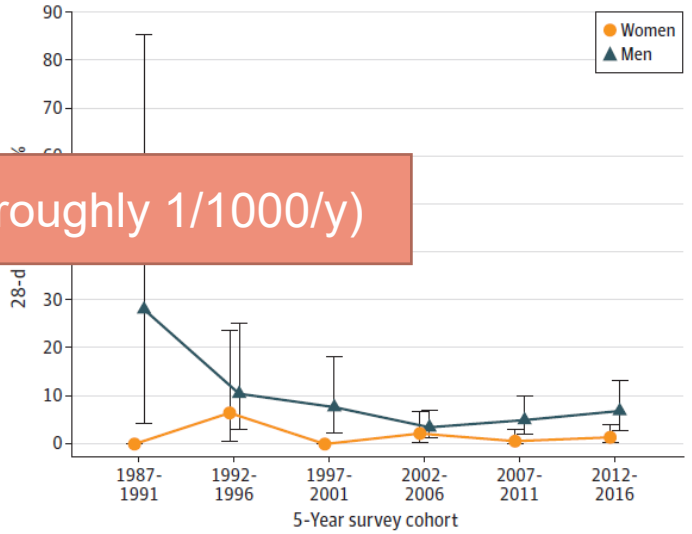
Epidemiology

Figure 1. Incidence Rate Trends in Major Upper and Lower Gastrointestinal Bleeding (GIB) for 5-Year Cohorts



Frequent, stable incidence (roughly 1/1000/y)

Figure 3. Twenty-Eight-Day Case Fatality Trends in Major Gastrointestinal Bleeding for 5-Year Cohorts



Error bars indicate 95% CIs.

Vora et al, JAMA Network Open. 2020;3(10):e2020172

Epidemiology

Table 4 Crude mortality by endoscopic diagnosis

Endoscopic diagnosis (n)	Crude mortality rate (%) Total* (5004) % (n)	New admissions (4109) % (n)	Inpatients (833) % (n)
Peptic ulcer	8.9 (162/1826)	5.8 (81/1403)	22 (70/322)
Varices	15 (82/544)	11 (51/469)	41 (29/70)
Malignancy	17 (31/187)	14 (22/156)	30 (9/30)
Oesophagitis	5.5 (65/1177)	2.8 (26/938)	17 (39/229)
Oesophagitis alone			10 (8/78)
Gastritis/erosions			24 (41/173)
Gastritis erosions alone			17 (9/54)
Erosive duodenitis	5.2 (33/640)	3.0 (16/539)	19 (17/90)
Erosive duodenitis alone	4.4 (5/114)	2.1 (2/94)	16 (3/19)
Mallory–Weiss	4.7 (10/213)	3.6 (7/193)	16 (3/19)
Mallory–Weiss alone	3.8 (4/106)	3.1 (3/96)	10.0 (1/10)
Other	12 (16/133)	11 (12/109)	17 (4/23)
Other alone	6.3 (5/80)	7.2 (5/69)	0 (0/10)
No diagnosis	5.8 (49/865)	3.7 (27/711)	15 (21/144)
All endoscoped	7.4 (371/5004)	5.0 (207/4109)	19 (162/833)
Not endoscoped	17 (304/1746)	12 (172/1441)	46 (126/274)
All patients	10 (675/6750)	6.8 (379/5550)	26 (288/1107)

30-d Mortality up to 10%

Hearshaw et al., Gut 2011;60:1327e1335. doi:10.1136/gut.2010.228437

Epidemiology - Costs

Table 3 Estimate of annual initial hospital costs for acute upper gastrointestinal bleeding (AUGIB) in the UK

Age bands (years)	UK Population*	AUGIB incidence per 100 000/year†	Annual number of patients with AUGIB in UK population	Mean total initial hospital cost estimates‡	Annual total costs
16–29	11 806 800			143 (n=91)	**£3 104 535**
30–44	12 843 400			053 (n=150)	**£10 811 709**
45–59	12 605 800			183 (n=224)	**£18 990 830**
60–64	3 624 400	109	3951	£2686 (n=78)	**£10 613 733**
65–74	5 820 900	214	12 457	£2749 (n=142)	**£34 248 977**
75+	5 020 000	485	24 347	£3190 (n=251)	**£77 667 271**
Total	**51 721 300**	–	**57 434**	–	**£155 437 055**

*Data on population from Office for National Statistics 2012.[19]
†AUGIB incidence figures taken from Rockall *et al*.[18]
‡Mean cost estimates based on analysis of TRIGGER data reported in this paper.

Significant cost and QoL decrease

Campbell HE, et al. BMJ Open 2015;5:e007230. doi:10.1136/bmjopen-2014-007230

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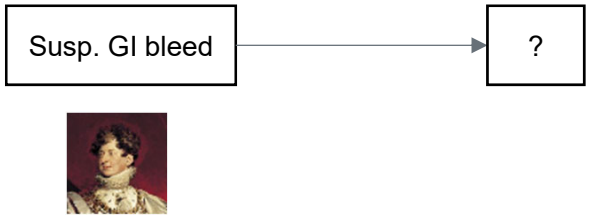
Risk factors and risk stratification

Clinical case 1

Patient brought to the ER with presyncope, coffee-ground emesis and melena in within the last 24h. No respiratory or cardiac complaints.

George IV 1762-1830



What do you want to know to better stratify this patient?

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Risk stratification

1. History: Age? Melena? Hematemesis? Syncope? Medications?
2. Status: stable vs unstable (SBP, HR), melena present
3. Objective findings: Hb, coagulation studies
4. Associated comorbodities (hepatic? renal? cardiac?)

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Clinical case 1 - Mr. George

85 yo male brought to the ER with presyncope, coffee-ground emesis and melena in within the last 24h. No respiratory or cardiac complaints.

- History: hip joint replacement 1 month earlier, hypertension, pseudogout, minor stroke ’97.
- Medications: Enalapril, Dafalgan, Plavix, Clexane (prophyl.), Oxynorm (R)

2 **1301 - Bluterbrechen , Teerstuhl (Meläna)**

Vitalparameter

Time	HF	Puls	AF	Zyan.	SpO2	O2	Kapno	ABPs	ABPd	BPS	BPD
19:42	78	76	16		99					102	54
19:02											
19:01	78	77	12		96					135	59

		venös	venös
Leukozyten	G/L	9.07	9.19
Hämoglobin	g/L	84 -	91 -
Hämatokrit	L/L	0.25 -	0.27 -
Erythrozyten	T/L	2.67 -	2.90 -
MCV	fL	95	94
MCH	pg	32	31
MCHC	g/L	332	335
RDW	%	13.1	13.7
Thrombozyten	G/L	425	275
MPV	fL	11.7 +	12.2 +
Normoblasten maschinell	/100 Leuk.	0.00	0.10 +

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Mr. George

Of the highlighted elements, which one contributes the most to this patient's Rockall score (bonus - how many total points?)

Answer

?

Mr. George

85 yo male presents to the ER with presyncope, coffee-ground emesis and melena in within the last 24h. No respiratory or cardiac complaints.

History: hip joint replacement 1 month earlier, hypertension, pseudogout, minor stroke ’97.

Medications: Enalapril, Dafalgan, Plavix, Clexane (prophyl.), Oxynorm (R)

2	1301 - Bluterbrechen , Teerstuhl (Meläna)

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		47559839	47533258
		NOTE	K NORD
		04.01.2022 15:44	20.12.2021 07:00
		04.01.2022 15:57	20.12.2021 08:03
		venös	venös
Leukozyten	G/L	9.07	9.19
Hämoglobin	g/L	84 -	91 -
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MPV	fL	11.7 +	12.2 +
Normoblasten maschinell	/100 Leuk.	0.00	0.10 +

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Mr. George

Age	<60 years	0
	60-79 years	+1
	≥80 years	**+2**
Shock	**No shock (SBP ≥100 AND HR <100)**	**0**
	Tachycardia (SBP ≥100 AND HR ≥100)	+1
	Hypotension (SBP <100)	+2
Comorbidities	No major comorbidity	0
	Any comorbidity EXCEPT renal failure, liver failure, and/or disseminated malignancy	**+2**
	Renal failure, liver failure, and/or disseminated malignancy	+3

Answer

2 + 2 = 4 points!

Scores are plentiful!

Glasgow-Blatchford

Rockall

AIMS65

Progetto Nazionale Emorragia Digestiva (PNED)

Match the score and its use!

Mortalità

Need for intervention / safe discharge

Rebleeding

Mortality

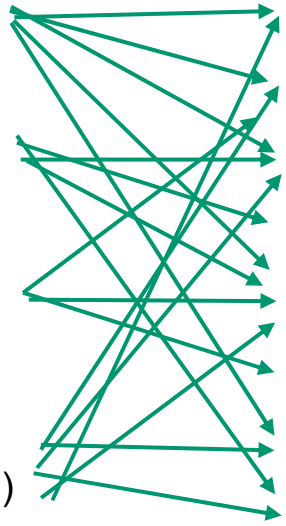
But also very confusing!

Glasgow-Blatchford

Rockall

AIMS65

Progetto Nazionale
Emorragia Digestiva (PNED)



Pre-endoscopy

Post-endoscopy

Need for intervention

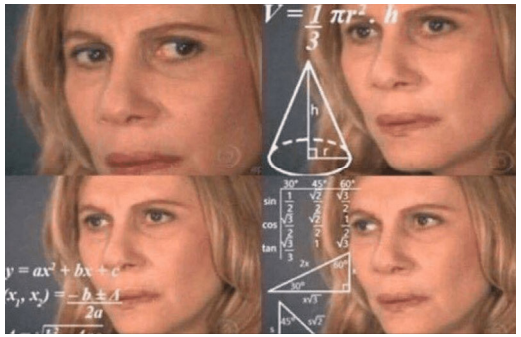
Safe discharge

Rebleeding

Mortality

Menu of the day in Stella

Francisco’s haircut

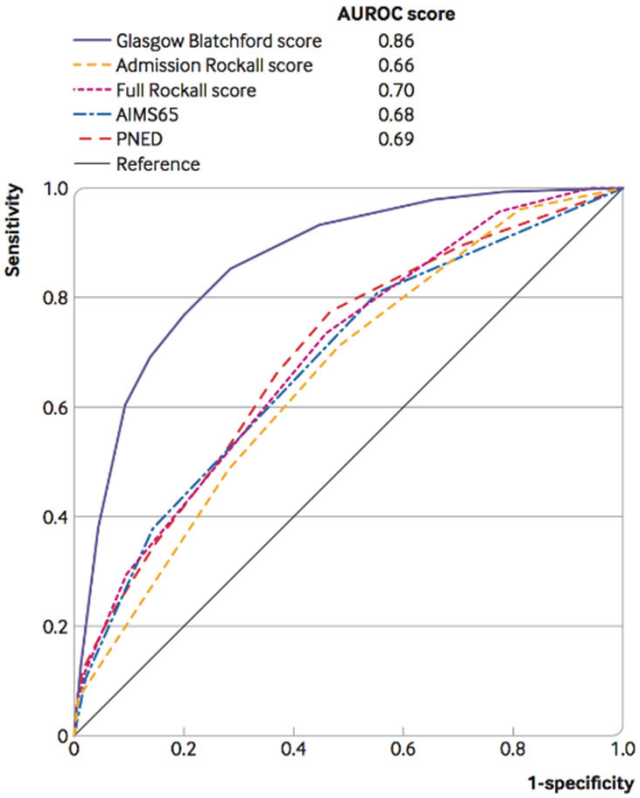


Clinical scoring systems - a brief overv

Progetto Nazionale Emorragia Digestive (PNED) [24]. The GBS was reported to have the highest accuracy (AUROC 0.86) for predicting need for hospital-based intervention (RBC transfusion, endoscopic treatment, arterial embolization, surgery) or death. Moreover, a GBS ≤ 1 was the optimal threshold to predict patient survival without need for hospital-based intervention, with a sensitivity of 98.6% and specificity of 34.6%. However, none of the evaluated risk scores were able to predict other outcomes with acceptable ability (AUROC ≤ 0.80).

- Much larger population database (>29'000 pts, 187 hospitals)
- Better predicts mortality, less so transfusion need

- Outcome: predi



Stanley AJ, Laine L, Dalton HR, *et al*. Comparison of risk scoring systems for patients presenting with upper gastrointestinal bleeding: international multicentre prospective study. *BMJ* 2017;356:i6432. doi:10.1136/bmj.i6432

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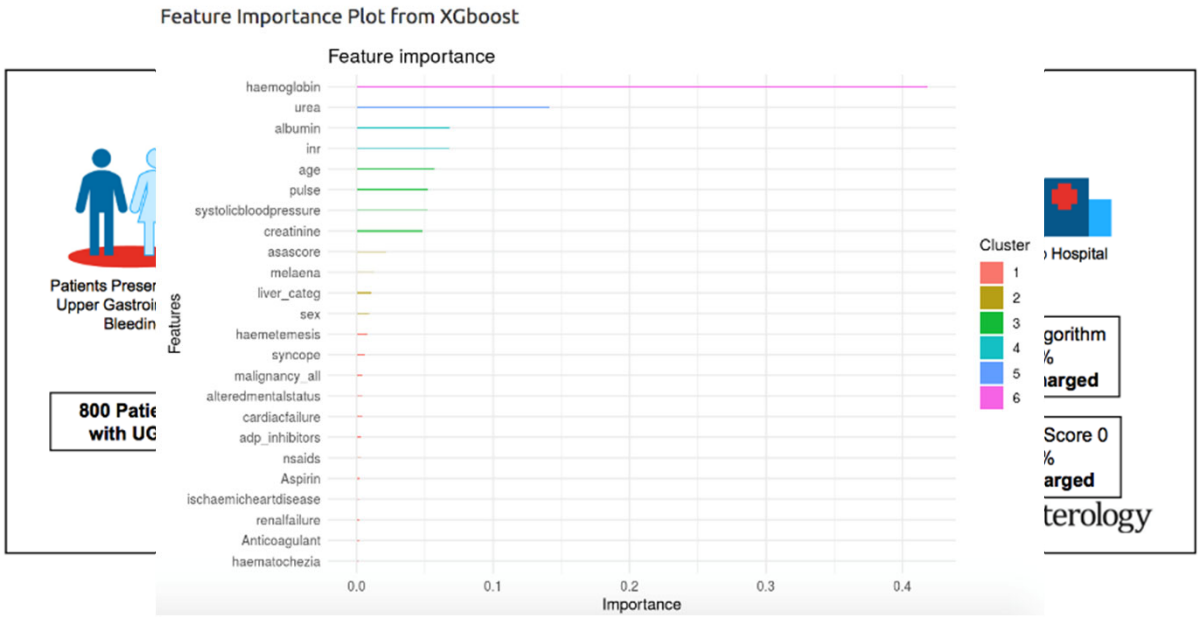
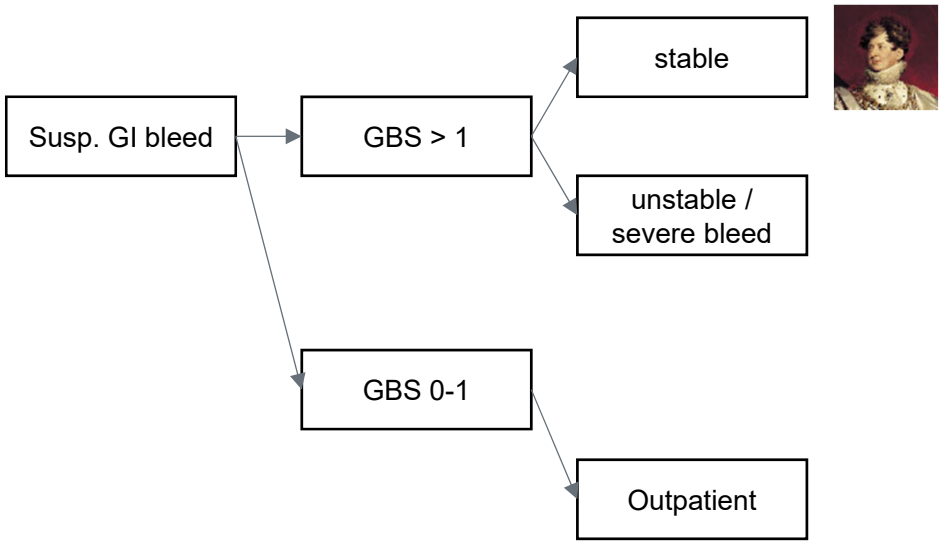
Future?



Shung DL, Au B, Taylor RA, *et al*. Validation of a machine learning model that outperforms clinical risk scoring systems for upper gastrointestinal bleeding. *Gastroenterology* 2020;158:160–7. doi:10.1053/j.gastro.2019.09.009

Risk stratification and triage



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Early management

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Back to Mr. George!

«He’s received a loading dose of Cyklokapron on his way to the ER as well as a loading PPI dose. His haemoglobin fell from 91g/L to 84g/L and we ordered 1 unit of packed RBCs. Should I do something else while waiting for the GI consult?»

1. **Do you agree with treatments so far?**
2. **What do you propose?**

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Resuscitation

- If unstable: restrictive fluid resuscitation regimen combined with an inotropic pharmacologic agent
- a restrictive RBC transfusion strategy is associated with significantly lower mortality (RR 0.65, 95%CI 0.44–0.97) and reduced rebleeding (RR 0.58, 95%CI 0.40–0.84).

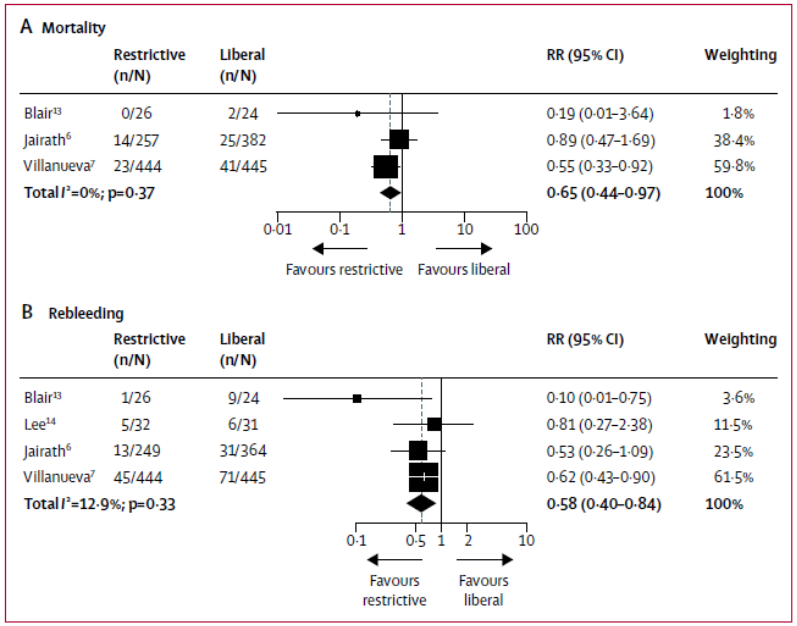

Figure 3: **Pooled RR of all-cause mortality (A) and rebleeding (B)**
No deaths occurred in either group in one trial (Villarejo and colleagues[15]) so it was not included in the meta-analysis. RR=relative risk.

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Tranexamic acid

Myocardial Infarction or Is
or Ischemia, and Other Th
Overall, administration o
ated with an increased risk
to 0.001; P = .56) (eTable
Supplement). Detailed an
in the Supplement.

RECOMMENDATION

ESGE does not recommend the use of tranexamic acid in patients with acute NVUGIH.
Strong recommendation, high quality evidence.

	Tranexamic acid (n=5956)	Placebo (n=5981)	Risk ratio (95% CI)
Bleeding	252 (4·2%)	262 (4·4%)	0·97 (0·82–1·15)
			1·54 (0·83–2·83)
			0·96 (0·74–1·25)
			1·36 (0·92–2·03)
			0·68 (0·44–1·05)
			1·63 (1·10–2·42)
			0·88 (0·49–1·58)
			1·03 (0·92–1·16)

Table 3: Effect of tranexamic acid on all-cause death

Taeuber et al., JAMA Surg. 2021;156(6):e210884

The HALT-IT Trial Collaborators, Lancet 2020; 395: 1927–36

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What about...?

Platel bjh guideline

The Ame

A practical guideline for the haematological management of major haemorrhage

ESGE

EASL

When laboratory results are available:	
IF:	**GIVE:**
Falling Hb	Red cells
APPT and/or PT ratio >1·5	FFP 15-20 ml/kg
Fibrinogen < 1·5 g/l	Cryoprecipitate (2 pools)
Platelet count < 50 x 10^9/l	Platelets 1 adult dose (order when < 100 x 10^9/l)

routine platelet transfusion
NVUGIH who are taking

atelet count and fibrinogen
ith the risk of failure to
leeding [...]should be
by-case basis»

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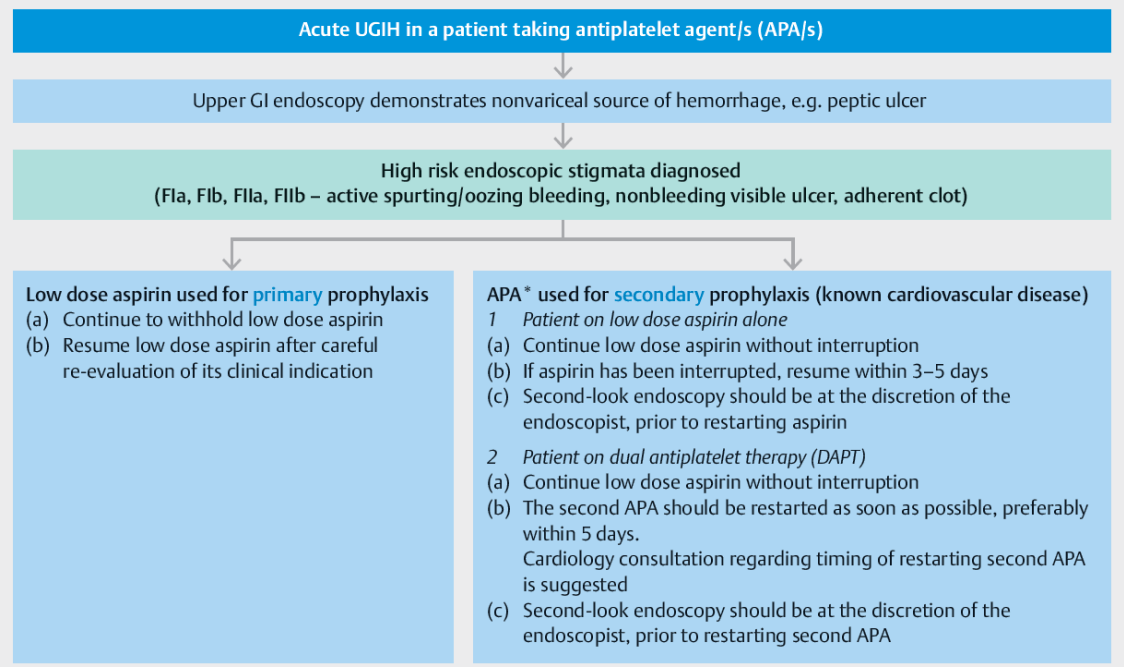
Antiplatelets and anticoagulants



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PPIs pre-endoscopy?

Why give them? To…..

- **A. Decrease mortality?**
- **B. Decrease the need for surgery?**
- **C. Decrease rebleeding rate after endoscopy?**
- **D. Decrease the need for endoscopic treatment?**
- **E. Decrease in the blood transfusion requirement?**

RECOMMENDATION

ESGE suggests that pre-endoscopy high dose intravenous proton pump inhibitor (PPI) therapy be considered in patients presenting with acute UGIH, to downstage endoscopic stigmata and thereby reduce the need for endoscopic therapy; however, this should not delay early endoscopy.

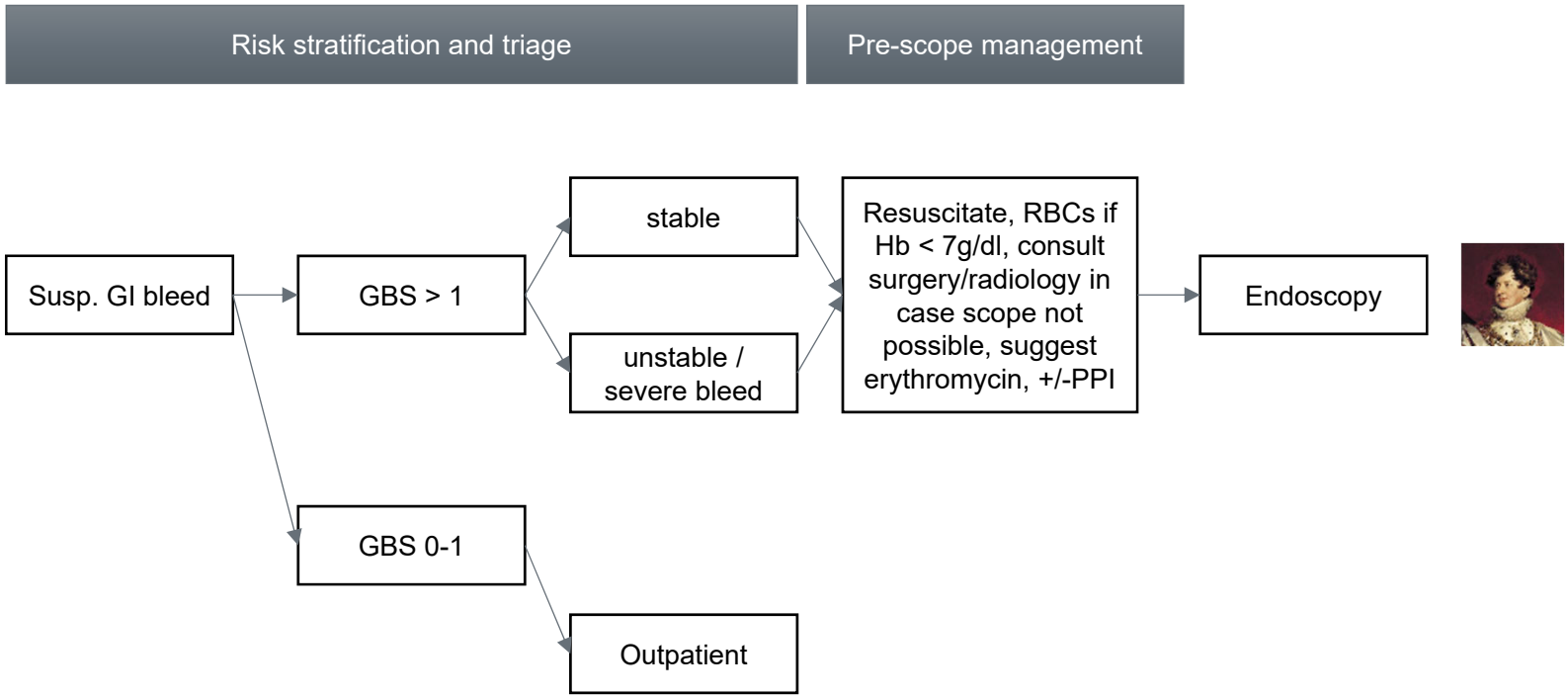
Weak recommendation, high quality evidence.

PPI therapy.

4. We could not reach a recommendation for or against pre-endoscopic PPI therapy for patients with UGIB.

Other measures

	Recommandation
NG tube	Does not differetiate U/LGIB
Sandostatin in NVUGIB	No benefit
Erythromycin	Selected patients w/ ongoing bleed


Risk stratification and triage
Pre-scope management
Susp. GI bleed
GBS > 1
GBS 0-1
stable
unstable / severe bleed
Outpatient
Resuscitate, RBCs if Hb < 7g/dl, consult surgery/radiology in case scope not possible, suggest erythromycin, +/-PPI
Endoscopy

Endoscopy

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Timing

Emergent	Urgent	Early	Delayed

RECOMMENDATION

ESGE does not recommend emergent (≤ 6 hours) upper GI endoscopy since this may be associated with worse patient outcomes.

Strong recommendation, moderate quality evidence.

RECOMMENDATION

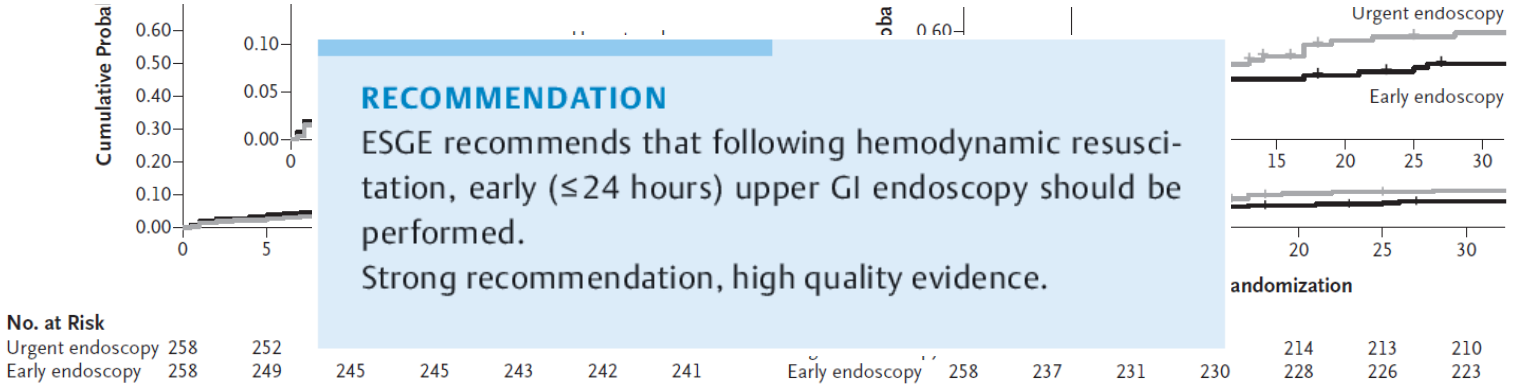
ESGE does not recommend urgent (≤ 12 hours) upper GI endoscopy since as compared to early endoscopy, patient outcomes are not improved.

Strong recommendation, high quality evidence.

RECOMMENDATION

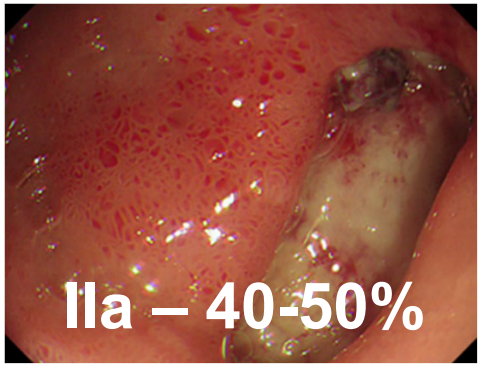
ESGE recommends that following hemodynamic resuscitation, early (≤ 24 hours) upper GI endoscopy should be performed.

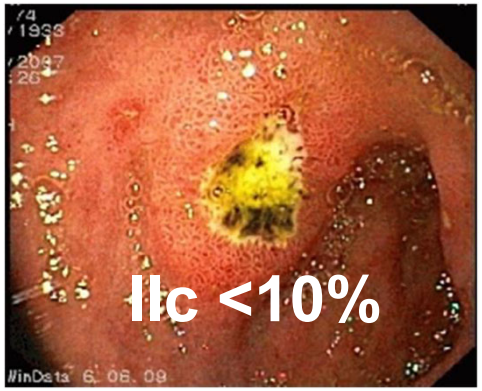
Strong recommendation, high quality evidence.

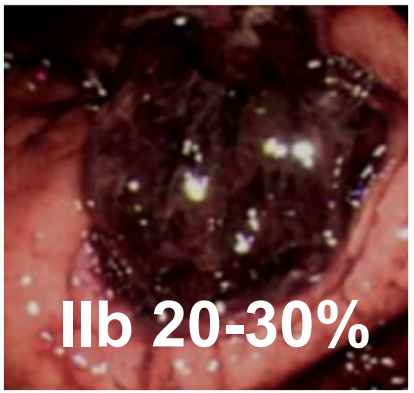


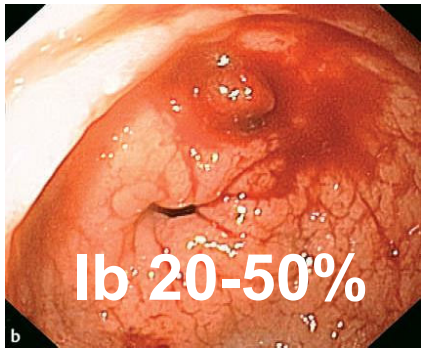
Lau et al., N Engl J Med 2020;382:1299-308.

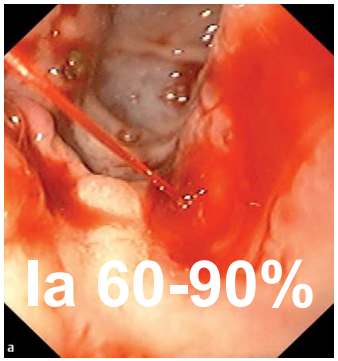
Endoscopic stratification - Stage and rebleeding risk (%)?

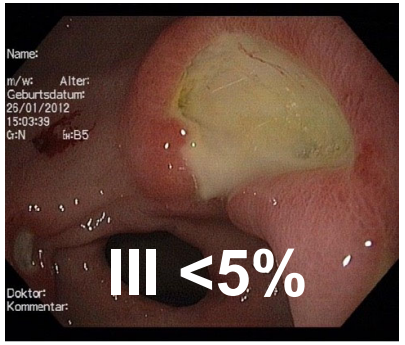












Endoscopic stratification - Stage and rebleeding risk (%)?

Class	Description	Rebleed rate
Ia	Spurting haemorrage	90%
Ib	Oozing haemorrage	20%
IIa	Visible vessel	50%
IIb	Adherent clot	30%
IIc	Haematin on ulcer base	<10%
III	Clean ulcer base	<5%

Endo. ttt

Epi + 2. modality

No endo. ttt

«high» vs. «low» risk

Sleisenger and Fordtran's Gastrointestinal and Liver Disease - 10th Edition

Endoscopy

- Corollary of rebleed rates < 20% as a whole is that **the majority of NVUGIH stop on their own!**
- Within 12H vs 12-24 vs >24: no difference in mortality / transfusions (even higher risk of needing repeat endoscopy in the early group) => **scoping too soon also puts the patient at risk of needing new procedure**
- Relevant exceptions: variceal, arterial ulcer - **which present usually differently**

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Endoscopic treatment

Additional considerations if…

- **Size >2cm**
- **Location : GDA / left gastric territories**
- **Excavated / fibrotic ulcer**

RECOMMENDATION

FIa, FIb (active bleeding)

(a) ESGE recommends for patients with actively bleeding ulcers (FIa, FIb), combination therapy using epinephrine injection plus a second hemostasis modality (contact thermal or mechanical therapy) .

Strong recommendation, high quality evidence.

(b) ESGE suggests that in selected actively bleeding ulcers (FIa, FIb), specifically those >2 cm in size, with a large visible vessel >2 mm, or located in a high risk vascular area (e.g., gastroduodenal, left gastric arteries), or in excavated/fibrotic ulcers, endoscopic hemostasis using a cap-mounted clip should be considered as first-line therapy.

Weak recommendation, low quality evidence.

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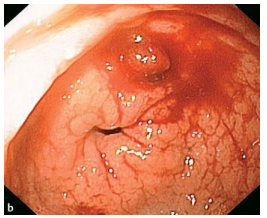
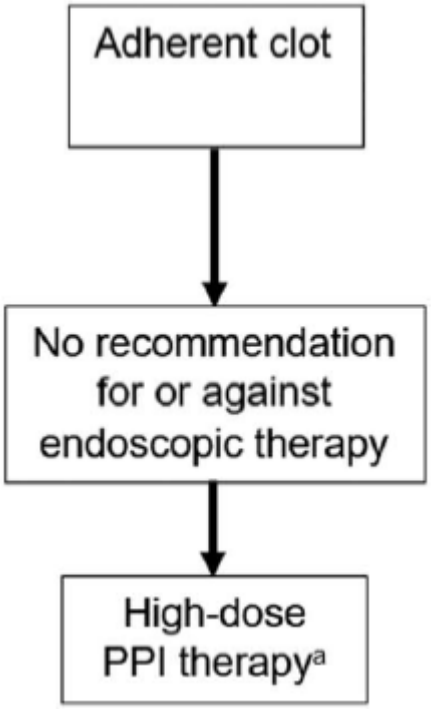
Adherent clots - ESGE / ACG





FIIb (adherent clot)

↓

Consider performing clot removal followed by endoscopic hemostasis of underlying high risk stigmata[4]
OR
Medical management with high dose PPI (intravenous bolus + continuous infusion for 72 hours or minimum twice-daily intravenous bolus dosing for 72 hours or oral dosing)

Adherent clots - ESGE / ACG

Table 6. Meta-Analyses Assessing Endoscopic Therapy Versus No Endoscopic Therapy Related to Stigmata of Hemorrhage (Excluding Trials With Second-Look Endoscopies Specifying Re-Treatment)

Stigmata	End point	Number of comparisons	RR (95% CI)	Pooled rate: no endoscopic therapy n/N (%)	NNT (95% CI)
Active bleeding					2 (2–2)
					2 (2–3)
					2 (2–3)
Nonbleeding visible vessel					—
					5 (4–6)
					9 (7–19)
					7 (5–9)
Clot					—
					—
	Surgery	3[65,71,78]	0.47 (0.10–2.26)	6/76 (8%)	—
	Mortality	2[65,71]	0.90 (0.23–3.58)	5/52 (10%)	—

[a]Statistical heterogeneity ($P \leq .10$) and random-effects model used.

therapy may play a role in provider decisions. Accessibility for application of endoscopic therapy based on ulcer location and availability of interventional radiological or surgical back-up if uncontrollable bleeding is provoked are other factors to be considered. When performing endoscopic therapy for clots, some endo-

Laine et al, Clinical Gastroenterology and Hepatology, 2009;7:33– 47

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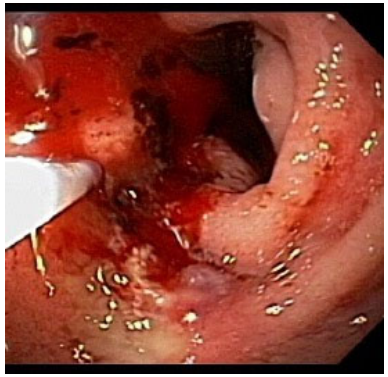
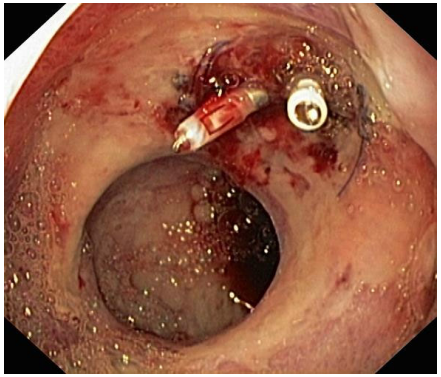
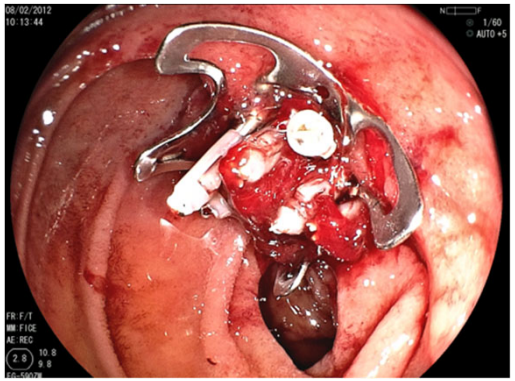
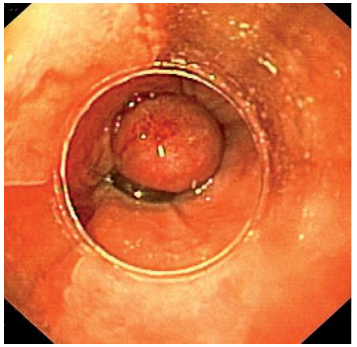
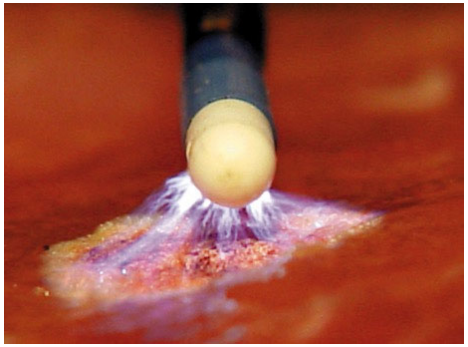
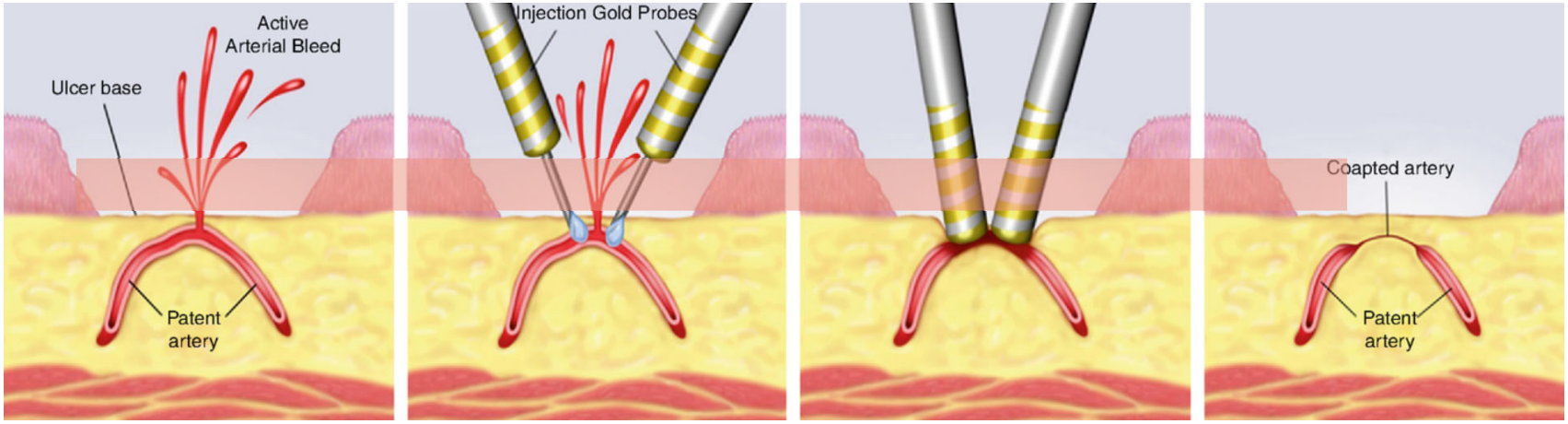
Endoscopic treatment

Contact thermal therapy - Settings?

- Cauterization of bleeding site
- Either direct contact (e.g. bipolar GoldProbe or monopolar Coaggrasper) or non-contact (APC)



Rrapi E., Narayan S., Siskin G., Stain S.C., Tadros M., Tafen M. (2021) Bipolar and Monopolar Cautery, Clips, Bands, Spray, Injections, Embolization, and Minimally Invasive Surgery. In: Tadros M., Wu G.Y. (eds) Management of Occult GI Bleeding. Clinical Gastroenterology. Humana, Cham.

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Contact thermal therapy - Settings?

Monopolar Coaggrasper:

safety. Monopolar hemostatic forceps are used for soft coagulation: The closed tip can be applied to the bleeding site or the forceps can be used to grasp the bleeding site (71–75). Soft monopolar electrocoagulation in RCTs was performed using soft coagulation mode at settings of 50–80 W with 1- to 2-second applications (72–75).

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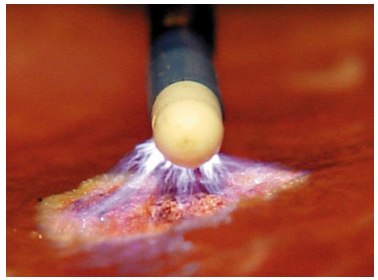
Argon plasma coagulation - Settings?



APC:

- helpfu
  same
- Gas: f
- Lowe
- Highe
- ACG
  tissue

forcedAPC preciseAPC® pulsedAPC® t the

Effective devitalization with forcedAPC

The preciseAPC® mode used in thin-walled structures

The pulsedAPC® mode used for tissue ablation and coagulation

https://www.uptodate.com/contents/argon-plasma-coagulation-in-the-management-of-gastrointestinal-hemorrhage, accessed 07.02.2022

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Post-endoscopy management

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PPIs after endoscopy

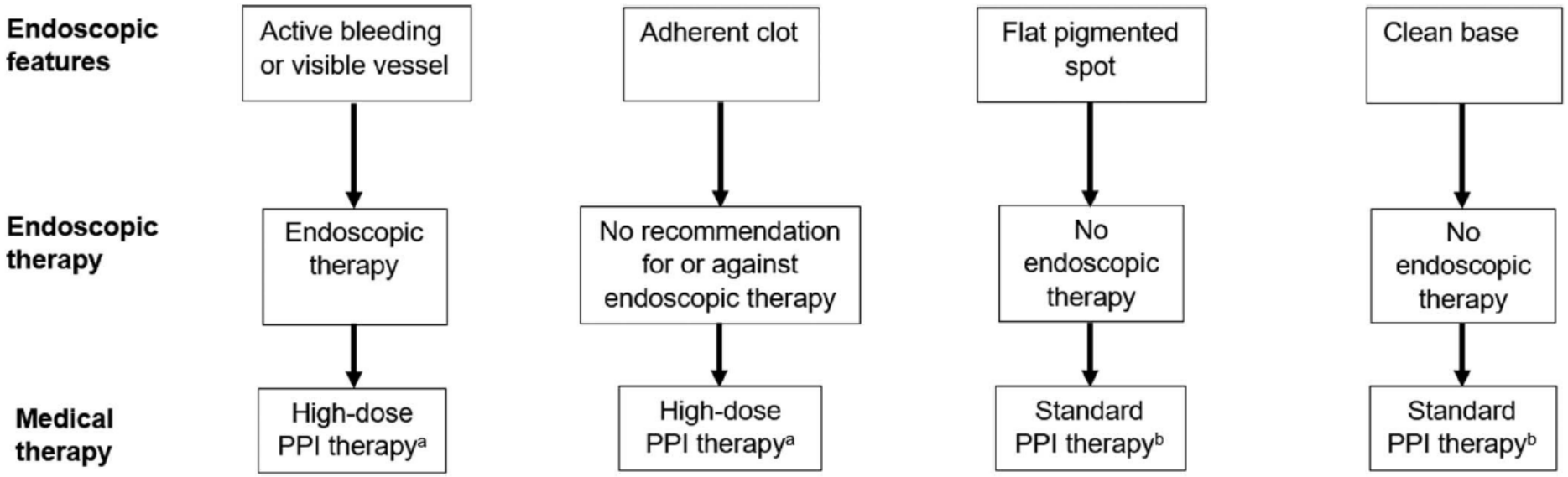

Figure 3. Endoscopic and medical therapy for ulcer bleeding based on endoscopic features of ulcer. [a]For continuous regimen, 80-mg bolus followed by 8-mg/min infusion for 3 days is recommended. For intermittent regimens, doses of 40 mg 2 to 4 times daily for 3 days are suggested, given orally if feasible, and an initial bolus of 80 mg may be appropriate. [b]Standard PPI therapy (e.g., oral PPI once-daily) has been recommended by previous guidelines (1,37) but is not assessed in the current document. PPI, proton pump inhibitor.

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HP Eradication

What do you achieve by eradicating Helicobacter pylori?

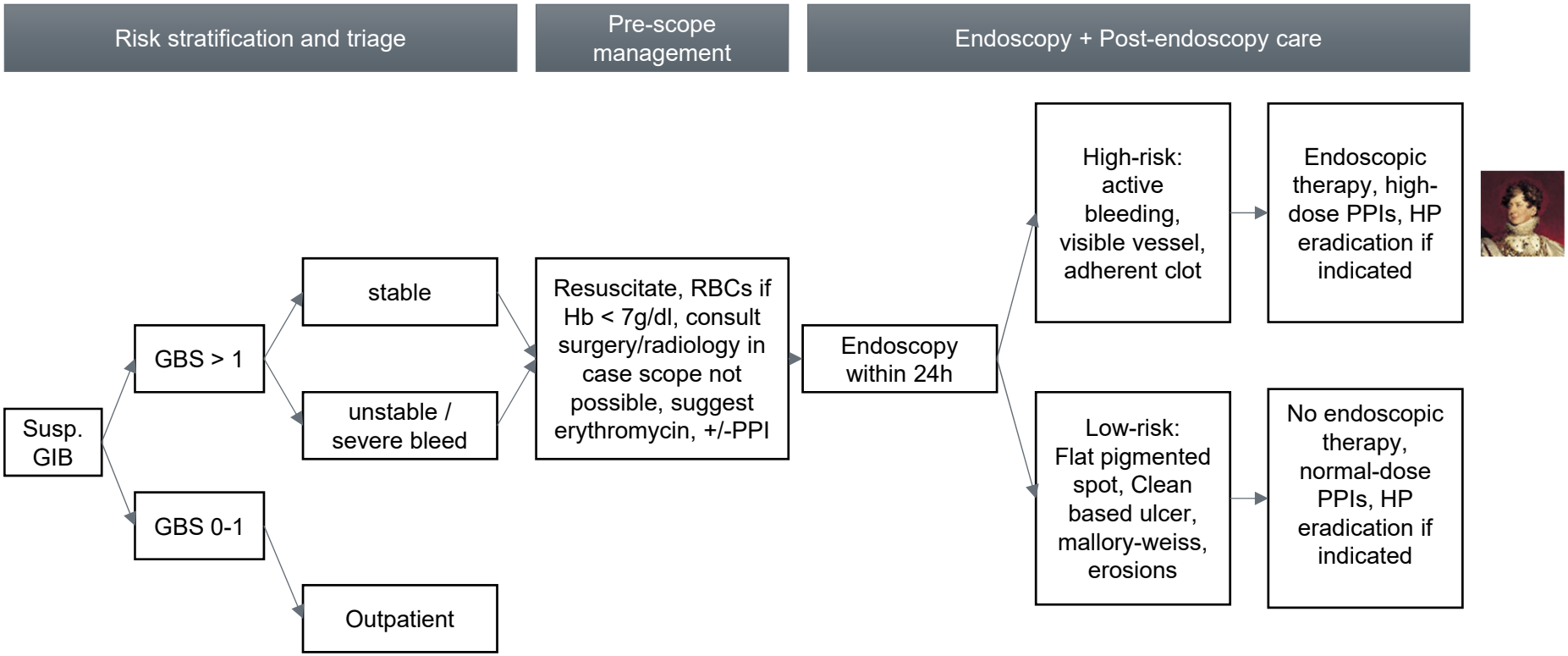
1. Speeds up ulcer healing in HP-positive ulcers
2. Prevents recurrence of duodenal and gastric ulcers vs. no therapy

Cochrane Library

Cochrane Database of Systematic Reviews

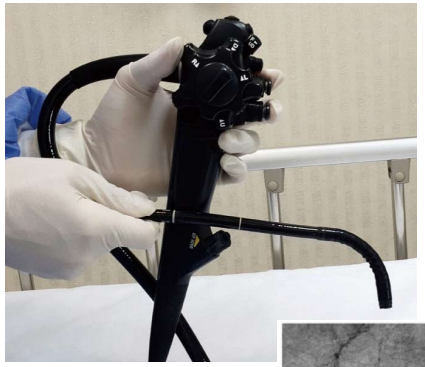
Eradication therapy for peptic ulcer disease in *Helicobacter pylori*-positive people (Review)

Ford AC et al. Eradication therapy for peptic ulcer disease in Helicobacter pylori-positive people. Cochrane Database of Systematic Reviews 2016, Issue 4.


Risk stratification and triage
Pre-scope management
Endoscopy + Post-endoscopy care
Susp. GIB
GBS > 1
GBS 0-1
stable
unstable / severe bleed
Outpatient
Resuscitate, RBCs if Hb < 7g/dl, consult surgery/radiology in case scope not possible, suggest erythromycin, +/-PPI
Endoscopy within 24h
High-risk: active bleeding, visible vessel, adherent clot
Low-risk: Flat pigmented spot, Clean based ulcer, mallory-weiss, erosions
Endoscopic therapy, high-dose PPIs, HP eradication if indicated
No endoscopic therapy, normal-dose PPIs, HP eradication if indicated

Recurrent bleeding / failed hemostasis

- On the next day, Mr. George, now on the ward, has a 20g/dL Hb loss…



What now?

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Recurrent bleeding / failed hemostasis

RECOMMENDATION

ESGE recommends that patients with clinical evidence of recurrent bleeding should receive repeat upper endoscopy, including hemostasis if indicated.
Strong recommendation, high quality evidence.

RECOMMENDATION

ESGE recommends that for patients with clinical evidence of recurrent peptic ulcer hemorrhage, use of a cap-mounted clip should be considered. In the case of failure of this second attempt at endoscopic hemostasis, transcatheter angiographic embolization (TAE) should be considered. Surgery is indicated when TAE is not locally available or after failed TAE.
Strong recommendation, moderate quality evidence.

RECOMMENDATION

ESGE recommends that in the case of failure of this second attempt at endoscopic hemostasis, transcatheter angiographic embolization (TAE) should be considered. Surgery is indicated when TAE is not locally available or after failed TAE.
Strong recommendation, high quality evidence.

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Last question… but not least

After careful consideration, you recommend TAE. The patient's family asks about the procedure. When thinking about possible outcomes of TAE vs. surgery, what would you **NOT** expect? (Bonus question: reference?)

1. An equal success rate with TAE compared to surgery
2. A lower complication rate with TAE compared to surgery
3. The same mortality rate with TAE compared to surgery
4. Shorter hospital stays with TAE compared to surgery
5. The spanish inquisition

Monty Python's Flying Circus, Series 2 Episode 2, first broadcast 22 September 1971

Recurrent bleeding / failed hemostasis: surgery vs. TAE

Table 2. Results: treatment for active or recurrent bleeding.

	TAE, $n = 24$	Surgery, $n = 43$	p
Hemostasis achieved with first attempt, *n* (%)	16 (66.7)	36 (83.7)	NS
Negative angiography, TAE not feasible, *n* (%)	2 (8.3)		
Recurrent bleeding, *n* (%)	6 (25)	7 (16.3)	NS
Mortality rate ≤30 d, *n* (%)	3 (12.5)	11 (25.6)	NS
Complication rate, periprocedural, *n* (%)	6 (25)	8 (18.6)	NS
Complication rate ≤30 d, *n* (%)	9 (37.5)	29 (67.4)	0.018[a]
Clavien-Dindo I–II	3 (33.3)	11 (37.9)	NS
Clavien-Dindo IIIa–b	3 (33.3)	3 (10.3)	NS
Clavien-Dindo IVa–b	3 (33.3)	15 (51.7)	NS
Need for blood transfusions, units of RBCs[b]	24 (6–37)	19 (6–54)	NS
0–10 units of RBCs, *n* (%)	2 (8.3)	3 (7)	
11–20 units of RBCs, *n* (%)	8 (33.3)	22 (5.1)	
> 20 units of RBCs, *n* (%)	14 (58.3)	15 (34.9)	
Duration of ICU treatment, d[b]	0 (0–7)	0 (0–17)	NS
0 d, *n* (%)	12 (60)	21 (52.5)	
1–3 d, *n* (%)	2 (10)	6 (15)	
4–7 d, *n* (%)	0	3 (7.3)	
8–14 d, *n* (%)	6 (30)	6 (15)	
> 14 d, *n* (%)	0	4 (10)	
Duration of hospital stay, d[b]	11 (5–39)	11 (2–43)	NS

TAE: transcatheter arterial embolization; NS: non-significant; $p > 0.05$; RBC: red blood cell; ICU: intensive care unit.
[a]Fisher's exact test, [b]median (range).

Conclusions: Mortality and rebleeding rates did not differ between TAE and surgery. With less postoperative complications, TAE should be the preferred hemostatic method when endoscopy fails.

Conclusion. In patients who fail endoscopic therapy, TAE shows marked reductions in complications and hospital stay with no difference in mortality as compared to surgery, but does have a higher rate of further bleeding. New evidence led to a change from the 2012 ACG Guidelines, which stated that either surgery or TAE is generally used (1).

Nykänen et al, Bleeding gastric and duodenal ulcers: case-control study comparing angioembolization and surgery, Scandinavian Journal of Gastroenterology, Volume 52, 2017 - Issue 5

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Thank you for your attention!