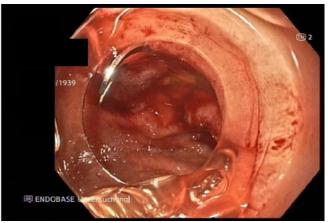


# Acute Upper GI Bleeding



Bible Class 21.08.2024 - Gastroenterologie - Jonas Brunner & Roy Frei







Bett / Lokalisation / Problem -

020-P-221-T

European Specialty Examination in Gastroenterology and Hepatology

Knowledge Examination

020-P-451-F

Akute hämodynamisch relevante erstmalige ...



European Society of Gastrointestinal Endoscopy - 2021 American College of Gastroenterology - 2021 British Society of Gastroenterology - 2019





## Goals



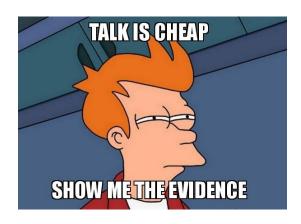
- 1. Practical: tools for everyday, focus on non-variceal GIB
- 2. Educational: ESEGH-like questions

Insel Gruppe -



#### **Contents**

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



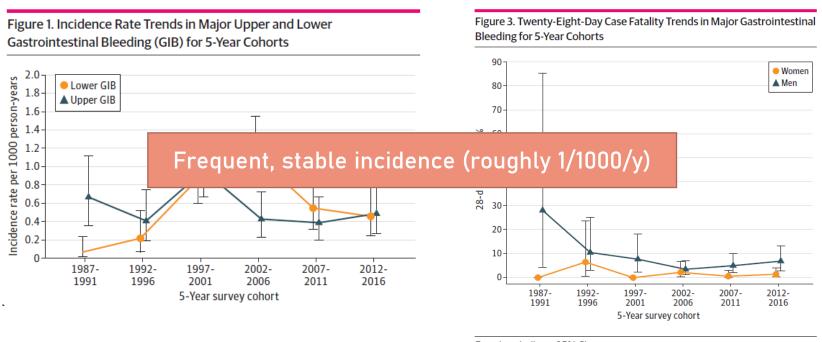


# Epidemiology and clinical presentation

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## **Epidemiology**



Error bars indicate 95% Cls.

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

19.08.2025

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# **Epidemiology**

Table 4 Crude mortality by endoscopic diagnosis

	Crude mortality rate	(%)	
Endoscopic diagnosis (n)	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 (26/038)	17 (39/229)
Oesophagitis alone			10 (8/78)
Gastritis/erosions	30-d Morta	lity up to 10%	24 (41/173)
Gastritis erosions alone		int) dip to 1070	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)

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



Table 3

45-59

60-64

65-74

## **Epidemiology - Costs**

Age bands (years)	UK Population*	AUGIB incidence per 100 000/year†	Annual number of patients with AUGIB in UK population	hosp	total initial ital cost ates‡	Annual total costs
16–29 30–44	11 806 800 12 843 400	Significant cost	and QoL decrea		3 (n=91) 3 (n=150)	£3 104 535 £10 811 709

0000

3951

12 457

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

12605800

3 624 400

5 820 900

109

214

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

== 183 (n=224)

£2749 (n=142)

£2686 (n=78)

£18 990 830

£10 613 733

£34 248 977

9

<sup>75+ 5 020 000 485 24 347 £3190 (</sup>n=251) £77 667 271
Total 51 721 300 - 57 434 - £155 437 055

<sup>\*</sup>Data on population from Office for National Statistics 2012. 19

<sup>†</sup>AUGIB incidence figures taken from Rockall et al. 18

<sup>#</sup>Mean cost estimates based on analysis of TRIGGER data reported in this paper.



## Risk factors and risk stratification

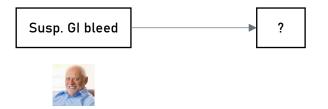


#### Clinical case 1

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







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



**MINSEL**GRUPPE

#### **Risk stratification**



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



#### Clinical case 1 - Mr. Jones

85 yo male brought to the ER with presyncope, coffeeground 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)												
Vitalpa	ramete	r										
Time	HF	Puls	AF	Zyan.	SpO2	02	Kapno	ABPs	ABPd	BPS	BPD	
19:42	78	76	16		99					102	54	
19:02												
19:01	78	77	12		96					135	59	Ι
10.10	70	70	43		03					100	15	1



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
<b>A</b> 🖂	<b>A</b> 🖂

		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	



### Mr. Jones



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

#### **Answer**

?



#### Mr. Jones

85 yo male presents to the ER with presyncope, coffeeground 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)



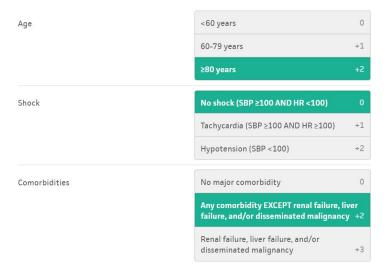


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		venös	venös
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#### **MINSEL**GRUPPE

## Mr. Jones



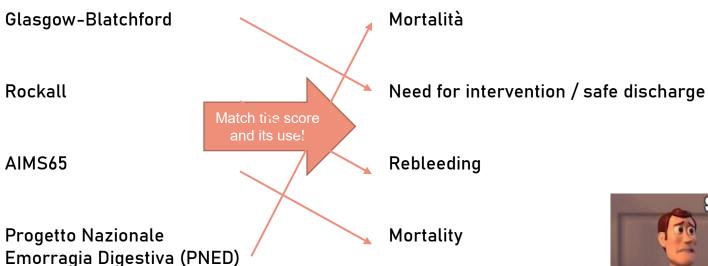


#### **Answer**

2 + 2 = 4 points!



## Scores are plentiful!







# Clinical scoring systems - a brief overview

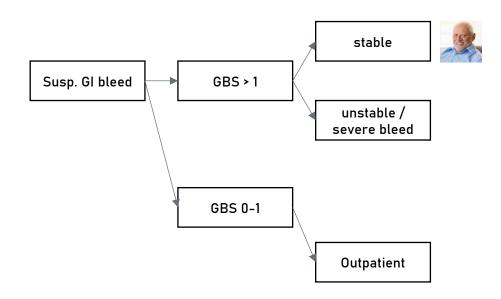
Rockall - Gut	Progetto Nazionale Emorragia Digestive (PNED) [24]. The GBS 6: 1318-21					
	was reported to have the highest accuracy (AUROC 0.86) for					
• 2,956 patiel Outcomes: predicting need for hospital-based intervention (RBC transfu-						
	sion, endoscopic treatment, arterial embolization, surgery) or					
	death. Moreover, a GBS ≤ 1 was the optimal threshold to predict					
	patient survival without need for hospital-based intervention,					
AIMS65 - Gas	with a sensitivity of 98.6% and specificity of 34.6%. However, 639-1647					
Newer, sim						
Albumin, IN outcomes with acceptable ability (AUROC ≤ 0.80).						
hospitals)	cts mortality, less so transfusion need					

Insel Gruppe – 19.08.2025 19.08.2025 19.08.2025 19.08.2025 19.08.2025 19.08.2025 19.08.2025 19.08.2025 19.08.2025 19.08.2025 19.08.2025 19.08.2025 19.08.2025 19.08.2025 19.08.2025



## **MINSEL**GRUPPE

#### Risk stratification and triage





# Early management



#### Back to Mr. Jones!

«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?»



- 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).

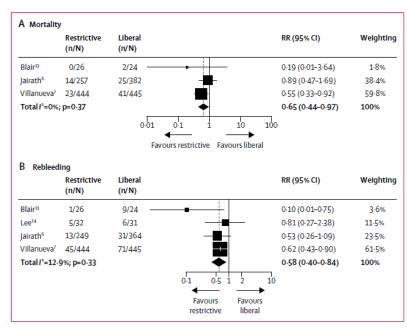


Figure 3: Pooled RR of all-cause mortality (A) and rebleeding (B)

No deaths occurred in either group in one trial (Villarejo and colleagues<sup>15</sup>) so it was not included in the meta-analysis. RR=relative risk.



## Tranexamic acid

# How do you manage a GI bleed?

#### RECOMMENDATION

ESGE does not recommend the use of tranexamic acid in patients with acute NVUGIH.

Strong recommendation, high quality evidence.



rable 3: Effect of traffexamic acid

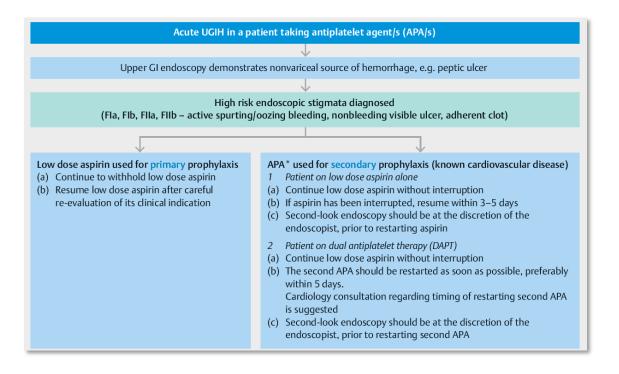


Taeuber et al., JAMA Surg. 2021;156(6):e210884

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



## Antiplatelets and anticoagulants





## 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.

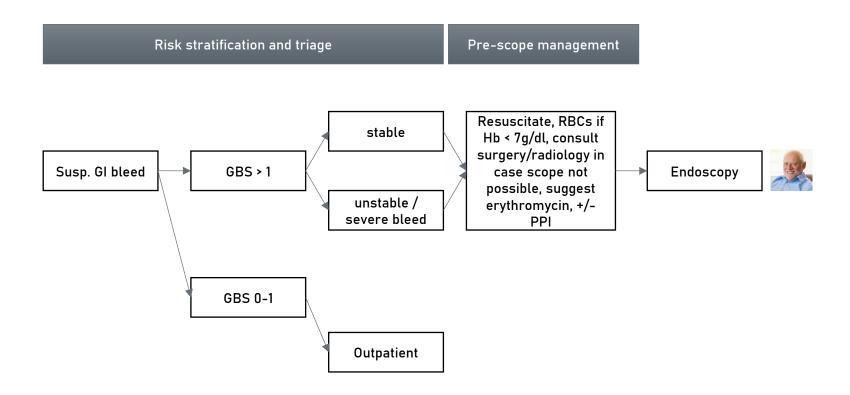
4. We could not reach a recommendation for or against preendoscopic PPI therapy for patients with UGIB.



## Other measures

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

#### **MINSEL**GRUPPE





# **Endoscopy**



#### **Timing Emergent Urgent Delayed Early** RECOMMENDATION RECOMMENDATION ESGE does not recommend emergent (≤ 6 hours) upper GI ESGE does not recommend urgent (≤12 hours) upper GI endoscopy since this may be associated with worse paendoscopy since as compared to early endoscopy, patient tient outcomes. outcomes are not improved. Strong recommendation, moderate quality evidence. Strong recommendation, high quality evidence. Cumulative Prob 0.60-0.60-0.10-0.50-0.05-RECOMMENDATION 0.40-Early endoscopy 0.30-ESGE recommends that following hemodynamic resusci-0.20tation, early (≤24 hours) upper GI endoscopy should be 0.10performed. 20 30 Strong recommendation, high quality evidence. andomization

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

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No. at Risk Urgent endoscopy 258

Early endoscopy

252

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245

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243

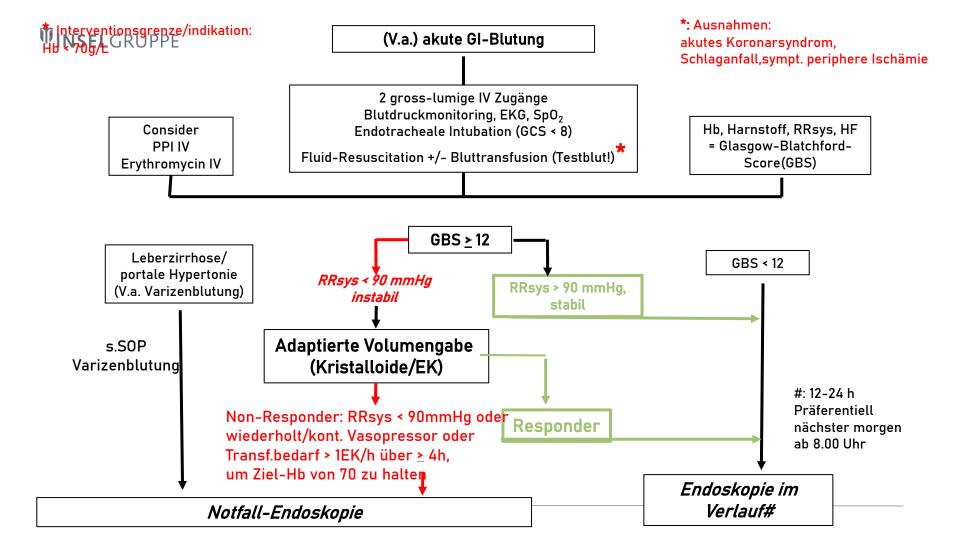
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Early endoscopy

237

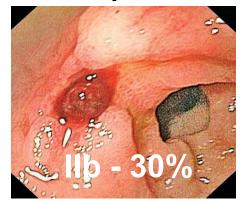
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223



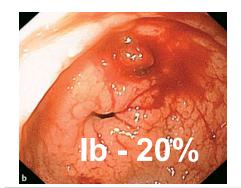
## **MINSEL**GRUPPE

## Endoscopic stratification - Stage and rebleeding risk (%)?















## Endoscopic stratification - Stage and rebleeding risk (%)?

Class	Description	Rebleed rate	
la	Spurting haemorrage	90%	
lb	Oozing haemorrage	20%	Francosia theres.
lla	Visible vessel	50%	Endoscopic therapy
Ilb	Adherent clot	30%	
IIc	Haematin on ulcer base	<10%	NI I II
Ш	Clean ulcer base	<5%	No endo. therapy

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



## **Endoscopic treatment**

Additional considerations if...

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



#### RECOMMENDATION

Fla, Flb (active bleeding)

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

Strong recommendation, high quality evidence.

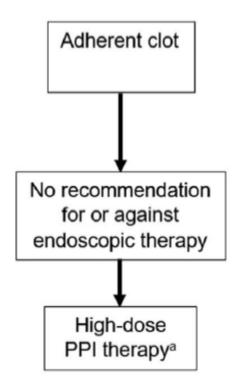
**(b)** ESGE suggests that in selected actively bleeding ulcers (Fla, Flb), specifically those > 2 cm in size, with a large visible vessel > 2 mm, or located in a high risk vascular area (e.g., gastroduodenal, left gastric arteries), or in excavated/fibrotic ulcers, endoscopic hemostasis using a cap-mounted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

Weak recommendation, low quality evidence.



## Adherent clots - ESGE / ACG





## FIIb (adherent clot)

Consider performing clot removal followed by endoscopic hemostasis of underlying high risk stigmata<sup>4</sup> 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	therapy ma	y play a role in provider deci	sions. Accessib	oility for ap-	2 (2–2) 2 (2–3)
	plication of	endoscopic therapy based or	n ulcer location	n and avail-	2 (2–3)
	ability of	interventional radiological	or surgical	back-up if	5 (4–6)
vessel	uncontrolla	ble bleeding is provoked are o	other factors to	be consid-	9 (7–19) 7 (5–9)
Clot	ered. When	performing endoscopic ther	apy for clots,	some endo-	
0.00	Surgery	3 <sup>65,71,78</sup>	0.47 (0.10–2.26)	6/76 (8%)	_
	Mortality	2 <sup>65,71</sup>	0.90 (0.23–3.58)	5/52 (10%)	

<sup>&</sup>lt;sup>a</sup>Statistical heterogeneity ( $P \leq .10$ ) and random-effects model used.

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

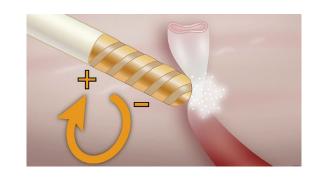


## **Endoscopic treatment**





### Contact thermal therapy - Settings?

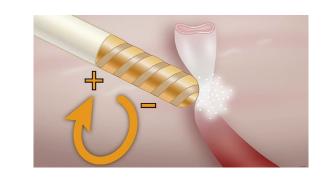


- Cauterization of bleeding site
- Either direct contact (e.g. bipolar GoldProbe or monopolar Coaggrasper) or non-contact (APC)
- Concerning settings for bipolar probes, which of the following is true?
  - A. High power (>50W) should be favored for adequate hemostasis
  - B. Moderate (8-10s) rather than short (<5s) application should be favored</li>
  - C. Current is generated at the base of the probe
  - D. Heater probes can coagulate arteries up to 1mm
  - E. Heater probes can deliver a variable energy depending on tissue resistance

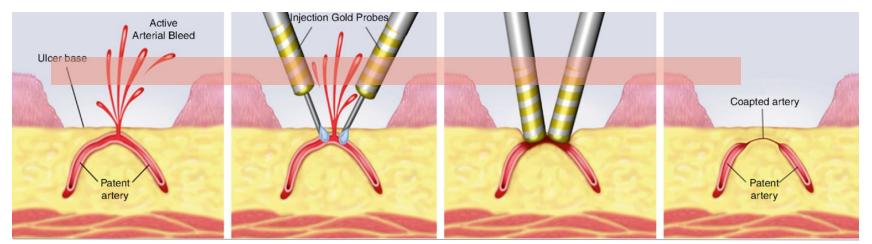
Rrapi E., Narayan S., Siskin G., Stain S.C., Tadros M., Tafen M. (2021) Bipolar and Monopolar Cautery, Clips, Bands, Spray, Injections, Embolization, and Minimally Invasive Surgery. In: Tadros M., Wu G.Y. (eds) Management of Occult GI Bleeding. Clinical Gastroenterology. Humana, Cham.



## Contact thermal therapy - Settings?



- Cauterization of bleeding site
- Either direct contact (e.g. bipolar GoldProbe or monopolar Coaggrasper) or non-contact (APC)
- Concerning settings for bipolar probes, which of the following is true?





### 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).



## Argon plasma coagulation - Settings?



#### APC:

- helpful for targets that are difficult to reach by direct contact and for treating multiple lesions at the same session
- Gas: flow rate usually 0.8-1L/min
- Lower settings (20-30W) in thinner regions colon and small bowel
- Higher settings (30-40W) for the thicker-walled stomach and for tumor ablation
- ACG 2021: in supporting RCTs 40-70W for duodenal and gastric ulcers, distance 2-8mm from tissue

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



## Argon plasma coagulation - Settings?



forcedAPC

preciseAPC®

pulsedAPC®



Effective devitalization with forcedAPC



The preciseAPC® mode used in thin-walled structures



The pulsedAPC® mode used for tissue ablation and coaquiation

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



# Post-endoscopy management

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#### PPIs after endoscopy

Table 2. Meta-analysis of Intermittent PPI vs Bolus With Continuous-Infusion PPIa

		No. of	(95% CI, Upper Boundary)		
Outcome	No. of Studies	Patients	Risk Ratio	Absolute Risk Difference, %	
Recurrent bleeding					
Within 7 d	1014,16,17,20-26	1346	0.72 (0.97)	-2.64 (-0.28)	
Within 30 d	1314-26	1691	0.89 (1.17)	-0.97 (1.49)	
Within 3 d	914,16,17,20-24,26	1146	0.73 (1.02)	-2.36 (0.17)	
Mortality	1114-16,18-24,26	1453	0.64 (1.21)	-0.74 (0.43)	
Surgery/RI	1214-24,26	1491	0.87 (1.49)	-0.30 (1.12)	
Urgent interventions	914-20,22,23	1283	0.95 (1.27)	-0.45 (2.43)	
Length of hospital stay, d	8 <sup>14-16,18,21-23,26</sup>	1204	-0.26 (0.09)b		
Blood transfusion, U	9 <sup>14-16,18,21-24,26</sup>	1242	-0.22 (-0.02) <sup>b</sup>		

- 3. High-dose for 72 hours post-endoscopy
- 4. ACG 2021: high dose 14d or standard dose 1

Figure 3. Forest Plot of Studies Comparing Intermittent With Bolus Plus Continuous-Infusion Proton Pump Inhibitors in Patients

O With High-Risk Bleeding Ulcers

Source	Intermittent Bolus, No.		Continuous Infusion, No.		Risk Ratio	Favors : Favors	Weight,
	Events	Total	Events	Total	(M-H, Fixed, 95% CI)	Bolus Infusion	%
Andriulli et al, <sup>14</sup> 2008	19	239	28	243	0.69 (0.40-1.20)	-	43.2
Chen et al, 16 2012	6	101	7	100	0.85 (0.30-2.44)		11.0
Choi et al, <sup>17</sup> 2009	3	21	1	19	2.71 (0.31-23.93)		1.6
Jang et al, <sup>24</sup> 2006	0	19	2	19	0.20 (0.01-3.91)		3.9
Javid et al, <sup>20</sup> 2009	4	53	4	53	1.00 (0.26-3.79)		6.2
Kim et al, <sup>21</sup> 2012	2	54	1	52	1.93 (0.18-20.60)		1.6
Sung et al, <sup>25</sup> 2012	3	105	2	95	1.36 (0.23-7.95)		3.3
Ucbilek et al, <sup>26</sup> 2013	3	37	10	36	0.29 (0.09-0.97)		15.8
Yamada et al, <sup>22</sup> 2012	4	13	5	15	0.92 (0.31-2.73)		7.2
Yüksel et al, <sup>23</sup> 2008	3	49	4	50	0.77 (0.18-3.24)		6.2
Total (95% CI)	47	691	64	682	0.74 (0.52-1.06)		100.0
Heterogeneity: $\chi_9^2 = 5.96$ Test for overall effect: $z =$					0.01	0.1 1.0 10 Risk Ratio (M-H, Fixed, 95% C	100

The outcome examined was rebleeding within 7 days in the intention-to-treat population. M-H indicates Mantel-Haenszel.

Sachar et al, JAMA Intern Med. 2014;174(11):1755-1762



## PPIs after endoscopy

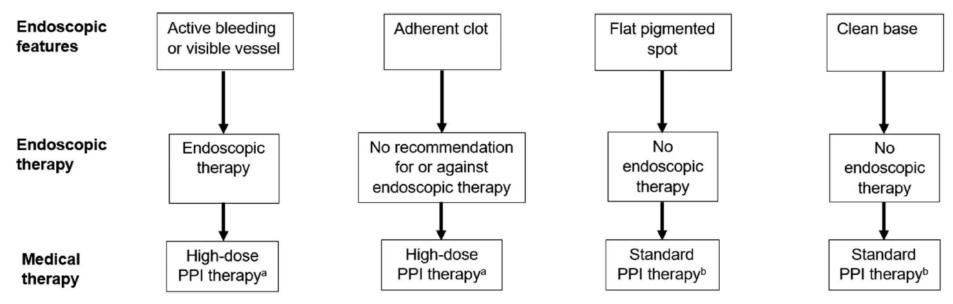


Figure 3. Endoscopic and medical therapy for ulcer bleeding based on endoscopic features of ulcer. <sup>a</sup>For continuous regimen, 80-mg bolus followed by 8-mg/min infusion for 3 days is recommended. For intermittent regimens, doses of 40 mg 2 to 4 times daily for 3 days are suggested, given orally if feasible, and an initial bolus of 80 mg may be appropriate. <sup>b</sup>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.



#### **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

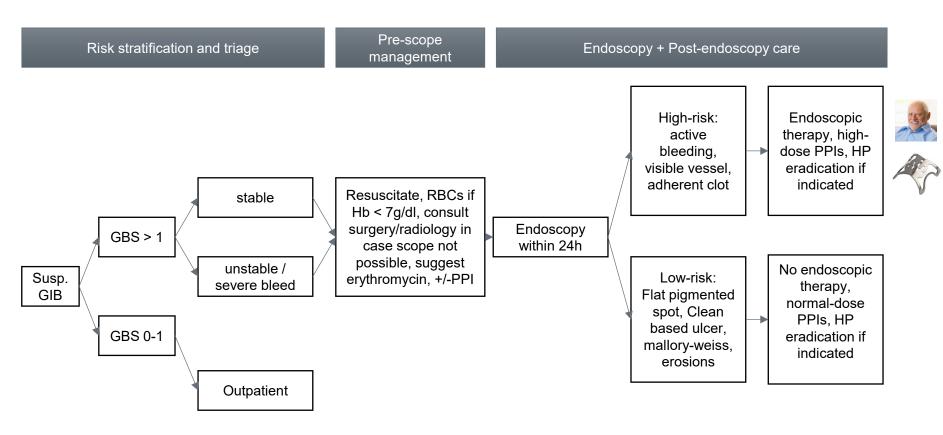


Cochrane Database of Systematic Reviews

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.

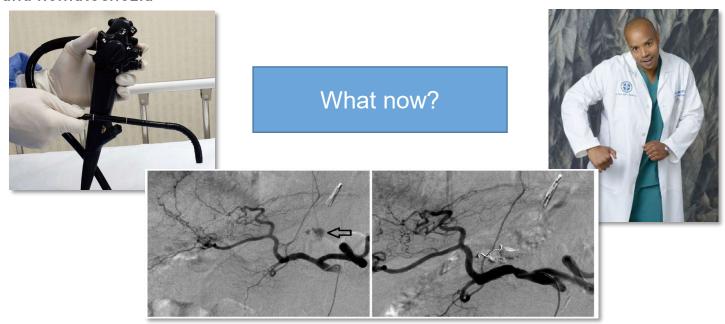
19.08.2025





## Recurrent bleeding / failed hemostasis

 On the next day, Mr. Jones, now on the ward, has a 20g/dL Hb loss and hematochezia





#### 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.

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ESGE recommends that for patients with clinical evidence of recurrent peptic ulcer hemorrhage, use of a capmounted 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.

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## Recurrent bleeding / failed hemostasis: surgery vs. TAE

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

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	TAE,	Surgery,					
	n = 24	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 $\leq$ 30 d, $n$ (%)	3 (12.5)	11 (25.6)	NS				
Complication rate, periprocedural, n (%)	6 (25)	8 (18.6)	NS				
Complication rate $\leq$ 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 Illa-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 <sup>b</sup>	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 <sup>b</sup>	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 <sup>b</sup>	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.

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

<sup>&</sup>lt;sup>a</sup>Fisher's exact test, <sup>b</sup>median (range).



Thank you for your attention!