Antithrombotic agents &

Gastrointestinal considerations

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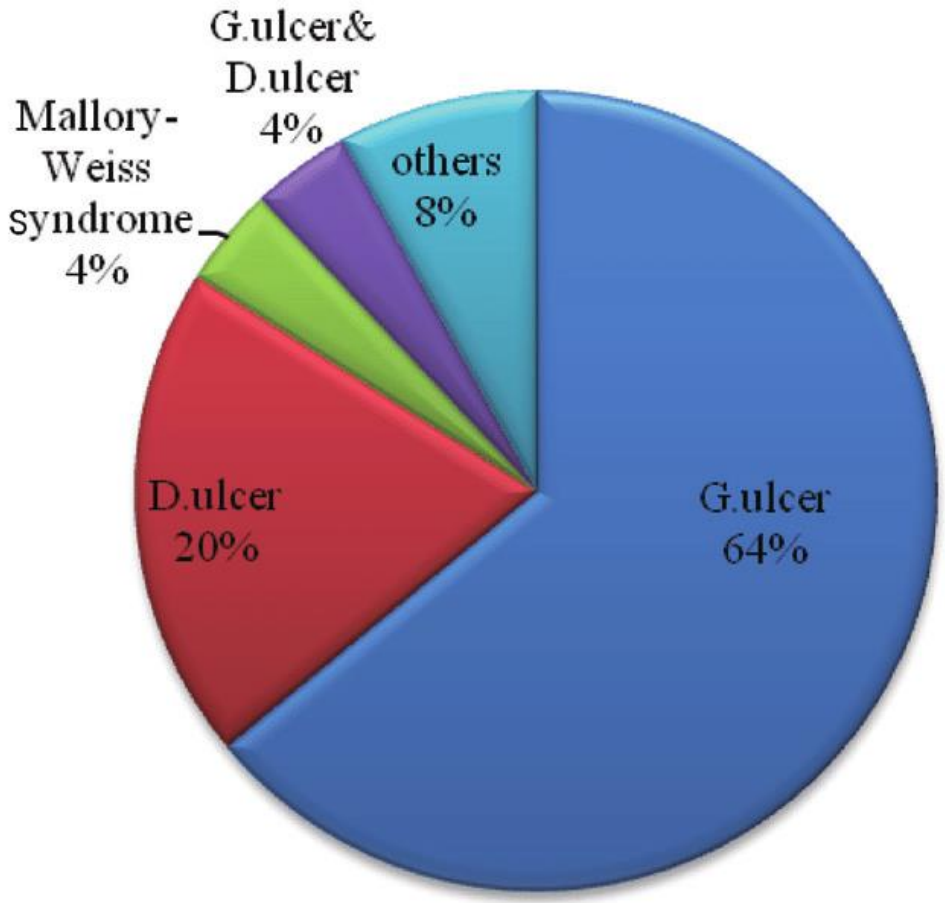
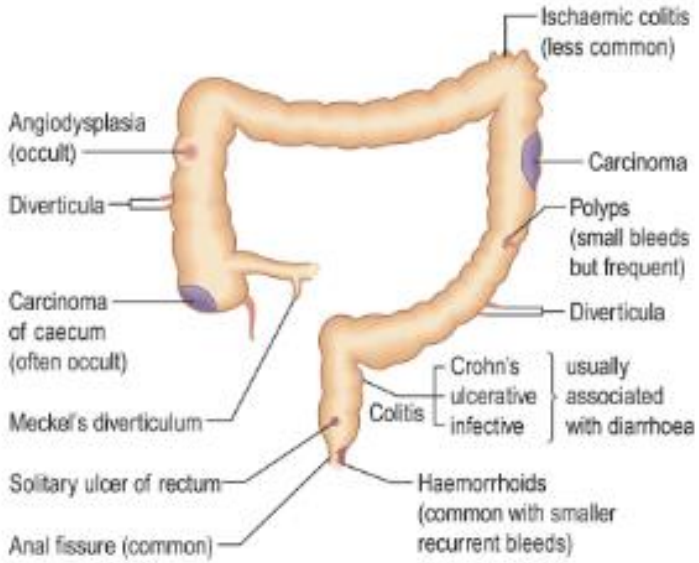
Analysis of gastrointestinal bleeding causes in patients with or without accompanying liver cirrhosis



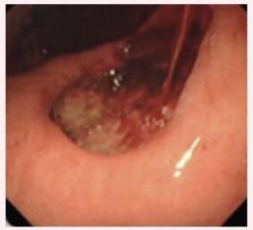


- Acute GI bleedingis defined as patients hospitalized or under observation with acute overt GI bleeding (upper and/or lower) manifesting as melena, hematochezia, or hematemesis.

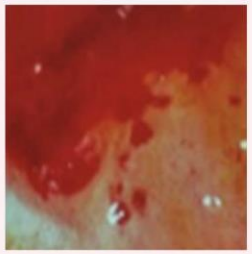
- Life-threatening hemorrhage is defined as major clinically overt or apparent bleeding, resulting in hypovolemic shock or severe hypotension requiring pressors or surgery; or associated with a decrease in hemoglobin of .5 g/dL, or requiring transfusion of >5 units of packed red blood cells, or causing death .

Forrest Classification

Acute Hemorrhage

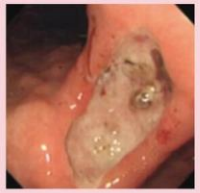


1a
Active Spurting
Rebleeding Risk:
60 to 100%

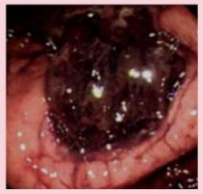


1b
Active Oozing
Rebleeding Risk:
50%

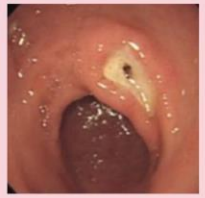
Signs of Recent Hemorrhage



IIa
Non-Bleeding Visible Vessel
Rebleeding Risk:
40 to 50%

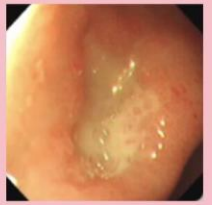


IIb
Adherent Clot
Rebleeding Risk:
20 to 30%



IIc
Flat Spot in Ulcer Base
Rebleeding Risk:
7 to 10%

Lesions without Active Bleeding



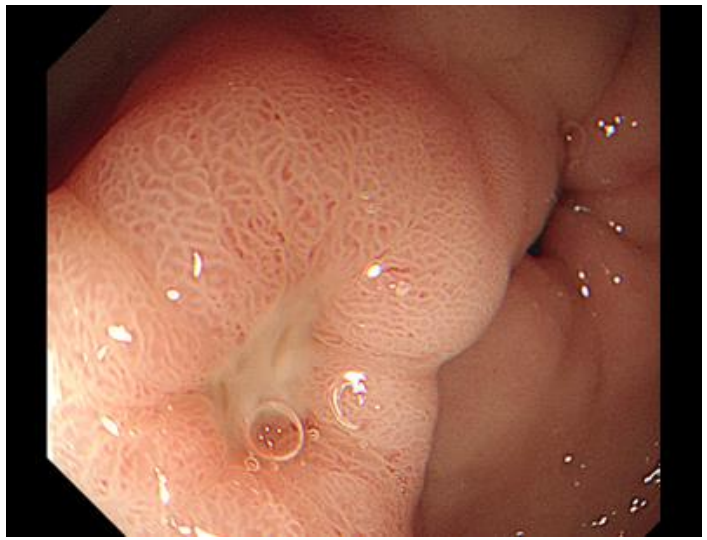
III
Clean-Based Ulcer
Rebleeding Risk:
3 to 5%

@enrrikke

Images from Alzoubaidi, et al, 2018

- First described in 1974 by J.A. Forrest et al. in The Lancet
- Standardized classification system for endoscopists to describe peptic ulcers
- Helps prognosticate and risk stratify patients based on stigmata of recent hemorrhage and decide on discharge versus close inpatient monitoring

Role of endoscopy in antiplatelet-induced gastrointestinal bleed	
Diagnostic	Assess the risk of rebleed
	Confirm the bleed is due to an antiplatelet agent by ruling out other causes like variceal bleed
	The severity of ulcer (Forest grading etc)
	H. pylori testing
Therapeutic	Sclerotherapy, clipping

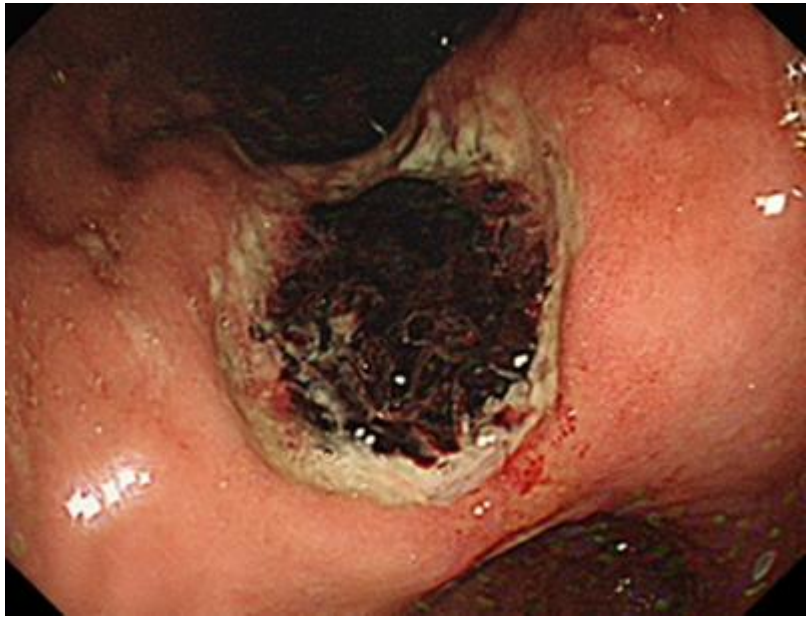


Forrest score	*Endoscopic appearance*	*Risk of rebleeding*[a]
Ia	Ulcer with active pulsating bleeding	55%
Ib	Ulcer with active nonpulsating bleeding	
IIa	Ulcer with a visible nonbleeding vessel	43%
IIb	Ulcer with an adherent clot	22%
IIc	Ulcer with hematin on ulcer base	10%
III	Ulcer with a clean base without signs of recent bleeding	5%

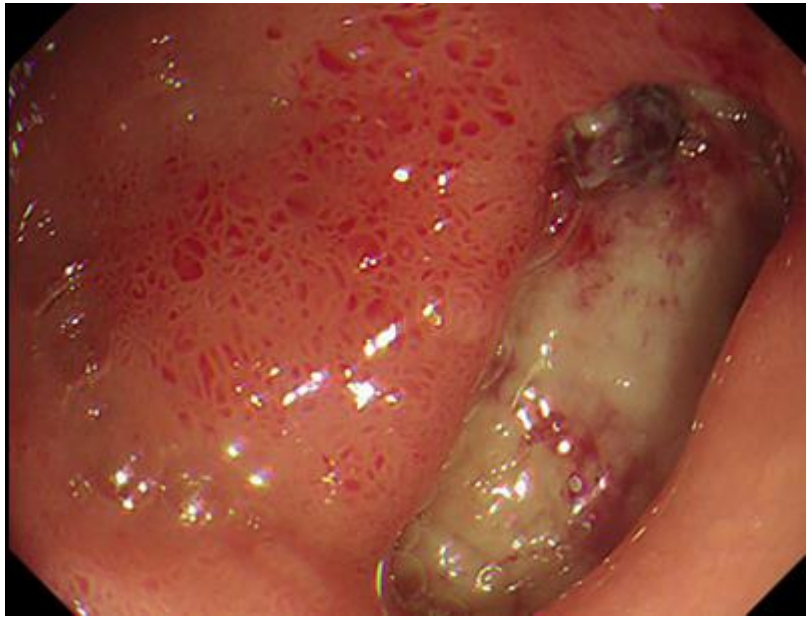
[a]Risk of rebleeding if endoscopic therapy is not performed.

Source: Adapted from Laine, L.; Peterson, W. L. Bleeding Peptic Ulcer. *N. Engl. J. Med.* **1994**, *331*, 717–727.

ENDOSCOPIC VIEW SOME ULCERS

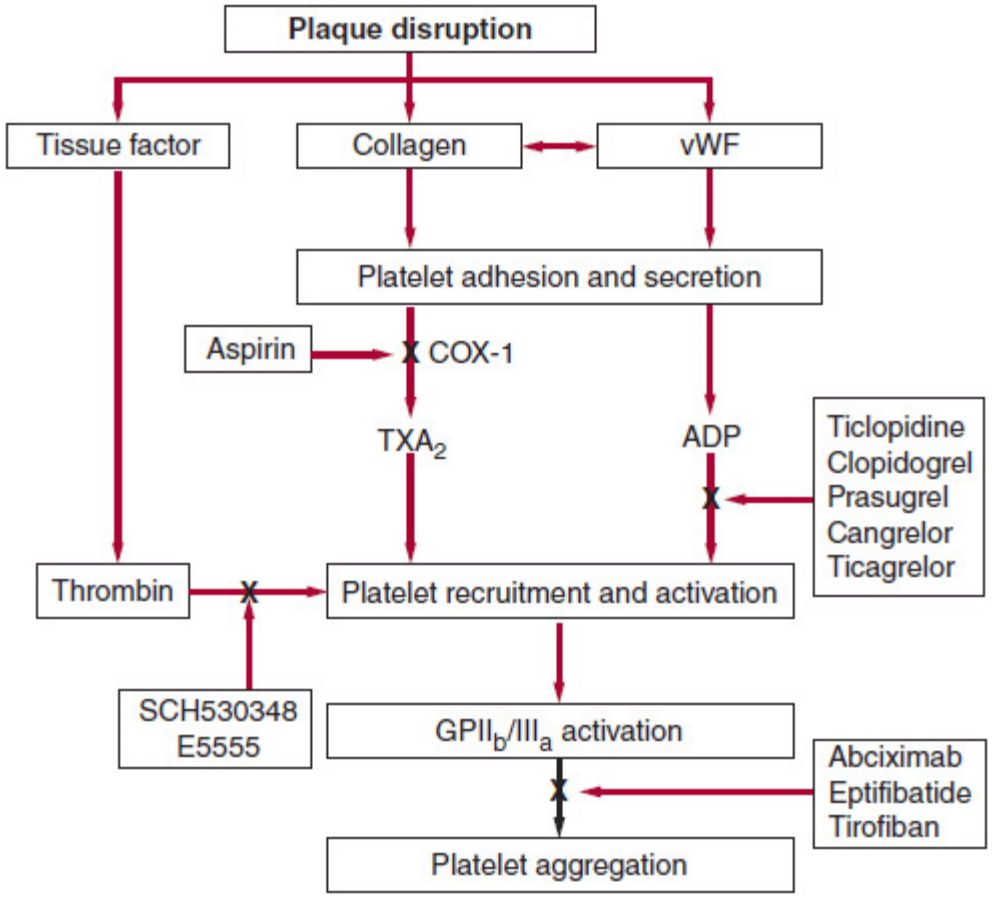


Forrest IIb ulcer at incisura. With ulcers with an adherent clot

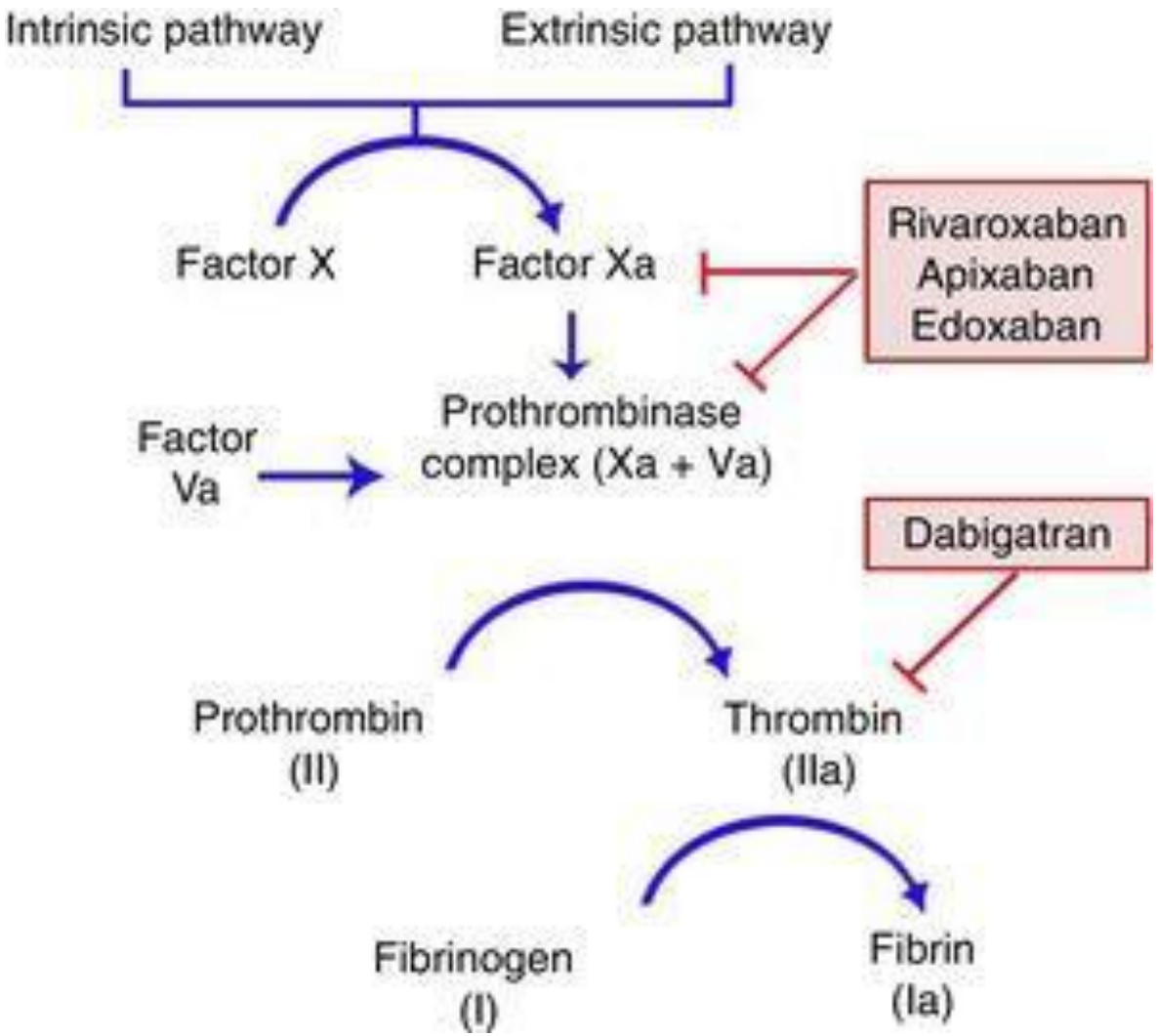


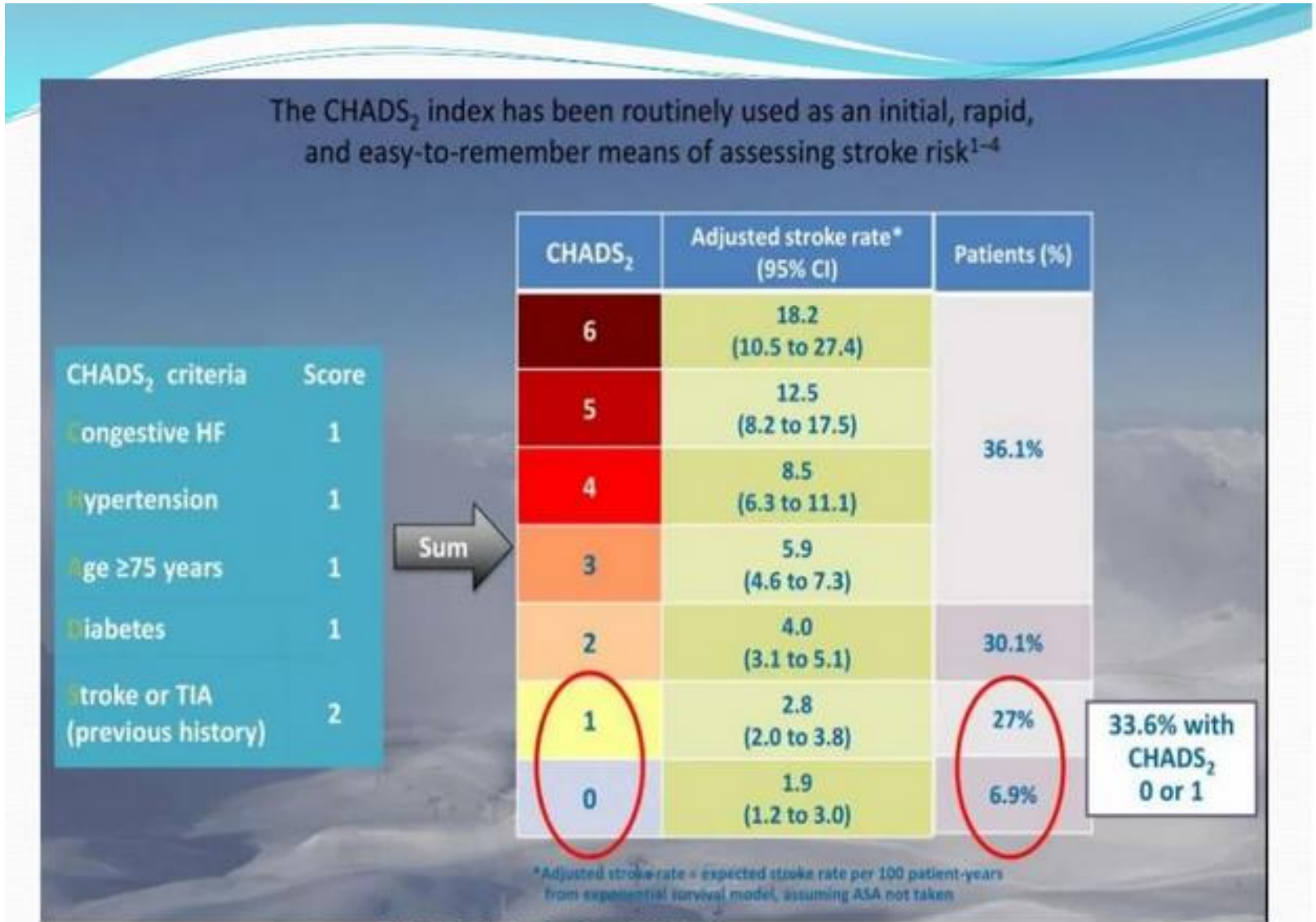
Forrest IIa ulcer with a visible vessel

INITIATION OF HEMOSTASIS



COAGULATION PATHWAY




The CHADS2 index has been routinely used as an initial, rapid, and easy-to-remember means of assessing stroke risk[1–4]
CHADS2 criteria
Score
Congestive HF
1
Hypertension
1
Age ≥75 years
1
Diabetes
1
Stroke or TIA (previous history)
2
Sum
CHADS2
Adjusted stroke rate* (95% CI)
Patients (%)
6
18.2 (10.5 to 27.4)
5
12.5 (8.2 to 17.5)
4
8.5 (6.3 to 11.1)
36.1%
3
5.9 (4.6 to 7.3)
2
4.0 (3.1 to 5.1)
30.1%
1
2.8 (2.0 to 3.8)
27%
0
1.9 (1.2 to 3.0)
6.9%
33.6% with CHADS2 0 or 1
*Adjusted stroke rate = expected stroke rate per 100 patient-years from exponential survival model, assuming ASA not taken

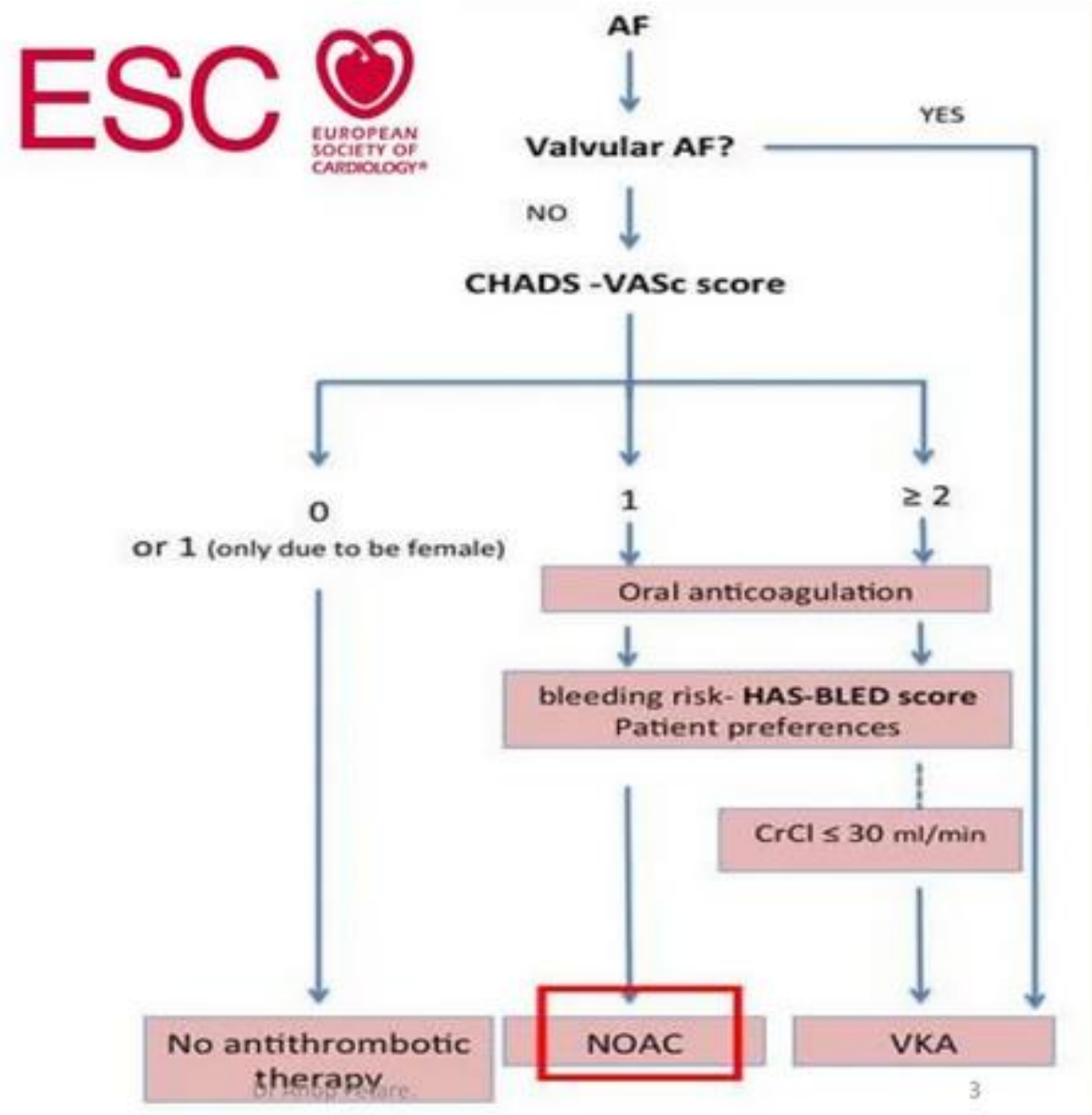
The CHA_2DS_2-VASc scheme was adopted by the ESC to complement the $CHADS_2$ scoring system

$CHADS_2$	Score	CHA_2DS_2-VASc	Score
Congestive heart failure	1	Congestive heart failure/left ventricular dysfunction	1
Hypertension	1	Hypertension	1
Aged ≥75 years	**1**	**Aged ≥75 years**	**2**
Diabetes mellitus	1	Diabetes mellitus	1
Stroke/TIA/TE	2	Stroke/TIA/TE	2
Maximum score	**6**	**Vascular disease (prior MI, PAD, or aortic plaque)**	1
		Aged 65–74 years	1
		Sex category (i.e. female gender)	1
		Maximum score	**9**

Camm et al. Eur Heart J 2010;31:2369–429.

CHA_2DS_2-VASc:

- In patients with a $CHADS_2$ score of 0–1, or
- When a more detailed stroke risk assessment is indicated


ESC
EUROPEAN SOCIETY OF CARDIOLOGY®
AF
Valvular AF?
YES
NO
CHADS -VASc score
0
or 1 (only due to be female)
1
≥ 2
Oral anticoagulation
bleeding risk- HAS-BLED score
Patient preferences
CrCl ≤ 30 ml/min
No antithrombotic therapy
NOAC
VKA
3

ASGE

TABLE 4. CHA_2DS_2-VASc scoring system

CHA_2DS_2-VASc score or assessment	Risk of stroke (CVA)	% Risk of annual CVA
0	Low	0
1	Moderate	1.3
2	High	2.2
3	High	3.2
4	High	4.0
5	High	6.7
6	High	9.8
7	High	9.6
8	High	6.7
9	High	15.2

CHA_2DS_2-VASc, Congestive heart failure [1 point], Hypertension [1 point], Age $\geq$ 75 years [2 points], Diabetes mellitus [1 point], Stroke [2 points], Vascular disease [1 point], Age 65-74 years [1 point], Sex category, ie, female sex [1 point].
CVA, cerebrovascular accident.

HAS-BLED

Letter	Clinical Characteristic	Points
H	Hypertension	1
A	Abnormal Liver or Renal Function	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INR	1
E	Elderly (age > 65)	1
D	Drugs or Alcohol	1 or 2
Maximum Score		9

Table 4 Components of HAS-BLED bleeding risk score

Clinical characteristics	Definition	Points
Hypertension	Systolic blood pressure > 160 mmHg	1
Abnormal liver or renal function	Chronic liver disease (*e.g.*, cirrhosis) or biochemical evidence of significantly impaired liver function (*e.g.*, bilirubin > 2 times the ULN plus one or more liver enzymes > 3 times the ULN Chronic dialysis, renal transplantation, or serum creatinine ⩾ 200 micromol/L	1 or 2
Stroke	Previous history of stroke	1
Bleeding tendency or predisposition	Bleeding disorder or previous bleeding episode requiring hospitalization or transfusion	1
Labile INRs	Labile INRs in patients taking warfarin (failure to maintain a therapeutic range at least 60% of the time)	1
Elderly	Age > 65 years	1
Drugs	Concomitant antiplatelet agents or NSAIDs Excessive alcohol use (⩾ 8 units per week)	1 or 2

Maximum score is 9. ULN: Upper limit of normal; INR: International normalized ratio; NSAIDs: Non-steroidal anti-inflammatory drugs.

Table 3 Risk factors for novel oral anticoagulant-related gastrointestinal bleeding

Risk factors	Definition
Higher dose of dabigatran and edoxaban	Dabigatran: a dose of 150 mg b.i.d Edoxaban: a dose of 60 mg daily
Concomitant use of ulcerogenic agents	Antiplatelet agents, NSAIDs or steroid
Older age	Age ⩾ 75 years
Renal impairment	Creatinine clearance < 50 mL/min
Prior history of peptic ulcers or GIB	
Helicobacter pylori infection	
Pre-existing GI tract lesions	Examples like diverticulosis, angiodysplasias
Ethnicity	Western population
HAS-BLED score	Score of ⩾ 3
Protective factors	**Definition**
Gastroprotective agents	Proton pump inhibitors or histamine H2-receptor antagonists

NOAC: Novel oral anticoagulant; GIB: Gastrointestinal bleeding; NSAIDs: Non-steroidal anti-inflammatory drugs.

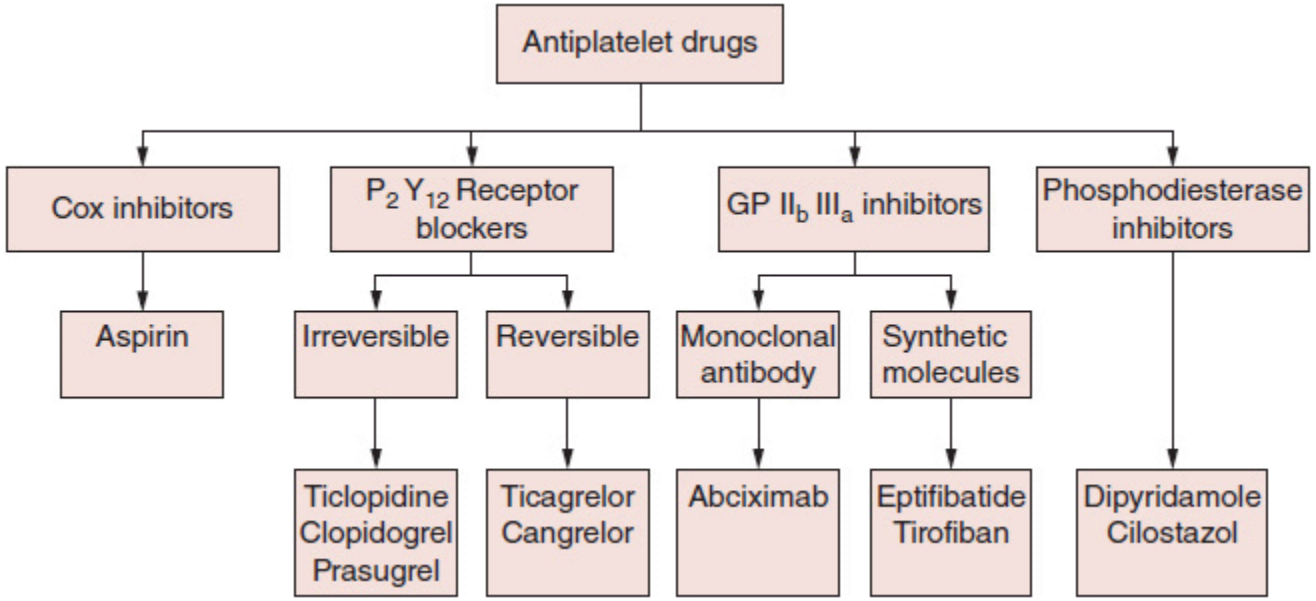
- ANTI- THROMBOTIC DRUGS

TABLE 2. Antithrombotic drugs: duration of action and approach to reversal when indicated

Drug class	Specific agent(s)	Duration of action	Approach to reversal based on procedural urgency	
			Elective	Urgent
APAs	Aspirin	7-10 days	NA	Hold, can give platelets
	NSAIDs	Varies	NA	Hold
	Dipyridamole (Persantine)	2-3 days	Hold	Hold
	Cilostazol (Pletal, Otsuka Pharmaceutical Co., Ltd., Tokushima, Japan)	2 days	Hold	Hold
	Thienopyridines: clopidrogrel (Plavix) prasugrel (Effient) ticlodipine (Ticlid) ticagrelor (Brilinta)	5-7 days: clopidogrel, 3-5 days: ticagrelor 5-7 days: prasugrel 10-14 days[98]: ticlopidine	Hold	Hold
	GPIIb/IIIa inhibitors: tirofiban (Aggrastat) abciximab (ReoPro) eptifibatide (Integrilin)	tirofiban: 1-2 seconds abciximab: 24 hours eptifibitide: 4 hours	NA	Hold HD: tirofiban
	PAR-1 inhibitor: vorapaxar (Zontivity)	5-13 days	Hold	Hold
Anticoagulants	Warfarin (Coumadin)	5 days	Hold	Vitamin K, PCC
	UFH	IV 2-6 hours SQ 12-24 hours	Hold	Protamine sulfate* (partial)
	LMWH: enoxaparin (Lovenox) dalteparin (Fragmin, Pfizer Inc, New York, NY, USA)	24 hours	Hold	Protamine sulfate, consider rVIIa
	Fondaparinux (Arixtra)	36-48 hours		Protamine sulfate, consider rVIIa
	Direct factor Xa Inhibitor: rivaroxaban (Xarelto) apixaban (Eliquis) edoxaban (Savaysa)	See Tables 7 and 8	Hold	Charcoal (if last intake within 2-3 hours); nonactivated PCC or activated PCC
	Direct thrombin inhibitor, oral: dabigatran (Pradaxa) IV: Desirudin (Iprivask, Aventis Pharmaceuticals Inc., Bridgewater, NJ, USA)	See Table 9	Hold	Charcoal (if last intake within 2-3 hours); nonactivated PCC or activated PCC; HD

NSAIDs, Nonsteroidal anti-inflammatory drugs; *NA*, not applicable; *HD*, hemodialysis; *PCC*, prothrombin complex concentrate; *rVIIa*, recombinant factor VIIa.
*Caution: Can cause severe hypotension and anaphylaxis.

Classification of antiplatelet drugs based on mechanism of action.



Cessation/mitigation of antiplatelet therapy - bleeding risk prevails

- History of recurrent bleeding (spontaneous or after modification of antithrombotic therapy)
- Life-threatening extracranial bleeding with no identifiable cause
- Lobar intracranial bleeding
- Untreatable haematological disorder leading to bleeding diathesis
- high-risk peptic ulcer (Forrest Ia, Ib, IIa, IIb) when adequate haemostasis cannot be established

Resumption of antiplatelet therapy - thrombotic risk prevails

- Recent ACS (<3months) or PCI (<30 days)
- High risk of stent-thrombosis
- Recurrent myocardial infarctions
- Recurrent Large-artery atherosclerosis ischemic strokes
- Multiple thrombotic risk factors
- Poly-vascular disease

Indications of antiplatelet agents

Monotherapy	Dual antiplatelet therapy (DAPT)	Antiplatelet + anticoagulant
Primary prevention of cardiovascular diseases	Post coronary stenting for 12 months	Cardioembolic stroke
Secondary prevention of cardiovascular diseases	Post coronary artery bypass grafting(CABG)	Acute myocardial infarction
	NSTEMI	Atrial fibrillation with myocardial infarction
	Short-term following high-risk transient ischemic attack and post-ischemic cerebrovascular accident	
	Secondary prevention of cardiovascular disease involving polyvascular bed (≥ 2 vascular beds)	

DRUG INTERCATIONS

Drug interactions with antiplatelet agents	
Antibiotic	
Amoxicillin	Increases aspirin levels by reducing renal clearance
Cefepime	Increases the effect of aspirin by competing for renal tubular clearance
Ceftazidime	Increases the effect of aspirin by competing for renal clearance
Piperacillin	Salicylic acid can be displaced from protein-binding sites
Other agents	
Hydrochlorothiazide	Increases the effect of aspirin by competing for renal clearance
Calcium carbonate	Calcium carbonate at moderate doses may cause aspirin toxicity while at higher doses it results in increased aspirin excretion

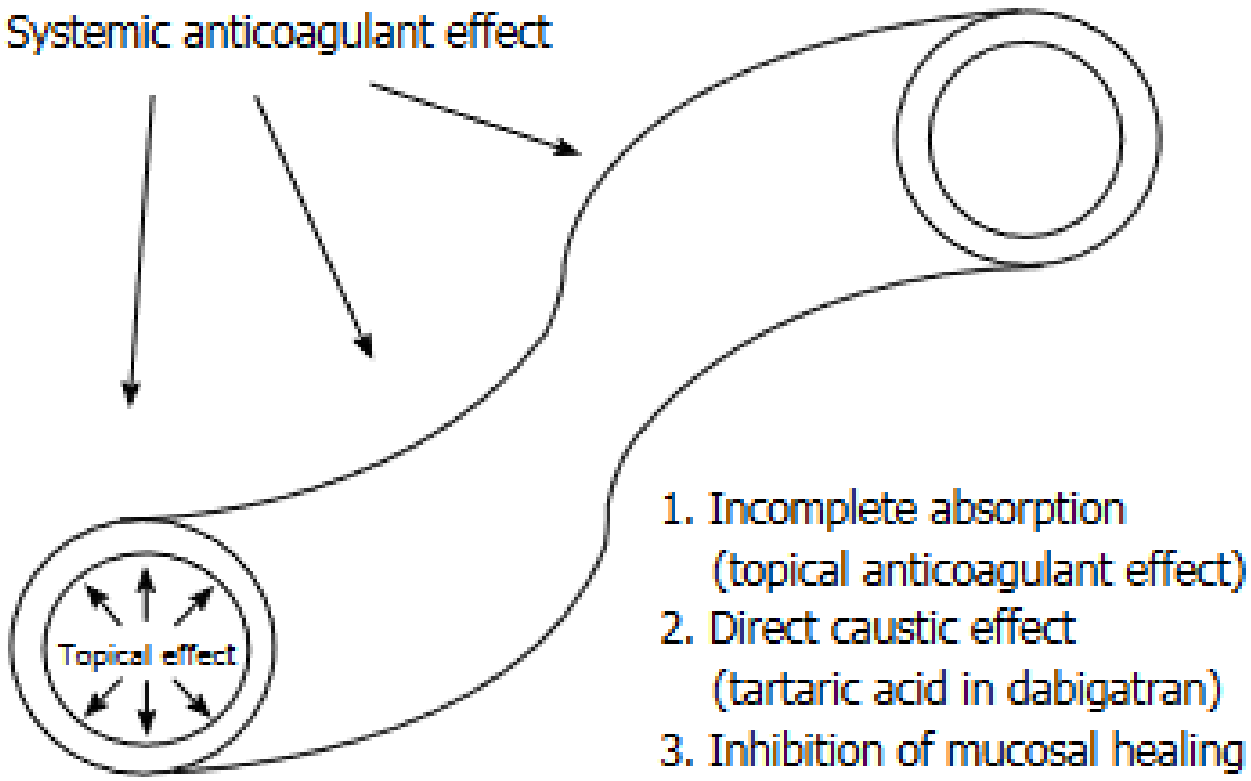


Figure 1 Pathogenesis of novel oral anticoagulant-related gastrointestinal bleeding. NOAC: Novel oral anticoagulant; GIB: Gastrointestinal bleeding.

Medication	Point of Action	½ Life	Treatment	Assays
Dabigatran (Pradaxa©)	Direct thrombin inhibitor	12-17 hours	• Hold medication • Oral charcoal (must give within two hours of last dose) • Praxbind© • Hemodialysis	• Thrombin Clotting time or Ecarin clotting time (ECT) • If normal no treatment needed
Rivaroxaban (Xarelto©)	Factor Xa inhibitor	5-9 hours (11 – 13 hours in elderly)	• Hold medication • KCentra© or Bebulin©	• Heparin Levels • If normal no treatment needed
Apixaban (Eliquis©)	Factor Xa inhibitor	12 hours	• Hold medication • KCentra© or Bebulin©	• Heparin Levels • If normal no treatment needed
Edoxaban (Savaysa©)	Factor Xa inhibitor	10-14 hours	• Hold medication • KCentra© or Bebulin©	• Heparin Levels • If normal no treatment needed

Table 1 Characteristics of different novel oral anticoagulants

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Mechanism of action	Anti-thrombin	Anti-factor Xa	Anti-factor Xa	Anti-factor Xa
Bioavailability	7%	66%	50%	60%
Tmax (h)	1.5	2.5	3	1-5
T½ (h)	9-17	6-13	12	12
Dosing	b.i.d	once daily	b.i.d	once daily
Renal excretion	High	Moderate	Moderate	Moderate
Hepatic metabolism	Low	Moderate	Moderate	Moderate
Reversal agents	Idarucizumab[1] Aripazine	Andexanet alfa Aripazine	Andexanet alfa Aripazine	Andexanet alfa Aripazine

[1]Idarucizumab is the only FDA-approved specific reversal agent currently. Tmax: Time to peak plasma level; T½: Half-life; GIB: Gastrointestinal bleeding.

QUESTION 1
WHICH DO YOU RECOMMEND

- **Aspirin vs Clopidogrel:**

- **Antiplatelet Agent of Choice for Those With Recent Bleeding or at Risk for Gastrointestinal Bleed**

Aspirin vs clopidogrel

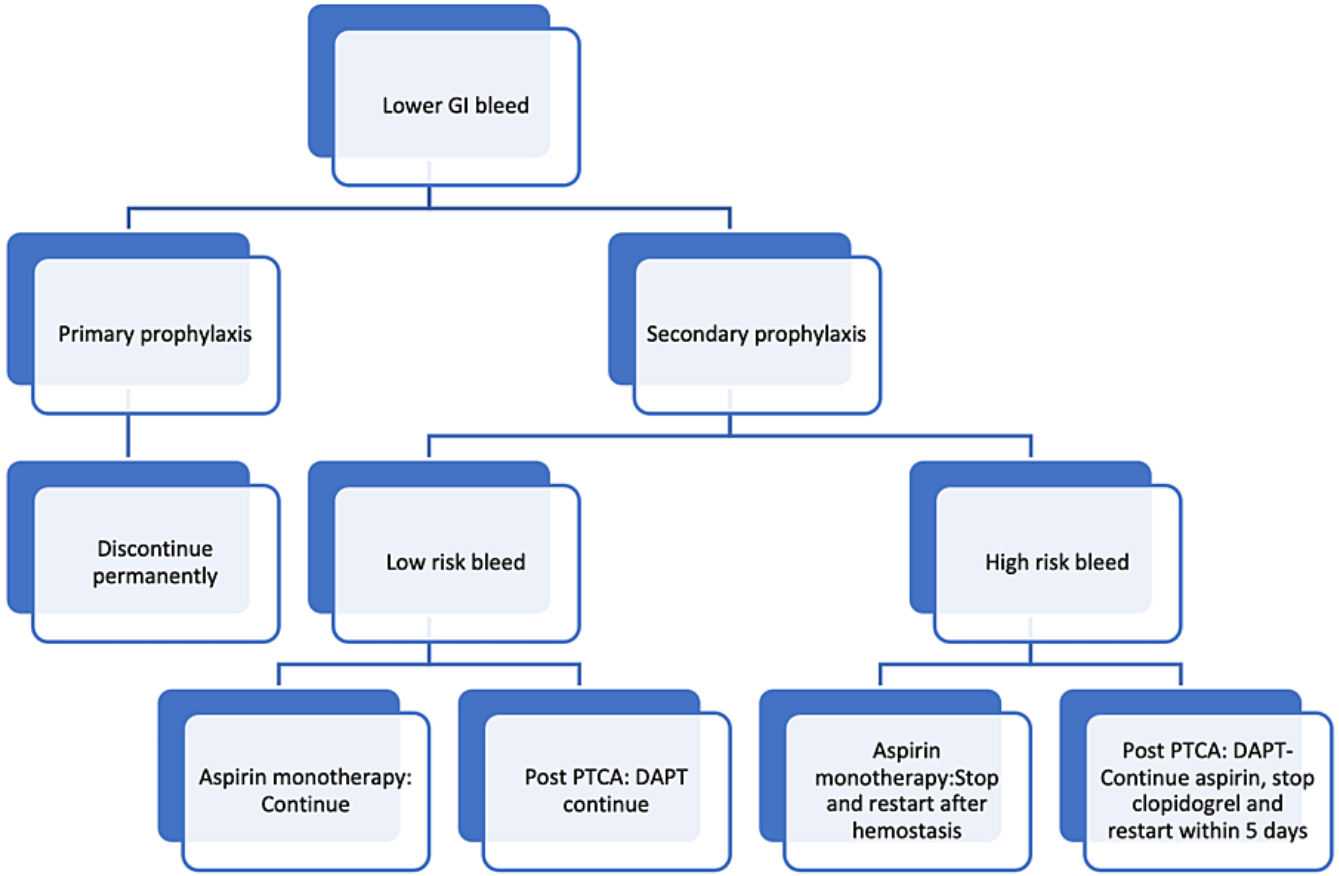
- **Studies comparing the incidence of antiplatelet-induced gastrointestinal bleeding**

Aspirin and clopidogrel having equal effects with respect to gastrointestinal bleed			
Han et al., 2021 [4]	RCT	Those with no ulcerations or bleeding on capsule endoscopy done after 6 months of DAPT post-percutaneous intervention were randomised to receive aspirin plus placebo, clopidogrel plus placebo or aspirin plus clopidogrel. For an additional 6 months following which a repeat capsule endoscopy was done to look for gastrointestinal mucosal injury.	Aspirin and clopidogrel monotherapy had similar effects on the gastrointestinal mucosa
Ng et al. 2008 [22]	RCT	Those with aspirin-induced peptic ulcer disease treated with omeprazole were randomised to receive clopidogrel or low-dose aspirin	A prospective study among those who had developed peptic ulcers while on aspirin was randomised to receive aspirin plus PPI or clopidogrel PPI. Minor gastrointestinal bleeding occurred in 45% of the clopidogrel group compared to 42% in the aspirin group, however, it was not statistically significant (p=0.709).

Strategies to reduce the risk of rebleeding

Strategies to reduce the risk of rebleed	
Number of agents	To review the indication for dual antiplatelet therapy
Dosage	Start with a lower dose and gradually escalate to the target dose
Frequency	Alternate day dosing followed by daily dosage
Drug interactions	Consider drug interactions that can potentially increase the dose of antiplatelet in the future
Proton pump inhibitor cover	While administering proton pump inhibitors, it is also important to consider interaction with clopidogrel that may reduce the efficacy of Clopidogrel. Clopidogrel is a prodrug that is converted to its active form in the liver by the CYP2C19 enzyme and is inhibited by proton pump inhibitors. The extent of inhibition of enzymes is as following: omeprazole>pantoprazole>lansoprazole>rabeprazole. Interaction can be reduced by changing the timing of administration with PPI given early morning and clopidogrel at bedtime
H.pylori	Testing for H.pylori and eradication
Patient education	Patient awareness regarding signs of bleed like dark-coloured stools and early presentation to the nearest healthcare facility
Dual antiplatelet therapy	In the case of dual antiplatelet therapy, prefer clopidogrel over ticagrelor as a second agent

Management of lower gastrointestinal bleed in a patient on antiplatelet therapy



- **Management of Patient with Simultaneous Overt Gastrointestinal Bleeding and Myocardial Infarction with ST-Segment Elevation – Priority Endoscopy**

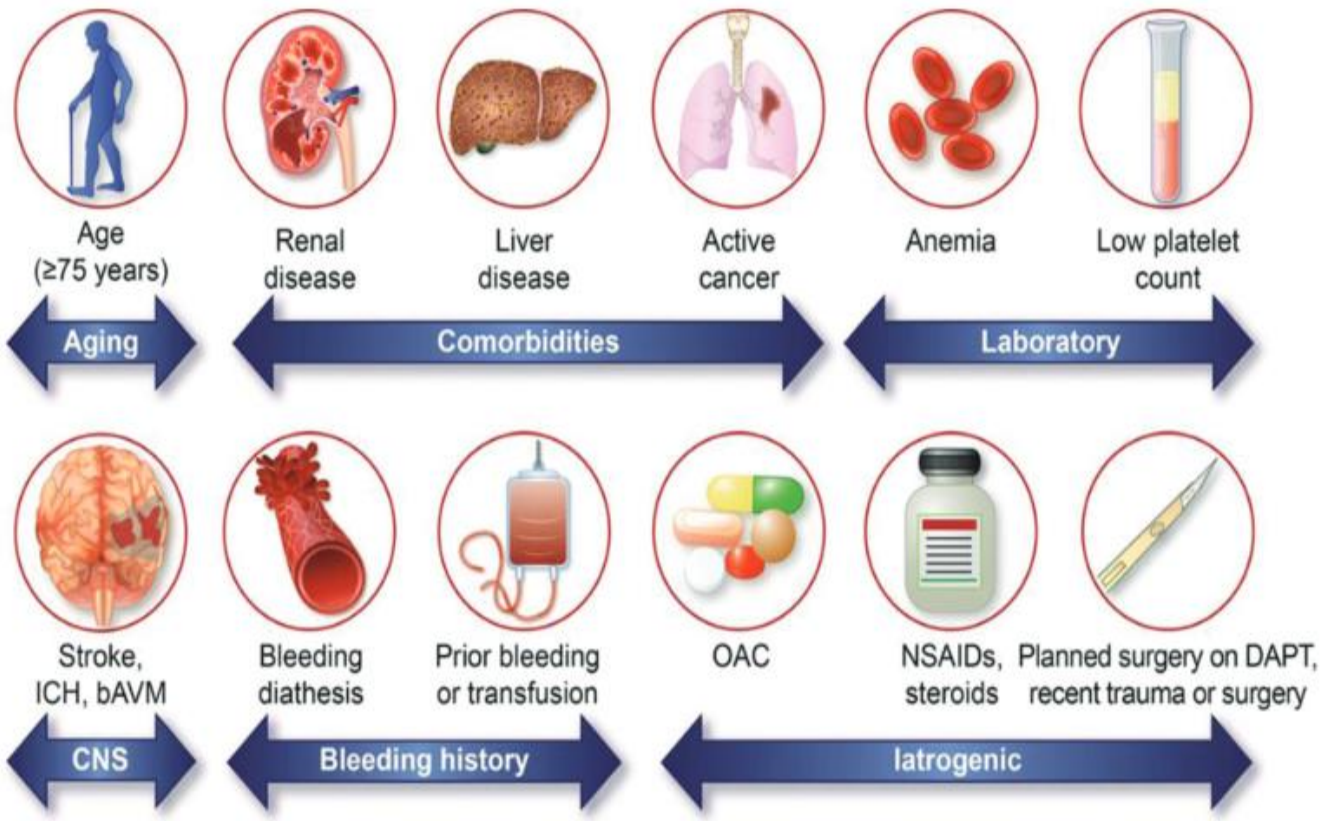
ENDOSCOPY BEFORE PCI AT THE ACS

- A patient with symptoms of upper gastrointestinal bleeding with a recent onset and co-occurring ASC should have an endoscopy before PCI.

- Medical history, drug used, precise examination, including rectal examination or gastric lavage after probe placement are not able to rule out bleeding with certainty.

Academic Research Consortium

Major and Minor Criteria for HBR(high bleeding risk) at the Time of PCI



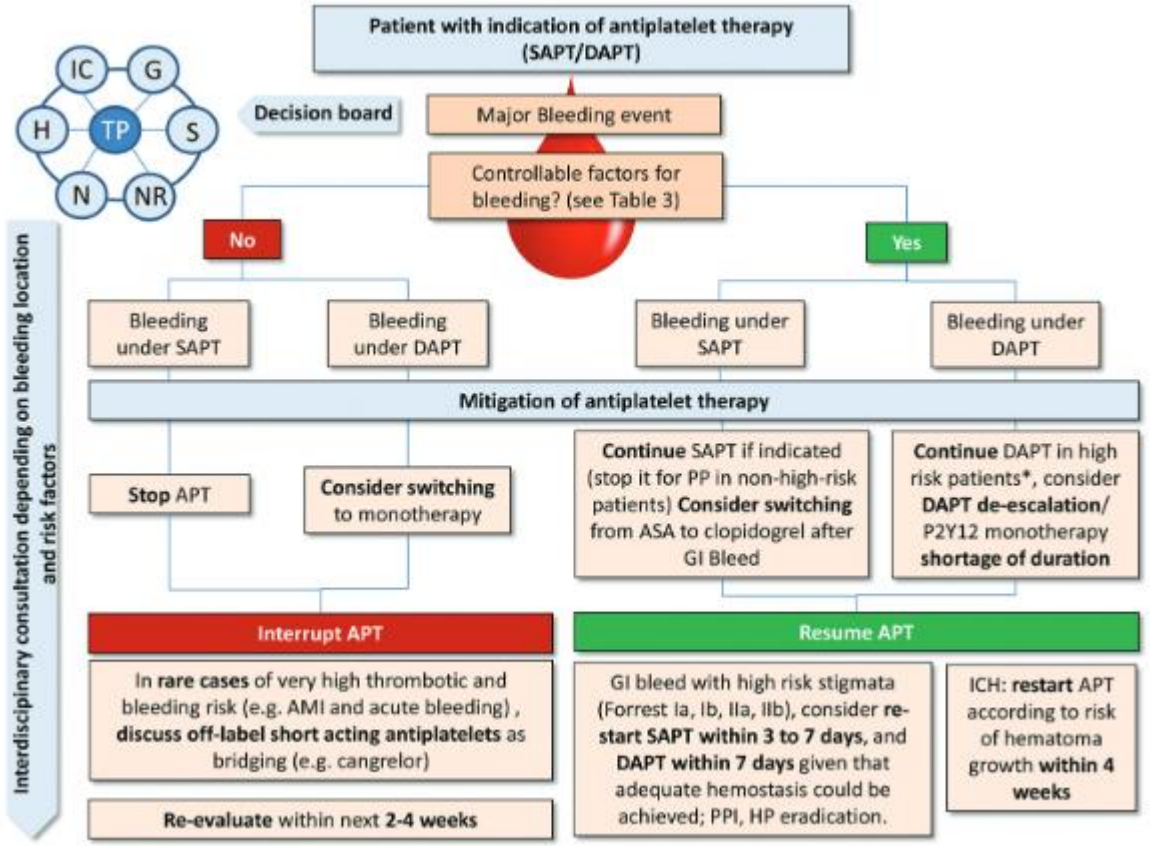
Major	Minor
	Age ≥75 y
Anticipated use of long-term oral anticoagulation*	
Severe or end-stage CKD (eGFR <30 mL/min)	Moderate CKD (eGFR 30–59 mL/min)
Hemoglobin <11 g/dL	Hemoglobin 11–12.9 g/dL for men and 11–11.9 g/dL for women
Spontaneous bleeding requiring hospitalization or transfusion in the past 6 mo or at any time, if recurrent	Spontaneous bleeding requiring hospitalization or transfusion within the past 12 mo not meeting the major criterion
Moderate or severe baseline thrombocytopenia† (platelet count <100×10⁹/L)	
Chronic bleeding diathesis	
Liver cirrhosis with portal hypertension	
	Long-term use of oral NSAIDs or steroids
Active malignancy‡ (excluding nonmelanoma skin cancer) within the past 12 mo	
Previous spontaneous ICH (at any time) Previous traumatic ICH within the past 12 mo Presence of a bAVM Moderate or severe ischemic stroke§ within the past 6 mo	Any ischemic stroke at any time not meeting the major criterion
Nondeferrable major surgery on DAPT	
Recent major surgery or major trauma within 30 d before PCI	

bAVM indicates brain arteriovenous malformation; CKD, chronic kidney

ACS AND DAPT

- **Dual Antiplatelet Therapy**
- The standard of care for patients with ACS is dual antiplatelet therapy (DAPT).
- It includes acetylsalicylic acid (ASA) and one of the P2Y receptor inhibitors. DAPT aims to reduce the activation of platelets and inhibit their aggregation at the site of damage to the endothelium (in which the atherosclerotic plaque has developed) or on the surface of exogenous materials.

Suggested algorithm for interruption of antiplatelet or anticoagulation according to bleeding severity type



Potential strategies to reduce future bleeding risk by modification of antithrombotic therapy

Bleeding occurred under treatment with	Possible strategies
SAPT	Consider cessation in particular in case of primary prevention, or if indicated switching from ASA to non-ASA (e.g., clopidogrel) treatment
DAPT	Consider cessation, switching to monotherapy (aspirin, clopidogrel, or ticagrelor), or de-escalation after ACS
Combination therapy	Consider switching from triple therapy to dual therapy, consider reducing the dose of NOAC in patients with HBR, consider LAA occlusion if high recurrent bleeding risk persists even under reduced NOAC dose

In case of <u>continued refractory bleeding</u>
→ *Emergency reversal* considered

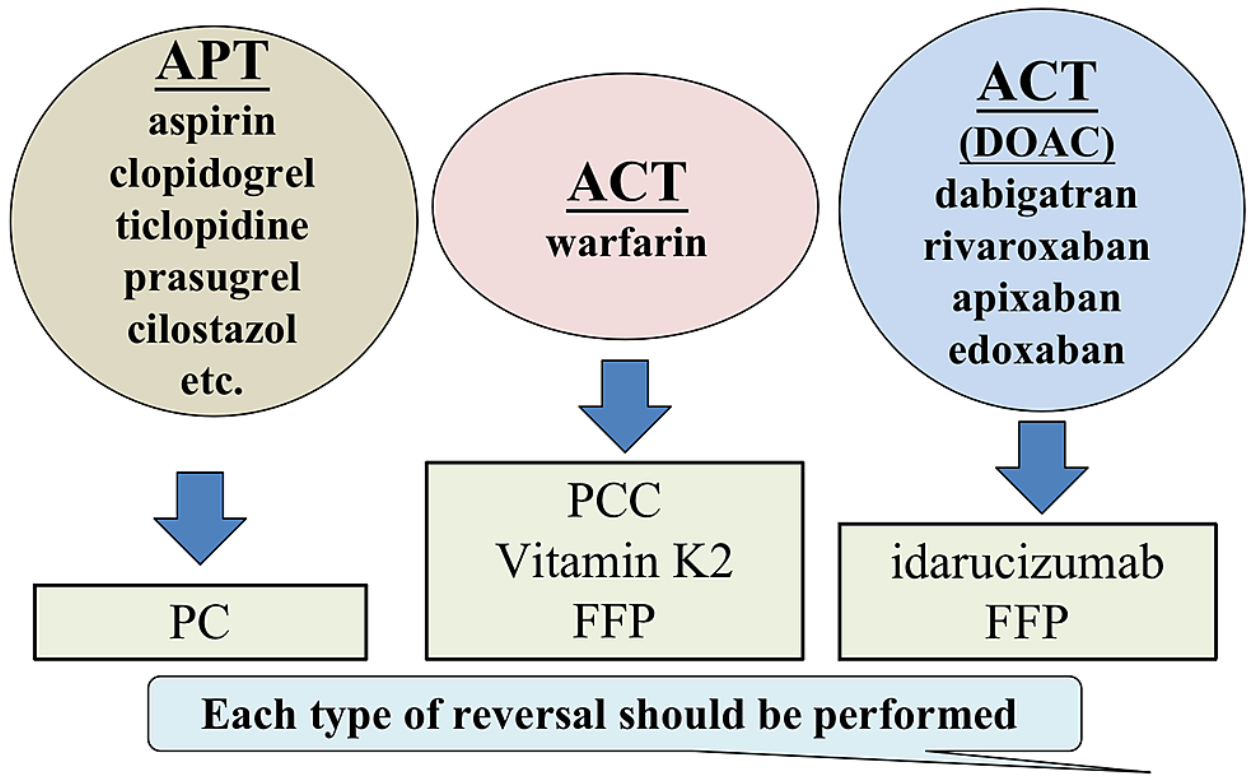


Table 2 Dosing of different novel oral anticoagulants according to indications and renal function

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Non-valvular AF				
United States	150mg b.i.d 75 mg b.i.d if CrCl 15-30 mL/min	20 mg daily 15 mg daily if CrCl 15-50 mL/min	5 mg b.i.d 2.5 mg b.i.d if Cr 15-29 mL/min OR two out of the following: age ≥ 80 years, BW ≤ 60 kg, Cr ≥ 1.5 mg/dL	60 mg daily 30 mg daily if CrCl 15-50 mL/min
	Avoid if CrCl < 15 mL/min	Avoid if CrCl < 15 mL/min	Avoid if CrCl < 25 mL/min or Cr > 2.5 mg/dL	Avoid if CrCl < 15 mL/min
Europe	150 mg b.i.d 110 mg b.i.d if age ≥ 80 years (may consider 110 mg b.i.d also if increased risk of bleeding)	20 mg daily -	5 mg b.i.d 2.5 mg b.i.d if Cr 15-29 mL/min OR two out of the following: age ≥ 80 years, BW ≤ 60 kg, Cr ≥ 1.5 mg/dL	60 mg daily 30 mg daily if one out of the following: CrCl 15-50 mL/min, BW ≤ 60 kg, concomitant use of p-gp inhibitors
	Avoid if CrCl < 30 mL/min	Avoid if CrCl < 15 mL/min	Avoid if CrCl < 15 mL/min	Avoid if CrCl < 15 mL/min
Postoperative DVT / PE thromboprophylaxis (hip or knee replacement)				
United States	Initial dose of 110 mg 1-4 h after operation, then 220 mg daily	Initial dose of 10 mg 6-10 h after operation, then 10 mg daily	Initial dose of 2.5 mg 12-24 h after operation, then 2.5 mg b.i.d	-
	-	-	-	-
	Avoid if CrCl < 30	Avoid if CrCl < 30 mL/min	Avoid if CrCl < 30 mL/min	-
Europe	Initial dose of 110 mg 1-4 h after operation, then 220 mg daily	Initial dose of 10 mg 6-10 h after operation, then 10 mg daily	Initial dose of 2.5 mg 12-24 h after operation, then 2.5 mg b.i.d	60 mg daily after 5 d of initial therapy with a parenteral anticoagulant
	Initial dose of 75 mg 1-4 h after operation, then 150 mg daily if CrCl 30-50 mL/min	-	-	30 mg daily after 5 d of initial therapy with a parenteral anticoagulant if one out of the following: CrCl 15-50 mL/min, BW ≤ 60 kg, concomitant use of p-gp inhibitors
	Avoid if CrCl < 30 mL/min	Avoid if CrCl < 15 mL/min	Avoid if CrCl < 15 mL/min	Avoid if CrCl < 15 mL/min
Treatment and prevention of recurrent DVT/PE				
United States	150 mg b.i.d after 5-10 d of initial therapy with a parenteral anticoagulant	15 mg b.i.d for 3 wk, then 20 mg daily	10 mg b.i.d for 1 wk, then 5 mg b.i.d	60 mg daily after 5-10 d of initial therapy with a parenteral anticoagulant
	-	-	-	30 mg daily after 5-10 d of initial therapy with a parenteral anticoagulant if one out of the following: CrCl 15-50 mL/min, BW ≤ 60 kg, concomitant use of p-gp inhibitors
	Avoid if CrCl < 30 mL/min	Avoid if CrCl < 30 mL/min	Avoid if CrCl < 25 mL/min or Cr > 2.5 mg/dL	Avoid if CrCl < 15 mL/min

QUESTION 2

- HAVE YOU SEEN AN ORDER CONSISTING ?

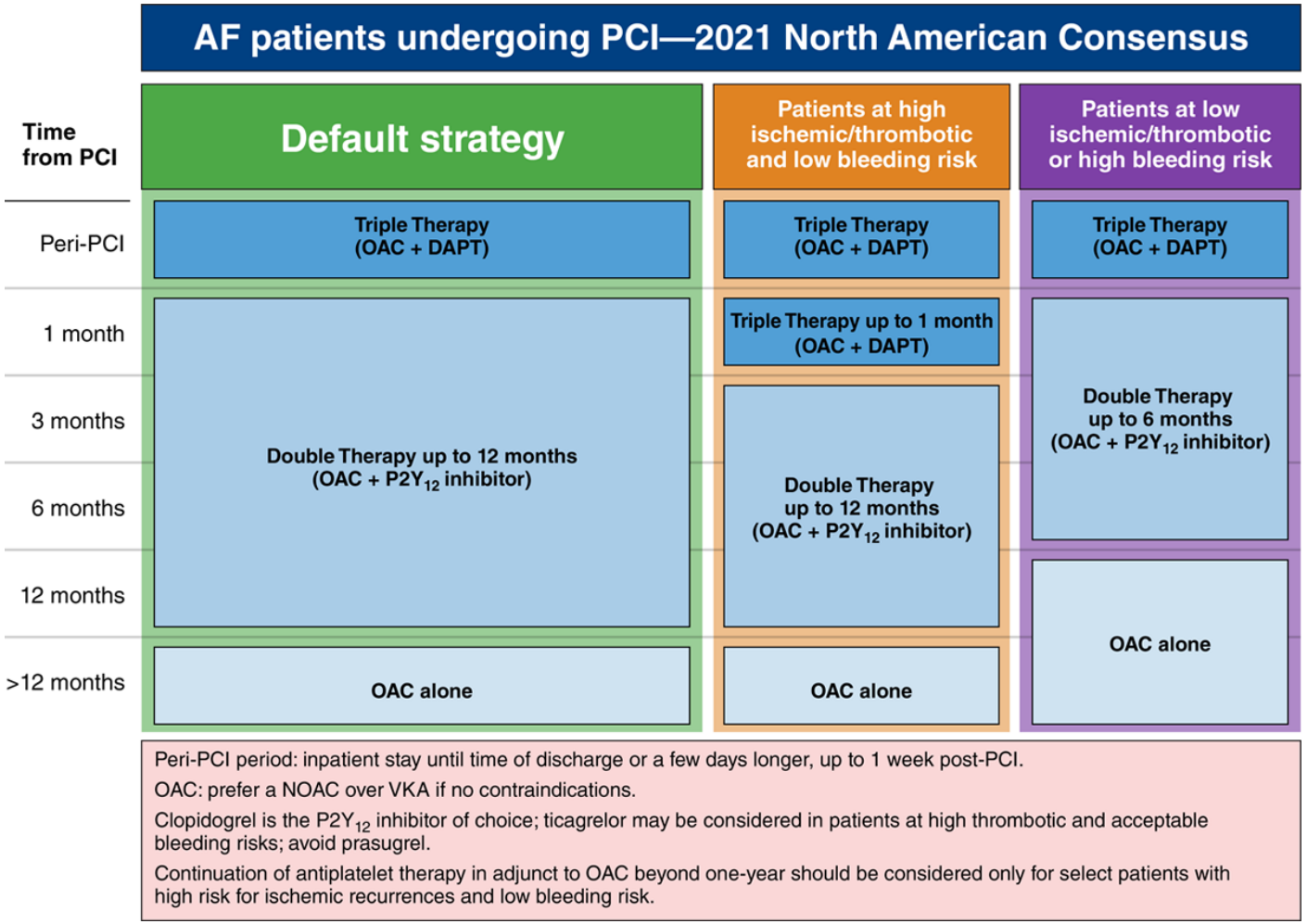
ASA +PLAVIX + APIXABAN

TRIPLE ANTI- THROMBOTIC THERAPY

- Triple therapy (TT) refers to the concurrent use of an oral anticoagulant (OAC), such as warfarin, and dual antiplatelet therapy (DAPT), such as acetylsalicylic acid (ASA) plus clopidogrel.

- The most common clinical indication for TT is patients with atrial fibrillation (AF) who have acute coronary syndrome (ACS) or who have undergone percutaneous coronary intervention (PCI) with stent insertion, which accounts for approximately 5% to 8% of all patients who undergo PCI.

Management of antiplatelet therapy in patients with atrial fibrillation (AF) undergoing percutaneous coronary intervention (PCI) treated with an oral anticoagulant triple therapy



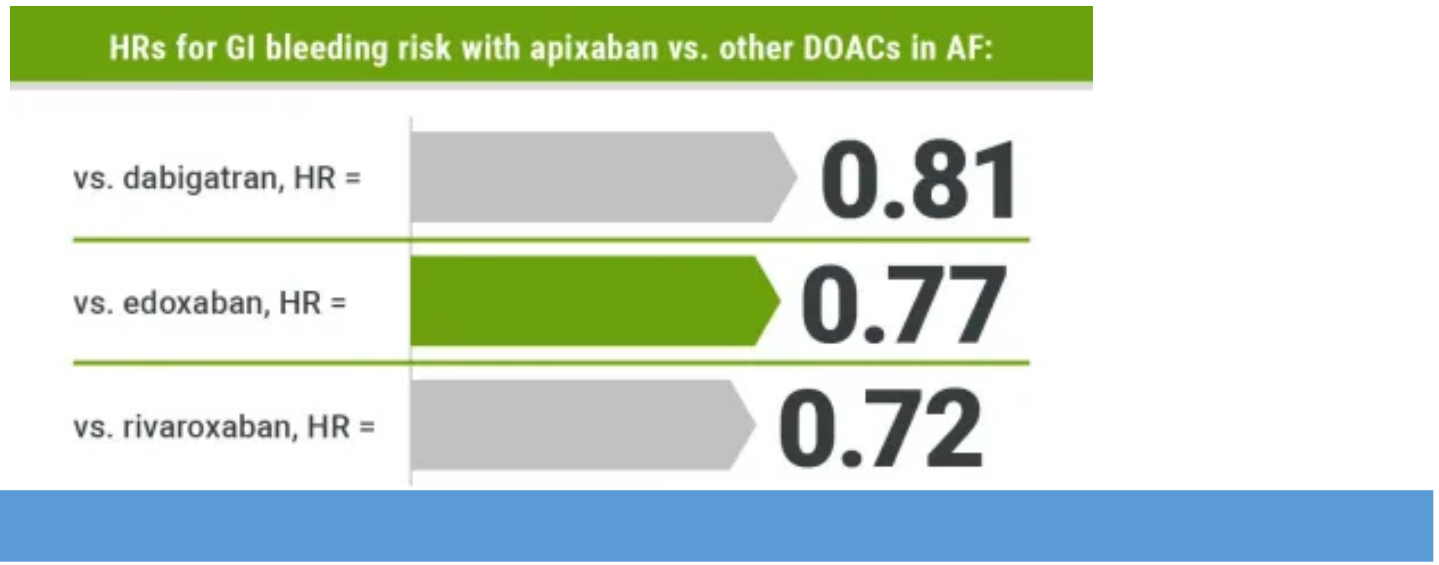
Question 3

What do you know about the role of SSRI (SERTRALINE)in GI BLEEDING risk?

Researchers find antidepressants significantly increase risk of gastrointestinal, intracranial bleeding.esp WITH NSAIDS

Choice of NOACs

High risk of stroke (high CHADS-VASC score)	Dabigatran 150 mg BID
Previous stroke	Rivaroxaban 20 mg QD
High risk of bleeding or previous life-threatening bleedings	Dabigatran 110 mg BID Apixaban 5 mg BID
Dyspepsia	Rivaroxaban 20 mg QD Apixaban 5 mg BID
GI bleeding	Apixaban 5 mg BID
Medication compliance problems	Rivaroxaban 20 mg QD
Elderly (≥80 years) and impaired renal function	Apixaban 2.5 mg BID



Apixaban is associated with lower risk for GI bleeding compared with dabigatran (HR = 0.81; 95% CI, 0.7-0.94), edoxaban (HR = 0.77; 95% CI, 0.66-0.91) or rivaroxaban (HR = 0.72; 95% CI, 0.66-0.79)

Guidelines For Management Of Bleeding Associated With NOAC

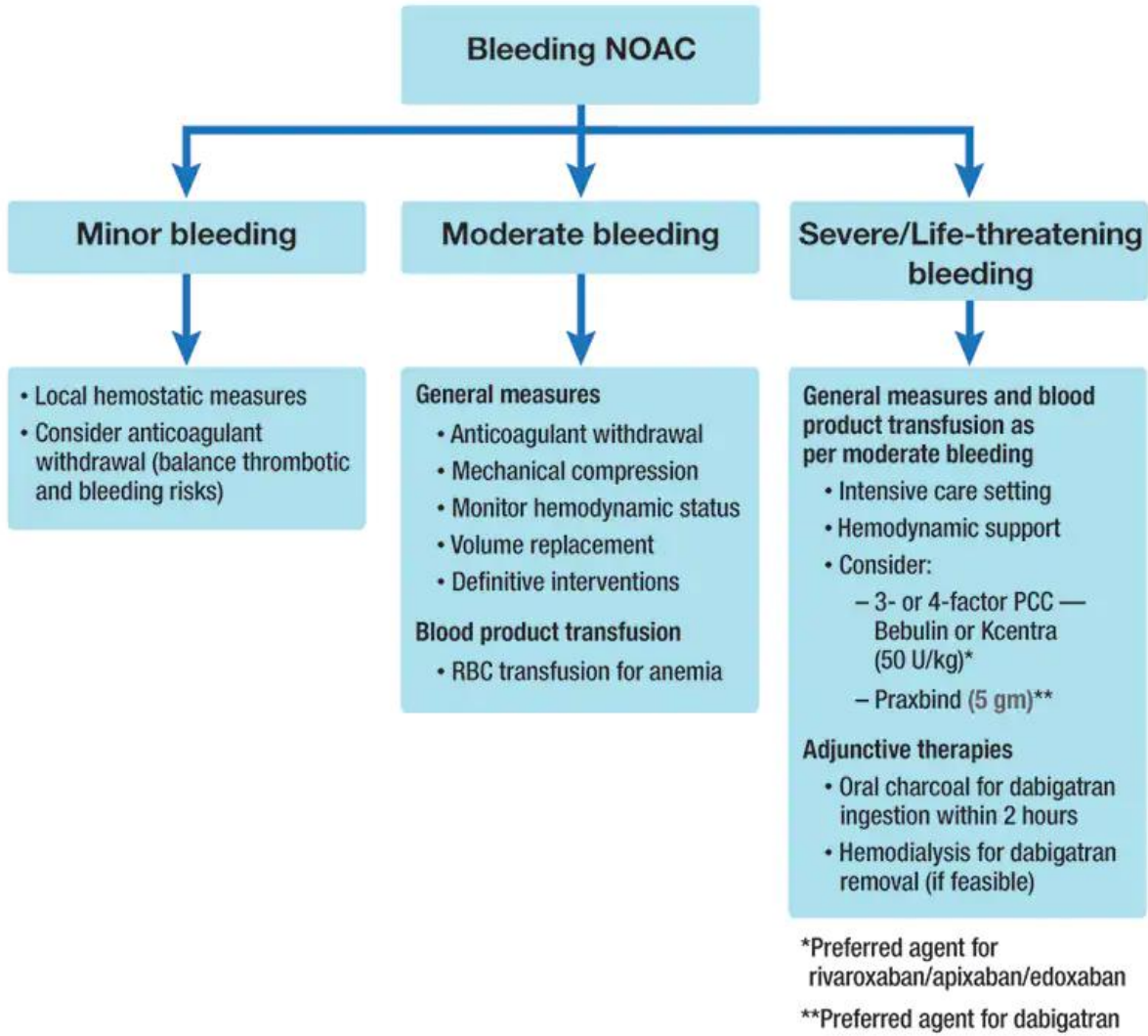


TABLE 6. Periprocedural management of dabigatran (Pradaxa)[53]

Creatinine clearance (mL/min)	Time to onset of action (h)	Half-life (h)	Timing of discontinuation before procedure	
			Moderate procedural bleeding risk (2-3 half-lives)	High procedural bleeding risk (4-5 half-lives)
>80	1.25-3	13 (11-22)	1-1.5 days	2-3 days
50-80	1.25-3	15 (12-34)	1-2 days	2-3 days
30-49	1.25-3	18 (13-23)	1.5-2 days	3-4 days
≤29	1.25-3	27 (22-35)	2-3 days	4-6 days

TABLE 7. Periprocedural management of apixaban (Eliquis)[54]

Creatinine clearance (mL/min)	Time to onset of action (h)	Timing of discontinuation before high-risk endoscopic procedure (day)
>60	1-3	1 or 2
30-59	1-3	3
15-29	1-3	4

TABLE 8. Periprocedural management of rivaroxaban (Xarelto)[54]

Creatinine clearance (mL/min)	Time to onset of action (h)	Timing of discontinuation before high-risk endoscopic procedure (day)
>90	2-4	≥1
60-90	2-4	2
30-59	2-4	3
15-29	2-4	4

Contraindications of NOAC

- Prevention of GIB relies on first reviewing the indications of NOACs and avoiding NOACs in patients with contraindications :

.renal impairment
.(CrCl less than 30 mL/min for dabigatran and

- CrCl less than 15 mL/min for other NOACs), and
- advanced liver disease with coagulopathy

Restarting Combination Therapy

Restarting Combination Therapy (Anticoagulation + APT) Triple therapy should be avoided in patients with atrial fibrillation (AFIB) undergoing PCI who experienced a prior major bleeding event.

The better safety of dual antithrombotic therapy consisting of non-vitamin-K-antagonist oral anticoagulants (NOACs) plus a P2Y 12 receptor inhibitor compared with triple therapy2,84 is established and highly recommended.

In HBR patients, switching from triple therapy (NOAC + DAPT) to dual therapy (NOAC + P2Y 12 in hibitor) and from vitamin-K antagonists to NOAC are possible strategies to reduce the bleeding risk.

In case bleeding occurred under dual antithrombotic therapy (NOAC + SAPT), dose reduction of NOAC to the lowest effective dose should be considered.

TABLE 12. Best practice recommendations for the management of DAPT[36]

Avoid cessation of all antiplatelet therapies after PCI with stent placement.
Avoid cessation of clopidogrel (even when aspirin is continued) within the first 30 days after PCI and either DES or BMS placement when possible.
Defer elective endoscopic procedures, possibly up to 12 months, if clinically acceptable from the time of PCI to DES placement.
Perform endoscopic procedures, particularly those associated with bleeding risk, 5-7 days after thienopyridine drug cessation. ASA should be continued.
Resume thienopyridine and ASA drug therapy after the procedure once hemostasis is achieved. A loading dose of the former should be considered among patients at risk for thrombosis.
Continue platelet-directed therapy in patients undergoing elective endoscopy procedures associated with a low-risk for bleeding.

DAPT, dual antiplatelet therapy; *BMS*, Bare metal stent(s); *DES*, drug-eluting stent(s); *PCI*, percutaneous coronary intervention; *ASA*, acetylsalicylic acid, or aspirin.

Urgent and emergent endoscopic procedures

Patients receiving anticoagulant therapy:

1. We recommend patients with acute GI bleeding on anticoagulation therapy have anticoagulant agents held to facilitate achievement of hemostasis.

2. We recommend either 4-factor PCC and vitamin K or fresh frozen plasma be given for life-threatening GI
bleeding in patients on warfarin anticoagulant therapy.

3. We suggest endoscopic therapy not be delayed in patients with serious GI bleeding and an INR < 2.5.

4. We suggest patients who require anticoagulation receive UFH because of its relatively short half-life after successful endoscopic hemostasis for high-risk stigmata.

Reversal of rivaroxaban or apixaban with andexanet alfa.

- For patients on rivaroxaban or apixaban who are hospitalized or under observation with acute GI bleeding, we suggest against andexanet alfa administration

- (conditional recommendation, very low certainty of evidence).

The US Food and Drug Administration (FDA) has granted accelerated approval for andexanet alfa (Andexxa®), the first antidote for the reversal of factor Xa inhibitors.

Andexanet alfa is approved for use in patients treated with rivaroxaban or apixaban when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding.

Direct thrombin inhibitor reversal

- For patients on **dabigatran** who are hospitalized or under observation with acute GI bleeding, we suggest <u>against</u> the administration of idarucizumab

- (conditional recommendation, very low certainty of evidence).

- Idarucizumab (Praxbind) is a specific reversal agent for dabigatran and is indicated in adult patients treated with dabigatran etexilate (Pradaxa) :

- when rapid reversal of its anticoagulant effects is required: For emergency surgery/urgent procedures; In life-threatening or uncontrolled bleeding.

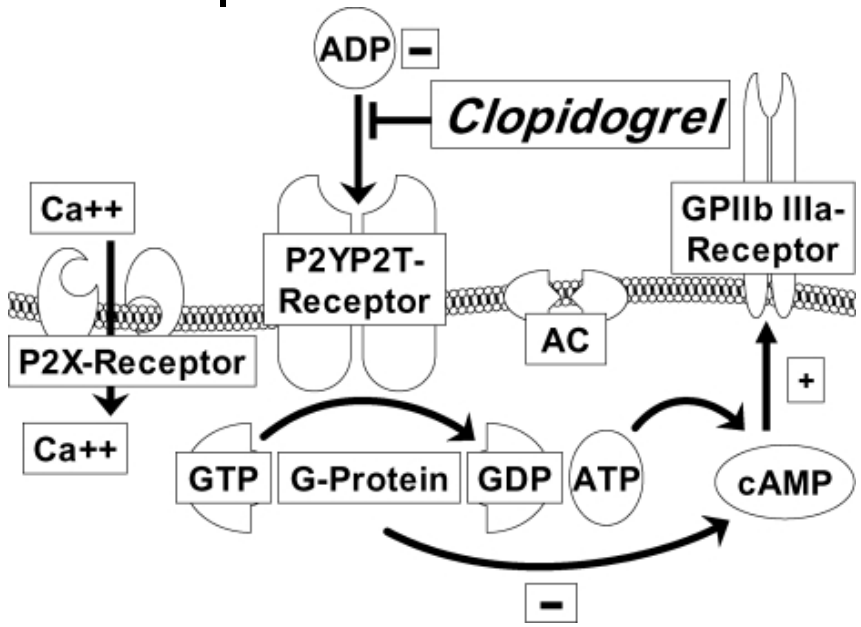
- For patients on warfarin who are hospitalized or under observation with acute GI bleeding, we suggest prothrombin complex concentrate administration compared with FFP administration

- (conditional recommendation, very low certainty of evidence).

- In patients receiving a VKA such as warfarin, :
- low-dose oral vitamin K 1–2 mg can be used when there is an elevated INR (typically an INR >10) to restore therapeutic level anticoagulation (i.e., INR 2.0–3.0) .

- In the setting of clinically significant GI bleeding requiring therapeutic intervention, vitamin K 2–5 mg (oral or intravenous) reverses anticoagulant effect (to INR #1.3) in 24–48 hours.
- Vitamin K use does not achieve rapid hemostasis in patients with acute bleeding

- For patients on dual antiplatelet therapy for secondary prevention who are undergoing elective endoscopic GI procedures, we suggest temporary interruption of the P2Y 12 receptor inhibitor while continuing ASA .



- (conditional recommendation, very low certainty of evidence).

Reversal of antiplatelet with platelet transfusion

- For patients on antiplatelet agents who are hospitalized or under observation with acute GI bleeding, we suggest against platelet transfusions who are not thrombocytopenic.

- (conditional recommendation, very low certainty of evidence)

Holding ASA vs continuing ASA

- For patients with GI bleeding on cardiac ASA for secondary cardiovascular prevention, we suggest against holding the ASA
- (conditional recommendation, very low certainty of evidence).

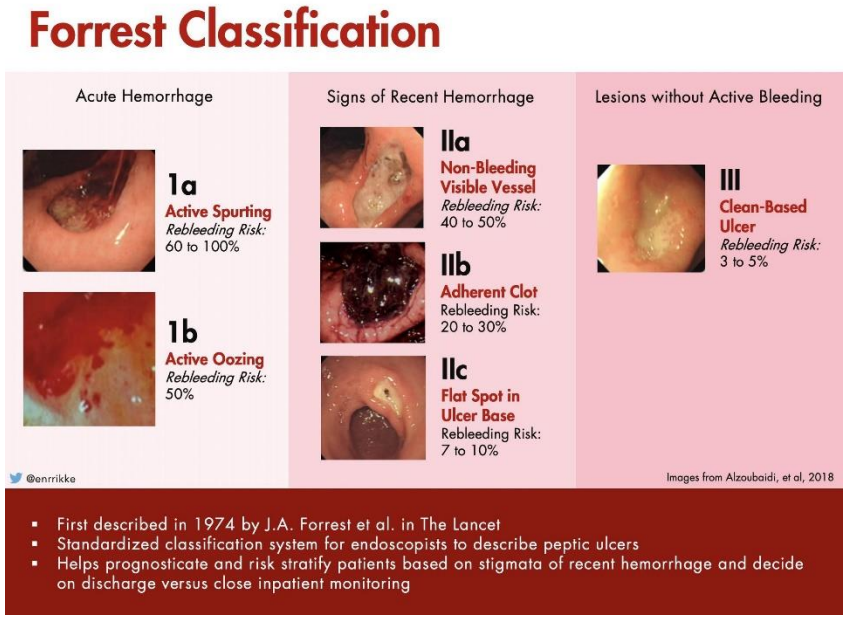
- For patients with GI bleeding on ASA for secondary cardiovascular prevention whose ASA was interrupted, we suggest the ASA be resumed on the day hemostasis is endoscopically confirmed .

- (conditional recommendation, very low certainty of evidence).

Resuming anticoagulants after hemostasis

Patients with low rebleeding risk

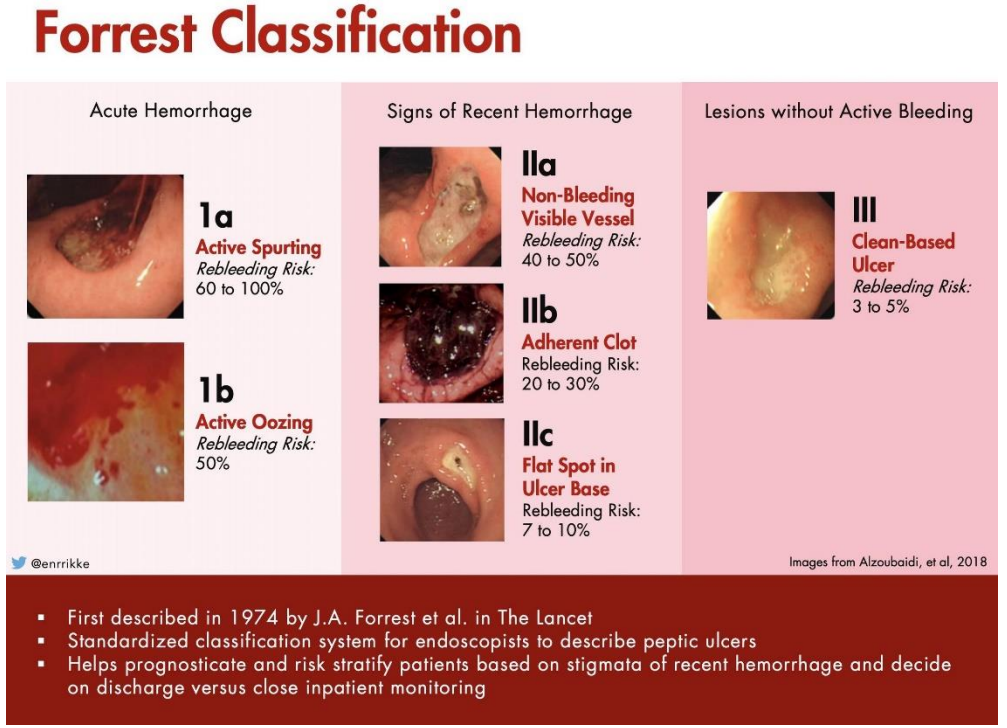
- We generally restart anticoagulation after hemostasis has been achieved for hemodynamically stable patients who have lesions with low-risk of rebleeding (eg, duodenal ulcer with a clean base)



Resuming anticoagulants after hemostasis

Patients with high rebleeding risk

- For patients with lesions at high risk of rebleeding, we delay restarting anticoagulation (if possible, depending on the patient's thrombotic risk) until the rebleeding risk is lower.



Patients on warfarin

- We restart warfarin in the evening of the procedure day, if no further bleeding occurs. Patients who resume warfarin will require several days to achieve therapeutic levels of anticoagulation.

- For those patients who had high enough thrombotic risk to warrant bridge therapy, we restart intravenous unfractionated heparin 48 hours after hemostasis is achieved for patients who require bridge therapy.

Patients on warfarin

- Initial postprocedure anticoagulation with intravenous unfractionated heparin is preferable to low molecular weight heparin (which is typically used in patients who have undergone surgery) due to its relatively short half-life of 1.5 hours .

- This allows for quick reversal following discontinuation of unfractionated heparin if bleeding recurs.

Patients on DOACs

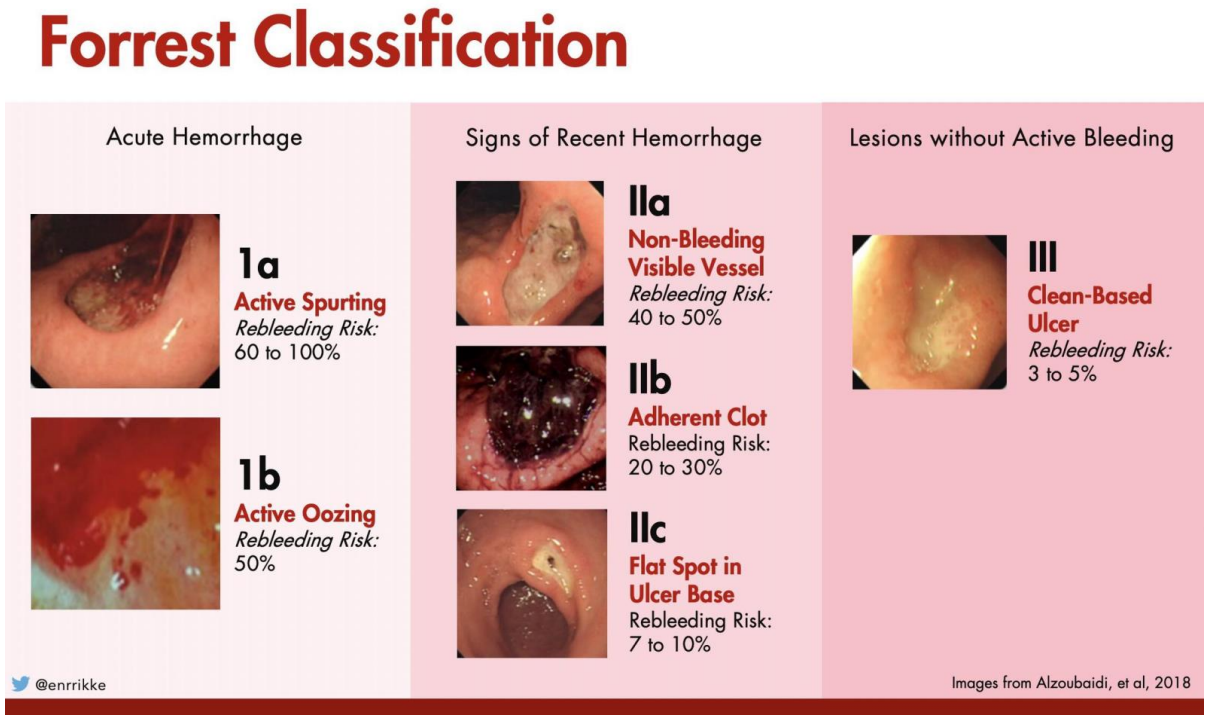
- We restart DOACs 48 to 72 hours after hemostasis has been achieved, if no further bleeding occurs.

- Administration of DOACs (dabigatran, rivaroxaban, apixaban, or edoxaban) results in therapeutic levels of anticoagulation within one to three hours of administration

Resuming anticoagulants after hemostasis

Patients with high rebleeding risk

- For patients with lesions at high risk of rebleeding, we delay restarting anticoagulation (if possible, depending on the patient's thrombotic risk) until the rebleeding risk is lower.



- **Management of antithrombotic agents in the elective endoscopy setting**

Empiric periprocedural thromboembolic risk stratification for patients receiving anticoagulant therapy

Risk stratum	Indication for anticoagulation		
	Mechanical heart valve	Atrial fibrillation	Venous thromboembolism
High[a]	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 3 mo) stroke or transient ischemic attack	• $CHADS_2$ score: 5 or 6 • CHA_2DS_2VaSc score: ≥ 7 • Recent (within 3 mo) stroke or transient ischemic attack • Rheumatic valvular heart disease	• Recent (within 3 mo) VTE • Severe thrombophilia (e.g., deficiency of protein C, protein S or antithrombin, antiphospholipid antibodies, and multiple abnormalities)

High-risk patients may also include patients with a previous stroke or transient ischemic attack occurring 3 mo ago and a CHADS2 score >5, patients with previous thromboembolism during temporary interruption of VKAs, or those patients undergoing certain types of surgery (e.g., cardiac valve replacement, carotid endarterectomy, and major vascular surgery).

International Society on Thrombosis and Haemostasis Guidance Statement

Empiric periprocedural thromboembolic risk stratification for patients receiving anticoagulant therapy

Moderate	• Bileaflet aortic valve prosthesis and ≥1 of the following: atrial fibrillation, previous stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, and age >75 yr	• $CHADS_2$ score: 2–4 (no previous stroke or transient ischemic attack) • CHA_2DS_2VaSc score: 5 or 6	• VTE within the past 3–12 mo • Nonsevere thrombophilia (e.g., heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 mo or palliative)

International Society on Thrombosis and Haemostasis Guidance Statement

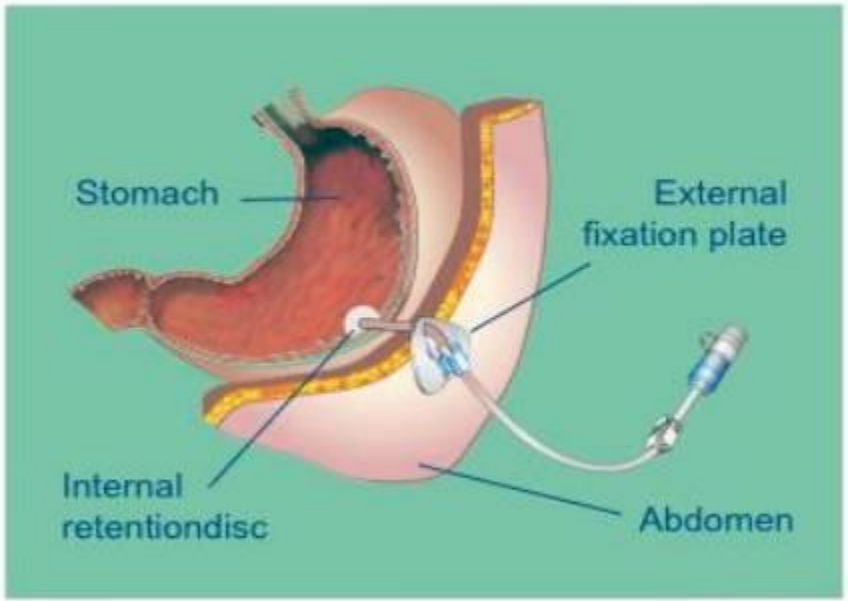
Empiric periprocedural thromboembolic risk stratification for patients receiving anticoagulant therapy

Low	• Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	• $CHADS_2$ score: 0 or 1 • CHA_2DS_2VaSc score: 1-4	• VTE more than 12 mo ago and no other risk factors

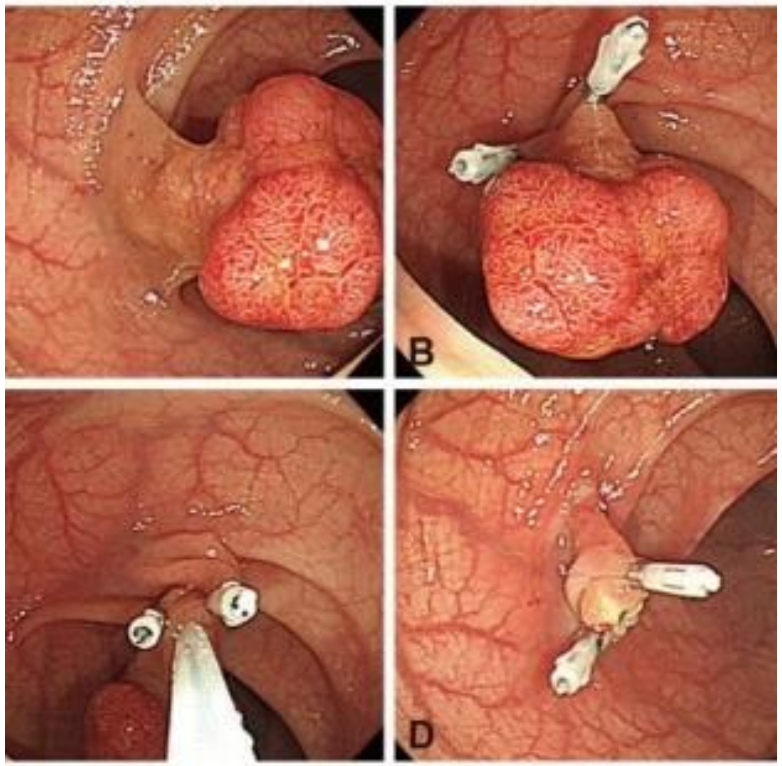
International Society on Thrombosis and Haemostasis Guidance Statement

QUESTION 4?

CAN YOU MENTION SOME HIGH RISK ENDOSCOPIC PROCEDURES?

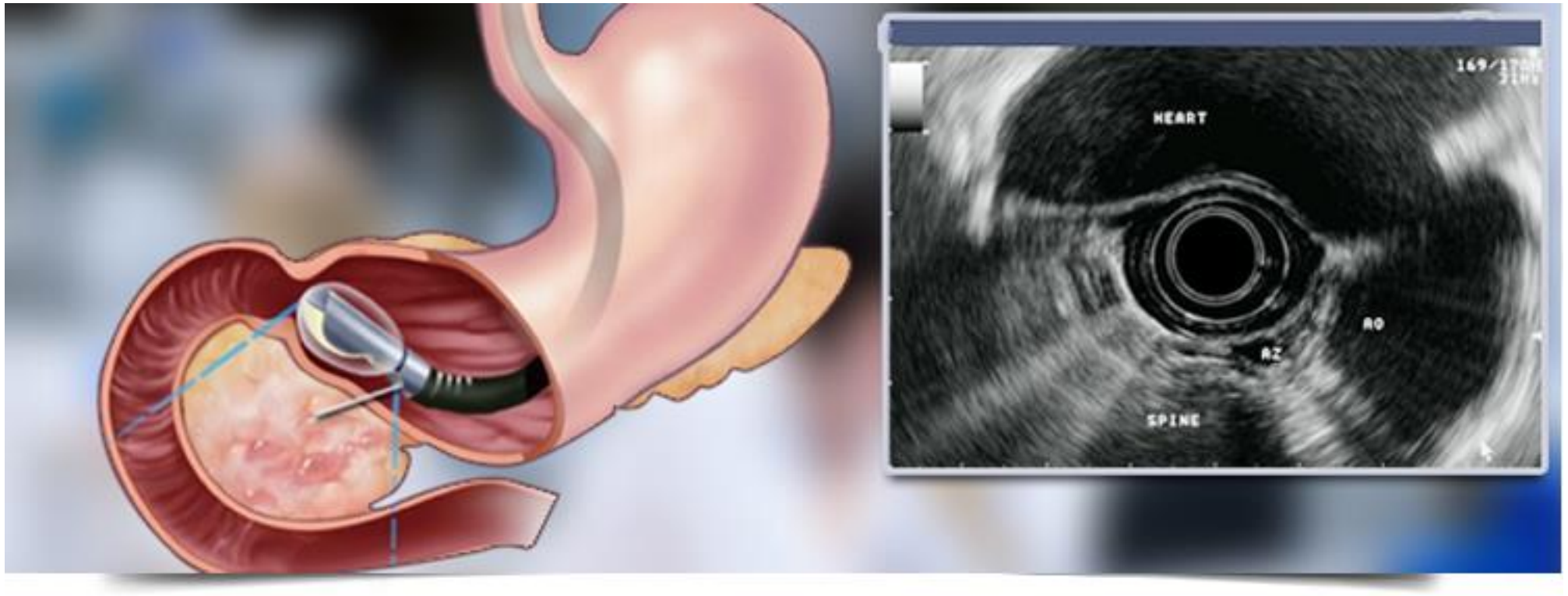


Percutaneous Endoscopic Gastrostomy (PEG)

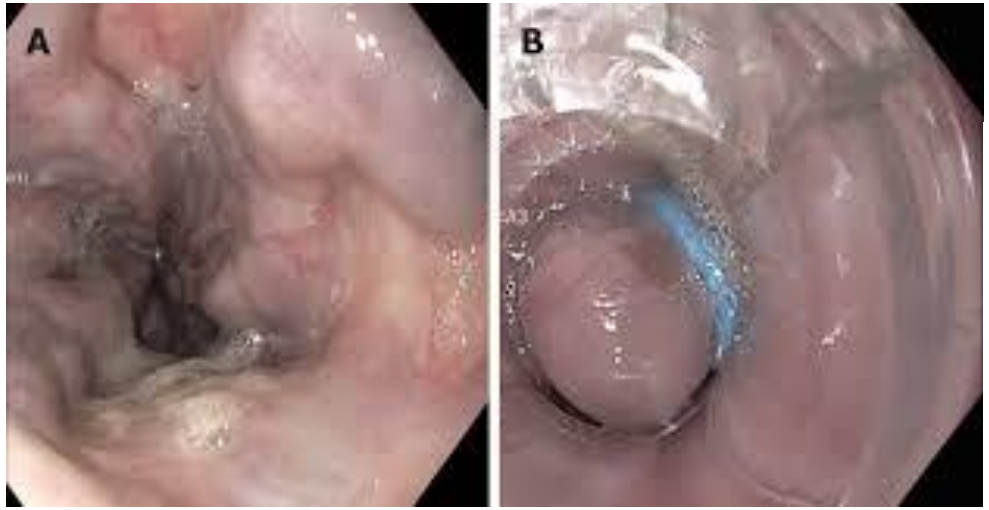


Endoscopic Polypectomy

Endoscopic Cystogastrostomy



Variceal ligation



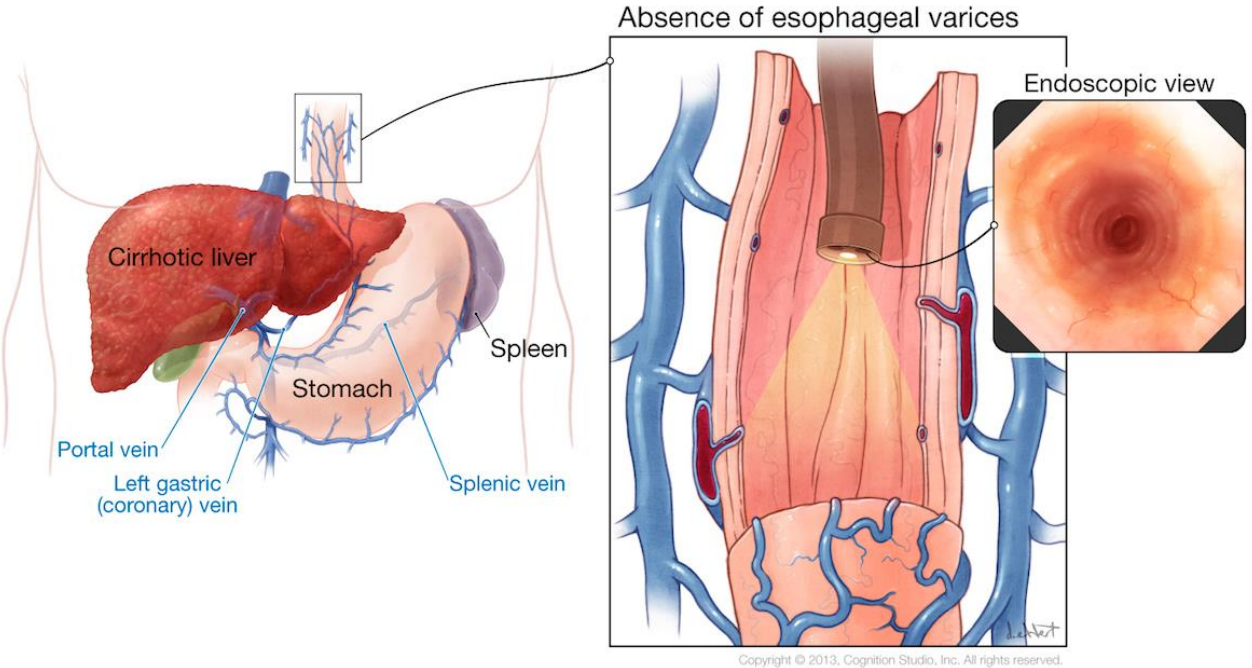


TABLE 3. Procedure risk for bleeding (overall)

Higher-risk procedures	Low-risk procedures
Polypectomy	Diagnostic (EGD, colonoscopy, flexible sigmoidoscopy) including mucosal biopsy
Biliary or pancreatic sphincterotomy	ERCP with stent (biliary or pancreatic) placement or papillary balloon dilation without sphincterotomy
Treatment of varices	
PEG placement*	Push enteroscopy and diagnostic balloon-assisted enteroscopy
Therapeutic balloon-assisted enteroscopy	Capsule endoscopy
EUS with FNA†	Enteral stent deployment (Controversial)
Endoscopic hemostasis	EUS without FNA
Tumor ablation	Argon plasma coagulation
Cystgastrostomy	Barrett's ablation
Ampullary resection	
EMR	
Endoscopic submucosal dissection	
Pneumatic or bougie dilation	
PEJ	

PEJ, Percutaneous endoscopic jejunostomy.
*PEG on aspirin or clopidogrel therapy is low risk. Does not apply to DAPT.
†EUS-FNA of solid masses on ASA/NSAIDs is low risk.

Empiric endoscopic procedural bleeding risk stratification

High bleeding risk procedures (30-d risk of major bleed >2%)	Low/moderate bleeding risk procedures (30-d risk of major bleed ≤ 2%)
Polypectomy (≥1 cm)	EGD with/without biopsy
PEG/PEJ placement	Colonoscopy with/without biopsy
ERCP with biliary or pancreatic sphincterotomy	Flexible sigmoidoscopy with/without biopsy
EMR/ESD	ERCP with stent (biliary or pancreatic) placement or papillary balloon dilation without sphincterotomy
EUS-FNA	EUS without FNA
Endoscopic hemostasis (excluding APC)	Push enteroscopy and diagnostic balloon-assisted enteroscopy
Radiofrequency ablation	Enteral stent deployment
POEM	Argon plasma coagulation
Treatment of varices (including variceal band ligation)	Balloon dilation of luminal stenoses
Therapeutic balloon-assisted enteroscopy	Polypectomy (<1 cm)
Tumor ablation	ERCP without biliary or pancreatic sphincterotomy
Cystogastrostomy	Marking (including clipping, electrocoagulation, and tattooing)
Ampullary resection	Video capsule endoscopy
Pneumatic or bougie dilation	
Laser ablation and coagulation	

ELECTIVE PROCEDURES

Patients with low to moderate thrombotic risk :

- Atrial fibrillation and a CHA_2DS_2-VASc score of 2 to 3 or $CHADS_2$ score of zero to 2 (assuming no prior stroke or transient ischemic attack)

- Venous thromboembolism >12 months previous and no other risk factors

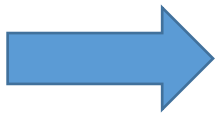


TABLE 5. Risk for thromboembolic event in patients with mechanical heart valve(s) or VTE on anticoagulation[37]

	Clinical indication for warfarin therapy	
Annual risk	**Mechanical heart valve**	**VTE**
High	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 months) CVA or TIA	• Recent (within 3 months) VTE • Severe thrombophilia (deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Medium	• Bileaflet aortic valve prosthesis and one or more of the following risk factors: AF, prior CVA or TIA, hypertension, diabetes, congestive heart failure, age $\geq$ 75 years	• VTE within the past 3-12 months • Nonsevere thrombophilia (heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 months or palliative)
Low	• Bileaflet aortic valve prosthesis without AF and no other risk factors for CVA	• VTE > 12 months previous and no other risk factors

VTE, venous thromboembolism; *CVA*, cerebrovascular accident; *TIA*, Transient ischemic attack; *AF*, atrial fibrillation.

Low risk procedures

- Patients at low or moderate risk for thrombosis require no change in anticoagulation prior to low-risk procedures (eg, upper gastrointestinal endoscopy [esophagogastroduodenoscopy [EGD] or colonoscopy, including mucosal biopsy) .

- However, for most patients scheduled for screening colonoscopy, the bleeding risk is uncertain because it is unknown whether or not polypectomy of a large polyp (≥1 cm) will be needed.

Low risk procedures

- If the international normalized ratio (INR) is >2.5, we postpone elective procedures for patients taking vitamin K antagonists (eg, warfarin) until the INR is ≤2.5.

TABLE 5. Risk for thromboembolic event in patients with mechanical heart valve(s) or VTE on anticoagulation[37]

	Clinical indication for warfarin therapy	
Annual risk	**Mechanical heart valve**	**VTE**
High	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 months) CVA or TIA	• Recent (within 3 months) VTE • Severe thrombophilia (deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Medium	• Bileaflet aortic valve prosthesis and one or more of the following risk factors: AF, prior CVA or TIA, hypertension, diabetes, congestive heart failure, age $\geq$ 75 years	• VTE within the past 3-12 months • Nonsevere thrombophilia (heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 months or palliative)
Low	• Bileaflet aortic valve prosthesis without AF and no other risk factors for CVA	• VTE > 12 months previous and no other risk factors

VTE, venous thromboembolism; *CVA*, cerebrovascular accident; *TIA*, Transient ischemic attack; *AF*, atrial fibrillation.

Patients with high thrombotic risk

- Atrial fibrillation with CHA_2DS_2-VASc score ≥4 ($CHADS_2$ score of ≥3)
- Atrial fibrillation with stroke or transient ischemic attack within three months
- Rheumatic valvular heart disease
- Venous thromboembolism within 12 months

- Thrombophilia (eg, antiphospholipid antibodies, heterozygous factor V Leiden, prothrombin gene mutation)
- Recurrent venous thromboembolism
- Active cancer (treated within six months or palliative)

High-risk procedures

- **Patients on warfarin**

- High-risk procedures generally warrant interruption of anticoagulation.
- For patients who are at high risk for thromboembolism and who are undergoing high- risk procedures , we ask the clinician who is managing the patient's anticoagulation if it is safe to hold warfarin for five days prior to the procedure and if bridging therapy is needed.
- Warfarin should be discontinued such that the INR is ≤ 1.5 by the day of the procedure.

bridging

- Peri procedural bridging may be appropriate in the subset of patients with:

- mechanical valves,
- atrial fibrillation with CHADS2 score >5,
- patients with previous thromboembolism during temporary interruption of VKAs,
- or those patients undergoing certain types of surgery (e.g., cardiac valve replacement, carotid endarterectomy, and major vascular surgery).

- The planned procedure type and its associated risk of postprocedural bleeding, and the baseline risk of thromboembolism will influence the recommendation

TABLE 13. Management of antithrombotic agents in the elective endoscopic setting

CV risk			Endoscopy-induced bleeding risk: Low		Endoscopy-induced bleeding risk: High
	Low	AC	1. Continue warfarin and NOAC	AC	1. Discontinue AC 2. Restart warfarin on same day of procedure 3. Delay reinitiating NOACs until adequate hemostasis is achieved
		APA	1. Continue standard doses of ASA/NSAIDs 2. Continue thienopyridines	APA	1. Continue standard doses of ASA/NSAIDs* 2. Discontinue thienopyridines at least 5 days before switch to ASA† 3. Dual APA, hold thienopyridines for at least 5 days, continue ASA†
	High	AC	1. Continue warfarin and NOAC	AC	1. Discontinue AC 2. Bridge therapy‡ 3. Restart warfarin on same day of procedure 4. Delay reinitiating NOACs until adequate hemostasis is achieved
		APA	1. Continue standard doses of ASA/NSAIDs 2. Continue thienopyridines	APA	1. Continue standard doses of ASA/NSAIDs 2. Discontinue thienopyridines at least 5 days before endoscopy or switch to ASA† 3. Dual APA, hold thienopyridines for at least 5 days, continue ASA†

AC, Anticoagulants; *APA*, antiplatelet agent; *NOAC*, novel oral anticoagulant; *ASA*, acetylsalicylic acid, or aspirin; *NSAID*, nonsteroidal anti-inflammatory drug; *CV*, cardiovascular.

*There is evidence to hold APA in patients undergoing ESD and EMR who have a low risk for a thromboembolic event.[116]

†Ticagrelor should be held for 3-5 days, and all other thienopyridines should be held for 5-7 days.

‡In moderate-risk patients (from Table 5), the decision to use bridging therapy and the degree of intensity should be individualized and the patient's wishes considered.[40]

Antiplatelet interruption vs continuation

- . For patients on dual antiplatelet therapy for secondary cardiovascular prevention who are undergoing elective endoscopic GI procedures, we suggest temporary interruption of the P2Y12 inhibitor while continuing ASA

- For patients on single antiplatelet therapy with P2Y12 inhibitor agents who are undergoing elective endoscopic GI procedures, we could not reach a recommendation for or against temporary interruption of the P2Y12 inhibitor.

- (conditional recommendation, very low certainty of evidence)

TABLE 2. Antithrombotic drugs: duration of action and approach to reversal when indicated

Drug class	Specific agent(s)	Duration of action	Approach to reversal based on procedural urgency	
			Elective	Urgent
APAs	Aspirin	7-10 days	NA	Hold, can give platelets
	NSAIDs	Varies	NA	Hold
	Dipyridamole (Persantine)	2-3 days	Hold	Hold
	Cilostazol (Pletal, Otsuka Pharmaceutical Co., Ltd., Tokushima, Japan)	2 days	Hold	Hold
	Thienopyridines: clopidrogrel (Plavix) prasugrel (Effient) ticlodipine (Ticlid) ticagrelor (Brilinta)	5-7 days: clopidogrel, 3-5 days: ticagrelor 5-7 days: prasugrel 10-14 days[98]: ticlopidine	Hold	Hold
	GPIIb/IIIa inhibitors: tirofiban (Aggrastat) abciximab (ReoPro) eptifibatide (Integrilin)	tirofiban: 1-2 seconds abciximab: 24 hours eptifibitide: 4 hours	NA	Hold HD: tirofiban
	PAR-1 inhibitor: vorapaxar (Zontivity)	5-13 days	Hold	Hold
Anticoagulants	Warfarin (Coumadin)	5 days	Hold	Vitamin K, PCC
	UFH	IV 2-6 hours SQ 12-24 hours	Hold	Protamine sulfate* (partial)
	LMWH: enoxaparin (Lovenox) dalteparin (Fragmin, Pfizer Inc, New York, NY, USA)	24 hours	Hold	Protamine sulfate, consider rVIIa
	Fondaparinux (Arixtra)	36-48 hours		Protamine sulfate, consider rVIIa
	Direct factor Xa Inhibitor: rivaroxaban (Xarelto) apixaban (Eliquis) edoxaban (Savaysa)	See Tables 7 and 8	Hold	Charcoal (if last intake within 2-3 hours); nonactivated PCC or activated PCC
	Direct thrombin inhibitor, oral: dabigatran (Pradaxa) IV: Desirudin (Iprivask, Aventis Pharmaceuticals Inc., Bridgewater, NJ, USA)	See Table 9	Hold	Charcoal (if last intake within 2-3 hours); nonactivated PCC or activated PCC; HD

NSAIDs, Nonsteroidal anti-inflammatory drugs; *NA*, not applicable; *HD*, hemodialysis; *PCC*, prothrombin complex concentrate; *rVIIa*, recombinant factor VIIa.
*Caution: Can cause severe hypotension and anaphylaxis.

Case report

- a 80-year-old woman known to you, presents to your clinic with shortness of breath, fatigue, and a “racing heart,” which started approximately 2 days ago.

- An electrocardiogram confirms AF with a heart rate of 120 beats/min. You review her chart to select an agent for AF stroke prevention and are reminded that she had a non-ST-segment elevation myocardial infarction 2 months ago, which was managed with 2 drug-eluting stents.
- She was prescribed 90 mg of ticagrelor twice daily for 12 months, 81 mg of ASA daily for life, 50 mg of metoprolol twice daily, 10 mg of ramipril daily, and 40 mg of atorvastatin daily.

- Her past medical history includes hypertension, type 2 diabetes mellitus, dyslipidemia, and osteoarthritis. Her other medications include 500 mg of metformin twice daily, 650 mg of acetaminophen twice daily, and 20 mg of paroxetine once daily, which was started during menopause for hot flashes.

- recent laboratory results revealed a hemoglobin A_{1c} level of 7.8% and a low-density lipoprotein cholesterol level of 2.6 mmol/L.

- Her complete blood count results, renal function, and liver enzyme levels were within normal limits.
- In the clinic today, her body mass index is 26 kg/m^2 and her blood pressure is 124/82 mm Hg.
- Her $CHADS_2$ (congestive heart failure, hypertension, age ≥ 75 y, diabetes mellitus, previous stroke or transient ischemic attack) score is 3.
- Her HAS-BLED (hypertension with a systolic blood pressure > 160 mm Hg, abnormal renal or liver function, stroke, bleeding, labile international normalized ratio [INR], elderly [age > 65 y], drugs [ASA, nonsteroidal anti-inflammatory drugs (NSAIDs)] or alcohol [≥ 8 drinks/wk]) score is 2, which is based on her age and ASA use.

- THE PATIENT has an indication for an OAC for AF stroke prevention; however, you decide to consult her cardiologist, as she is currently taking DAPT for her recent ACS and coronary stents.

Selection of anticoagulants for TT.

- Most of the limited evidence regarding TT is for warfarin.

- The aforementioned meta-analyses that assessed TT only included vitamin K antagonists—these studies provide the largest body of evidence (15 and 18 studies, N = 7182 and N = 17 708, respectively), although both are largely based on observational data.

- If warfarin is used, consider an INR target of 2.0 to 2.5 and monitor INR frequently (eg, every 2 weeks), although this narrow target can be difficult to achieve.

- The 2016 CCS AF guidelines suggest, based on extrapolation of data from the direct oral anticoagulant (DOAC) AF trials, using a DOAC, such as apixaban, dabigatran, or rivaroxaban, preferentially to warfarin for patients with nonvalvular AF and recent ACS.
- However, the clinical efficacy and safety of DOACs in a TT regimen has not been established.

- Of the DOACs, only rivaroxaban and dabigatran have randomized controlled *safety* data compared with warfarin (as part of TT) in patients with AF .

- The PIONEER-AF-PCI study compared 15 mg of rivaroxaban daily plus 75 mg of clopidogrel daily, and 2.5 mg of rivaroxaban twice daily plus DAPT (75 mg/d of clopidogrel plus 75 to 100 mg/d of ASA), with warfarin plus DAPT (target INR of 2.0 to 3.0).

Selection of antiplatelets for TT

- Clopidogrel is the preferred antiplatelet to be used in combination with ASA and an OAC.

- The newer, more potent antiplatelet agents, prasugrel and ticagrelor, are not recommended owing to an increased risk of bleeding compared with clopidogrel

- The addition of a proton pump inhibitor (PPI) should be considered as gastroprotection for patients taking TT, particularly for those with a history of gastrointestinal bleeding or ulcers.

- While there is a lack of data addressing the efficacy of gastroprotection in TT, evidence does show that PPIs reduce the risk of upper gastrointestinal bleeding by at least 50% in patients taking DAPT.
- Previously, concerns were raised regarding a potential drug-drug interaction between PPIs and clopidogrel based on observational trial data.

- PATIENT'S cardiologist asks you to stop her ticagrelor and initiate 75 mg of clopidogrel daily (starting in the morning after her last evening dose of ticagrelor) for 10 months (ie, she will receive a $P2Y_{12}$ inhibitor for a total of 12 months after coronary stent insertion).
- She is to continue taking her low-dose ASA for another month, then stop (ie, she will receive ASA therapy for a total of 3 months after coronary stent insertion).
- She is prescribed 3 mg of warfarin daily, with a suggested INR target of 2.0 to 2.5 while taking TT.

- You decide to initiate 40 mg of pantoprazole daily while she is receiving TT, and also decide to increase her metoprolol to 75 mg twice daily to achieve better rate control.
- You reassess her paroxetine, as selective serotonin reuptake inhibitors can increase the risk of gastrointestinal bleeding.
- You also emphasize to her the importance of adhering to TT for the length of time prescribed, describe the signs and symptoms of bleeding, and
- recommend she avoid using any over-the-counter products that might increase her risk of bleeding (eg, NSAIDs, vitamin E, high-dose omega-3 [3 to 4 g/d], *G* natural health products such as ginkgo, ginseng, and garlic).

THANKS FOR YOUR ATTENDANCE