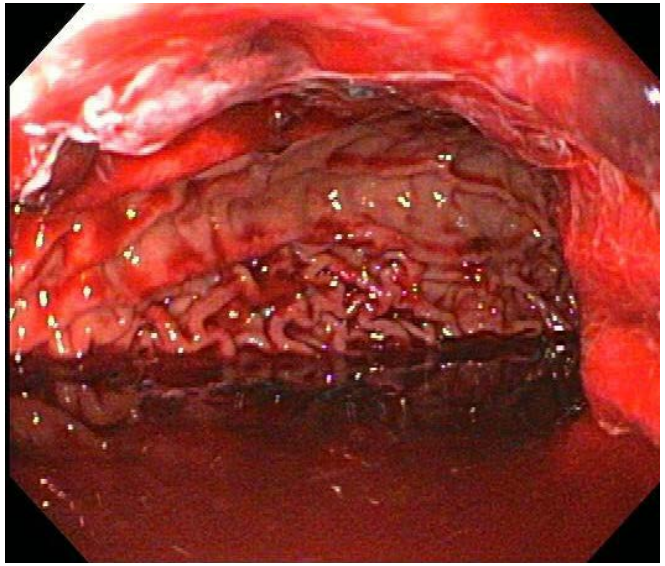
Management of Antithrombotic Therapy in the Peri-endoscopic Period: An Update



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- None

Objectives

- Accurately assess the risk of bleeding in patients on anticoagulants and antiplatelet agents before endoscopic procedures
- Describe the cardiovascular risk of modifying antithrombotic therapy in the periendoscopic setting
- Provide current best-practice recommendations for management of antithrombotic therapy before and after endoscopic procedures

Case Presentation

- 66 M admitted with chest pain
- Cardiac cath: significant stenosis of prox/mid LAD → DES x 2, now on ASA/clopidogrel
- Next day: N/V, abd pain and lipase > 2,000
- MRCP: 12mm CBD with distal filling defects
- Hospital course c/b cholangitis and strep viridans bacteremia
- ERCP with temporary biliary stent placement without sphincterotomy
- Discharged home

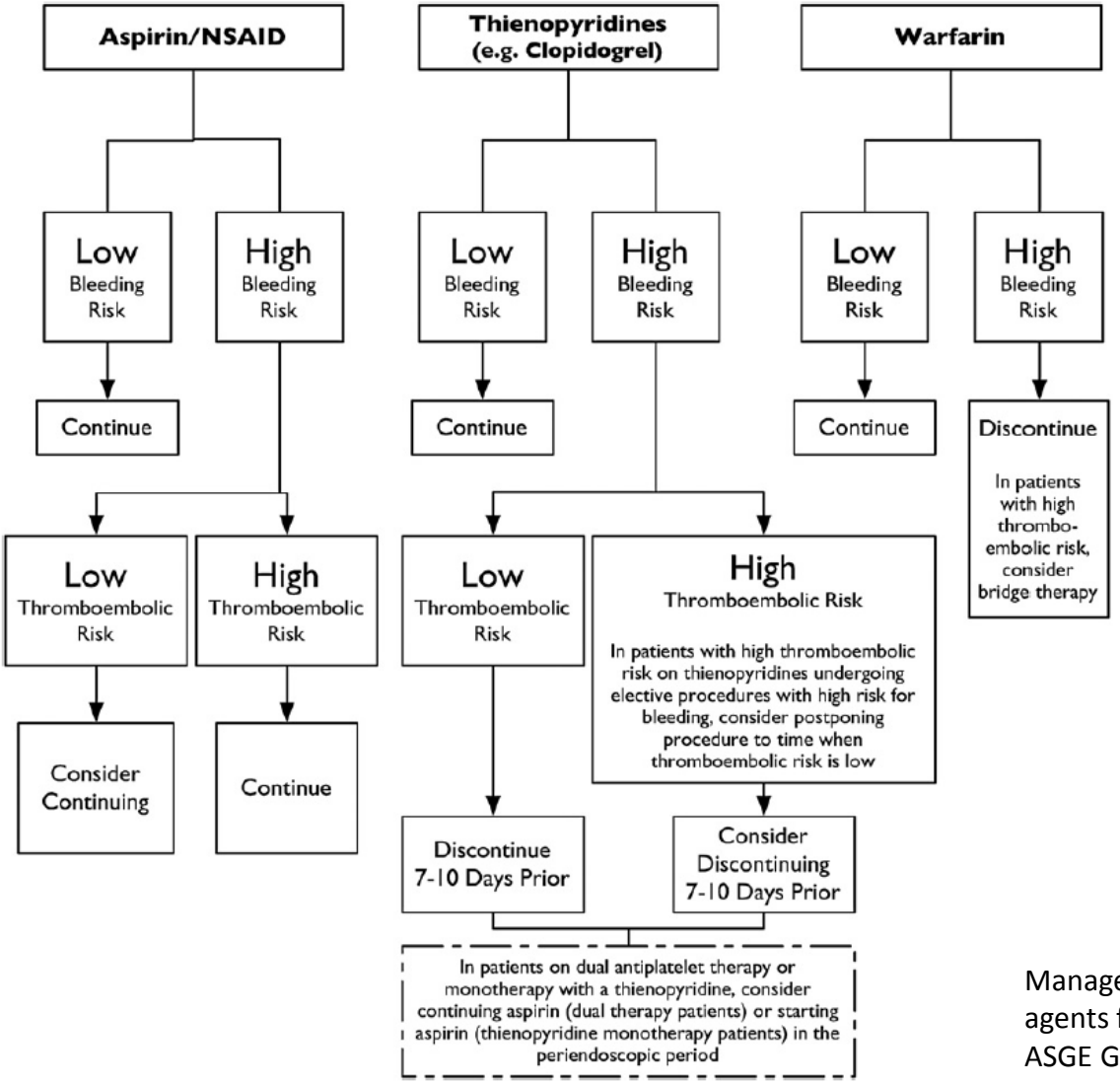
Options for Our Patient?

- Eventually needs definitive management of biliary stones with ERCP *(and cholecystectomy)*
- Can we stop ASA and/or clopidogrel?
- Standard ERCP with sphincterotomy?
- Alternatives?

  (1) ERCP with papillary balloon dilation without sphincterotomy

  (2) ERCP with repeated stent exchange until safe to come off of dual antiplatelet therapy

Management of antithrombotic agents for endoscopic procedures



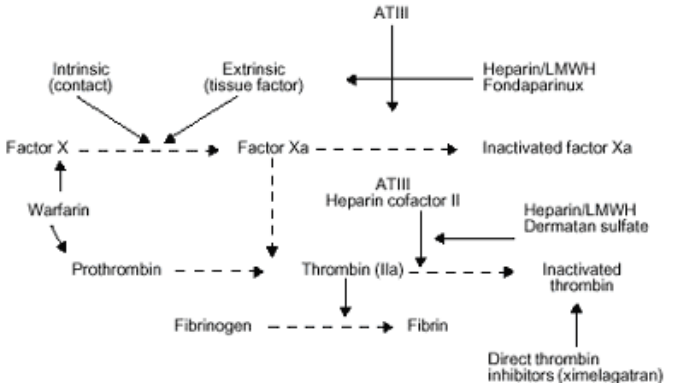
Management of antithrombotic agents for endoscopic procedures. ASGE Guideline 2009.

The Problem

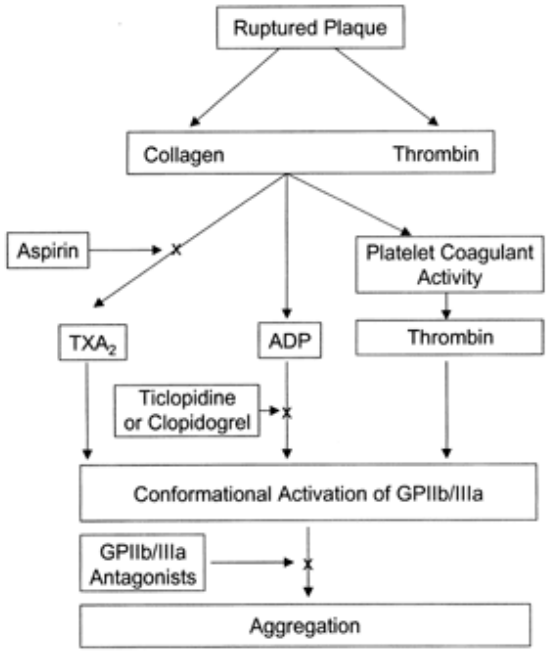
- Guidelines rely heavily on observational studies and expert opinion
- Personal experience vs published guidelines
  - 55.5% pts had antithrombotics managed incorrectly
    (M. Bruno et al. Digestive and Liver Disease 47 (2015) 45-49)
- Differences between international guidelines
- Peri-endoscopic management of antithrombotics often done by non-GI specialists
- Little known about novel anticoagulant and antiplatelet agents and not addressed in GI guidelines
- Medico-legal issues

Antithrombotic Agents

- **Anticoagulants**
  - Warfarin
  - Heparin
  - LMWH
  - New Oral Anticoagulants (NOACs)



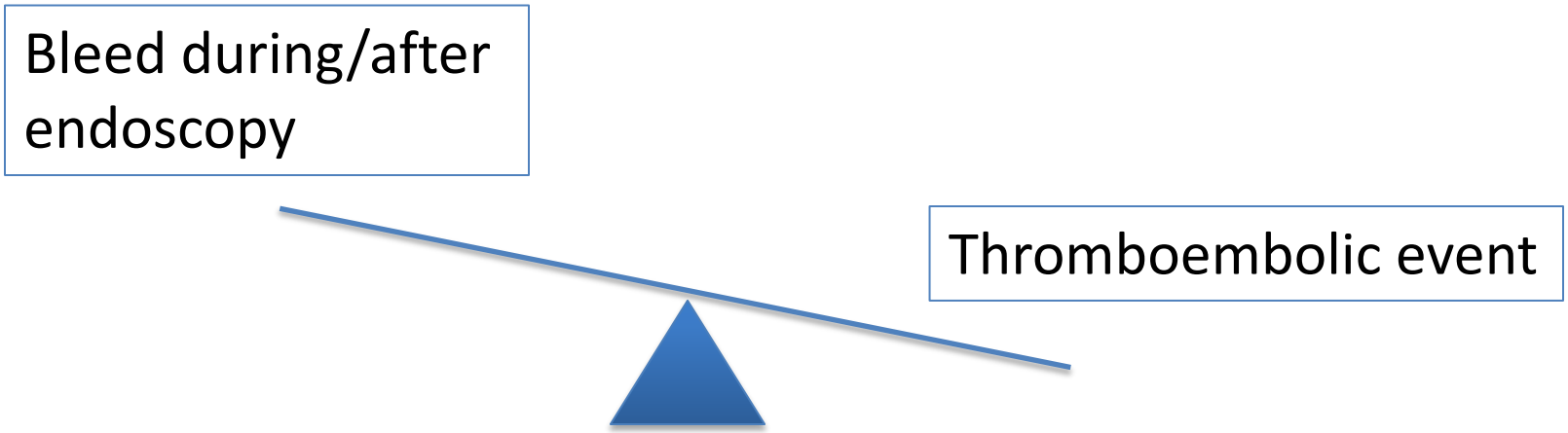
- **Antiplatelets**
  - ASA
  - NSAIDs
  - Thienopyridines (eg, clopidogrel)
  - New Oral Antiplatelet Agents



www.medscape.com

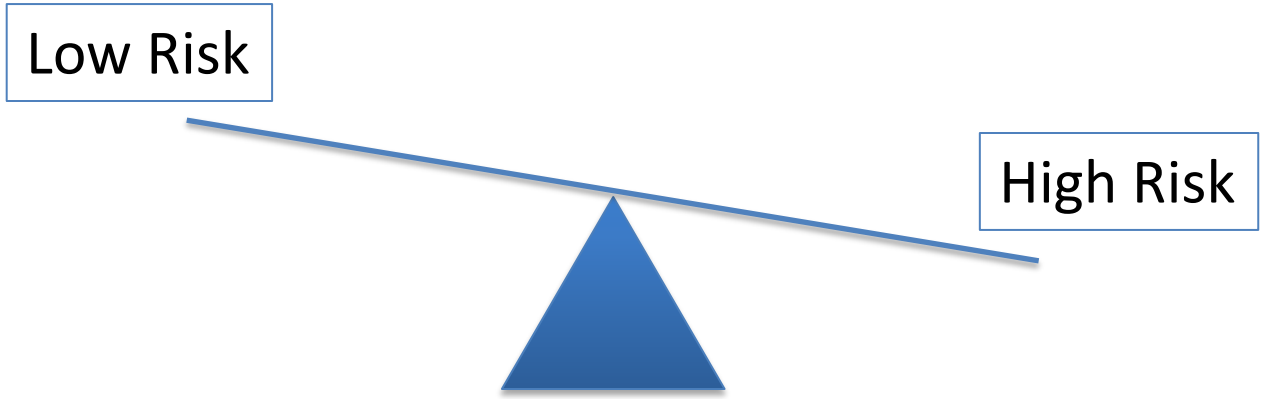
Managing Antithrombotics

- Urgency of procedure
- Risk of thromboembolic event from stopping antithrombotic therapy
- Risk of bleeding from endoscopic procedure
- Risk of bleeding with antithrombotic agent



What are the Risks of Thromboembolic Events Around Endoscopy?

- Depends on the condition for which antithrombotic therapy is being used



Conditions with High Risk of Thromboembolic Events: > 10% Annual Risk

Atrial fibrillation	Previous stroke/transient ischemic attack
	$CHADS_2 \geq 4$
	Associated valvular heart disease
Prosthetic valve	Discontinuing antiplatelet/anticoagulant in bioprosthetic valve <3 months
	Mechanical valve in mitral position
	Mechanical valve with previous thromboembolic event
Coronary disease and stents	Recent acute coronary event <4–6 weeks
	Discontinuing dual antiplatelet therapy in:
	Drug-eluting stent <1 year
	Bare metal stent <1 month
DVT/PE	Discontinuing anticoagulation in event <3 months
	Recurrent DVT/PE
	Severe hypercoagulable states: active cancer, paroxysmal nocturnal hemoglobinuria, myeloproliferative syndromes

$CHADS_2$ Score

Clinical parameters	Points
Congestive heart failure	1
Hypertension	1
Age ≥75 years	1
Diabetes mellitus	1
Secondary prevention in patients with previous ischemic stroke, transient ischemic attack	2

$CHADS_2$ score	Stroke rate (per 100 patient-years) without antithrombotic therapy	95% CI
0	1.9	1.2–3.0
1	2.8	2.0–3.8
2	4.0	3.1–5.1
3	5.9	4.6–7.3
4	8.5	6.3–11.1
5	12.5	8.2–17.5
6	18.2	10.5–27.4

Kwok A, et al. Am J Gastroenterol 2009.

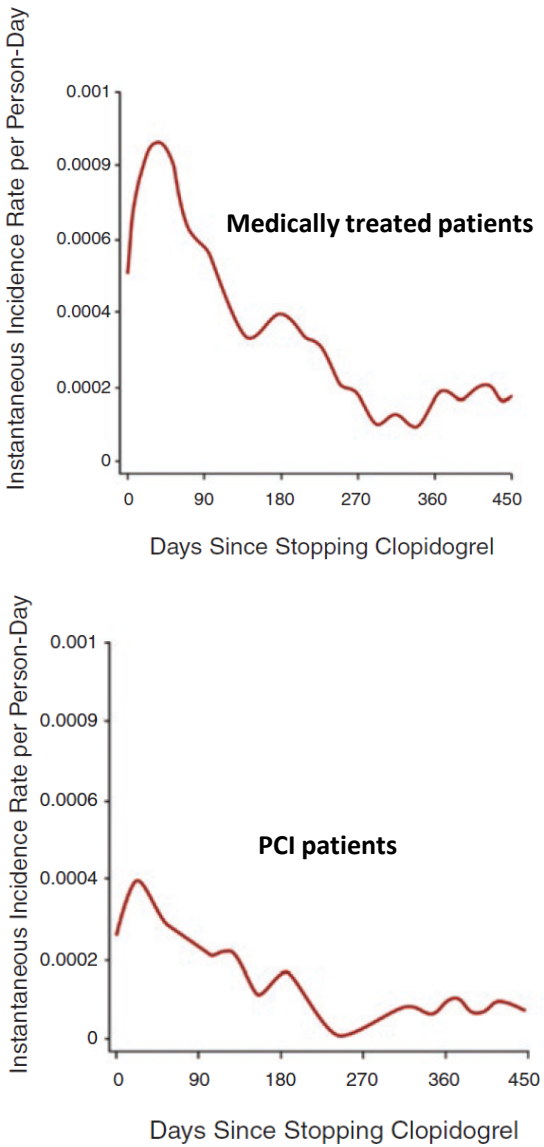
Risk of Discontinuing Anticoagulation

- Risk of stroke in anticoagulated patients with atrial fibrillation (AF)
  - Anticoagulation adjusted for endoscopy including EGD or colonoscopy
- 1137 procedures in 987 patients
  - 12 CVAs
  - **30 day risk:** **0.31% for nonvalvular AF**
    2.93% for complex patients with comorbid disease
- 10x higher in patients with complex clinical situations – stroke increased with
  - Age
  - History of stroke
  - Hypertension
  - Hyperlipidemia
  - Family history of vascular disease

Blacker DJ, et al. Neurology 2003.

Risk of Discontinuing Antiplatelet Therapy

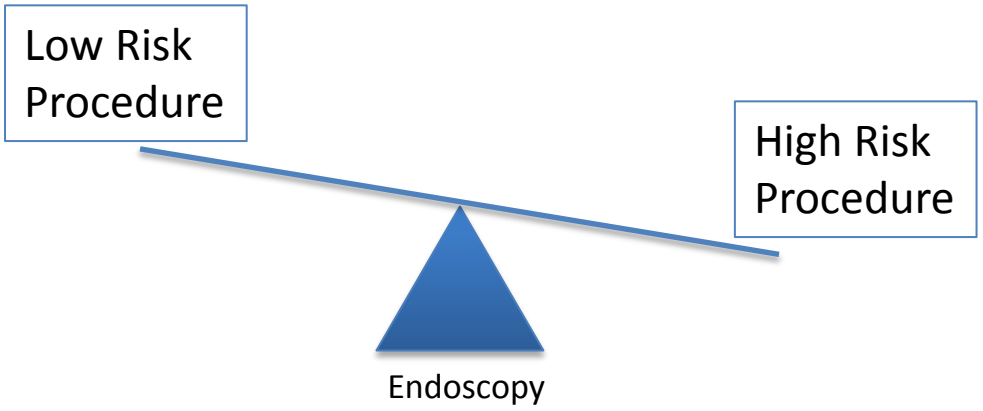
- Primary CV prophylaxis: 0.7% / year
- Secondary CV prophylaxis: 1.5% / year
- Percutaneous coronary intervention
  - Bare metal stent (BMS) and drug eluting stent (DES)
    - first 30 days: 30% rate of major adverse CV event during procedure if stop ASA/clopidogrel, 4% clopidogrel only
  - Risk off antiplatelet agents never drops down to zero
    - 5-10% risk of CV event or ST even after 2 years
    - BMS: minimum 1 month therapy, ideal 12 months
    - DES: minimum 6 months therapy, ideal 12 months



Perioperative Management of Antithrombotic Therapy. CHEST 2012.
Glenn Eisen, MD. ACG 2013 Annual Scientific Meeting.
Becker RC, et al. AJG 2009.

What are the Endoscopic Risks for GI Bleeding?

- Depends upon the procedure being performed



* Delay elective endoscopy until patient at lower risk for thromboembolism if possible

Endoscopy Risk for GIB

LOW RISK OF BLEEDING (< 1%)

Procedure	Risk of bleeding
Diagnostic endoscopy with or without biopsy	
EGD	0.01 – 0.13%
Double balloon enteroscopy	0.1%
Colonoscopy	0 – 0.02%
Biliary/pancreatic stent without sphincterotomy	0.26%
EUS without FNA	----
Capsule endoscopy	----

HIGH RISK OF BLEEDING (≥1%)

Procedure	Risk of bleeding
Polypectomy	
Gastric	7.2%
Duodenal/ ampullary	4.5 – 10.3%
Colonic	0.7 – 3.3%
EMR	22% * (mostly with >2cm lesions)
Biliary sphincterotomy	2 – 3.2%
Pneumatic dilation in achalasia	1.7%
Esophageal stenting	0.5 – 5.3%
PEG	2.5%
EUS with FNA	1.3 – 6% *negligible for solid lesions
Variceal sclerotherapy	4 – 25.4%
Variceal band ligation	2.4 – 5.7%
Thermal ablation and coagulation	5%
Laser ablation and coagulation	1.1%

Kwok A, et al. Am J Gastroenterol 2009.

Diagnostic Endoscopy is Safe on Warfarin

- Gerson LB, et al. Am J Gastroenterol 2000
  - Retrospective review, 104 pts, single VA center
  - EGD and colonoscopy w/ bx on therapeutic warfarin
  - 171 procedures (99 colo + 63 EGD + 9 ERCP)
  - 0/104 pts with thromboembolism or hemorrhage
    - adverse-event rate 0% (95% CI, 0-3%)

Diagnostic Endoscopy is Safe on ASA/NSAIDs

Widely cited paper is 20 years old and retrospective series
(Shiffman ML, et al. GIE 1994)

- 694 pts undergoing EGD or colonoscopy: 320 NSAIDs, 374 controls
- Minor bleeding: 20/320 NSAIDs vs 8/374 controls (p=0.009)
- Major bleeding: 2/320 NSAIDs vs 2/374 controls (p=NS)

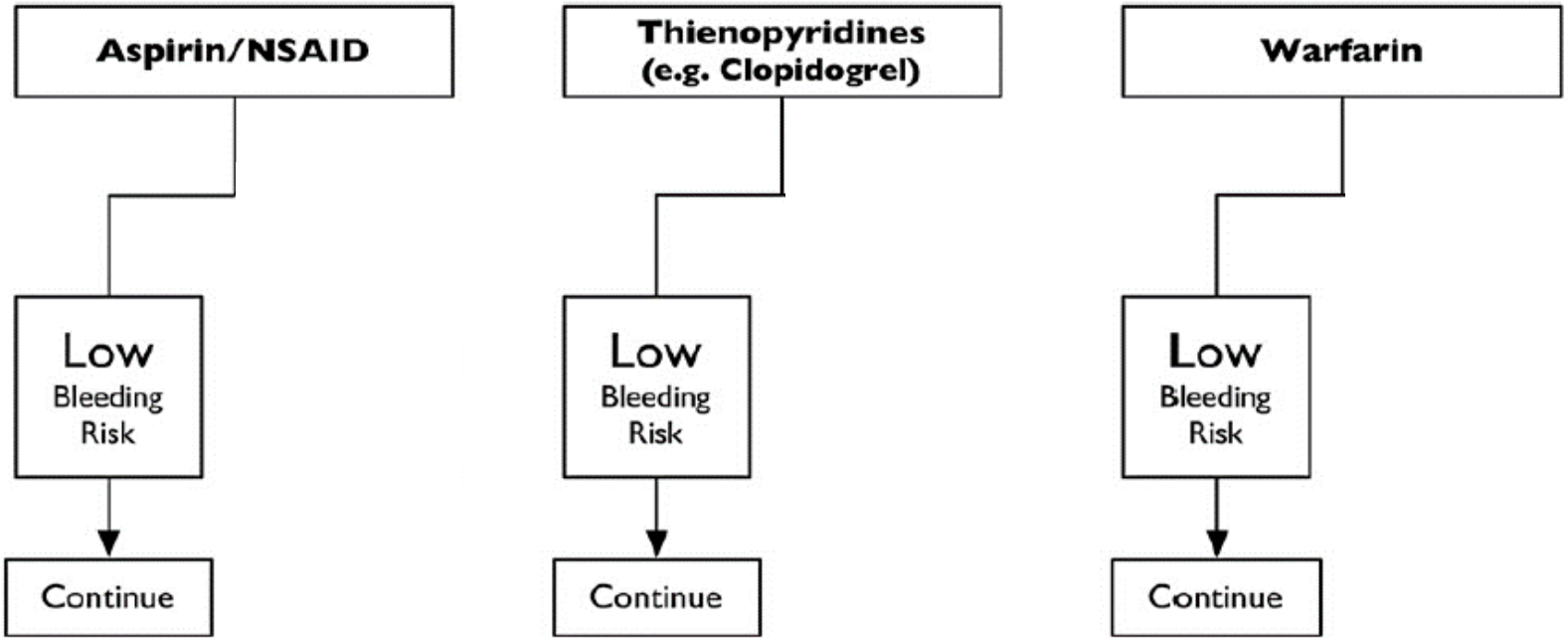
Diagnostic Endoscopy is Safe on Antiplatelets

- Whitson MJ, et al. J Clin Gastroenterol 2011
  - Prospective, single-blind, randomized study
  - EGD with biopsy on either ASA or clopidogrel

		Antral Biopsies		Duodenal Biopsies		
Drug	Subjects	Normal	Rim	Normal	Rim	Total
CPG	25	125	100	75	50	350
ASA	20	100	80	60	40	280

Drug	Biopsies	Endoscopic Bleeding Events	Clinical Bleeding Events
CPG	350	0	0
ASA	280	1	0

ASGE Guidelines

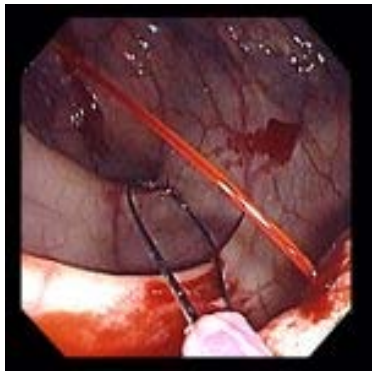


- **Endoscopy (EGD and colonoscopy) +/- biopsy is a LOW risk procedure for bleeding, regardless of antithrombotic therapy**
- **May delay elective procedure if INR supratherapeutic**

Management of antithrombotic agents for endoscopic procedures. ASGE Guideline 2009.

Colonoscopic Polypectomy

- Increasing use of colonoscopy
  - Aging population, many on ASA/NSAIDs, clopidogrel or anticoagulation
- Polyps
  - Screening colonoscopy (25% men, 15% women)
  - Incidental finding on diagnostic colonoscopy
- Post-polypectomy bleed (PPB) is most common complication of colonoscopic polypectomy
  - High bleeding risk procedure
  - 0.7 - 8.6% risk, up to 22% with EMR



Heldwein W, et al. Endoscopy 2005.
Kwok A, et al. Am J Gastroenterol 2009.

Risk Factors for Hemorrhage After Colonoscopic Polypectomy

	Adjusted odds ratios (95% confidence interval)†
Patient-related risk factors	
Definite risk factors	
– Age >65 years	1.37 – 1.69 (range, 1.02 – 2.42)
– Anticoagulation	3.71 – 5.2 (range, 1.05 – 13.05)
– Cardiovascular disease	2.08 – 3.0 (range, 1.45–6.2)
Likely risk factors	
– Male gender	1.92 (1.35 – 2.77)
– Arterial hypertension	5.60 (1.80 – 17.20)
– Chronic renal disease	3.29 (1.84 – 5.87)
Polyp-related risk factors	
Definite risk factor	
– Size ≥1cm	2.38 – 4.40 (range, 1.78 – 10.30)
Likely risk factor	
– Morphology (sessile, laterally spreading tumor)	1.42 (1.06 – 1.89)
Technique-related risk factors	
Likely risk factors	
– Use of pure-cutting current	6.95 (4.42 – 10.04)
– Inadvertent cold polypectomy	7.15 (3.13 – 16.36)
– Endoscopist case volume <300 colonoscopies/year‡	2.32 (1.25 – 4.3)
– Poor bowel preparation	1.54 (1.06 – 1.89)

Pre-procedure RF

Intra-procedure RF

Endoscopy and antiplatelet agents. ESGE Guideline 2011.

GIE
GASTROINTESTINAL ENDOSCOPY 2004 Jan;59(1):44-8.

Risk of colonoscopic polypectomy bleeding with anticoagulants and antiplatelet agents: analysis of 1657 cases

Aric J. Hui, MD, Ronald M. Y. Wong, Jessica Y. L. Ching, MPH, Lawrence C. T. Hung, MD, S. C. Sydney Chung, MD, Joseph J. Y. Sung, MD, PhD

- Retrospective audit of colonoscopies, 1/2000 to 12/2001
- Tertiary referral endoscopy center (HK)
- 5593 colonoscopies, 1657 with polypectomy
- Use of ASA, NSAIDs, warfarin assessed

- Post-polypectomy bleeding = 37 cases (2.2%)
  - 32 immediate (31 mild, 1 moderate)
  - 5 delayed (1 mild, 2 moderate, 2 severe)
- Use of antiplatelets and anticoagulation and risk of post-polypectomy bleeding

Variables	No bleeding N = 1620	Bleeding N = 37	Univariate *p* value
Use of antiplatelet agents	213 (13.2%)	6 (16%)	0.62
Aspirin	122 (7.5%)	5 (13.5%)	
NSAID	84 (5.2%)	1 (2.7%)	
Concomitant Aspirin and NSAID	7 (0.4%)	0 (0%)	
Use of warfarin	13 (0.8%)	4 (10.8%)	< 0.001*

*Significant in a multivariate logistic regression analysis

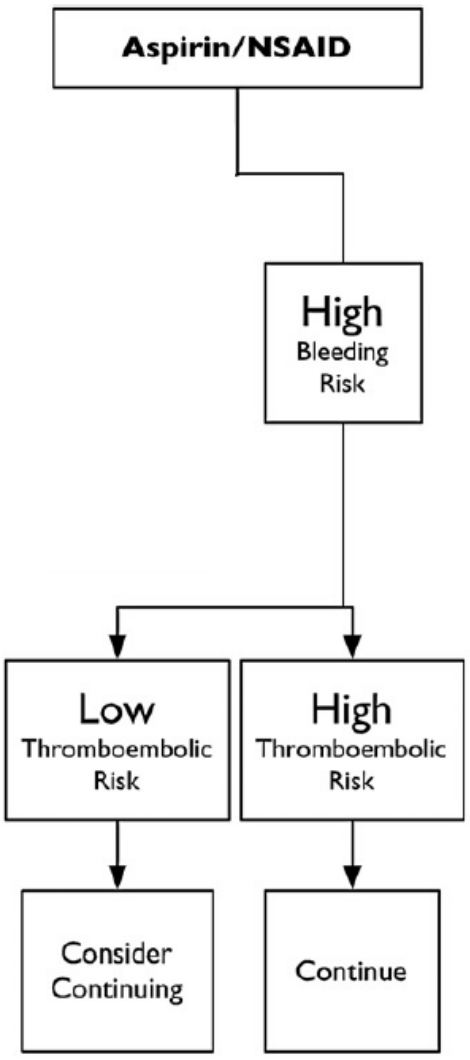
Case-Control Studies Evaluating Risk of PPB Relative to ASA Intake

First author, year	Study design Number of patients	Incidence of PPB in the whole study population		Patients taking aspirin % (n/n)		*P* value
		Type of PPB	Incidence	Cases (PPB)	Controls (no PPB)	
Shiffman, 1994 [38]	Prospective 464	Any	6.5%	73% (22/30)	47% (206/434)	0.009
		Major*	0.9%	100% (2/2)	0% (0/2)	0.73
Yousfi, 2004 [39]	Retrospective 20636	Any	0.5%	40% (32/81)	33% (27/81) †	0.36
Hui, 2004 [40]	Retrospective 1657	Any	2.2%	14% (5/37)	8% (122/1620)	0.62
Heldwein, 2005 [22]	Prospective 2257	Any	8.6%	n. d.	n. d.	n. s.
		Major*	1.6%	n. d.	n. d.	n. s.
Sawhney, 2008 [23]	Retrospective 4592	Delayed	0.9%	41% (17/41)	39% (51/132) †	0.80

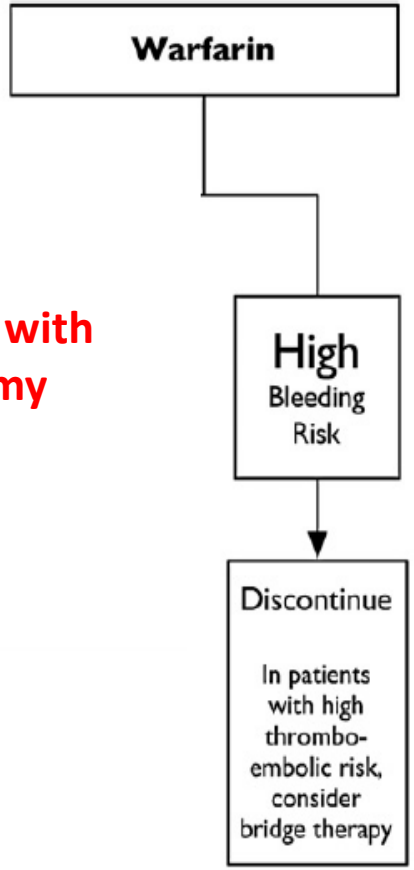
PPB = post-polypectomy bleed

Endoscopy and antiplatelet agents. ESGE Guideline 2011.

Management of ASA/NSAIDs and Warfarin for High Bleeding Risk Procedures

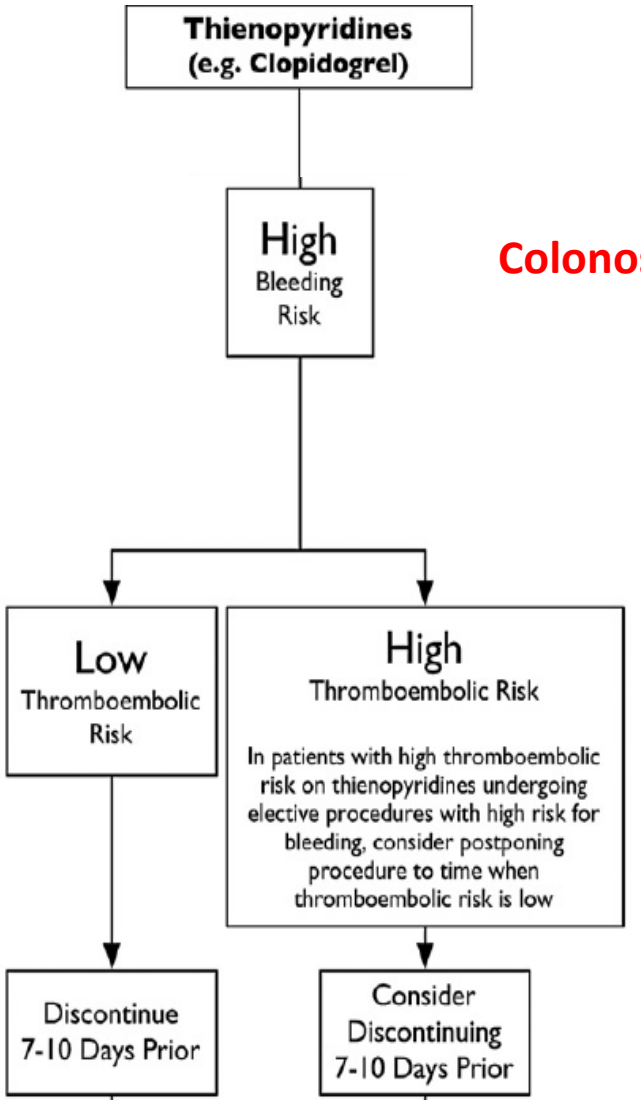


Colonoscopy with polypectomy



Management of antithrombotic agents for endoscopic procedures. ASGE Guideline 2009.

Colonoscopic Polypectomy on Thienopyridines (e.g., Clopidogrel)



Colonoscopy with polypectomy

- **Monotherapy clopidogrel: hold clopidogrel, start ASA**
- **Dual antiplatelet therapy: hold clopidogrel, cont ASA**

Management of antithrombotic agents for endoscopic procedures. ASGE Guideline 2009.

Limitations to Guidelines on Clopidogrel Management

- Current recommendations regarding thienopyridine drug management based largely on inference and expert opinion
  - Limited prospective data
- ASGE and ESGE recommend stopping clopidogrel 7-10 days prior to polypectomy, with ASA replacement/continuation, irrespective of thromboembolic risk

Management of antithrombotic agents for endoscopic procedures. ASGE Guideline 2009.
Endoscopy and antiplatelet agents. ESGE Guidelines 2011.

Dig Dis Sci (2011) 56:2631–2638
DOI 10.1007/s10620-011-1682-2

ORIGINAL ARTICLE

The Rate of Post-Polypectomy Bleeding for Patients on Uninterrupted Clopidogrel Therapy During Elective Colonoscopy Is Acceptably Low

Linda A. Feagins · Fatema S. Uddin · Raquel E. Davila · William V. Harford · Stuart J. Spechler

- Retrospective, case–control study of patients who had colonoscopic polypectomy (VA hospital from July 2008 - December 2009)
- 1,967 patients: 118 on clopidogrel and 1,849 controls
- Assessed frequency of delayed PPB (within 30 days) for patients on uninterrupted clopidogrel therapy vs matched controls

Age (years)	Clopidogrel use	ASA or NSAID use	Number of polyps	Largest polyp	Technique	Time to bleed	Hct drop	Hospital days	Intervention
61	Yes	Yes	7	8 mm	Hot snare with hemoclip	8 days	42–29	2	Colonoscopy, no transfusion
60	No	Yes	3	5	Hot snare with saline lift	<1 day	44–24	2	Colonoscopy, 2 units pRBC
77	No	No	3	5	Cold forceps	2 days	35–24	2	Colonoscopy, 2 units pRBC
72	No	Yes	2	12	Hot snare	<1 day	48–36	1	
81	No	No	1	15	Hot snare with saline lift	<1 day	41–26	1	Colonoscopy, no transfusion
69	No	Yes	1	20	Hot snare	7 days	40–23	1	Colonoscopy, 2 units pRBC
50	No	Yes	2	25	Hot snare	<1 day	47–30	1	Colonoscopy, 2 units pRBC

No significant difference in frequency of PPB between clopidogrel users and non-users (0.8% vs. 0.3%, P = 0.37, unadjusted OR = 2.63, 95% CI 0.31–22).

Is Clopidogrel Safe During Colonoscopic Polypectomy?

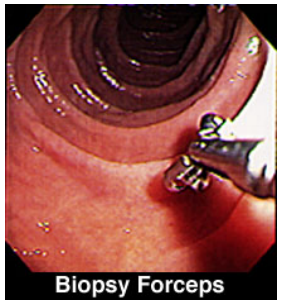
- 3 recent retrospective studies[1-3]
  - Total of 320 patients receiving clopidogrel
  - 860 polypectomies
  - Evaluated effect of uninterrupted clopidogrel therapy on PPB

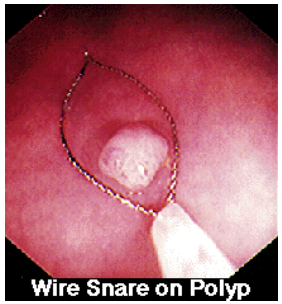
Unnecessary to interrupt clopidogrel therapy for colonoscopic polypectomy, esp in patients on clopidogrel monotherapy and for polyps < 1cm

1. Singh M, et al. GIE 2010.
2. Friedland S, et al. Gastroenterol Res 2009.
3. Feagins LA, et al. Dig Dis Sci 2011.

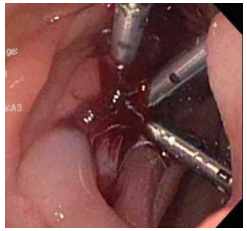
Are We Ready to Change Our Practice for Polypectomy on Clopidogrel?

- Limitations of most studies
  - most polyps small (<1cm)
  - removed using variety of techniques with varying risks of PPB
    - Cold biopsy forceps vs snare polypectomy





  - use of hemoclips

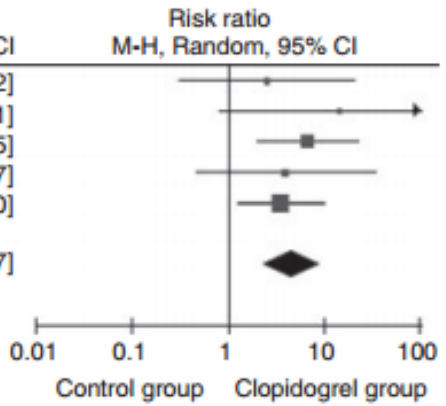


Are We Ready to Change Our Practice for Polypectomy on Clopidogrel?

- Recent meta-analysis showed increased risk of *delayed* bleeding
  - RR 4.66 (95% CI, 2.37-9.17; p<0.00001)

Study or Subgroup	Clopidogrel Events	Clopidogrel Total	Control Events	Control Total	Weight	Risk ratio M-H, Random, 95% CI
Feagins 2011	1	118	6	1849	10.3%	2.61 [0.32, 21.52]
Feagins and Iqbal 2013	5	210	0	286	5.5%	14.96 [0.83, 269.11]
Grossman 2010	3	70	15	2380	31.0%	6.80 [2.01, 22.95]
Rodino 2011	1	25	4	400	9.9%	4.00 [0.46, 34.47]
Singh 2010	5	142	12	1243	43.3%	3.65 [1.30, 10.20]
Total (95% CI)		565		6158	100.0%	4.66 [2.37, 9.17]
Total events	15		37			

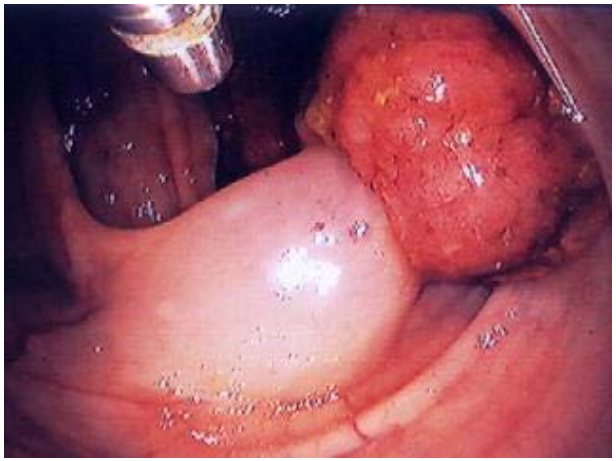
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.58$, df = 4 ($P = 0.81$); $I^2 = 0\%$
Test for overall effect: $Z = 4.45$ ($P < 0.00001$)

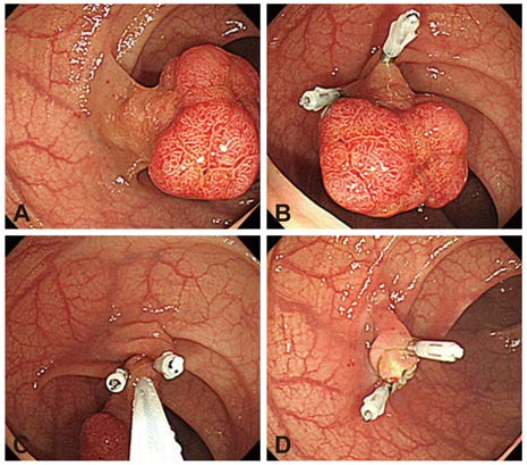


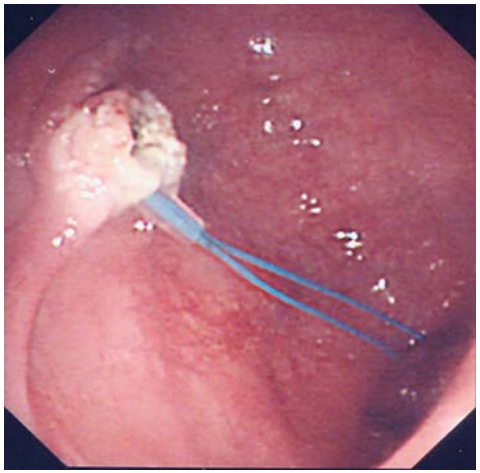
Gandhi S, et al. Aliment Pharmacol Ther 2013.

Endoscopic Interventions Can Decrease Bleeding After Elective Polypectomy

First author, year	Patients, n	Methods compared	Polyp size, mm	Bleeding incidence (immediate + delayed)	P value
Dobrowolski, 2004 [28]	69	Adrenaline vs. no intervention	>10	2% vs. 16%	<0.05
Lee, 2007 [29]	486	Adrenaline vs. saline injection	>20	4.9% vs. 10.4%	0.03*
Iishi, 1996 [30]	89	Detachable loop ligating device vs. no intervention	>10	0 vs. 12%	0.02*
Di Giorgio, 2004 [31]	488	Detachable loop ligating device vs. adrenaline vs. no intervention	22.1 vs. 24.7 vs. 21.5	1.8% vs. 3.1% vs. 7.9%	n.s.†
Kouklakis, 2009 [32]	64	Adrenaline vs. detachable loop ligating device + clip	>20	12.5% vs. 3.1%	0.02
Paspatis, 2006 [33]	159	Adrenaline vs. adrenaline + detachable loop ligating device	>20	10.6% vs. 2.3%	0.02
Lee, 2009 [34]	475	Argon plasma coagulation vs. no intervention	9.8 vs. 9.5	2.5% vs. 4.3%	n.s.







Endoscopy and antiplatelet agents. ESGE Guideline 2011.

Judging the Need for Polypectomy Before Colonoscopy?

- Impractical to classify *a priori* the preprocedural risk of bleeding
  - Every elective colonoscopy could involve need to remove polyps
- All patients at potential high risk of bleeding
- Diagnostic colonoscopy followed by therapeutic colonoscopy off antithrombotic agent vs hold antithrombotic agent initially?
  - Cost effective to withhold warfarin before screening colonoscopy (Gerson LB, et al. Am J Med 2004)

Back to Our Patient

- Definitive management of biliary stones with ERCP
- High risk for thromboembolic complications
  - Cannot discontinue ASA/clopidogrel for 6-12 months
- ERCP with sphincterotomy inc risk of GI bleeding

Post-ERCP Sphincterotomy Hemorrhage (PESH)

- Endoscopic biliary sphincterotomy (ES) bleeding rates 0.3 – 2%[1]
- Risk factors: cholangitis, coagulation disorders, institution of anticoag w/in 3d of sphincterotomy, bleeding observed during procedure[2]
- 2% of pts regardless of use of ASA or NSAIDs in the 3d preceding procedure[3]
  - PESH and APA (6/298) vs PESH and no APA (42/2299); p=0.99
- No adequately powered studies assessing risk of PESH in patients taking thienopyridines

1. Kwok A, et al. Am J Gastroenterol 2009.
2. Freeman ML. Curr Gastroenterol Rep 2003.
3. Freeman ML, et al. N En J Med 1996.

Options for Removing Biliary Stones in Dual APA Therapy

- **ERCP with repeated biliary stenting until APA monotherapy**
  - Risk of cholangitis, risk of multiple procedures
- **ERCP with standard biliary sphincterotomy**
  - No PESH in retrospective review of 8 patients undergoing ES with dual APA therapy[1]
- **ERCP with balloon dilation (EPBD)**
  - High risk of post-ERCP pancreatitis (PEP)
    - Higher rates of severe morbidity following EPBD c/t ES (p=0.004) including severe PEP (p=0.01)[2]
  - May reduce risk with temporary pancreatic stent
- **ERCP with small sphincterotomy + balloon dilation**
  - No data for this technique with pts on dual APA therapy
  - Intraprocedural oozing 32%, clinically significant bleeding 7%[3]

ES = endoscopic sphincterotomy

1. Samie A, et al. Hepatogastroenterology 2013.
2. Disario JA, et al. Gastroenterology 2004.
3. Misra SP, et al. Endoscopy 2008.

When to Stop Antithrombotic Before Elective Endoscopy

Drugs	Timing of cessation	Grade of recommendation	Special considerations
Warfarin	3-5 days	Grade 1B	INR before procedure Vitamin K Bridging therapy
Heparin	4-6 hours	Grade 1C	
LMWH	Daily dose – 24h Twice daily – last dose morning before	Grade 1C	
ASA/NSAIDs	If decision made to cease: 7-10 days	Grade 2C	
Clopidogrel	5-10 days	Grade 1C	Start ASA for pts on monotherapy

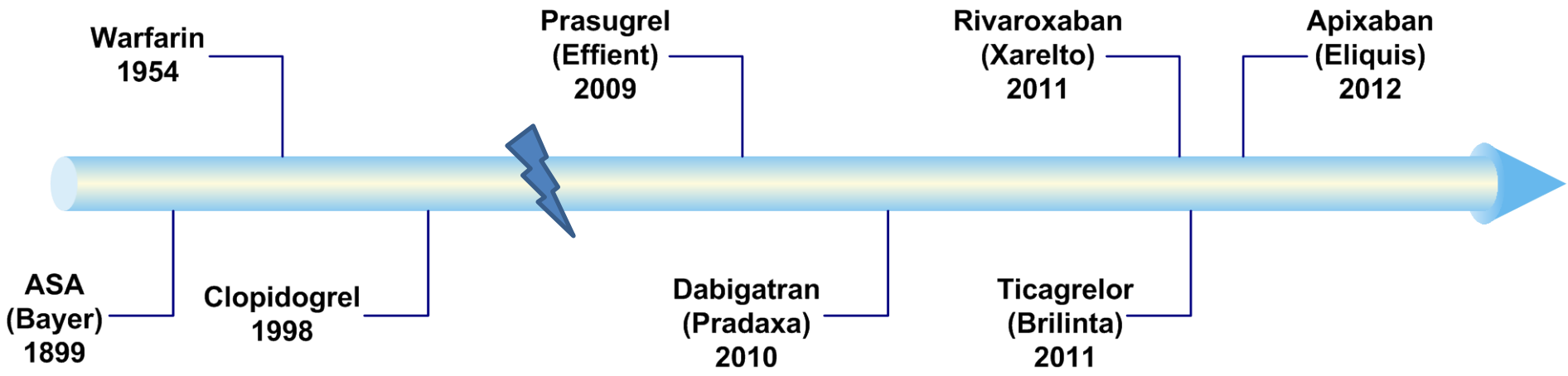
Kwok A, et al. Am J Gastroenterol 2009.

When to Resume Antithrombotic Therapy Following Elective Endoscopy

Drug	Timing of Reinstitution	Grade of recommendation	Special considerations
Warfarin	Same night	Grade 1C	Consider starting ≥ 3 days if sphincterotomy, polypectomy, EMR
Heparin	2-6 hours after procedure	N/A	
LMWH	24 hours after procedure	Grade 1C	Higher risk procedure: start 48-72h after and at lower dose
ASA/NSAIDs	Next day (if decision made to hold)	Grade 2C	
Clopidogrel	Next day	Grade 2C	Consider delayed reinstitution if higher risk procedure performed

Kwok A, et al. Am J Gastroenterol 2009.

Changing Face of Antithrombotics



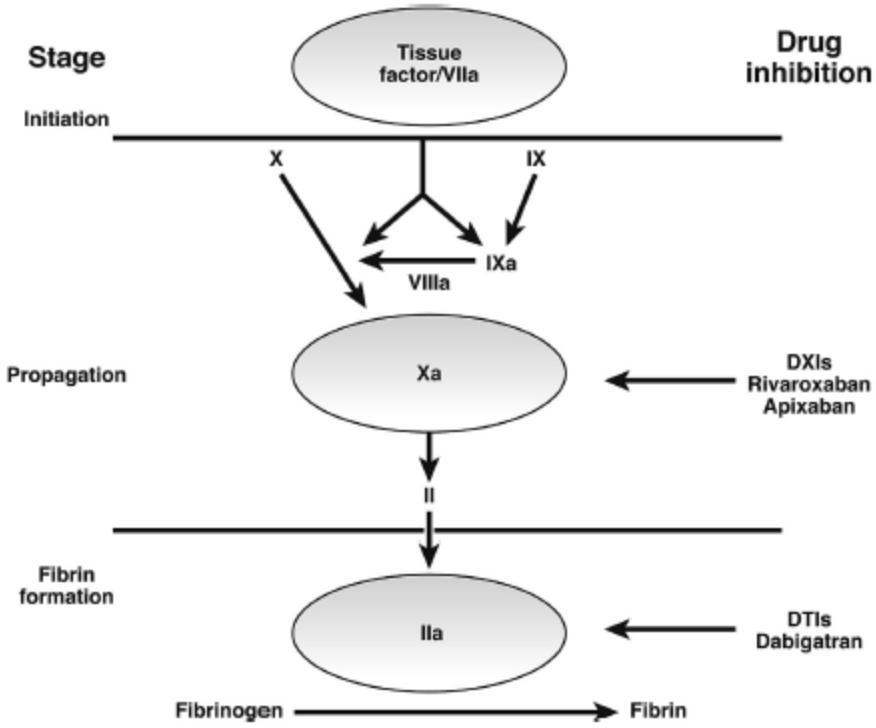
Year drug first marketed

New Oral Anticoagulant and Antiplatelet Agents

- Many physicians unfamiliar on mechanism of action, indications for use, pharmacokinetics
- Limited data on management during elective endoscopic setting
- Limited data on management during urgent/emergent endoscopic procedures for acute GI bleed

Novel Oral Anticoagulants (NOACs)

- **Dabigatran (Pradaxa)**
  - Prophylaxis for nonvalvular afib
- **Rivaroxaban (Xarelto)**
  - Prophylaxis for nonvalvular afib
  - Prophylaxis of DVT/PE after surgery
  - Acute DVT/PE
- **Apixaban (Eliquis)**
  - Prophylaxis for nonvalvular afib



Baron T, et al. CGH 2014.

Overview of NOACs

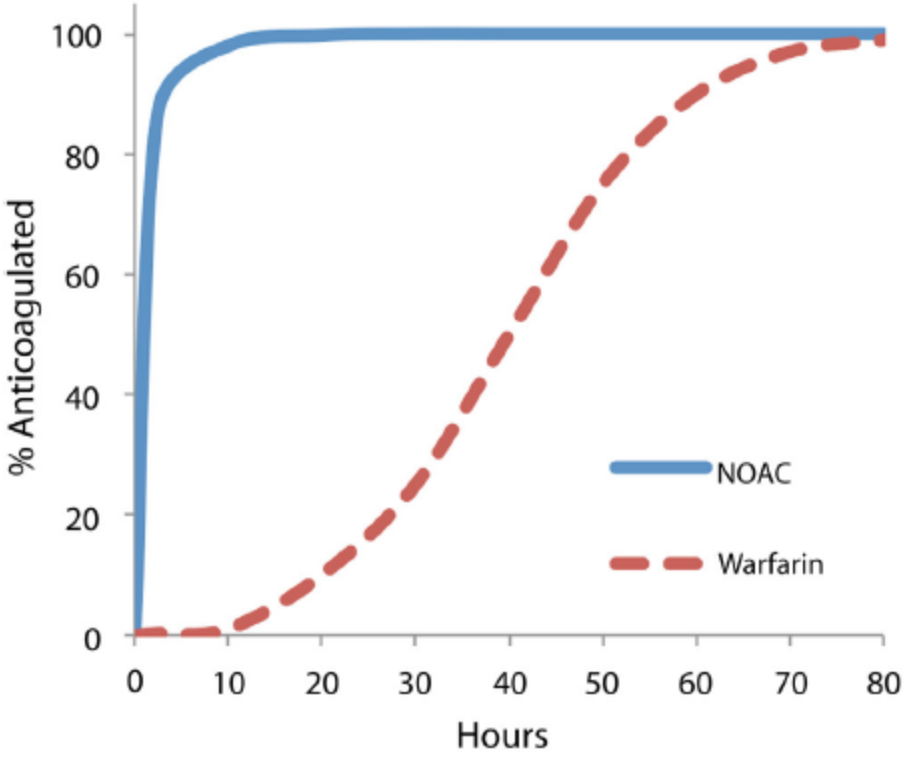
Agent	Onset of action (hours)	Half-life based on CrCl	Management of uncontrolled bleeding
Dabigatran	1-3	> 80 mL/min, 14h 50-79 mL/min, 17h 30-49 mL/min, 19h < 30 mL/min, 28h	Hemodialysis, charcoal hemoperfusion, consider FEIBA or recombinant activated Factor VIIa
Rivaroxaban	1-3	> 80 mL/min, 8h 50-79 mL/min, 9h 30-49 mL/min, 9h < 30 mL/min, 9.5h	Consider PCCs
Apixaban	1-3	> 50 mL/min, 15h < 30-49 mL/min, 18h	Charcoal hemoperfusion, consider PCCs

PCC = prothrombin complex concentrates
FEIBA = factor eight inhibitor bypass activity

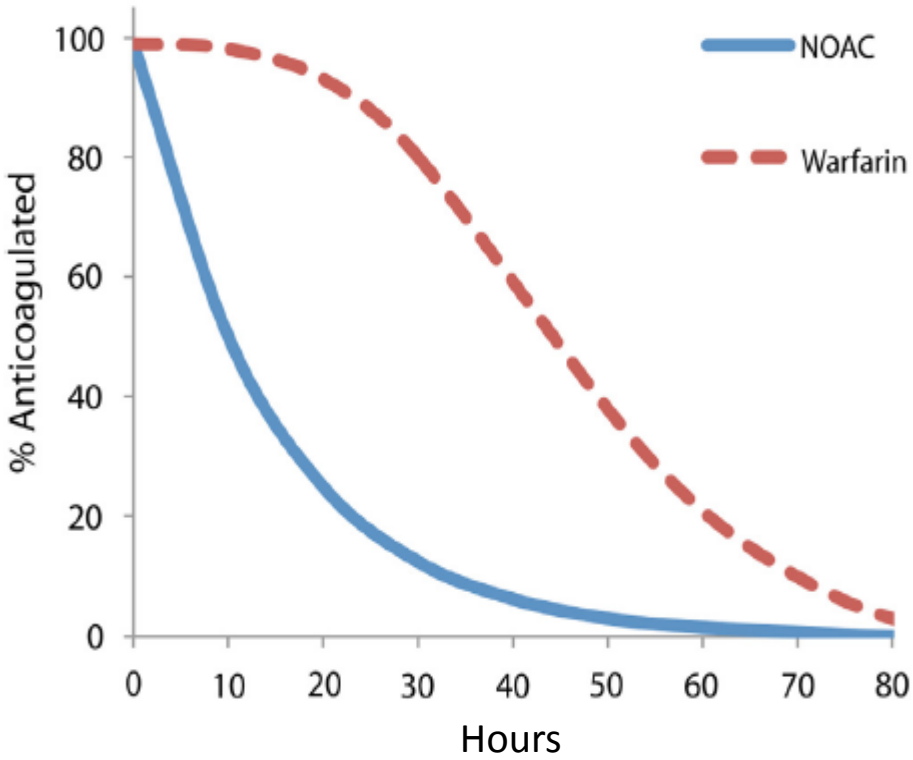
Baron T, et al. CGH 2014.

Pharmacodynamics: Warfarin vs NOACs

ONSET



OFFSET



* Based on normal liver and kidney function

Desai J, et al. GIE 2013.

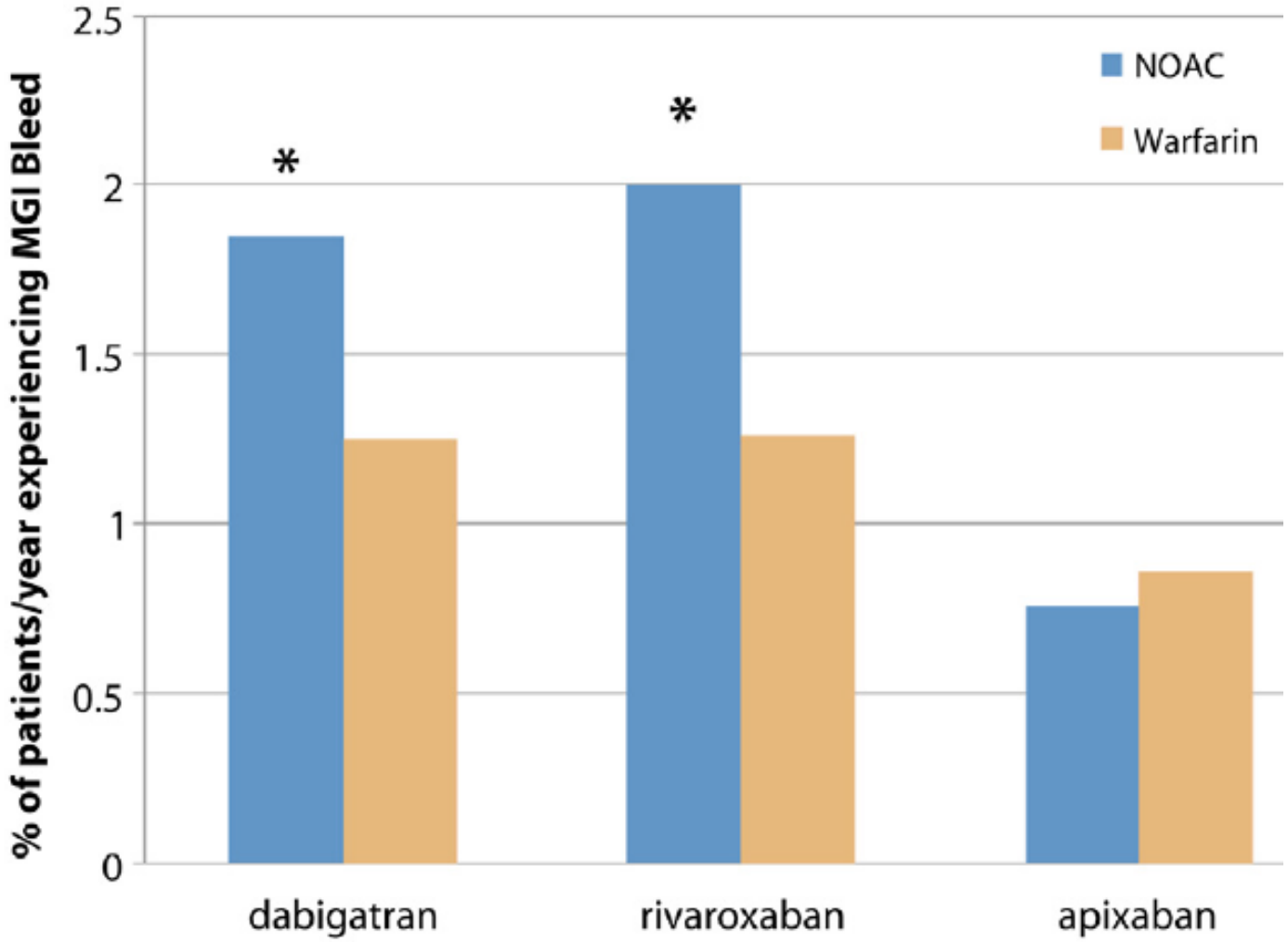
Effects of NOACs on Routine Hemostatic Tests

Drug	aPTT	PT	TT	ECT	Anti-FXa activity assays	Comment
Dabigatran	Moderately sensitive; reflects relative intensity of effect	Insensitive	Highly sensitive	Sensitive; good linear relationship; not uniformly available	Not useful	Normal aPTT and TT likely exclude substantial drug effect
Rivaroxaban	Reasonably sensitive	Insensitive and reagent-dependent	No effect	No effect	Probably accurate	A normal PT or anti-Xa level likely exclude clinically relevant circulating drug
Apixaban	Reasonably sensitive	Insensitive and reagent dependent	No effect	Unlikely to have effect	Probably accurate	A normal anti-Xa level exclude clinically relevant circulating drug

TT = thrombin time

Baron T, et al. CGH 2014.

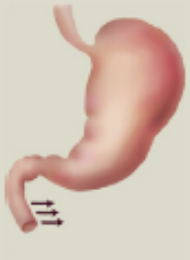
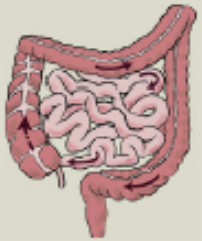
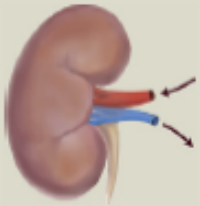
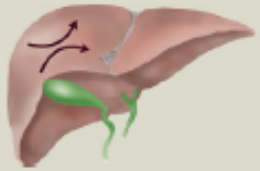
NOACs Associated with Higher GIB Rates



* Statistically significant inc rate of GIB c/t warfarin based on RE-LY, ROCKET-AF and ARISTOTLE studies

Desai J, et al. GIE 2013.

Absorption and Elimination of Warfarin and NOACs

	Bioavailability	Active anticoagulant present in GI tract	Renal excretion	Hepatic metabolism
				
Warfarin	100%	None	None	High
Dabigatran	7%	High	High	Low
Rivaroxaban	66%	Moderate	Moderate	Moderate
Apixaban	50%	Moderate	Moderate	Moderate

Desai J, et al. GIE 2013.

When to Hold and Resume NOACs Before and After Elective Endoscopy

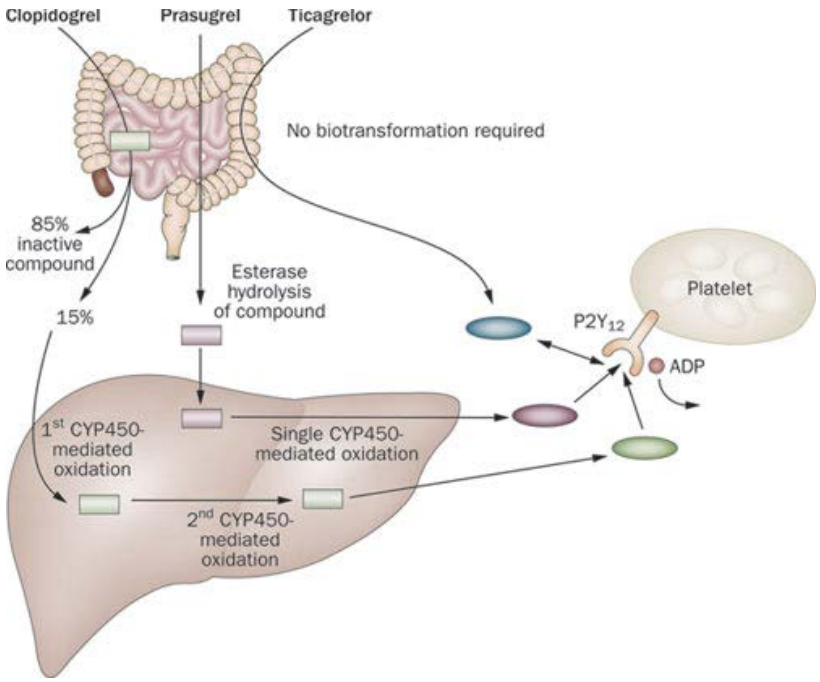
	Dabigatran	Rivaroxaban	Apixaban
HOLD*			
Standard bleeding risk procedure	Continue NOAC or hold morning dose		
High bleeding risk procedure	1-2 days minimum, consider 2-4 days		
RESUME*			
Standard risk of bleeding	Within 12-24 hours		
High risk of bleeding	Delay for at least 48 hours		

* based on normal renal function

Desai J, et al. GIE 2013.
Baron T, et al. CGH 2014.
Parekh P, et al. Am J Gastroenterol 2014.

New Oral Antiplatelet Agents

- **Prasugrel (Effient)**
  - Prevention of thrombotic cardiovascular complications in acute coronary syndromes with PCI
- **Ticagrelor (Brilinta)**
  - Prevention of thrombotic cardiovascular complications in acute coronary syndromes with or without coronary stents



Nature Reviews Cardiology 8, 547-559 (October 2011).

New Oral Antiplatelet Agents

	Clopidogrel	Prasugrel	Ticagrelor
Mechanism of action	ADP P2Y12-receptor antagonist		
Reversibility	Irreversible	Irreversible	Reversible
Onset of effect	2-4 hours	30 minutes	30 minutes
Duration of effect	3-10 days	5-10 days	3-4 days
Withdraw before endoscopy	**5-10 days**	**7 days**	**5 days**
Resume after endoscopy	**Within 48 hours**	**Discuss with cardiologist. Caution as these drugs have more rapid onset.**	
Lab monitoring	None (consider platelet function testing)		
Emergency reversal agents	Consider platelet transfusion		

Desai J, et al. GIE 2013.
Baron T, et al. CGH 2014.

Conclusions

- Risks for GI bleeding and thrombotic events can be classified as high vs low risk
- Decision to stop, reverse or continue antithrombotic agents should be based on balance of these risks
- ASA/NSAIDs do not need to be stopped prior to procedures but decision can be individualized
- Data for managing antithrombotics for screening colonoscopy and polypectomy is evolving
- Guidelines are valuable but not a substitute for careful personalized risk assessment strategy involving patient, endoscopist and consulting physicians