Exploring the Gray Areas of Anticoagulation

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Objectives

- Re-assess historical "gray areas" for Direct Oral Anticoagulant (DOAC) use including in obesity, mechanical heart vales, antiphospholipid syndrome (APS) mechanical heart valves, and treatment of left ventricular (LV) thrombus
- Explore the anticoagulation pipeline including Factor XI inhibitors

DOAC FDA labeled indications

	Apixaban (Eliquis)	Rivaroxaban (Xarelto)	Dabigatran (Pradaxa)	Edoxaban (Lixiana)
Approved Indication	• Stroke prevention in non-valvular afib • Treatment of DVT/PE • Reduction of recurrence of DVT/PE following initial treatment • Post-operative VTE prophylaxis	• Stroke prevention in non-valvular afib • Treatment of DVT/PE • Reduction of recurrence of DVT/PE following initial treatment • Post-operative VTE prophylaxis • Extended VTE prophylaxis in acutely medically ill • Reduction in risk of major cardiovascular events in patients with chronic CAD or PAD	• Stroke prevention in non-valvular afib • Treatment of DVT/PE • Reduction of recurrence of DVT/PE following initial treatment • Post-operative VTE prophylaxis	• Stroke prevention in non-valvular afib • Treatment of DVT/PE

Lexi-Drugs. UpToDate Lexidrug

DOAC Dosing

	Apixaban (Eliquis)	Rivaroxaban (Xarelto)	Dabigatran (Pradaxa)	Edoxaban (Lixiana)
Afib	5mg BID	20mg daily	150mg BID	60mg once daily
VTE Treatment	**10mg BID x7 days** following by 5mg BID	**15mg BID x21days** followed by 20mg daily	150mg BID after* **>5 days of parenteral therapy**	60mg daily after* **5-10 days of parenteral therapy**
Reduction of recurrence	2.5mg BID	10mg daily	150mg BID	
Surgical prophylaxis	2.5mg BID	10mg daily	110 mg once then 220 mg daily (Post-op)	
Other		**Reduction in risk of CV events**: 2.5mg BID		

Lexi-Drugs. UpToDate Lexidrug

Warfarin vs DOAC

Indication	Warfarin	DOAC
Non-valvular atrial fibrillation	✓	✓*
Valvular atrial fibrillation	✓*	X
Mechanical heart valve	✓*	X
Venous thromboembolism (VTE)	✓	✓*
Antiphospholipid Syndrome (APS)	✓*	X
Left Ventricular (LV) thrombus	✓*	✓

✓ denotes preferred agent**

Benjjani A, et al. JACC. 2024; 3: 444-465

Anticoagulation Special Populations: Obesity

DOAC use in Obesity: VTE

J Thromb Haemost, 2021; 19:1874-1882

Per International Society on Thrombosis and Hemostasis (ISTH) guidance 2021:

- For treatment of VTE and primary prevention of VTE:
  - May use standard doses of **rivaroxaban or apixaban** regardless of high BMI and weight
  - AVOID **Dabigatran, edoxaban** in patients with a BMI >40 kg/m^2 or weight >120 kg in VTE

	Phase 3 Studies Comparing DOACs with Vitamin K Antagonist (VKA) in VTE		Phase 4 Studies Comparing DOAC with Vitamin K Antagonist (VKA) in VTE (Including retrospective, prospective & meta-analyses)	
	BMI >35 or BW >120kg	BMI >40	BMI >35 or BW >120kg	BMI >40
Apixaban	X	X	**Similar outcomes**	**Similar outcomes**
Dabigatran	X	X	X	X
Edoxaban	X	X	X	X
Rivaroxaban	**Similar outcomes**	X	**Similar outcomes**	**Similar outcomes**
Pooled DOAC	**Similar outcomes**	X	**Similar outcomes**	**Similar outcomes**

DOAC use in Obesity: Atrial fibrillation

Patel et al (2024):

- Analyzed data from COMBINE AF (pooled patient data from 4 pivotal randomized trials of NOAC vs warfarin in atrial fibrillation)
- Effect of DOAC on outcomes of stroke/systemic embolism generally consistent across spectrum of BMI and body weight relative to warfarin
- Reduction in intracranial hemorrhage by DOAC appears preserved across spectrum of BMI and body weight relative to warfarin

Circulation. 2024;1349:932-943

DOAC use in Obesity

- For both treatment of VTE and stroke prophylaxis in atrial fibrillation in obesity ≥40kg/m^2 consider DOAC therapy
  - The use of apixaban and rivaroxaban at standard doses is appropriate
  - Avoid use of dabigatran and edoxaban
- Data remains limited in patient with **BMI ≥ 50kg/m^2** and **weight >150kg** as these populations remain underrepresented in trials
  - Risk vs benefit discussion in these populations
  - Potentially more data for rivaroxaban > apixaban
- Recommend against routine monitoring of DOAC levels

Anticoagulation Special Populations: Mechanical Heart Valve

DOAC use in Mechanical Heart Valves

RE-ALIGN (2013)

- Dabigatran vs. warfarin in patients undergoing bileaflet mechanical aortic and/or mitral valve replacement OR prior valve replacement >3 months prior
- Interim analysis showed **excess thromboembolism and bleeding** compared to warfarin
- Trial stopped early as a result

PROACT Xa (2023)

- Apixaban vs. warfarin in patients with On-X aortic mechanical aortic valve implanted at least 3 months prior to enrollment
- Interim analysis showed **excess thromboembolism** compared to warfarin
- Trial also stopped early as a result

N Engl J Med 2013;369:1206-1214
NEJM Evid 2023; 7: doi: 10.1056/EVIDoa2300067

DOAC use in Mechanical Heart Valves

Given the results of the previous two trials, **DOAC use** in Mechanical Heart Valves is contraindicated and **should be avoided due to excess thromboembolic risk**

Anticoagulation Special Populations: Antiphospholipid Syndrome (APS)

DOAC use in APS

Blood. 2018; 132:1365-1371
Ann Interm Med. 2019; 171: 685-694
J Am Coll Cardiol. 2023; 81: 16-30

TRAPS (2018) Randomized controlled trial; non-inferiority

- Rivaroxaban vs VKA in patients with triple-positive APS (n=120)
- Trial was **terminated early** after primary outcome of thromboembolic events, major bleeding, or death 19% in rivaroxaban arm vs 3% VKA; HR 6.7; 95% CI 1.5-30.5; P=0.01

Ordi-Ros et al (2019) Randomized controlled trial; non-inferiority at RR 1.40

- Rivaroxaban vs VKA in patients with thrombotic APS (n=190)
- Primary efficacy outcome of proportion of patients with new thrombotic events
- Recurrent thrombosis occurred in 11 patients (11.6%) in rivaroxaban, 6 (6.3%) VKA; RR **1.83** [95% CI, 0.71 to 4.76]
- Stroke occurred 9 times in rivaroxaban arm, 0 in VKA RR, 19.00 [CI, 1.12 to 321.9]

Khairani et al (2022) Meta-analysis of 4 Randomized controlled trials

- DOACs compared to VKA associated with increase of subsequent arterial thrombotic events; OR: 5.43; 95% CI: 1.87-15.75; P < 0.001
- DOACS compared to VKA associated with increase of composite arterial thrombotic events or VTE OR: 4.46; 95% CI: 1.12-17.84; P = 0.03

DOAC use in APS

- 2019 EULAR Recommendations for the management of antiphospholipid syndrome in adults
  - DOACs should be avoided in patients with triple aPL positivity and history of arterial events
  - DOACS may be considered in patients with difficulty achieving target INR or contraindications to VKA
- However, given information published after the guidelines it appears DOACS are associated with **increased risk of arterial thrombosis and stroke** regardless of history of arterial thrombosis and positivity status (triple vs. double vs. single)

Anticoagulation Special Populations: LV Thrombus

Treatment of LV Thrombus

LV thrombus in non-ischemic cardiomyopathy

- Typically anticoagulation for 3-6 months. May consider discontinuation if LVEF improves to >35% in addition to resolution of thrombus
- May consider indefinite anticoagulation without improvement in LVEF despite optimal GDMT, persistent apical akinesis/dyskinesis or patients with proinflammatory/hypercoagulable states

•LV thrombus after Acute Myocardial Infarction

- Optimal duration of anticoagulation is unknown, consider 3-6 months
- Risk vs. benefit of anticoagulation in addition to antiplatelet therapy

Mural (laminated) thrombus

- If persistent (particularly if organized/calcified) risk of embolization likely low and shared-decision making regarding continuation of oAC

Circulation. 2022; 146:e205–e223

DOAC use in LV Thrombus

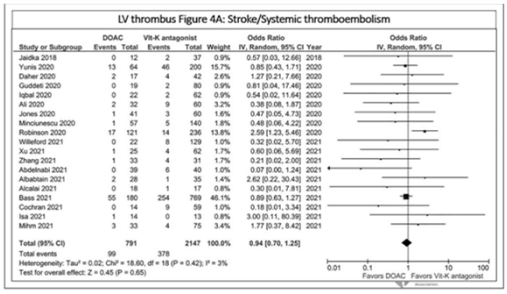
Per Management of Patients at Risk for and With Left Ventricular Thrombus: A Scientific Statement From the American Heart Association (2022):

"DOACs are considered by this writing group to be a reasonable alternative to VKA in patients with LV thrombus"

Circulation. 2022; 146:e205–e223

DOAC use in LV Thrombus

Circulation. 2022; 146:e205–e223



DOAC use in LV Thrombus

- Per currently available data, DOACs (apixaban and rivaroxaban) are non-inferior to warfarin in treatment of LV thrombus
- DOACs may be preferable in several patient populations:
  - Patients at higher bleed risk
  - Need for concomitant anti-platelet therapy (DAPT)
  - Patients with barriers to regular INR monitoring or a time in therapeutic range (TTR) < 50%
- Limited data exists regarding appropriate DOAC dosing strategies (dosing for use in atrial fibrillation vs. treatment of acute VTE)

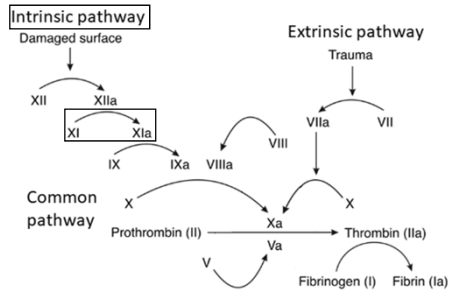
Circulation. 2022; 146:e205–e223

Anticoagulation Pipeline: Anti-Xi inhibitors

Anti-XIa

- Anti-Xa inhibitors (apixaban, rivaroxaban) have become first line anticoagulant in many indications as previously discussed
- Gaps in anticoagulation therapy remain
  - Warfarin still preferred in certain patient populations (mechanical valve, antiphospholipid syndrome)
  - Optimal anticoagulation in populations at higher risk of bleeding (elderly, ESRD)

Anti-XIa



Anti-XIa

- Stroke prevention in atrial fibrillation
- Thromboprophylaxis in orthopedic surgery
- Secondary prevention following Acute Coronary Syndrome (ACS)
- Secondary prevention after non-cardioembolic stroke
- Thromboprophylaxis after foreign material implantation

Anti-Xia

Pharmaceuticals (Basel). 2023; 16:866

*Study completed, data available

Drug	Type	Admin/dosing	Trial
Abelacimab	Monoclonal antibody FXI/FXIa	Subcutaneous (SQ), monthly	Phase III (treatment of cancer-associated VTE) Phase III (atrial fibrillation) Phase II (atrial fibrillation)*
Asundexian	Small molecule	Oral, daily	Phase III (atrial fibrillation)* Phase II (post-ACS) Phase II (post-stroke)
Fesomersen	Antisense oligonucleotide of FXI	SQ, weekly	Phase II (thrombosis in ESRD)*
Milvexian	Small molecule	Oral, daily	Phase III (atrial fibrillation) Phase III (post-ACS) Phase III (post-stroke) Phase II (VTE prophylaxis)* Phase II (post-stroke)*
Osocimab	Monoclonal antibody FXIa	Intravenous (IV)/SQ, monthly	Phase II (ESRD)*
Xisomab 3G3	Monoclonal antibody FXI	Intravenous	Phase II (prevention of catheter-associated thrombosis in cancer)

Anti-Xia: asundexian

Stroke prevention in atrial fibrillation

- Phase II: PACIFIC-AF (safety)
  - Asundexian 20/50mg daily vs apixaban BID: 0.42 (0.25-0.67) **significantly lower rate** of all **bleeding** events
- Phase III: OCEANIC-AF (safety/efficacy)
  - Asundexian 50mg daily vs apixaban BID: Stopped early due to **inferior efficacy** in preventing **stroke/systemic embolism**, data not yet released

The Lancet. 2022; 10333:1383-1390
Bayer Global. https://www.bayer.com/media/en-us/oceanic-af-study-stopped-early-due-to-lack-of-efficacy

Anti-Xia: abelacimab

Stroke prevention in atrial fibrillation

- Phase II: AZALEA-TIMI 71 (safety)
  - Abelacimab 90mg/150mg monthly vs rivaroxaban 20mg daily: terminated early due to **greater than expected benefit** in major/non-clinically relevant major **bleeding** (1.0% vs 0.7% vs 3.7%; $p < 0.05$)
- Phase III: LILAC-TIMI 76 (safety/efficacy)
  - TBD

AHA Scientific Session Late Breaking Clinic Trial. November 12, 2023. Philadelphia, PA

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- Ruff, CT on behalf of the AZALEA-TIMI 71 Committee. AZALEA-TIMI 71. AHA Scientific Session Late Breaking Clinic Trial. November 12, 2023. Philadelphia, PA

Antiplatelets for Chronic Coronary Disease and Acute Coronary Syndromes

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Objectives

- Describe the role of aspirin and oral $P2Y_{12}$ inhibitors for patients with chronic coronary disease (CCD) or acute coronary syndromes (ACS) with or without percutaneous coronary intervention (PCI)
- Evaluate the advantages and disadvantages of the different $P2Y_{12}$ inhibitors
- Discuss how antiplatelet recommendations change if oral anticoagulation is indicated

Case #1

62 YO F admitted to the Emergency Department (ED)
- Abdominal pain and nausea. A couple of days before she took a test capsule for GI study.
- Sudden urge to have a bowel movement.
- In bathroom had sudden onset of severe chest pain
  - EKG showed ST-elevation

PMH:
CAD – LAD stent (unknown type) 2016
Hyperlipidemia
Chronic diarrhea

PSH:
Cholecystectomy 1992

Case #1

- **Patient instructed to stop both clopidogrel (Plavix) and aspirin 9 days prior to GI workup**

- STEMI alert
  - Acute thrombosis of previous Left Anterior Descending (LAD) stent
  - Left heart catheterization with successful thrombectomy and balloon angioplasty

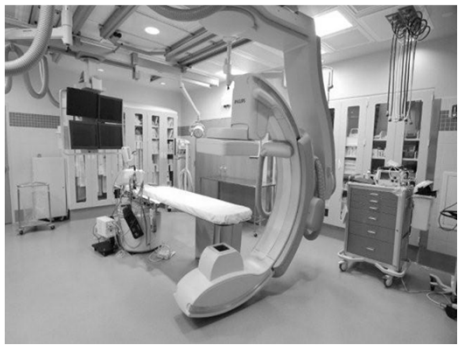
Case #2

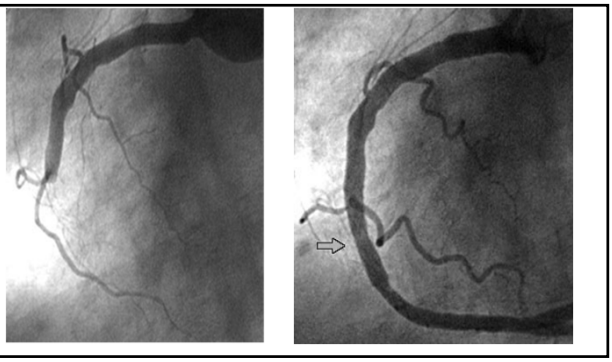
57 YO M
- Admitted for an elective urology procedure

PMH
CAD with a history of 3 cardiac stents (unknown type) in 2019
Peyronie's and Erectile Dysfunction

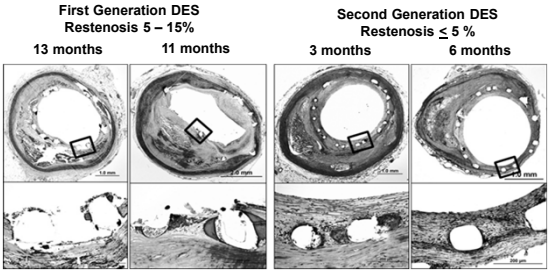
PSH
Colonoscopy

- **Post Procedure**
- Chest Pain and diaphoresis
- EKG showed ST-elevation
- Emergent cath - 100% thrombotic occlusion of prox and mid Right Coronary Artery (RCA) at site of previous stents S/P thrombectomy and PCI with bare metal stent placement x 3
- **Patient instructed to discontinue aspirin for 10 days prior to procedure**





Stent Evolution: Restenosis vs Stent Thrombosis



Otsuka F. Circulation 2014;129:211-223

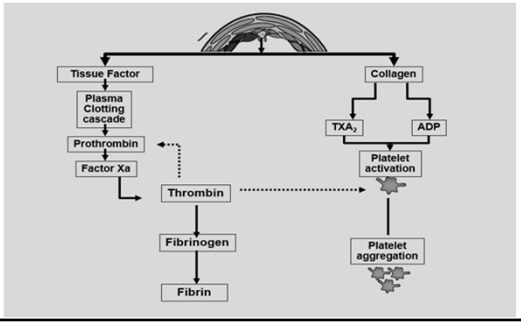
Risk of Mortality
Stent Thrombosis versus Bleeding

Mortality associated with stent thrombosis	
Drug Eluting Stents	Bare Metal Stents
17 - 45%	9 - 21%

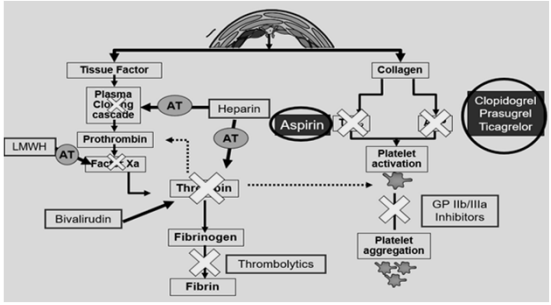
Mortality associated with bleeding after PCI at 12-24 months
7.3 - 13%

Thrombosis 2012;2012:956-962
JACC 2015;66:1036-45
Circ Cardiovasc Interv 2016;9:e003519
Circ Cardiovasc Interv 2010;3:140-7
JACC 2015;65:1411-20
JACC Cardiovasc Interv 2016;9:1450-7

Essentials of Thrombosis



Sites of Antithrombotic Action

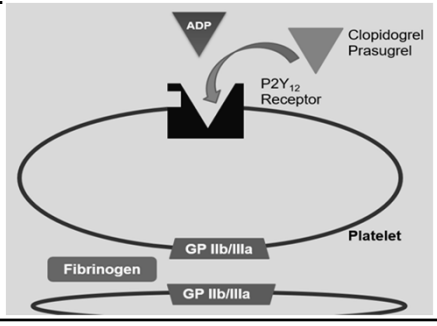


Oral $P2Y_{12}$ Inhibitor Comparison

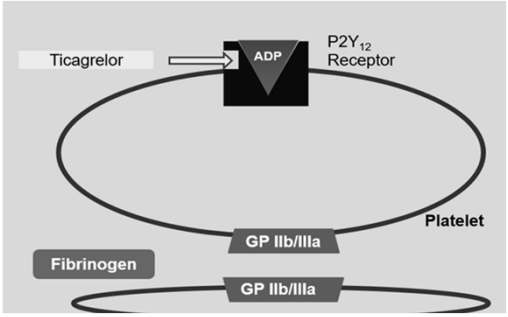
	Clopidogrel	Prasugrel	Ticagrelor
Loading Dose	300-600 mg	60 mg	180 mg
Maintenance Dose	75 mg daily	10 mg daily	90 mg BID
Prodrug	Yes	Yes	No
Reversible	No	No	Yes
Metabolism	CYP 2C19	CYP 3A, 2B6	CYP 3A
Time to 50% Platelet Inhibition (min)	120-240 (600 mg)	60	30
Maximal Platelet Inhibition (%)	35	79	88

Potency →

$P2Y_{12}$ Mechanism of Action



$P2Y_{12}$ Mechanism of Action



Benefits of Dual Antiplatelet Therapy (DAPT) in Acute Coronary Syndromes

Study	Indication	Duration (months)	Antiplatelet Therapy	Incidence of Primary Composite Endpoint* (%)	
CURE	ACS	12	Aspirin vs Aspirin + Clopidogrel	11.4 9.3	p<0.001
Triton-TIMI 38	ACS/PCI	15	Aspirin + Clopidogrel vs Aspirin + Prasugrel	12.1 9.9	p<0.001
PLATO	ACS	12	Aspirin + Clopidogrel vs Aspirin + Ticagrelor	11.7 9.8	p<0.001

***Primary Composite Endpoint** – Death from Cardiovascular (CV) Causes, Non-fatal myocardial infarction (MI) or Non-fatal stroke

N Engl J Med 2001;345:494-502
N Engl J Med 2007;357:2001-2015
N Engl J Med 2009;361:1045-1047

Risks of Dual Antiplatelet Therapy (DAPT) in Acute Coronary Syndromes

Study	Indication	Duration	Antiplatelet Therapy	Incidence of Major Bleeding (%)	
CURE	ACS	12	Aspirin vs Aspirin + Clopidogrel	2.7 3.7	p=0.001
Triton-TIMI 38	ACS/PCI	15	Aspirin + Clopidogrel vs Aspirin + Prasugrel	1.8 2.4	p=0.03
PLATO	ACS	12	Aspirin + Clopidogrel vs Aspirin + Ticagrelor	2.2 2.8	p=0.03

These rates are under the umbrella of a clinical trial **NOT** real world
Patients who require oral anticoagulation are excluded

N Engl J Med 2001;345:494-502
N Engl J Med 2007;357:2001-2015
N Engl J Med 2009;361:1045-1047e

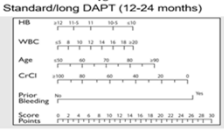
Find the Balance

Increased Ischemic Risk/Risk of Stent Thrombosis (May Favor Longer-Duration DAPT)	Increased Bleeding Risk (May Favor Shorter-Duration DAPT)
Advanced age Acute coronary syndrome presentation Extensive coronary artery disease Diabetes mellitus Chronic kidney disease Prior myocardial infarction Prior stent thrombosis Heart failure Current smoker	• Advanced age • Diabetes mellitus • History of prior bleeding • **Oral anticoagulant therapy** • Female sex • Low body weight Chronic kidney disease • Liver disease • Anemia • Chronic steroid or NSAID therapy
Multi-vessel disease Stent undersizing or underexpansion Small stent diameter Long stent length (>60 mm) Short stent length (<3mm) Bifurcation stents In-stent restenosis Multiple stents (> 3 stents) First-generation drug-eluting stent	

PATIENT FACTORS · ANGIOGRAPHIC FACTORS · PATIENT FACTORS

Levine GN. Circulation 2016;68:1082-1115
Rogiani G. Eur J Intern Med 2020;77:27-29

Tools to Find the Balance

	PRECISE-DAPT Score	DAPT Score
Time of use	At time of coronary stenting	After 12 months of uneventful DAPT
DAPT duration strategies assessed	Short DAPT (3-6 months) vs Standard/long DAPT (12-24 months)	Standard DAPT (12 months) vs Long DAPT (30 months)
Score calculator		
Score range	0 to 100 points	-2 to 10 points
Decision making cut-off	≥ 25 → 3-6 months of DAPT <25 → 12-24 months of DAPT	≥2 → Long DAPT <2 → Standard DAPT
Limitations	• Clopidogrel 88% • Validated in PLATO cohort (Ticagrelor) • **Excluded patients on long term anticoagulation**	• Clopidogrel 65%; prasugrel 35% • Excluded prior bleeding/thrombotic events • **Excluded patients on long term anticoagulation**

Yeh RW. JAMA. 2016;26:315:1735-49
Costa F. The Lancet. 2017;389:192-34

Dual Antiplatelet Therapy (DAPT) Recommendations (without oral anticoagulation)

Bare Metal Stent for Acute Coronary Syndrome *(2016 DAPT Guidelines)*
Aspirin 81 mg daily uninterrupted lifelong plus clopidogrel 75mg daily or prasugrel 10mg daily or ticagrelor 90mg twice daily for a minimum of 1 month (Class 2) ideally at least 12 months (Class 1)
Drug-eluting Stent for Acute Coronary Syndrome
Aspirin 81 mg daily plus clopidogrel 75mg daily or prasugrel 10mg daily or ticagrelor 90mg twice daily for ideally at least 12 months (Class 1) up to 3 years (Class 2b) followed by SAPT
Bare Metal Stent for Chronic Coronary Disease *(2016 DAPT Guidelines)*
Aspirin 81 mg daily uninterrupted lifelong plus clopidogrel 75mg daily for a minimum of 1 month (Class 1) consider up to 12 months (Class 2)
Drug-eluting Stent for Chronic Coronary Disease
Aspirin 81 mg daily plus clopidogrel 75 mg daily for 6 months followed by SAPT (Class 1) **Option for High bleeding risk:** Aspirin 81 mg daily plus clopidogrel 75 mg daily for 1 – 3 months followed by clopidogrel 75 mg daily for up to 12 months (Class 2a) followed by SAPT (Class 1)
Medical Management of Acute Coronary Syndrome
Aspirin 81 mg daily uninterrupted lifelong (Class 1) plus clopidogrel 75 mg daily or Ticagrelor 90 mg twice daily for ideally at least 12 months (Class 1)

SAPT = Single Antiplatelet Therapy

Virani SS. J Am Coll Cardiol 2023 82:833-955
Levine GN. Circulation 2016;68:1082-1115

DAPT Recommendations Focus on DES (without oral anticoagulation)

Drug-eluting Stent for Acute Coronary Syndrome
Aspirin 81 mg daily plus clopidogrel 75mg daily or prasugrel 10mg daily or ticagrelor 90mg twice daily for ideally at least 12 months (Class 1) up to 3 years (Class 2b) followed by SAPT
Drug-eluting Stent for Chronic Coronary Disease
Aspirin 81 mg daily plus clopidogrel 75 mg daily for 6 months followed by SAPT (Class 1) **Option for High bleeding risk:** Aspirin 81 mg daily plus clopidogrel 75 mg daily for 1 – 3 months followed by clopidogrel 75 mg daily for up to 12 months (Class 2a) followed by SAPT (Class 1)
Acute Coronary Syndrome without Stent
Aspirin 81 mg daily uninterrupted lifelong (Class 1) plus clopidogrel 75 mg daily or Ticagrelor 90 mg twice daily for ideally at least 12 months (Class 1)

SAPT = Single Antiplatelet Therapy

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DAPT Recommendations Focus on DES (with oral anticoagulation)

Drug-eluting Stent for Acute Coronary Syndrome or Chronic Coronary Disease
Aspirin 81 mg daily plus **clopidogrel** 75 mg daily plus DOAC for up to 1 month followed by **clopidogrel** plus DOAC for up to 6 months (Class 1) followed by DOAC alone (Class 2b) **Option for High bleeding risk:** Aspirin 81 mg daily plus **clopidogrel** 75 mg daily plus DOAC for 1 month followed by **clopidogrel** 75 mg daily plus DOAC for up to 6 months followed by DOAC alone (Class 2a)
Acute Coronary Syndrome or Chronic Coronary Disease without Stent
DOAC Alone (Class 2b)

DOAC = Direct Oral Anticoagulant

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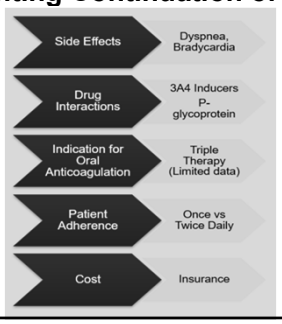
Factors Preventing Continuation of Ticagrelor



Drug Interactions with Ticagrelor

- Ticagrelor is metabolized by CYP 3A
- Weak CYP 3A inhibitor

Strong CYP 3A inhibitors	CYP 3A inducers	CYP 3A substrates
Antiretrovirals	Carbamazepine	Cyclosporine
Clarithromycin	Rifampin	Tacrolimus
Ketoconazole	Phenytoin	Amlodipine
Itraconazole	Dexamethasone	Diltiazem, Verapamil
Voriconazole	Phenobarbital	Ator, simva, lovastatin

- Ticagrelor and active metabolite are P-glycoprotein (PgP) substrates and weak inhibitors PgP
  - Monitor digoxin levels
  - Dabigatran

Switching Between $P2Y_{12}$ Inhibitors

$P2Y_{12}$ Receptor Inhibitors: Dosing and Switching

Loading Dose	Maintenance Dose	If converting to alternative $P2Y_{12}$	
Clopidogrel 600 mg x 1	Clopidogrel 75 mg daily (start the next day)	Ticagrelor 180 mg x 1 then Ticagrelor 90 mg every 12 hours (12 hours after loading dose)	Prasugrel 60 mg x 1 then Prasugrel 10 mg daily (start the next day)
		When escalating to prasugrel or ticagrelor from clopidogrel, the dose can be given regardless of the timing and dosing of the previous clopidogrel regimen	
Prasugrel 60 mg x 1 **Indicated for ACS patient who are managed with PCI. In the setting of an ACS loading dose of prasugrel 60 mg can be given during or after the PCI once the coronary anatomy is known.** Contraindications: History of ICH, TIA/CVA, thrombolytic use in the past 24 hours Relative contraindications: Age ≥75, weight <60 kg, recent trauma/surgery, oral anticoagulant use	Prasugrel 10 mg daily (start the next day)	Clopidogrel 600 mg x 1 (24 hrs after last prasugrel dose) then Clopidogrel 75 mg daily (start the next day)	Ticagrelor 180 mg x 1 (24 hrs after last prasugrel dose) then Ticagrelor 90 mg every 12 hours (12 hours after loading dose)
Ticagrelor 180 mg x 1 **In the setting of an ACS a loading dose of ticagrelor 180 mg can be given immediately at the time of presentation, during, or after the PCI.** Contraindications: History of ICH Relative contraindications: Risk for bradycardia, severe hepatic dysfunction, strong CYP3A4 inhibitor/inducer, severe dyspnea at baseline, oral anticoagulant use, thrombolytic use in the past 24 hours	Ticagrelor 90 mg every 12 hours (12 hours after loading dose)	Clopidogrel 600 mg x 1 (24 hrs after last ticagrelor dose) then Clopidogrel 75 mg daily (start the next day)	Prasugrel 60 mg x 1 (24 hrs after last ticagrelor dose) then Prasugrel 10 mg daily (start the next day)

If converting from ticagrelor or prasugrel to clopidogrel because patient is high bleed risk or has a recent bleed, regardless of time from event, can consider omitting or reducing loading dose after discussion with Interventional Cardiology.

ACS = Acute Coronary Syndrome; CVA = Cerebral Vascular Accident; ICH = intracranial hemorrhage, PCI = Percutaneous Coronary Intervention; TIA = transient ischemic attack

Conclusions

- Understanding the current recommendations for DAPT is clinically important
- Balancing the ischemic and bleeding risk is key
  - Early cessation of DAPT is problematic
  - Patients should remain on at least one antiplatelet medication following stent placement unless on oral anticoagulation
- Patient education is key
  - Pharmacists can be instrumental in providing this education
- Involve the patient's cardiologist to ensure safe transitions of care