Anticoagulation and Antiplatelet update: A case based approach

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No disclosures relevant to this talk

Objectives

1. Discuss the indication for antiplatelet therapy for cardiac diagnosis

2. Discuss the indication for anticoagulation therapy for cardiac diagnosis

3. Discuss the different treatment options and length of treatment with antiplatelet and anticoagulation therapy

Case #1

75 year old female Mrs Ann T Coagulation comes in feeling “heart jumping” with atrial fibrillation and rapid ventricular response. She has mild left ventricular dysfunction and atrial dilation at 5.5 cm. She receives metoprolol and rate is controlled. Her daughter asks “are we going to fix her back to the normal rhythm?”

What are your treatment options?

Does the patient need anticoagulation?

Atrial Fibrillation

Most common arrhythmia in the hospital setting

Preventable cause of stroke

Atrial rate > 300 places the patient at risk for atrial thrombus as well as rapid ventricular response

Rapid ventricular response can lead to hypotension, syncope, congestive heart failure, fatigue

Risks are are CAD, CHF, obesity, diabetes, hypertension, age

Recurrence rates

Upto 70% at 1 year

Majority of the episodes are asymptomatic even when 17% are over 48 hours in duration

At 5 years 25% of patients will have permanent atrial fibrillation

Patients with left ventricular dysfunction, hypertension, advanced age and enlarged atria are likely to have recurrence

New onset afib

Treatment for reduction in thrombus embolization

- Asa
- anticoagulation

How do you determine who to anticoagulate?

Prevention of embolization

CHA2DS2-VASc score is calculated to guide anticoagulation

All patients undergoing pharmacological or DC cardioversion need anticoagulation at least short term

CHADS2-VASC score

Congestive heart failure 1

Hypertension 1

Age >= 75 2

Stroke/tia 2

Diabetes 1

Vascular disease (including aortic plaque) 1

Age 65 to 74 1

Female sex 1

Anticoagulation

Embolization can occur with paroxysmal, permanent or persistent atrial fibrillation

Warfarin reduces risk of cerebrovascular accident if score >=2

Anticoagulation reduces cerebrovascular accident by ⅔

There is 0.4% risk of serious bleeding but this is less than stroke risk

NOAC compared to warfarin

Reduce risk of stroke and bleeding

Significant reduction in hemorrhagic stroke which many times is fatal

Dabigatran has increased risk of gastrointestinal bleeding

What about aspirin and clopidogrel?

Aspirin monotherapy

Even with CHADS2 score of 0 not be studied adequately

2007 meta analysis demonstrated a 20% risk reduction in CVA but not statistically significant

Did not reduce disabling stroke

In one observational study there is higher incidence of stroke compared to no therapy

Aspirin + clopidogrel

Active A trial demonstrated superiority to aspirin alone

Active W trial demonstrated warfarin superior

Turns out bleeding risk of dual antiplatelet therapy is similar to warfarin anticoagulation and NOACs have less bleeding in comparison to dual antiplatelet therapy so if a patient can take aspirin + clopidogrel, they can take anticoagulation

Bridging for warfarin

Not necessary in patient without history of thromboembolism

In patients who present with cerebrovascular accident the net benefit with heparin bridging is neutral when combined with the ICH risk

What about patients undergoing PCI who later develop afib. How many agents do they need?

WOEST trial demonstrated less bleeding and MACE with warfarin + clopidogrel vs triple therapy

NEJM 2016;375:2423-34 Trial randomizing over 2000 patients to:

rivaroxiban (Xarelto) at 15 mg daily with P2Y12 inhibitor (clopidogrel)

Very low dose Xarelto 2.5 mg mg by mouth twice a day (not available in US) and dual antiplatelet therapy

Warfarin with dual antiplatelet therapy

Results

The rates of clinically significant bleeding were lower in the two groups receiving rivaroxaban than in the group receiving standard therapy (16.8% in group 1, 18.0% in group 2, and 26.7% in group 3.

The rates of death from cardiovascular causes, myocardial infarction, or stroke were similar in the three groups (Kaplan-Meier estimates, 6.5% in group 1, 5.6% in group 2, and 6.0% in group 3; P values for all comparisons were nonsignificant).

Conclusion: Avoid triple therapy

In participants with atrial fibrillation undergoing PCI with placement of stents, the administration of either low-dose rivaroxaban plus a P2Y12 inhibitor for 12 months or very-low-dose rivaroxaban plus DAPT for 1, 6, or 12 months was associated with a lower rate of clinically significant bleeding than was standard therapy with a vitamin K antagonist plus DAPT for 1, 6, or 12 months.

The three groups had similar efficacy rates, although the observed broad confidence intervals diminish the surety of any conclusions regarding efficacy.

NOAC dosing

Dabigatran (Pradaxa) 150 mg by mouth twice a day is typical dose if normal renal function. For GFR < 30 may use 75 mg twice daily however ACCP considers it contraindicated at this level of renal function. Reduce dose also with dronedarone or ketoconazole. There is antidote.

Apixaban 5 mg by mouth twice a day but reduced dosing based on age, weight and renal function.

Rivaroxaban 20 mg by mouth daily but reduced dose based on renal function.

Mrs Ann T Coagulation needs surgery soon

Our lady is taking dabigatran

You receive a phone call from the surgeon who wants to do surgery in 2 days and wants to know if that amount of time is good enough

You notice that her calculated GFR has decreased from her previous labs to 28

What do you recommend?

Dabigatran discontinuation

- CrCl 50-30 ml/min – stop **48 hours** prior to the procedure
- If high risk for bleeding stop for **4 days**
- CrCl < 30 - hold drug for 2 – 5 days and > 5 days for high risk bleeding
- In patients at high risk of bleeding a **thrombin time** can be checked 6 – 12 hours prior to surgery – if normal there is no dabigatran present

Apixaban (Eliquis)

- Discontinued at least 48 hours prior to invasive procedure

Rivaroxaban (Xarelto)

- “Stop medication 24 hours prior to procedure”
- However, in elderly patients the half-life can be 11 to 13 hours and therefore at 4 half lives it can be upto and over 48 hours

You later receive a phone call that the medication is too expensive and Mrs Ann does not mind warfarin

Apixaban: Start warfarin and stop apixaban 3 days later, or stop apixaban, begin a parenteral anticoagulant (UFH or LMWH) and warfarin at the time apixaban would have been due, and then stop LMWH or UFH when INR therapeutic.

Dabigatran:

CrCl >50 mL/min: Start warfarin and stop dabigatran 3 days later

CrCl 31-50 mL/min: Start warfarin and stop dabigatran 2 days later

CrCl 15-30 mL/min: Start warfarin and stop dabigatran 1 day later

Rivaroxaban: Start warfarin and stop rivaroxaban 3 days later, or stop rivaroxaban, begin LMWH/UFH and warfarin at same time when the next dose of rivaroxaban would have been given, and then stop LMWH/UFH when INR is acceptable.

*For all warfarin to NOAC conversion. Stop warfarin and start when INR <2. However, the manufacturer advises when INR <3 for rivaroxaban.

Prosthetic valves

-A 76 year old female visits your office 4 months after a valve replacement

-You do not hear a mechanical click and an echo report confirms a bioprosthetic mitral valve

-The patient asks you how long should she be anticoagulated

Mechanical valves

-Aortic. Rec: ASA < 100 mg + warfarin. INR goal is 2-3 unless patient has history of LV dysfunction, prior embolism

    -No need to bridge for surgery but monitor INR closely

-Mitral. Rec: ASA < 100 mg + warfarin. INR goal 2.5-3.5

    -Bridging necessary with heparin or LMWH

Bioprosthetic valves

-Anticoagulation for the first 3 months with warfarin with INR goal 2-3

-Followed by ASA < 100 mg daily

70 year old female with history of bare metal stent to the circumflex

-Above patient with history of bare metal stent (BMS) to the circumflex coronary artery 5 months ago due to ACS presentation at that time

-BMS was implanted as patient had anemia with hemoglobin 8.0 of unknown etiology

-you receive a phone call about discontinuation of clopidogrel as well as aspirin prior to knee surgery which has disabled the patient to the point where she is unable to walk

What do you recommend?

Dual Antiplatelet therapy (DAPT) and non cardiac surgery a common question to the PCP

-stopping too early increases risk of stent thrombosis or myocardial infarction

-continuation may cause bleeding

-3 million PCI worldwide, 7-17% of patients need non-cardiac surgery in the first year

Timing of thrombotic complications post PCI

-6 months irrespective of the stent type (BMS or DES)

-second generation DES fare better than first generation from a safety standpoint in meta-analysis

-ACS is an independent predictor of perioperative ischemic complications and recommendation of at least delay for elective non-cardiac surgery

Urgency of surgery and DAPT

Incorporating 2016 ACC/AHA guideline focused update on duration of antiplatelet therapy

Low	Intermediate	High
>4 weeks after PCI with POBA	>2 weeks and ≤4 weeks after PCI with POBA	≤2 weeks after PCI with POBA
>6 months after PCI with BMS	>1 month and ≤6 months after PCI with BMS	≤1 month after PCI with BMS
>12 months after PCI with DES	>6 months and ≤12 months after PCI with DES	≤6 months after PCI with DES
	>12 months after complex PCI with DES (long stents, multiple stents, overlapping, small vessels, bifurcations, left main, last remaining vessel)	≤12 months after complex PCI with DES
		≤6 months after PCI for MI Previous ST

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What is considered high risk for thrombotic complications?

-PCI for myocardial infarction

-Complex PCI defined as > 3 stents, > 60 mm stent length, chronic total occlusion, stent thrombosis ACS, bifurcation 2 stent

Aspirin discontinuation

-Oscarsson et. al

-To continue or discontinue aspirin in the perioperative period

-Randomized controlled trial

-There was 80% reduction in MACE with continuation of ASA (1.8% vs 9% p=0.02)

-There was a high risk of MACE with discontinuation of aspirin without increase in bleeding although it was not powered to assess bleeding

Your recommendation

-stop clopidogrel 5 days prior to knee surgery after a total of 6 months post ACS event

-hold ticagrelor(Brilinta) 5 days before surgery

-hold prasugrel(Effient) 7 days before surgery

-continue aspirin 81 mg daily during the perioperative period

-only exception would be if this was intracranial or intraspinal neurosurgery

What if the patient was taking DAPT after 1 year post MI and wants a recommendation about continuation

-no trial has shown reduction in mortality with continuation past 1 year

-PEGASUS-TIMI 54 trial randomized patients 1 year post MI taking ticagrelor to discontinuation, continuation at 90 mg bid or 60 mg bid

-There was a reduction in MACE driven by MI

-No difference in overall mortality

-Higher risk of bleeding

DAPT TRIAL

-randomized patients 12 months post PCI to continuation of clopidogrel for another 18 months or placebo

-there was a reduction in MACE driven by stent thrombosis and MI

-there was an increase in bleeding

-mortality was numerically higher almost statistically significant

Outcome	Continued Thienopyridine (N = 5020)	Placebo (N = 4941)	Hazard Ratio, Thienopyridine vs. Placebo (95% CI)†	P Value†
	no. of patients (%)			
Stent thrombosis‡	19 (0.4)	65 (1.4)	0.29 (0.17–0.48)	<0.001
Definite	15 (0.3)	58 (1.2)	0.26 (0.14–0.45)	<0.001
Probable	5 (0.1)	7 (0.1)	0.71 (0.22–2.23)	0.55
Major adverse cardiovascular and cerebrovascular events§	211 (4.3)	285 (5.9)	0.71 (0.59–0.85)	<0.001
Death	98 (2.0)	74 (1.5)	1.36 (1.00–1.85)	0.05
Cardiac	45 (0.9)	47 (1.0)	1.00 (0.66–1.52)	0.98
Vascular	5 (0.1)	5 (0.1)	0.98 (0.28–3.39)	0.98
Noncardiovascular	48 (1.0)	22 (0.5)	2.23 (1.32–3.78)	0.002
Myocardial infarction	99 (2.1)	198 (4.1)	0.47 (0.37–0.61)	<0.001
Stroke	37 (0.8)	43 (0.9)	0.80 (0.51–1.25)	0.32
Ischemic	24 (0.5)	34 (0.7)	0.68 (0.40–1.17)	0.16
Hemorrhagic	13 (0.3)	9 (0.2)	1.20 (0.50–2.91)	0.68
Type uncertain	0	1 (<0.1)	—	0.32

So what do you recommend?

-ACC/AHA guidelines recommend DAPT for 12 months post ACS

-In this patient with severe anemia you can recommend discontinuation after 1 year of ACS

-based on CURE trial which randomized ACS patients to clopidogrel for 3 to 12 months post myocardial infarction with a mean follow up of 9 months

-there was reduction in MACE but increased risk of bleeding

Switching between antiplatelet agents

-If this patient needed to be switched to clopidogrel from prasugrel or ticagrelor due to cost or bleeding risk a loading dose of clopidogrel needs to be given

-In the PLATO trial approximately 50% of the patients received loading dose of clopidogrel prior to receiving ticagrelor

68 y/o male with DES to the proximal LAD 2 weeks ago needs urgent non-cardiac surgery. What are your options?

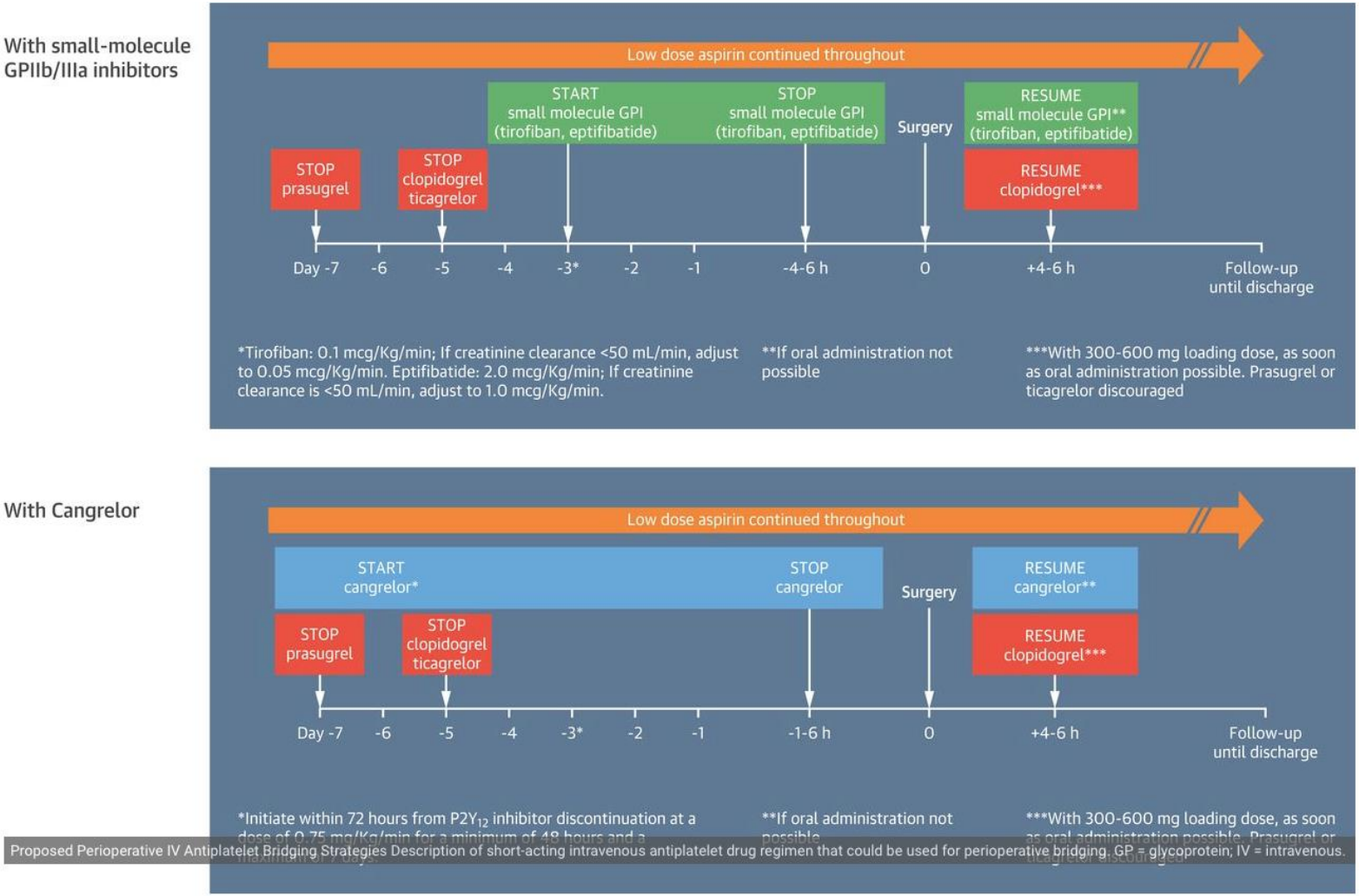
-use of unfractionated heparin or low molecular weight heparin is not recommended

-heparin paradoxically potentiates platelet aggregation and may potentiate vessel thrombosis

-short acting small-molecule IV IIb/IIIa inhibitors tirofiban and eptifibatide can be used

-recently approved ultra-short acting cangrelor can also be used for bridging

Thromb Haemost 2015 2015;114:423-31



Proposed Perioperative IV Antiplatelet Bridging Strategies Description of short-acting intravenous antiplatelet drug regimen that could be used for perioperative bridging. GP = glycoprotein; IV = intravenous.

Thank you