New oral anticoagulant and antiplatelet drugs

Implications for Endoscopy

Dr. Daniel Sadowski
Royal Alexandra Hospital
Edmonton, Ab.

Faculty Disclosure

- **Faculty:** Daniel Sadowski
- **Relationships with commercial interests:**
  - **Grants/Research Support:** none
  - **Speakers Bureau/Honoraria:** none
  - **Consulting Fees:** none
  - **Other:** none

August 05, 2014 Appointment:

Dr. Daniel Sadowski
331 Community Services Ct
Royal Alexandra Hospital
Edmonton, AB
T5H 3Y9
Phone:(780)735-6837
Fax:(780) 735-5650

Re:
15174 - 19 street
Edmonton, AB
T5Y 2R7
DOB: April 11, 1937
AHC: 116637400
Phone: (780)478-2009
Cell: (780) -

Dear Dr. Sadowski:,

Thank you for your consultation of this above named patient whom you have seen before. Was diagnosed with Carcinoma of the cecum, a right hemicolectomy with primary anastomosis was done last November 2013. I would like to ask for your kind care for a follow up or post operative colonoscopy for her which is due on November 2014. I am referring this patient for your kind assessment and management. If you require any further information regarding this patient please contact me at 780-478-2995.

Sincerely,

Name: i
Chart No: **15101**
15174 - 19 street
PHN/Reg: **11663-7400**
Edmonton, AB T5Y2R7
Gender: **Female** DOB: **APR 11, 1937**

Allergies:
SULFA

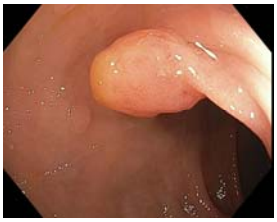
Problems:

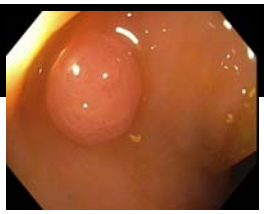
Problem Type	Severity	Status	Start Date	End Date
cwA blood test every 3mons for 3y		Active	26-03-2014	
CT Scan due on Nov 22, 2014 ans		Active	26-03-2014	
Hysterectomy/BSO		Active	01-01-2013	
Appendectomy		Active	01-01-2013	
TonsELLECTOMY		Active	01-01-2013	
Hypertension		Active	27-08-2012	
Hypothyroidism		Active	27-08-2012	
Hypercholesterolemia		Active	27-08-2012	
Depressive disorder, not elsewhor		Active	27-08-2012	
Anxiety		Active	27-08-2012	
Congestive heart failure 2 TO RAF ECHO AUG 2012 EF 55%/MILD RV DYSFXN/MR		Active	27-08-2012	

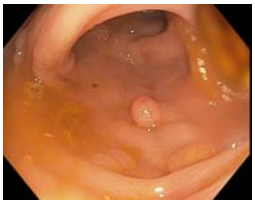
Active Medications

Drug	Dosage	Last Prescribed
BISOPROLOL 5 MG po od for 3 month		Jun 12, 2014
XALERTO 20 MG OD FOR 3 MONTHS		Jun 12, 2014
TYLENOL 4 QID PRN	QID (PRN) 1MTH	Jun 12, 2014
spiriva ONCE A DAY 100 days		Jun 12, 2014
ADVAIR 250 2 puff BID x3		Jun 12, 2014
OMEPRAZOLE 20 MG po od 3 months		Jun 12, 2014
Salbutamol Sulfate 100mcg Inhalation qid prn 3 months		Jun 12, 2014
NORVASC	5mg ONCE 100tab	Jun 12, 2014
effexor 75+75 mg od for 3 months		Jun 12, 2014
LASIX	40mg BID 3MTH	Jun 12, 2014
K-DUR 20 MEQ TABLET 1 tab BID 3 MONTHS		Jun 12, 2014

Case







Learning objectives

- Management of NOACS in the setting of elective endoscopy
- Management of platelet inhibitors in the setting of elective endoscopy

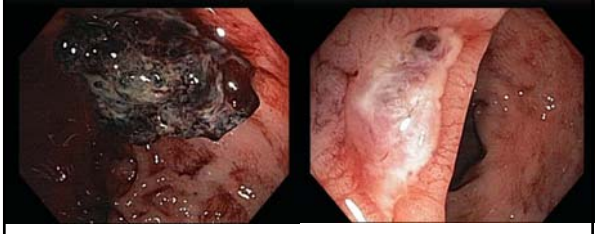
VIT K antagonists (coumadin/warfarin)

- Advantages:
  - Wide range of approved indications: DVT/PE, AF, mechanical heart valves, AMI
  - Reversible with Vit K and plasma, PCC's
- Disadvantages:
  - Monitoring required
  - Levels affected by dietary factors and other drugs
  - Narrow therapeutic window
  - Slow onset and offset

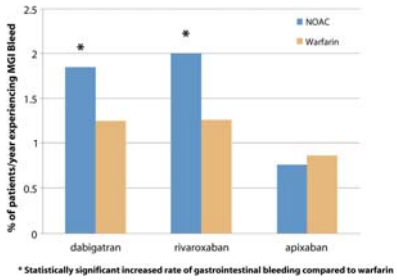
New Oral Anticoagulants

- Monitoring not required
- Stable anticoagulation levels
- Reversal not uniformly possible
- Agents:
  - Dabigatran (Pradaxa)
  - Riveroxaban (Xaralto)
  - Apixaban (Eliquis)
  - Coming soon:
    - Edoxaban (Lixiana -Japan) , Savaysa -US/Europe)

Case: 6 days post-polypectomy



NOACs and GI Bleeding



The rate of major GI bleeding in the 3 pivotal novel oral anticoagulant trials

Gastrointestinal Endoscopy 2013;78:p227 - 239

Bleeding vs. Thrombosis

	Low Procedural Bleeding Risk	High Procedural Bleeding Risk
Low risk of Thrombosis or Embolism	May continue anti-thrombotic agents	Stop anti-thrombotic agents
High Risk of Thrombosis or Embolism	Continue anti-thrombotic agents	Stop anti-thrombotic agents (consider bridge therapy)

High-risk Procedures	Low Risk Procedures
Polypectomy	Diagnostic (EGD, colonoscopy, flexible sigmoidoscopy) including biopsy
Biliary or pancreatic sphincterotomy	ERCP without sphincterotomy
Pneumatic or bougie dilation	EUS without FNA
PEG placement	Enteroscopy and diagnostic balloon-assisted enteroscopy
Therapeutic balloon-assisted enteroscopy	Capsule endoscopy
EUS with FNA	Enteral stent deployment (without dilation)
Endoscopic hemostasis	
Tumor ablation by any technique	
Cystogastrostomy	
Treatment of varices	

Management of antithrombotic agents for endoscopic procedures *GIE 2009*

NOACs: Pharmacokinetics

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Target	Thrombin	Fxa	Fxa	Fxa
Half-life (h)	12-17	9-13	9-14	9-11
Dosing	110 – 150 mg bid	10-30 mg od	2.5-5 mg bid	15-30 mg od
Peak plasma conc.	2-3 h	2-4 h	1-3 h	1-3 h
Plasma protein binding	34-35%	92-95%	87%	40-59%
Renal elimination	80%	66%	25%	35%

Suggested Management of Anti-thrombotic Agents Prior to Screening-Related Colonoscopy

Anti-thrombotic Agent	Recommended interval between last dose and procedure	Recommended interval between procedure and next dose	If therapeutic intervention performed*
Anticoagulant agent			
Warfarin (Coumadin)	5 d	<24 hr	<24 hr
Low-Molecular weight heparin	24 hr	<24 hr	48 hr
Pradax (dabigatran) *Predominantly renal excretion* *Assessment of creatinine clearance essential*	48 hr GFR ≥60 5 d GFR <60	1 d	48 hr
Xarelto (rivaroxaban)	24-48 hr	1 d	48 hr
Eliquis (apixaban)	24-48 hr	1 d	48 hr
Antiplatelet agent			
Aspirin	continue		N/A
Plavix (clopidogrel)	5 d	1 d	1 d
Effient (Prasugrel)	5 d	1-2 d	1-2 d**
Brilinta (Ticagrelor)	5 d	1-2 d	1-2 d**
Aggrenox (dypiridamole/ASA)	7-10 d *(consider starting ASA bridge)*	1 d	1 d

GFR creatinine clearance in ml/min.
*Restarting antithrombotics is dependent on endoscopic intervention performed during procedure. Use caution when large polyps have been removed with electrocautery. NOAC's produce full anti-coagulation within a few hours of restarting the drug.
**Restarting Prasugrel and Ticagrelor should be approached cautiously after polypectomy. Both drugs achieve full anti-platelet effect in 4 hours.

Risks of Thromboembolism

- Low
  - AF with CHADS2 Score 0-1
  - Bioprosthetic valve or mechanical mitral valve
  - Previous DVT
- Intermediate
  - AF CHADS2 score 2-3
  - DVT/PE in last 3-6 months
- High –? Use bridging?
  - Recent CVA/TIA
  - AF with CHADS2 4-6
  - DVT/PE in last 3 months
  - Mechanical Mitral Valve
  - Severe/multiple thrombophillic abnormalities
  - Recent placement of coronary stent

Anti-platelet agents - periendoscopic management:

Agent (ADH Inhibitors)	Stop when?	Restart when?	Time to maximal platelet inhibition
Aspirin	Continue for all procedures	-	
Aspirin/dypyridamole (Aggrenox)	7-10 d *?start ASA?*	1 d	7 days
Clopidogrel (Plavix)	5 d	1 d	3-5 days (consider loading dose 600 mg)
Prasugrel (Effient)	7 d	1-2 d	4 hours
Ticagrelor (Brilinta)	5 d	1-2 d	4 hours

Adapted from Baron T, NEJM 2013

Anti Platelet agents: Clinical Caveats

- Continue ASA even in high risk procedures
- Most patients are on dual antiplatelet therapy for a drug eluting stents
- Exercise caution in discontinuing therapy:
  - Within 6 weeks of bare metal stent insertion
  - Within 3-6 months of drug eluting stent insertion
  - Consider delay of procedure?

Summary

- NOACs need to be managed cautiously in the setting of elective endoscopy
- Clear communication in the referral letter is essential
- Use caution in discontinuing NOACs and newer antiplatelet agents in patients at high risk for thrombosis

- Discussion and Questions