Challenges in Anticoagulation: A Panel Discussion

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Learning Objectives

- To discuss and apply the evidence in the context of case-based discussions for common practice challenges faced by pharmacists managing anticoagulation, including:
  - Stroke Prevention in Elderly AF patients
  - Anticoagulation (DOAC/warfarin) for stroke prevention for AF patients with renal dysfunction
  - Use of DOACs in extremes of weight
  - Bleeding risk and resumption of anticoagulation after bleeding

Disclosures

Lynette Kosar:
- No relevant industry relationships to disclose

Lori Albers:
- Paid speaking for: AstraZeneca

Bill Semchuk:
- Participation on advisory boards or paid speaking for: Bayer, BI Canada, Pfizer/BMS Alliance, Servier, Sanofi
- Member of the Heart and Stroke Canada Secondary Prevention of Stroke Guidelines Primary Panel

Sheri Koshman:
- No relevant industry relationships to disclose

Challenges in Anticoagulation

- https://youtu.be/4HavF5f3VoA

Patient Case

- Ms. Knitter, Age: 87, Female, Weight: 63 kg
- Medical History
  - Hyperlipidemia
  - Hypertension
  - MI, 15 years ago; CABG x 5
- Current Medications
  - ASA EC 81 mg po daily
  - Bisoprolol 5 mg po daily
  - Atorvastatin 80 mg po HS
  - Perindopril 8 mg po daily
- Social History
  - Family assists with medications
  - Lives independently in her own home
  - Occasional accidental fall at home

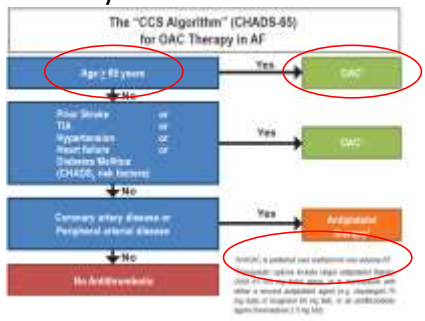
Patient Case

- Presents to ER with complaints of fluttering in her chest and periods of feeling tired and faint
- Relevant Findings
  - ECG: Atrial fibrillation, HR: 102 irregular,
  - BP: 135/85
  - Echo: LVEF: 55%, no significant valvular heart disease
- Labs
  - Scr: 100 micromol/L, Liver: WNL, CBC: WNL

Question

- What is the best course of action given her overall clinical and social history
  - Is oral anticoagulation indicated for Ms. Knitter?
  - If so, what are her options? Which agent & dose?

What do Canadian Cardiovascular Society AF Guidelines tell us?



2018 CCS AF Guidelines

What does the Saskatchewan Drug Plan tell us?

- Saskatchewan Drug Plan Exception Drug Status Criteria for DOACs

a) At-risk patients with non-valvular atrial fibrillation who require rivaroxaban for the prevention of stroke and systemic embolism **AND** in whom:
- Anticoagulation is inadequate following a reasonable trial on warfarin;

OR

- Anticoagulation with warfarin is contraindicated or not possible due to inability to regularly monitor via International Normalized Ratio (INR) testing (i.e. no access to INR testing services at a laboratory, clinic, pharmacy, and at home).

http://formulary.drugplan.ehealthsask.ca/PDFs/APPENDIXA.pdf

What's the reality for Elderly Patients with Atrial Fibrillation?

- Elderly patients: ≥ 75 years
- Common arrhythmia, prevalence ↑ with age
- AF is associated with substantial mortality & morbidity, including a 5 fold ↑ in risk of stroke
  - Stroke risk from AF ↑ exponentially with age
  - Annual stroke risk at 80-90 yrs is as high as 23.5%
- Patients fear stroke more than bleeding

Benedetti et al. Minerva Cardioangiologica 2018 June; 66 (3): 301-13; Cavallari et al. Anatol J Cardiol. 2018 Jan: 19 (1): 67-71; Belmonte et al. ESC E-Journal of Cardiology Practice. Vol 16 N6 (24 Apr 2019; Barco et al. Best Practice & Research Clinical Hematology 26 (2013) 215-224; Zweiker at al. BMJ Open. 2017; 7 (9): e018242

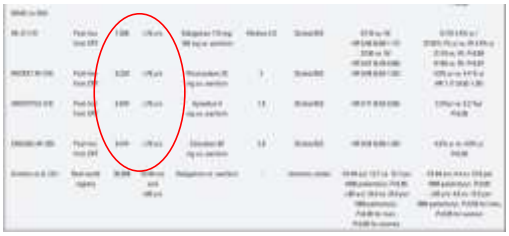
What's the reality for Elderly Patients with Atrial Fibrillation?

- Physicians are less likely to anticoagulate
- Patients frequently refuse anticoagulation
  - 25-65% of elderly patients are not Rx'd OAC
- Warfarin (>60% TTR INR 2–3) is superior to placebo, ASA, or ASA & clopidogrel (ACTIVE –W)
  - Absolute benefit of warfarin over antiplatelet therapy continues to ↑ as patients age (ATRIA, WASPO, & BAFTA)

Edholm et al. Med Clin North Am. 2015 March; 99(2): 417-430; Benedetti et al. Minerva Cardioangiologica 2018 June; 66 (3): 301-13
Cavallari et al. Anatol J Cardiol. 2018 Jan: 19 (1): 67-71; Barco et al. Best Practice & Research Clinical Hematology 26 (2013) 215-224

In the Era of DOACs

- Proportion of patients 75 years or over enrolled in the phase III RCTs was over 30-40% (over 27,000 patients)



Cavallari et al. Anatol J Cardiol. 2018 Jan: 19 (1): 67-71

In the Era of DOACs

	% Patients ≥75 years	Stroke/SE	Major Bleeding	ICH	GI Bleeding
	Compared to warfarin				
Dabigatran 110 mg (RE-LY)	40%	↔	↔	↓	↑ Women ≥75 & men ≥85 years
Dabigatran 150 mg (RE-LY)		↓	↑	↓	
Rivaroxaban (ROCKET AF)	38%	↔	↔	↓	↑
Apixaban (ARISTOTLE)	31%	↓ (all cause mortality)	↓ (renal dysfunction)	↓	↔
Edoxaban (ENGAGE AF-TIMI 48)	40.2%	↔	↓	↓	↑ (high dose)
	Compared to acetylsalicylic acid (ASA)				
Apixaban (AVERROES)	40.4%	↓ (Trial terminated early)	↔	↔	↔

Trader D. ESC E-Journal of Cardiology Practice. Vol. 17 NS – 17 Apr 2019
Cavallari et al. Anatol J Cardiol. 2018 Jan; 19 (1): 67-71
Benedetti et al. Minerva Cardioangiologica 2018 June; 66 (3): 301-13;

American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults

*By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel**

Table 4. 2019 American Geriatrics Society Beers Criteria® for Potentially Inappropriate Medications Drugs To Be Used With Caution in Older Adults*

Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Dabigatran, Rivaroxaban	Increased risk of gastrointestinal bleeding compared with warfarin and reported cases with other direct oral anticoagulants when used for long-term treatment of VTE or atrial fibrillation in adults ≥75 years.	Use with caution for treatment of VTE or atrial fibrillation in adults ≥75 years	Moderate	Strong
Use With Caution (Table 4)				
Rivaroxaban	Emerging evidence of increased risk of serious bleeding compared with other anticoagulant options			
Medications That Should Be Avoided or Have Their Dosage Reduced With Decreased Kidney Function (Table 6)				
Apixaban, dabigatran, edoxaban, and rivaroxaban		Revised CrCl at which action is required, cautions and recommendations to reflect current labeling, and CrCl estimation parameters in clinical trials		

Fick et al. J Am Geriatr Soc. 2019 Apr, 67(4):674-694

OAC in the Elderly Patient with AF

- ✓Comprehensive individual patient assessment required
- ✓OAC is required to ↓risk of stroke
- ✓DOACs associated with better efficacy and safety profiles compared to warfarin
  - ✓Apixaban or edoxaban *may* be preferred
  - ✓If using warfarin, refer to an anticoagulation clinic
- ✓Minimize the impact of each modifiable risk factor for bleeding
- ✓The use of ASA for stroke prevention in AF is difficult to justify

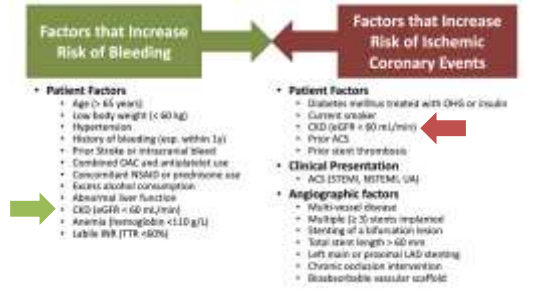
Back to Patient Case

- Ms. Knitter, Age: 87, Female
- Weight: 63 kg
- $CHADS_2$ = 2
- HASBLED = 1
- Renal function has decline, but is stable:
  - SCr has increased from 100 micromol/L to 174 micromol/L
  - CrCl decreased from 35mL/min to 20mL/min (Cockcroft-Gault)

Question

- What are her options for an oral anticoagulant given her decline in renal function?

AF Stroke Prevention Challenges in CKD

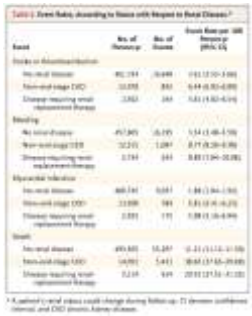


Andrade JG et al; CCS Atrial Fibrillation Guidelines Committee. 2018 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. Can J Cardiol. 2018 Nov;34(11):1371-1392.

AF Stroke Prevention Challenges in CKD

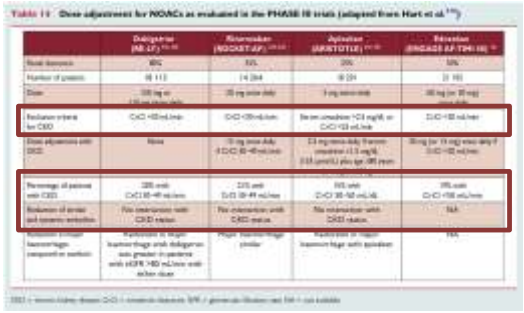
↑ risk of thrombosis & risk of bleeding

- Risk increases as renal function declines
- Due to physiological changes & incorrect OAC dosing



Olesen JB et al. Stroke and bleeding in atrial fibrillation with chronic kidney disease. N Engl J Med. 2012 Aug 16;367(7):625-35.

AF Stroke Prevention Challenges in CKD



Kirchhof P et al. 2016 ESC Guidelines for the management of AF developed in collaboration with EACTS. 2016 Nov;18(11):1609-1678.

AF Stroke Prevention Challenges in CKD

CCS AF Guidelines

Recommendation 5 – Warfarin when mechanical valve, mitral stenosis or renal dysfunction (2014)

We recommend that when OAC is indicated, warfarin be used rather than one of the NOACs for those patients with a mechanical prosthetic valve, those with rheumatic mitral stenosis and those with a CrCl of 15 – 30 mL/min (Strong Recommendation, Moderate Quality Evidence).

Values and preferences (2014)

This recommendation places high value on the evidence from one RCT of the inferiority of dabigatran compared to warfarin for the prevention of thromboembolism in patients with a mechanical prosthetic valve. It places relatively high value on the long experience and clinical reports of the use of warfarin in patients with rheumatic mitral stenosis and patients with CrCl 15 – 30 mL/min and the absence of such information for NOACs.

Verma, Atul et al. 2014 Focused Update of the CCS Guidelines for the Management of AF. Can J Cardiol 2014;30:1114-1130

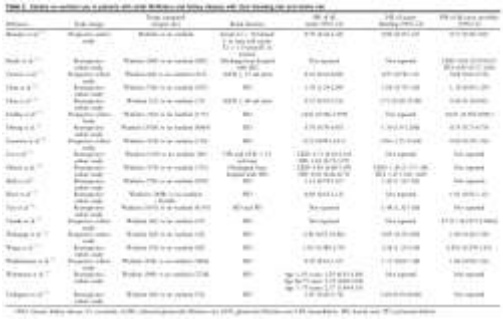
AF Stroke Prevention Challenges in CKD

Dosage of Oral Anticoagulants Based on Renal Function

CrCl	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
CrCl >90 mL/min	Dose adjusted for INR 2.0-3.0	150 mg bid*	20 mg daily	5 mg bid	60 mg daily**
CrCl 30-89 mL/min	Dose adjusted for INR 2.0-3.0	Consider 110 mg bid in patients ≥ 75 yrs	15 mg daily	5 mg bid (Consider 2.5 mg bid†)	30 mg daily
CrCl 15-29 mL/min	No RCT Data **	No RCT Data‡	No RCT Data	Very limited RCT Data‡	No RCT Data‡
CrCl < 15 mL/min (or on dialysis)	No RCT Data‡	No RCT Data‡	No RCT Data‡	No RCT Data‡	No RCT Data‡

http://www.ccs.ca/images/Guidelines/PocketGuides_EN/AF_Gui_2018_PG_EN_web.pdf

AF Stroke Prevention Challenges in CKD



Jegatheswaran, J et al. Anticoagulation in Patients With Advanced Chronic Kidney Disease: Walking the Fine Line Between Benefit and Harm. Canadian Journal of Cardiology, Volume 35, Issue 9, 1241 - 1255

AF Stroke Prevention Challenges in CKD

Apixaban

Table 12 – Dosage and Administration for Patients According to Renal Function

Creatinine Clearance (eCrCl) / Indication	Renal Impairment: Normal	Mild	Moderate	Severe		
	> 80 mL/min	>50–≤80 mL/min	>30–≤50 mL/min	≥25–≤30 mL/min	≥15–<24 mL/min	<15 mL/min or patients undergoing dialysis
Prevention of stroke and systemic embolism in patients with atrial fibrillation	5 mg bid Dose adjustment to 2.5 mg bid, if ≥2 of following criteria are met‡: • age ≥ 80 years • body weight ≤60 kg • serum creatinine ≥133 µmol/L (1.5 mg/dL)				No dosing recommendation due to very limited clinical data	ELIQUIS is not recommended

‡ These patients have been determined to be at higher risk of bleeding.

Eliquis Product Monograph. Pfizer Canada 2019.

AF Stroke Prevention Challenges in CKD

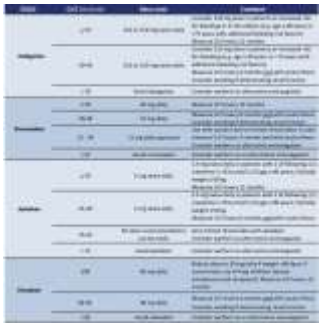
Rivaroxaban

Xarelto Product Monograph. Bayer Canada 2019.

AF Stroke Prevention Challenges in CKD

- Rivoxaban data in CrCl 15-29mL/min:
  - **Limited RCT data:**
    - ROCKET-AF: ad-hoc analysis of primary efficacy endpoint & safety endpoint by baseline CrCl (n=8 CrCl <30mL/min)
    - EINSTEIN-DVT and EINSTEIN-PE: n=21 CrCl <30mL/min, none of which experienced a recurrent VTE or major bleed
  - **Observational data:** XANTUS
    - n=75 CrCl 15-29mL/min
    - CrCl <50mL/min was similar to ROCKET-AF results
  - **PK/PD single dose study** (n=32 for all renal subgroups)
    - $t_{1/2}$ 9.5hr in those with CrCl <30mL/min (vs 8.3hrs)
    - AUC was higher, but maximum plasma concentrations similar (AUC CrCl <30mL/min 64%, CrCl 30-49mL/min 52%, CrCl 50-79mL/min 44%

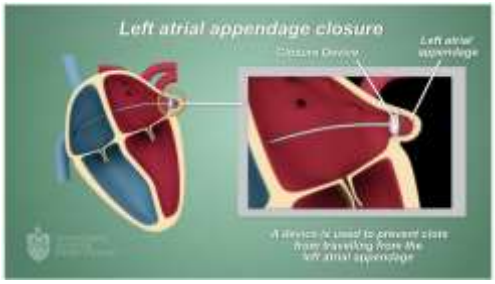
AF Stroke Prevention Challenges in CKD



Thrombosis Canada. Suggested Use of NOACs According to Patient Renal Function for Stroke Prevention in AF.

AF Stroke Prevention Challenges in CKD

AF Stroke Prevention Challenges in CKD



https://www.svhhearthealth.com.au/procedures/procedures-treatments/left-atrial-appendage-closure

AF Stroke Prevention Challenges in CKD

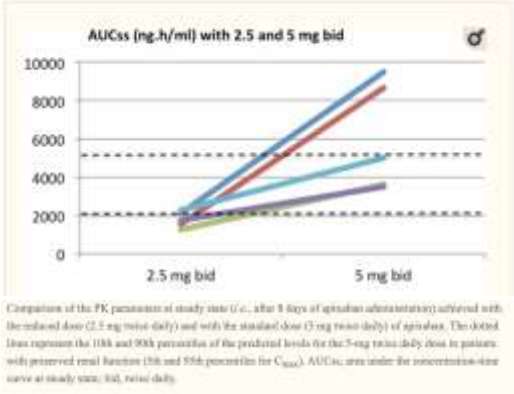
CCS AF Guidelines

AF Stroke Prevention Challenges in CKD

Burlacu A et al. Pros and cons of antithrombotic therapy in ESKD: a 2019 update. Nephrol Dial Transplant. 2019 Jun 1;34(6):923-933.

AF Stroke Prevention Challenges in CKD

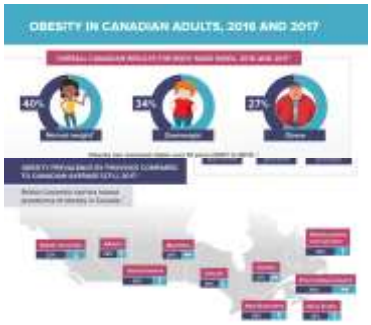
Turakhia MP et al. Chronic kidney disease and arrhythmias: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Eur Heart J. 2018 Jun 21;39(24):2314-2325.



Mavrakanas TA et al. Apixaban Pharmacokinetics at Steady State in Hemodialysis Patients. J Am Soc Nephrol. 2017 Jul;28(7):2241-2248.

What if Ms. Knitter was large or small?

What if she weighed 112 or 122 kg?



- Estimated that by 2019 (now), more than 55% of the Canadian population Will by overweight or obese. (Twells L et al. CMAJ Open 2014;2(1):E18.

Weight Based Dosing of NOACs Go To Sources….

- CCPN SPAF Tool - X
- Thrombosis Canada: DOACs in Obese Patients – Guide
  - "data on the clinical efficacy and safety of DOACs in obese patients are limited. NO randomized controlled trials have examined the safety and efficacy of DOACs only in obese patients. Overall, <20% of patients in DOAC trials weighted >90-100kg…"
  - "if DOACs are to be used in patients with a BMI>40 or >120 kg, this should be as a last resort (ie. When vitamin K antagonists cannot be used) and patients should be informed of the limitations of the available information and potential risk of underdosing"
- 2018 European Practical Guide[1]:
  - "because of limited data in extreme obesity, the use of VKA in patients with a BMI≥ 40 kg/m² or weight > 120 kg should be considered… in rare cases when a NOAC is needed in such circumstances, specific measurements of drug trough levels should be considered… under the guidance of a hematologist…"

Steffel J et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation European Heart Journal 2018;39:1330-1393

ARISTOTLE Subgroup analysis: Efficacy and Safety Outcomes Stratified by Weight Categories for Apixaban vs Warfarin Use - Weight > 120 kg (n=982)

Weight > 120 kg	Apixaban Rate (n)*	Warfarin Rate (n)*	Hazard Ratio (95% CI) Apixaban vs Warfarin
Efficacy Endpoints			
Stroke or systemic embolism	0.44 (4)	1.13 (11)	0.387 (0.123 to 1.215)
Stroke	0.44 (4)	1.03 (10)	0.426 (0.134 to 1.357)
Ischemic or uncertain stroke	0.44 (4)	0.61 (6)	0.711 (0.201 to 2.521)
Hemorrhagic stroke	0.00 (0)	0.41 (4)	
All cause death	3.00 (28)	2.52 (25)	1.190 (0.694 to 2.042)
Myocardial infarction	0.33 (3)	0.41 (4)	0.806 (0.180 to 3.600)
Safety Endpoints			
Major bleeding	1.55 (13)	2.08 (19)	0.742 (0.366 to 1.502)
Major or CRNM bleeding	2.77 (23)	4.83 (43)	0.575 (0.347 to 0.954)
Intracranial bleeding	0.00 (0)	0.43 (4)	-
GI bleeding	0.47 (4)	0.33 (3)	1.436 (0.321 to 6.416)
Any bleeding	16.44 (119)	25.13 (176)	0.670 (0.531 to 0.846)

*Rates per 100 patient-years.
CI, confidence interval; CRNM, clinically relevant non-major; GI, gastrointestinal.

0 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5 5.5 6 6.5

Favor Apixaban Favor Warfarin

Hohnloser et al. Efficacy and safety of apixaban versus warfarin in patients with atrial fibrillation and extremes in body weight: Insights from the ARISTOTLE trial. Circ 2019 (10.1161/CirculationAHA.118.037955)

Comparative Effectiveness and Safety of Rivaroxaban and Warfarin among Morbidly Obese Patients with AF: Propensity Matched Cohort

	Rivaroxaban (n=3563)	Warfarin (n=3563)	OR (95% CI)	P value
Follow up time (months), mean (SD)	10.27 (2.89)	10.56 (2.70)	-0.29 (-0.42, -0.16)	<0.0001
Composite risk of ischemic stroke/ systemic embolism, n(%)	52 (1.5%)	59 (1.7%)	0.88 (0.60, 1.28)	0.5028
Time to first composite event (days), mean (SD)	111.87 (107.01)	125.90 (105.65)	0.90 (0.62.1.30)	0.5690
Risk of major bleeding, n (%)	77 (2.2)	96 (2.7)	0.80 (0.59, 1.08)	0.1447
Time to first major bleeding event (days), mean (SD)	127.99 (97.22)	147.56 (110.65)	0.82 (0.61, 1.10)	0.1878

Peterson E et al. Comparative effectiveness, safety and costs of rivaroxaban and Warfarin among morbidly obese patients with atrial fibrillation. Am Heart J 2019; doi.10.1016/j.ahj.2019.02.001

What if she were small?

- What drugs cause less bleeding?
- What guidance do we have?

Risks and Benefits of NOACs Compared with Warfarin (NNT/NNH)

Clinical Outcome	Apixaban (5mg bid), HR, NNT per 2 years	Dabigatran (150 mg bid), RR, NNT or NNH per 2 years	Edoxaban (60 mg daily) HR, NNT or NNH per 3 years	Rivaroxaban (20mg daily), HR or RR, NNT or NNH per 3 years
Stroke or SE	Superiority vs W HR = 0.79 (0.66-0.95) NNT=168	Superiority vs W RR = 0.66 (0.53-0.82) NNT=91	Non-inferiority vs W HR <0.79 (0.63-0.99), NNT=141*	Non-inferiority vs W HR = 0.79 (0.65 – 0.95), NNT = 134*
Intracranial bleed	Superiority vs W HR = 0.51 (0.35 to 0.75) NNT=238	Superiority vs W RR=0.26 (0.14-0.49), NNT=182	Superiority vs W HR=0.54 (0.38 – 0.77), NNT = 172	Superiority vs W HR = 0.67 (0.47 – 0.93), NNT=247
Major bleed	Superiority vs W HR 0.69 (0.60-0.80) NNT = 79	RR = 0.93 (0.81 – 1.07), NS	Superiority vs W HR = 0.80 (0.71 – 0.91), NNT 66	HR = 1.04 (0.90 – 1.20), NS
GI bleed	HR =0.89 (0.70-1.15), NS	Inferior vs W RR = 1.50 (1.19 – 1.89), NNH = 100	Inferior vs W HR = 1.23 (1.02 – 1.50), NNH 167	Inferior vs W RR = 1.45, NNH 101
Any cause of death	Superiority vs W HR =0.89 (0.80-0.99), NNT=132	RR = 0.88 (0.77 – 1.00), NS	HR = 0.92 (0.83 – 1.01), NS	HR = 0.85 (0.70-1.02), NS

* indicates on treatment analysis used to calculate NNT as superiority was not demonstrated in ITT analysis

1. Hijazi Z, et al. Circulation 2016;133(9):863-72.
2. Fox KA, et al. Eur Heart J 2011;32:2387-94.
3. Hohnloser SH, et al. Eur Heart J 2012; 33:2821-30.
4. Bohula EA, et al. Circulation 2016;132:23-38.

Dosing of DOACs is Important (AF):

DOAC	Usual Starting Dose	Dosing adjustment Criteria
Apixaban (Eliquis)	5 mg BID	2.5 mg BID if any 2 of the following criteria: - Age ≥80 years - Body weight ≤60 kg - Creatinine ≥133 µmol/L
Dabigatran (Pradaxa)	150 mg BID	110 mg BID if - Age ≥80 or - 75 ≤ a one hemorrhagic risk factors* or - CrCl 30-50 ml/min
Edoxaban (Lixiana)	60 mg OD	30 mg once daily if: - CrCl 30-50 ml/min - body weight ≤60 kg - Concomitant use of P-gp inhibitors except amiodarone and verapamil
Rivaroxaban (Xarelto)	20 mg OD taken with food	15 mg OD taken with food if CrCl 30-49 mL/min

Rates of Major Bleeding and the Effect of Apixaban Compared with Warfarin

Subgroup	No of Events (Annual %)		
	Apixaban Tx	Warfarin Tx	HR (95% CI)
No dose reduction criteria	204 (1.8)	279 (2.5)	0.7 (0.6-0.9)
1 dose reduction criteria	102 (3.2)	145 (4.8)	0.7 (0.5-0.9)
Criteria:			
Age ≥ 80	46 (3.5)	61 (4.9)	0.7 (0.5-1.1)
Weight ≤ 60kg	26 (2.3)	44 (4.0)	0.6 (0.4-0.9)
Creat ≥133	30 (4.2)	40 (5.8)	0.7 (0.5-1.2)

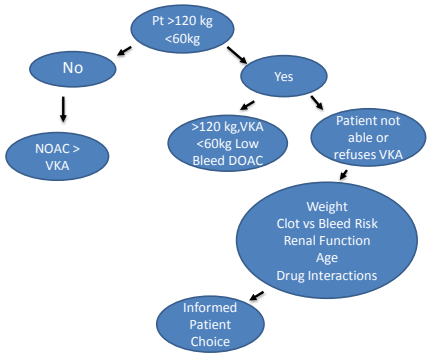
Alexander J et al. JAMA Card 2016;1(6):673-681

ARISTOTLE Subgroup analysis: Efficacy and Safety Outcomes Stratified by Weight Categories for Apixaban vs Warfarin

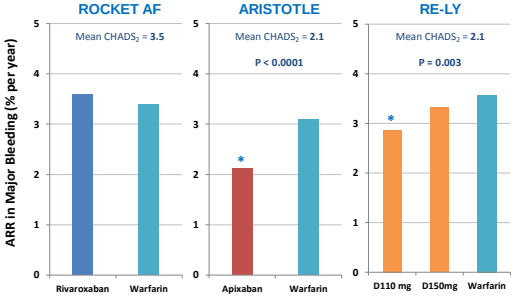
	Apixaban	Warfarin	Apixaban vs Warfarin HR
Major Bleeding			
≤ 60 kg	2.33 (36)	4.28 (62)	0.55 (0.36-0.82)
61-120kg	2.15 (277)	3.02 (370)	0.71 (0.61-0.93)
>120kg	1.55 (13)	2.08 (19)	0.74 (0.37-1.50)
GI Bleeding			
≤ 60 kg	0.90 (14)	1.09 (16)	0.84 (0.41-1.72)
61-120kg	0.67 (87)	0.79 (100)	0.85 (0.64-1.13)
>120kg	0.47 (4)	0.33 (3)	1.44 (0.32-6.42)
Any Bleeding			
≤ 60 kg	18.68 (244)	30.86 (344)	0.62 (0.53-0.73)
61-120kg	18.15 (1987)	25.29 (2528)	0.73 (0.69-0.78)
>120kg	16.44 (119)	25.13 (176)	0.67 (0.53-0.85)

Distribution of patients: ≤ 60 kg (n=1985), >60-120kg (n=15172), ≥120kg (n=982)
Hohnloser et al. Circ 2019 (10.1161/CirculationAHA.118.037955)

Bill's Clinical Approach:



New Anticoagulants vs. Warfarin: Major Bleeding

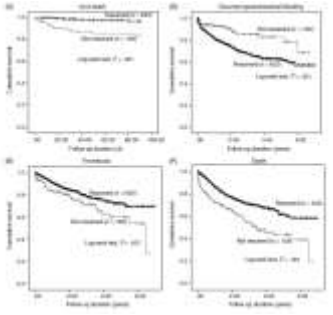


Patel et al. *NEJM* 2011;365(10):883-91; Connolly et al. *NEJM* 2009;361(12):1139-51; Granger et al. *NEJM* 2011;365:981-92

If she does develop an anticoagulant-related major bleed (GI, ICH) what approach do you take?

- Do you restart anticoagulation?
- If so, when?
- Do you change anticoagulant to minimize bleed risk?
- What else can you do to minimize bleed risk?

Outcomes Post GI Bleed



Sostres C et al. Aliment Pharmacol 2019:00:1-11.

What is the risk for TE with anticoagulation interrupted?

- High –risk (>10%/yr if not anticoagulated)
  - – Mechanical mitral valve or older aortic valve, AF and CHADs2 - ≥ 4
  - – Recent (within 3 months) – VTE
- Moderate –risk (5-10%/yr)
  - – Bileaflet aortic valve
  - – AF and CHADs2 – 2-3
- Low-risk (<5%/yr)
  - – AF and CHADS2 - low

Tomaselli G et al. JACC 2017. ACC Expert Consensus Decision Pathway on Mgmt of Bleeding in Patients on Oral Anticoagulants

When to resume OAC Post GI Bleed and empiric bleed risk

Low

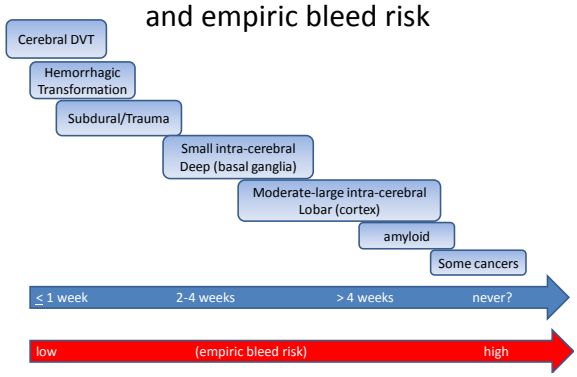
High

- Upper:
  - M-W tear
  - EtOH Gastritis/esophagitis
  - Gastric/duodenal ulcer (healed)
  - Gastic/duodenal ulcer (bleeding)
  - GAVE
  - Unresectable neoplasm
- Lower
  - Hemorrhoid
  - Diverticulosis
  - Angiodysplasia
  - Ulcerative colitis
  - C.difficile colitis
  - Unresectable neoplasm

≤ 1 week

≥ 4 week, ?never

When to resume OAC Post IC Bleed and empiric bleed risk



Timing of Restart OAC after GI or IC Bleed

- No prospective data to drive decisions…
- Generally reasonable to restart 7-15 days post GIB and generally longer post ICH
- Individualized patient assessment of risk/benefits should be completed to optimize outcomes

Kido K. Ann Pharmcother 2017;5(11)1000-1007.

After a DOAC bleed, should we switch anticoagulants? Is it safer?

- If taking VKA and develops ICH:
  - Better INR control, control modifiable risk factors
  - Change to DOACs (40-60% RRR for ICH)
- If taking DOAC and develops GI bleed:
  - Apixaban/edoxaban instead of rivaroxaban/dabigatran
- If taking DOAC and any bleed, is dose correct?
  - Dose adjustment guidelines

Eikelboom JW et al. Am J Emerg Med 2016;34:3
Liew A et al. J Thromb Haemost 2014;12:1419
Abraham NS et al. Gastroenterology 2017;152:1014

Other things to decrease bleeding risk…