Antithrombotic Therapy in Atrial Fibrillation, Venous Thromboembolism and Cerebral Vascular Accident

Presented by:

Nibal R. Chamoun, PharmD, BCPS

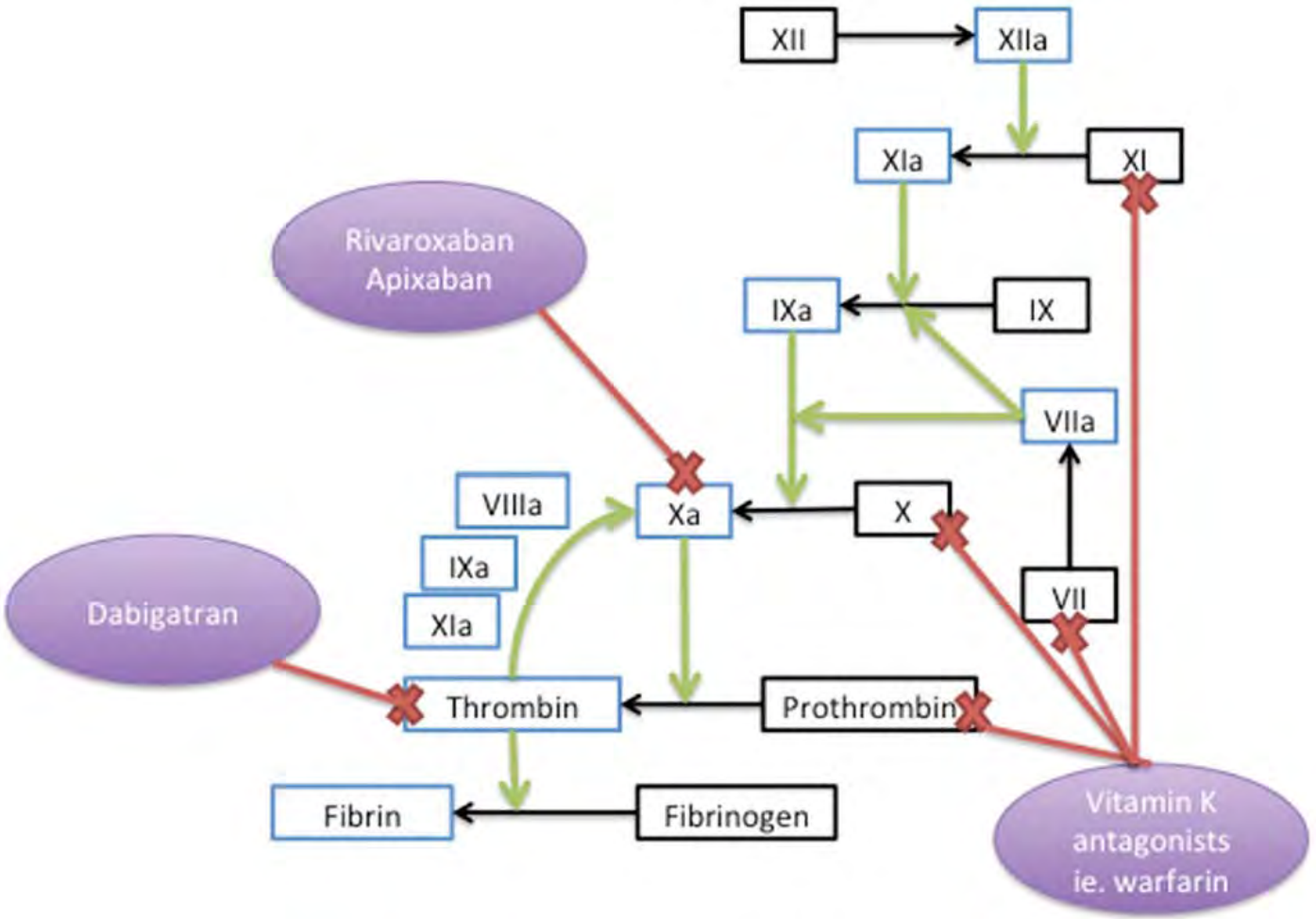
Objectives

- Review the mechanism of action, indications and contraindications of vitamin K antagonists versus new oral anticoagulation
- Identify patients who may benefit from specific antithrombotic therapy
- Discuss pertinent monitoring
- Review important counseling tips

Abbreviations

- AC: Anticoagulation
- NOACS: Novel oral anticoagulants
- SPAF: Stroke prevention in Atrial Fibrillation
- VTE: Venous thromboembolism
- DVT: Deep venous thrombosis
- PE: Pulmonary embolus
- Hb/Hct: hemoglobin/hematocrit
- PK and PD: pharmacokinetic and pharmacodynamic

Mechanism of Action: VKA versus NOACS



Saraf K, et al. Postgrad Med J 2014;90:520–528

VKAs versus NOACS

VKAs (acenocoumarol, hydroxycoumarol)

- Variability in dosing
- More monitoring
- Long half life
- Numerous drug/food interactions

NOACS (rivaroxaban, dabigatran, apixaban)

- Fixed dosing
- Less monitoring
- Shorter half lives➔ compliance is important
- Less drug food interactions
- Dosage adjustment required for renal impairment

Vitamin K antagonists (VKAs)

- Mode of Action(MOA):
  - Inhibits the formation of vitamin K dependent clotting factors. Factors IX, VII, X, II & protein C& S

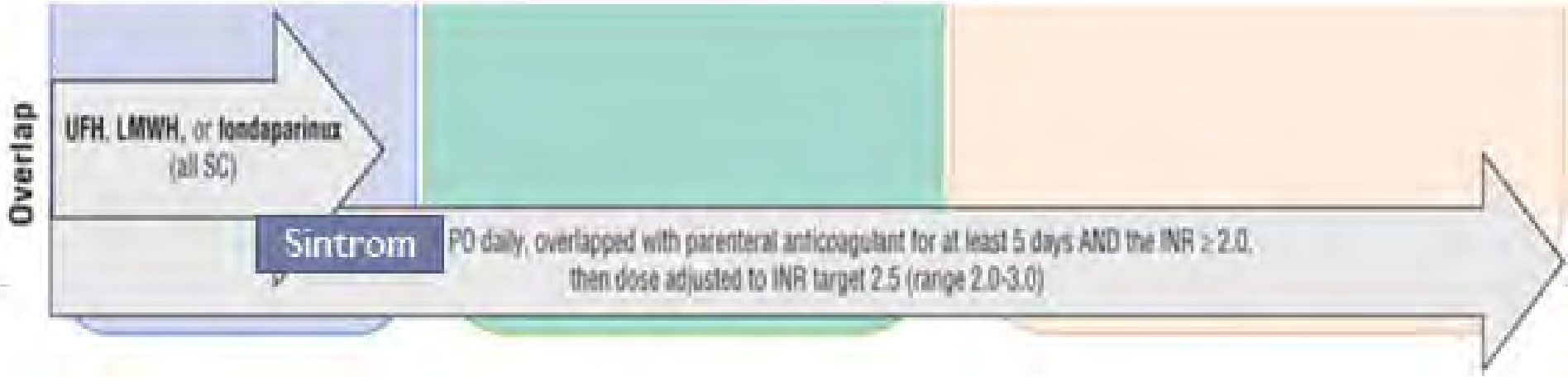
- Onset of action is slow due to:
  - Half life of the medication to reach steady state
    - Hydroxycoumarol: 20-60 hours
    - Acenocoumarol: 8 to 11 hours

  - Full therapeutic effect of VKA antagonist:
    - Hydroxycoumarol: 5-7 days
    - Acenocoumarol: 5 days

Vitamin K antagonists (VKAs)

- Because the full therapeutic effect of VKA antagonist takes 5 days (even if the INR will change fast with sintrom), this doesn't mean full therapeutic effect has been achieved.

- Overlap parenteral and VKAs for a minimum of 4-5 days and until we reach therapeutic INR goal and discontinue parenteral AC upon having 2 consecutive therapeutic INR readings



	Dabigatran	Rivaroxaban	Apixaban
Target	Thrombin	Factor Xa	Factor Xa
Bioavailability	6	80	50
Frequency	Bid	Bid or daily	bid
T- max (h)	2	3	3
Half life (h)	12-17	7-11	9-14
Protein binding(%)	35	95	87
CYP metabolism (%)	None	32	15
P-gp transport	Yes	Yes	yes
Renal excretion (%)	80	66	25
Non renal excretion(%)	20	34	75
Available in Lebanon	Yes	Yes	Yes

CHEST 2012; 141(2)(Suppl):e120S–e151S

Laboratory Tests to Monitor AC

Oral Anticoagulant	Routine laboratory test	Other monitoring parameters
VKA Antagonists	PT/ INR	LFTs
Oral DTI (Dabigatran)	No routine test	SrCr
Direct Xa inhibitor (Rivaroxaban)	No routine test	SrCr
Direct Xa inhibitor (Apixaban)	No routine test	SrCr

CHEST 2012; 141(2)(Suppl):e24S–e43S

Indications for Antithrombotic Therapy

- Stroke prevention in Atrial Fibrillation (SPAF)
- Treatment of VTE (PE and DVT)
- Antithrombotic therapy for CVA

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Risk Assessment Scores: Stroke Assessment Scores

Risk	Point Value
Prior stroke or TIA	2 points
Age > 75 years	1 point
Hypertension	1 point
Diabetes	1 point
Heart Failure	1 point
No risk factors	0 points

Am J Cardiol 2010; 105: 502- 10

Use of CHA_2DS_2-VASc for Stroke Risk Stratification

- ESC AF guideline recommendations
  - $CHADS_2$ should be used as the initial method for stroke risk stratification in patients with AF
    - $CHADS_2$ score ≥ 2 → Warfarin (target INR 2-3)
    - $CHADS_2$ score of 0-1 → Perform CHA_2DS_2-VASc

Camm AJ et al. *Eur Heart J* 2010;31:2369-2429.

CHA2DS2-VASc: Stroke Risk Stratification

Table 9 Approach to thromboprophylaxis in patients with AF

Risk category	CHA_2DS_2-VASc score	Recommended antithrombotic therapy
One 'major' risk factor or ≥2 'clinically relevant non-major' risk factors	≥ 2	OAC[a]
One 'clinically relevant non-major' risk factor	1	Either OAC[a] or aspirin 75–325 mg daily. Preferred: OAC rather than aspirin.
No risk factors	0	Either aspirin 75–325 mg daily or no antithrombotic therapy. Preferred: no antithrombotic therapy rather than aspirin.

AF = atrial fibrillation; CHA_2DS_2-VASc = cardiac failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled)-vascular disease, age 65–74 and sex category (female); INR = international normalized ratio; OAC = oral anticoagulation, such as a vitamin K antagonist (VKA) adjusted to an intensity range of INR 2.0–3.0 (target 2.5).

European Heart Journal (2010) 31, 2369–2429

HASBLED Score: Bleeding Risk Score

Table 10 Clinical characteristics comprising the HAS-BLED bleeding risk score

Letter	Clinical characteristic[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

European Heart Journal (2010) 31, 2369–2429

Case 1

- MM is a 67 year old woman who underwent a mechanical mitral valve replacement 7 months ago. She presents to clinic with atrial fibrillation and during work up expresses interest in being started on rivaroxaban instead on acenocoumarol. Creatinine Clearance ~ 90ml/min.
- At home is on:
  - acenocoumarol regimen: MWFSS 2mg & TTH 3mg
  - INR goal 2.5-3.5
  - Last INR (1 week ago, 2.7)

- **Which of the following is the best treatment plan for this patient?**
  A. Switch to rivaroxaban 20mg po daily
  B. Switch to rivaroxaban 15 mg po daily
  C. Switch to dabigatran 150mg po bid
  D. Keep on acenocoumarol

NOACS:
Stroke Prevention in Atrial Fibrillation

- Data randomized controlled trials (~ 70,000 patients)
  - Majority are non-inferiority trials in terms of decrease in stroke (Ischemic & hemorrhagic) in comparison to VKA
  - Less incidence of intracranial hemorrhage

- NOACs are associated with an increase in GI bleeds as compared to warfarin

NOACS:
Stroke Prevention in Atrial Fibrillation

Non-valvular atrial fibrillation

+

Indication for Anticoagulation

Dose adjustments of NOACS are necessary for renal impairment in Stroke Prevention in Atrial Fibrillation (SPAF)

NOACS in SPAF Trials

	RE-LY[a]	ROCKET-AF[b]	ARISTOTLE[c]	ENGAGE AF[d]
Drug	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
# Randomized	18,113	14,266	18,201	21,105
Dose, mg	150, 110	20	5	60, 30
Frequency	Twice Daily	Once Daily	Twice Daily	Once Daily
Dose adjustment	No	20 → 15	5 → 2.5	60 → 30 30 → 15
• At baseline	0	21	5	25
• After randomization	No	No	No	> 9%
Target INR (warfarin)	2.0-3.0	2.0-3.0	2.0-3.0	2.0-3.0
Design	PROBE*	2x blind	2x blind	2x blind

a. Connolly AJ, et al. *N Engl J Med*. 2009;361:1139-1151[18];
b. Patel MR, et al. *N Engl J Med*. 2011;365:883-891[19];
c. Granger CB, et al. *N Engl J Med*. 2011;365:981-992[20];
d. Giugliano RP, et al. *N Engl J Med*. 2013;369:2093-2104.[21]

Dose Reduction TSOACS in SPAF Trials

RE-LY[a]	ROCKET-AF[b]	ARISTOTLE[c]	ENGAGE-AF[d]
Not studied in CrCl< 30ml/min ! 2 doses studied: 150mg PO BID 110mg PO BID Approved on the market is also 75mg po BID	• 20→15 mg QD for: – Creatinine clearance < 30-49 mL/min	• 5→2.5 mg BID for ANY TWO of: – Age ≥ 80 years – body weight ≤ 60 kg – Serum creatinine ≥ 1.5 mg/dL	• 60→30 mg QD or 30→15 mg QD for: – Creatinine clearance 30-50 mL/min – body weight ≤ 60 kg – Use of quinidine, verapamil, or dronedarone

a. Connolly SJ,et al. *N Engl J Med*. 2009;361:1139-1151[18]
b. Patel MR, et al. *N Engl J Med*. 2011;365:883-891[19];
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WHY NOT NOACS IN VAVULAR ATRIAL FIBRILLATION

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dabigatran versus Warfarin in Patients with Mechanical Heart Valves

John W. Eikelboom, M.D., Stuart J. Connolly, M.D., Martina Brueckmann, M.D., Christopher B. Granger, M.D., Arie P. Kappetein, M.D., Ph.D., Michael J. Mack, M.D., Jon Blatchford, C.Stat., Kevin Devenny, B.Sc., Jeffrey Friedman, M.D., Kelly Guiver, M.Sc., Ruth Harper, Ph.D., Yasser Khder, M.D., Maximilian T. Lobmeyer, Ph.D., Hugo Maas, Ph.D., Jens-Uwe Voigt, M.D., Maarten L. Simoons, M.D., and Frans Van de Werf, M.D., Ph.D., for the RE-ALIGN Investigators*

- **N= 256 patients**
- **Terminated early:**
  - The use of dabigatran in patients with mechanical heart valves was associated with increased rates of thromboembolic and bleeding complications, as compared with warfarin, thus showing no benefit and an excess risk.

N ENGL J MED 369;13 september 26, 2013

WHAT IS THE EXACT DEFINITION OF VAVLUAR AFIB?

Europace Advance Access published August 31, 2015

Europace
doi:10.1093/europace/euv309

EHRA PRACTICAL GUIDE

Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation

Valvular Indications and Contraindications to NOACs in Afib

- **Contraindicated for NOACS**
  - Mechanical prosthetic heart valves
  - Mitral stenosis(moderate to severe)

- **Eligible for NOACS**
  - Other native valve diseases (mild to moderate)
  - Severe aortic stenosis
  - Bioprosthetic heart valves (except in the first 3 months)
  - Mitral valve repair (except in the first 3 -6 months)

Recognizing Drug Interactions: Community or Hospital Setting

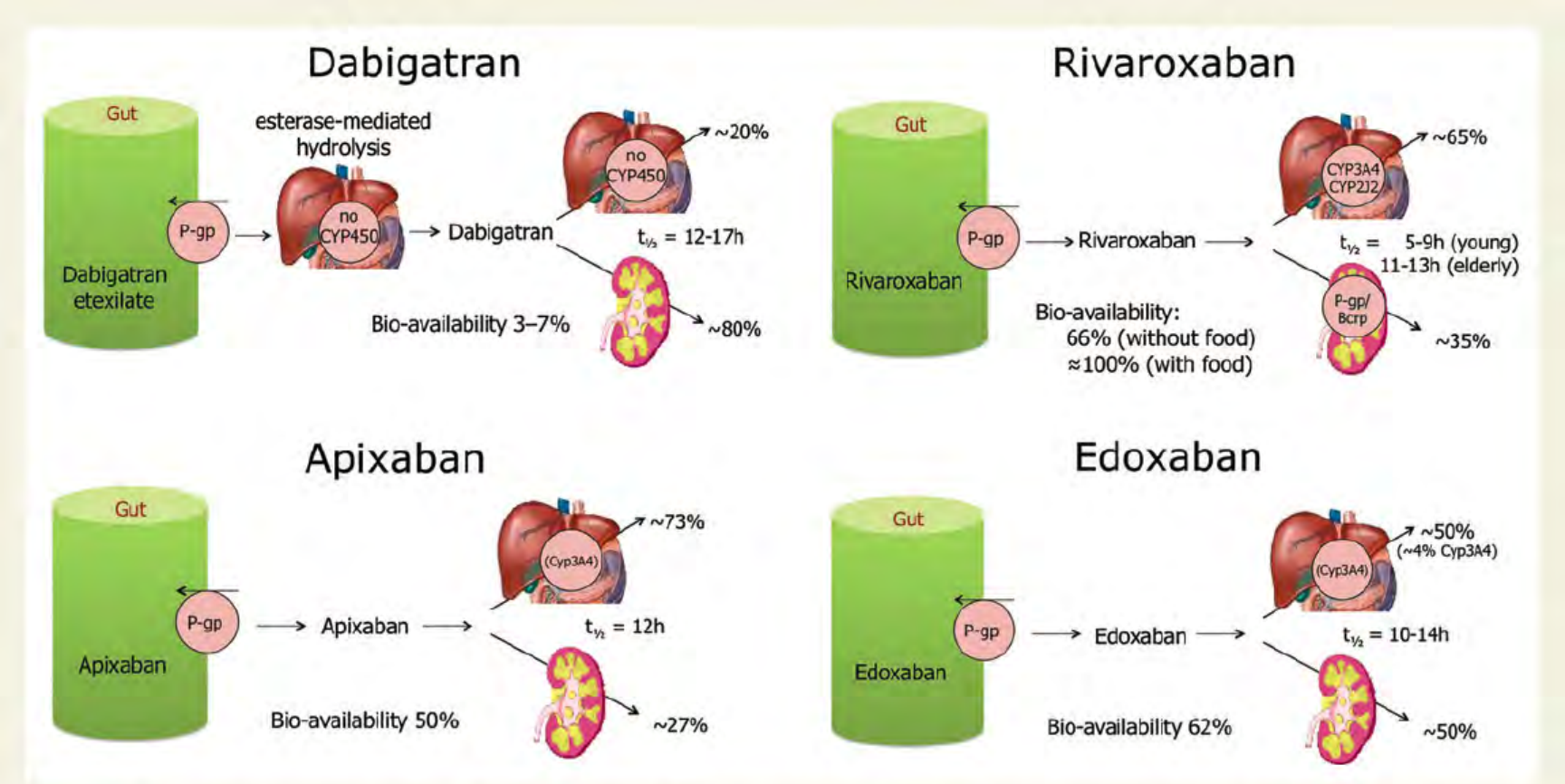

Figure 3 Absorption and metabolism of the different new anticoagulant drugs. There are interaction possibilities at the level of absorption or first transformation, and at the level of metabilization and excretion. See also *Table 5* for the size of the interactions based on these schemes.

Europace doi:10.1093/europace/euv309

Recognizing Drug Interactions: Community or Hospital Setting

- **Mechanism of interaction:** cytochrome P450 3A4 and P-glycoprotein (P-gp)

- **Concern:** minimal guidance for dose adjustments & monitoring is not possible

- **Interacting medications:**
  - Antimicrobials (antifungals, antibiotics, antiretrovirals)
  - Antiepileptics
  - Immunosuppressant
  - Verapamil

Interpreting medication interactions with NOACs based on the EHRA

- **Red:** contra-indicated/not recommended.
- **Orange:** reduce dose (from 150 to 110 mg BID for dabigatran; from 20 to 15 mg OD for rivaroxaban; from 5 to 2.5 mg BID for apixaban).
- **Hatching:** no clinical or PK data available.
- **Brown:** contraindication for interactions that lead to reduced NOAC plasma levels
- **Yellow:** consider dose reduction if 2 or more 'yellow' factors are present.

Table 6 *Continued*

	via	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
Fungostatics					
Fluconazole	Moderate CYP3A4 inhibition	No data yet	No data yet	No data yet	+42% (if systemically administered)[247]
Itraconazole; Ketoconazole; Posaconazole; Voriconazole;	potent P-gp and BCRP competition; CYP3A4 inhibition	+140-150% (US: 2 x 75 mg if CrCl 30-50 ml/min)	+100%[60]	+87-95%[64] (reduce NOAC dose by 50%)	Up to +160%[247]
Immunosuppressive					
Cyclosporin; Tacrolimus	P-gp competition	Not recommended	No data yet	+73%	Extent of increase unknown
Antiphlogistics					
Naproxen	P-gp competition	No data yet	+55%[254]	No effect (but pharmacodynamically increased bleeding time)	No data yet
Carbamazepine***; Phenobarbital***; Phenytoin***; St John's wort***	P-gp/ BCRP and CYP3A4/CYP2J 2 inducers	minus 66%[253]	minus 54%[SmPC]	minus 35%	Up to minus 50%
Other factors:					
Age ≥ 80 years	Increased plasma level		#	%	
Age ≥75 years	Increased plasma level			%	
Weight ≤ 60 kg	Increased plasma level		#		
Renal function	Increased plasma level	See Table 8			
Other increased bleeding risk		Pharmacodynamic interactions (antiplatelet drugs; NSAID; systemic steroid therapy; other anticoagulants); history of GI bleeding; recent surgery on critical organ (brain; eye); thrombocytopenia (e.g. chemotherapy); HAS-BLED ≥3			

Take Home Message: Anticoagulation in Stroke Prevention in Atrial Fibrillation

- VKA
  - Approved for both valvular and non-valvular atrial fibrillation
  - **VKA and bridging with parenteral anticoagulation is recommended**
- NOACS:
  - Approved for **non-valvular atrial fibrillation**
  - Imperative to **dose adjust in renal dysfunction**
  - **Less intracranial hemorrhage** but **more gastrointestinal bleeding** (except apixaban)
  - Necessitate that pharmacists **screen for drug interactions**

Case 1

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- At home is on:
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- **Which of the following is the best treatment plan for this patient?**
  A. Switch to rivaroxaban 20mg po daily
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  D. **Keep on acenocoumarol**

Indications for Antithrombotic Therapy

- Stroke prevention in Atrial Fibrillation (SPAF)
- **Treatment of VTE (PE and DVT)**
- Antithrombotic therapy for CVA

Clinical Practice Guideline Recommendations: Treatment of Venous Thromboembolism (DVT & PE)

- 2016 ACCP Guidelines (Jan 2016)
  - NOACs (dabigatran, apixaban, edoxaban or rivaroxaban) are first line options
  - Conventional treatment (VKA (sintrom or warfarin) + parenteral anticoagulation)is second line option

Chest. 2016. doi:10.1016/j.chest.2015.11.026

Clinical Practice Guideline Recommendations: Treatment of Venous Thromboembolism (DVT & PE)

1. **Bridging: (Conventional Therapy)**
   - Parenteral anticoagulant + bridge to oral therapy VKA (we start oral VKA and the parenteral at the same time, we keep the patient on the parenteral AC, for at least 4-5 days and until we are sure that the VKA is therapeutic, then we stop the parenteral and keep the patient on oral VKA)

2. **Directly oral treatment: (using target specific oral anticoagulants(TSOACS))**
   - Rivaroxaban 15mg PO BID for 21 days, followed by 20mg PO daily
   - Apixaban 10 mg twice daily for 7 days followed by 5 mg twice daily

3. **Switching: (using target specific oral anticoagulants(TSOACS))**
   - Start parenteral anticoagulant for 2 weeks, then switch to Dabigatran 150mg PO BID
   - Start parenteral anticoagulant, then switch to Edoxaban 60mg po daily or if impared renal function (CrCrl 30-50ml/min, weight<60kg or taking potent pgp inhibitors) 30mg PO daily

NOACS: Treatment of Venous Thromboembolism (DVT & PE)

- Randomized controlled trials (~ 25,000 patients)
  - Non-inferior to conventional treatment for VTE recurrence(margins of non-inferiority between 1.5-2.75)
  - Less bleeding (notably more GI bleeding, except apixaban)
  - Superior to placebo for the prevention of recurrent VTE and are associated with lower bleeding rates.

J Thromb Thrombolysis (2015) 39:264-272 Blood 2014;124(7):1020-1028

Case 2

- A 70 yo woman (wt=80kg, ht=173cm) is diagnosed with a DVT. No significant PMH. Pertinent history is that she's not very active and had recent travel. Her CrCl is estimated at 25ml/min. **Which of the following treatment choices is most suitable for this patient?**
  A. Enoxaparin that is bridged to acenocoumarol 2mg po daily
  B. Rivaroxaban 15mg po BID for 21 days followed by 20mg po daily
  C. Enoxaparin for 7 days followed by Dabigatran 150mg po BID
  D. Dabigatran 150mg po BID

NOACS: Treatment of Venous Thromboembolism (DVT & PE)

DVT or PE

+

Good renal function defined as CrCl(≥ 30 ml/min)

NO DOSE ADJUSTMENTS EXIST

for CrCL < 30ml/min for Apixaban, Dabigatran or Rivaroxaban in the treatment of VTE

Patients who should NOT receive NOACS in VTE

- Severe renal impairment defined as: CrCl<30 mL/min for rivaroxaban, dabigatran and edoxaban; and <25 mL/min for apixaban
- VTE in the setting of Cancer
- VTE in the setting of thrombophilic conditions
- When compliance is a concern
- History of GI bleeds
- Nursing mothers
- Pregnancy
- Extreme body weight

Blood 2014;124(7):1020-1028
Konstantinides et al. European Heart Journal. doi:10.1093/eurheartj/ehu283

Appropriate candidates for NOACS in VTE

- On VKA antagonists with erratic INRs
- Those who find INR testing burdensome
- Reliable and compliant patients

Blood 2014;124(7):1020-1028

NOACs in VTE: Which agent is the best for your patient?

Patient specific criteria	NOAC selection
Prefers to avoid injections	Apixaban or Rivaroxaban
CrCl between 30-50 ml/min	Apixaban, rivaroxaban, edoxaban (not dabigatran)
Dyspepsia or GERD	Rivaroxaban, apixaban, edoxaban
Recent GI bleed	Apixaban
Poor compliance with twice daily dosing	Rivaroxaban or edoxaban
Recent myocardial infarction	Rivaroxaban, apixaban ,edoxaban

Blood 2014;124(7):1020-1028

Take Home Message: Anticoagulation in VTE Treatment

- **Verify** appropriate renal function **CrCl> 30ml/min**
- Screen for interactions & caution providers
- **Remember the strategies:**
  - Start **directly oral** therapy with **Rivaroxaban or Apixaban**
  - If **dabigatran or edoxaban** are selected, **the first week** should be **parenteral** treatment, **then SWITCH to NOACS**
- Emphasize on **compliance, especially the switch in doses**

- **VKA and bridging with parenteral anticoagulation is recommended if:**
  - **CrCl< 30ml/min & in** special populations: cancer, pregnancy, thrombophilic conditions, extreme body weight

Case 2

- A 70 yo woman (wt=80kg, ht=173cm) is diagnosed with a DVT. No significant PMH. Pertinent history is that she's not very active and had recent travel. **Her CrCl is estimated at 25ml/min. Which of the following treatment choices is most suitable for this patient?**

A. **Enoxaparin that is bridged to acenocoumarol 2mg po daily**
B. Rivaroxaban 15mg po BID for 21 days followed by 20mg po daily
C. Enoxaparin for 7 days followed by Dabigatran 150mg po BID
D. Dabigatran 150mg po BID

Indications for Antithrombotic Therapy

- Stroke prevention in Atrial Fibrillation (SPAF)
- Treatment of VTE (PE and DVT)
- **Antithrombotic therapy for Cerebral Vascular Accident (CVA)**

Classification of CVA

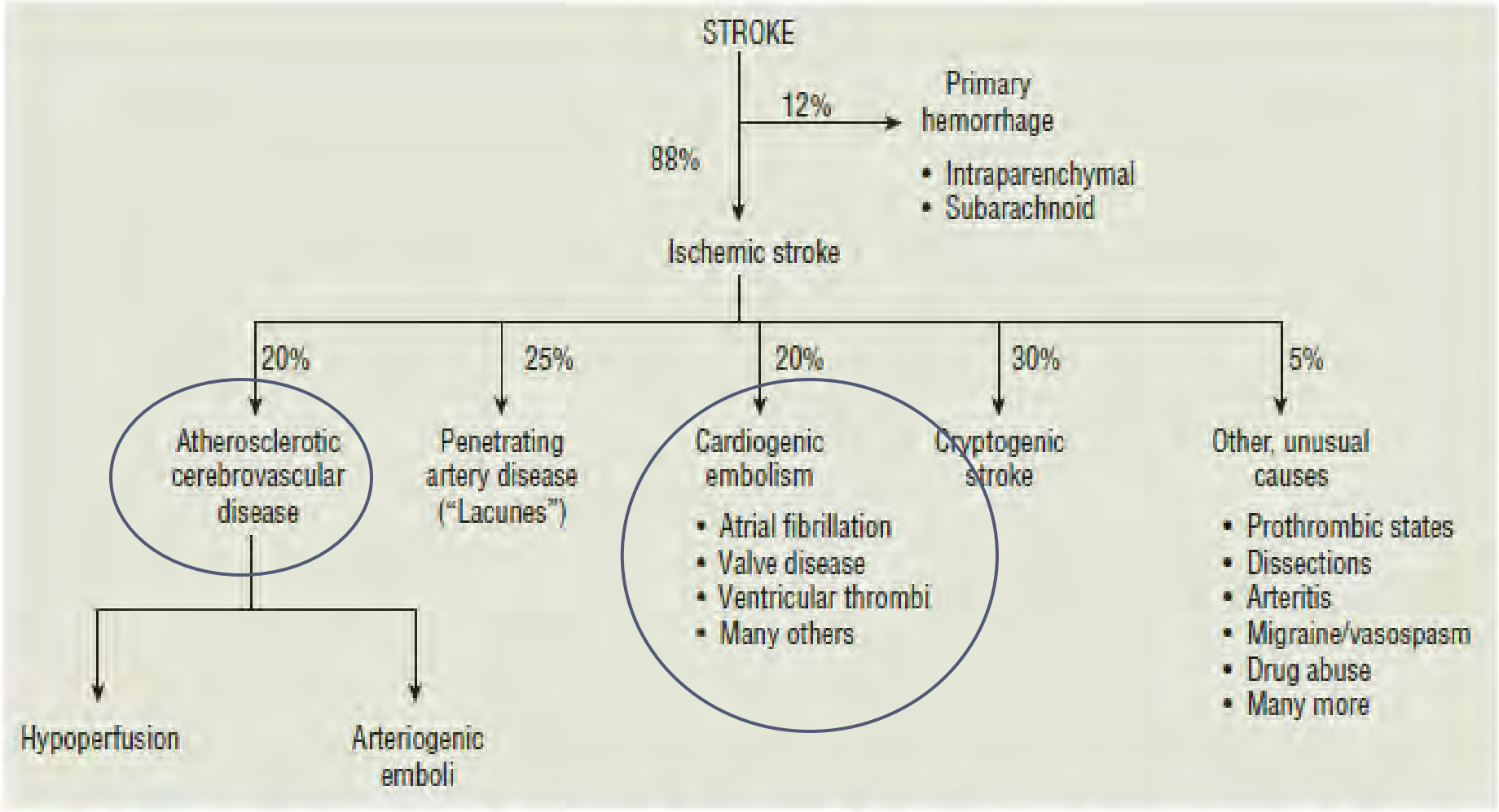

FIGURE 22-1. A classification of stroke by mechanism with estimates of the frequency of various categories of abnormalities. Approximately 30% of ischemic strokes are cryptogenic.

Antithrombotics for Secondary Stroke Prevention

- Pharmacologic categories used in secondary stroke prevention
  - Antiplatelets
  - Anticoagulants

Selection of the appropriate antithrombotic agent: Cardioembolic Vs Non-cardioembolic

Non-cardioembolic Stroke or TIA

- Antiplatelet
  - ASA
  - Plavix
  - Extended Release Dipyridamole+ ASA

Cardioembolic Stroke or TIA (Presence of Afib or Valvular disease)

- **Afib:**
  - Anticoagulation (CHADS2 score automatically ≥2)
    - NOACs or VKA anticoagulant based on the presence of valvular or non-valvular AFIB)
  - Non-tolerant ➔ give antiplatelets
- **Valvular heart disease** (ex. Mechanical valve)
  - Antithrombotic therapy depending on:
    - Valve type
    - Location (mitral or aortic)
    - when the valve was placed (> or < 3 mo ago)

Case

- G.R is a 55 year old man with a PMH of a non-cardioembolic stroke, CAD, dyslipidemia and peptic ulcers. **What would be the best option for secondary stroke prevention?**

a) Aspirin 81mg po daily
b) Acenocoumarol 2mg po daily
c) Clopidogrel 75mg daily
d) Rivaroxaban 20mg po daily

Non-cardioembolic strokes: Antiplatelet options for Secondary Stroke Prevention

- Antiplatelet options (all acceptable options for initial therapy):
  - Aspirin (50 mg/d to 325 mg/d) monotherapy
  - The combination of aspirin 25 mg and extended-release dipyridamole 200 mg twice daily
  - Clopidogrel 75 mg monotherapy

- Combination aspirin/extended release dipyridamole or clopidogrel is preferred over aspirin alone (Guyatt, 2012).

- The combination of ASA +clopidogrel might be considered in minor non-cardioembolic stroke/TIA and continued for 90 days

Antiplatelet Agent Comparison

Drug	Aspirin	Clopidogrel	ASA+ERDP
The selection of an antiplatelet agent should be individualized on the basis of patient risk factor profiles, cost, tolerance, and other clinical characteristics			
Side Effects	GI upset GI bleed	• Less GI bleed • Less diarrhea • Rash	• GI upset • Headache (usually self limiting)
Monitor	Periodic assessment of : Hemoglobin, Hct, platelets and signs of bleeding		

Case

- G.R is a 55 year old man with a PMH of a non-cardioembolic stroke, CAD, dyslipidemia and peptic ulcers. **What would be the best option for secondary stroke prevention?**

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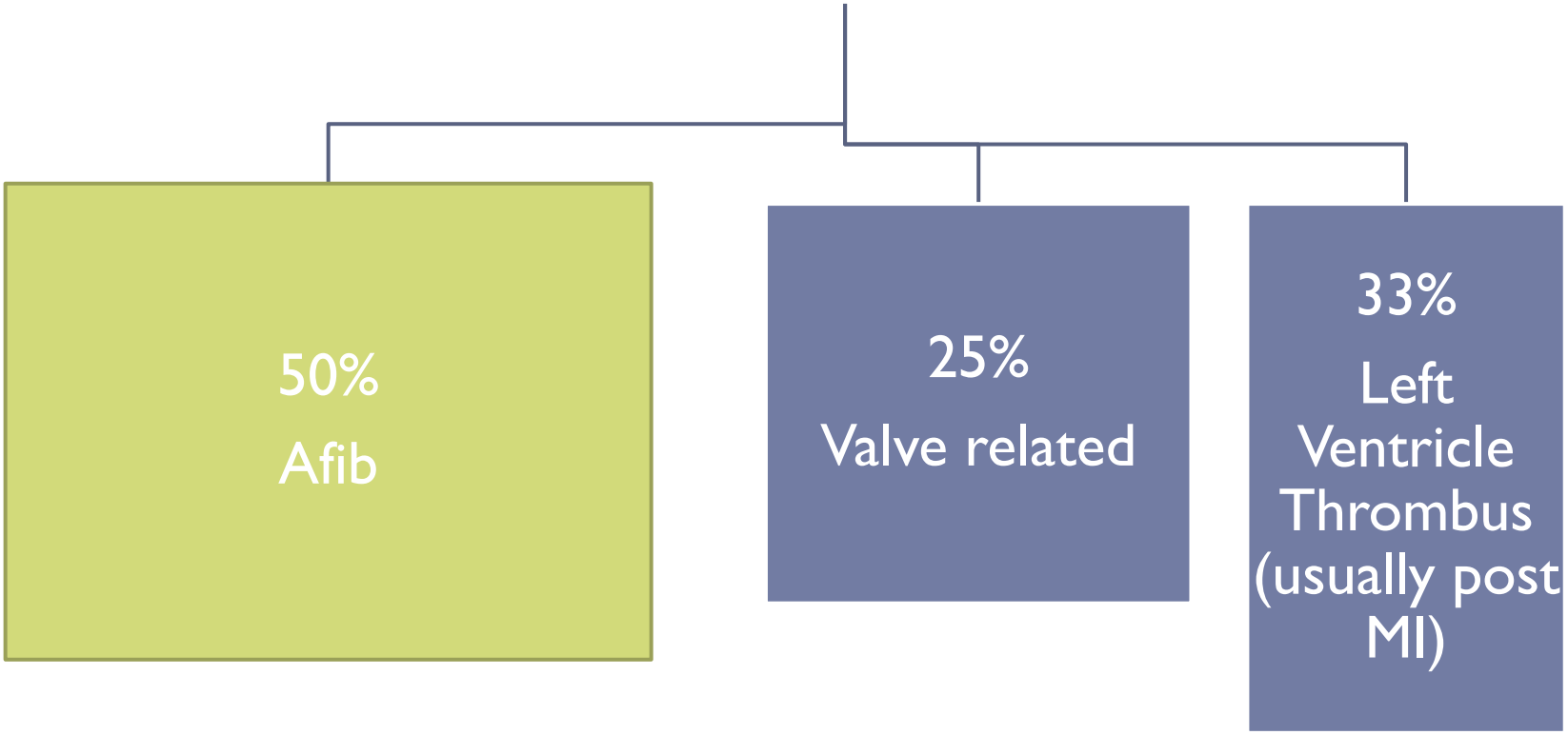
Cardioembolic Stroke make up 20% of IS



Stroke.2006;37:577-617

Case

- G.R is a 55 year old man with a PMH of a cardioembolic stroke, with a history of atrial fibrillation, CAD, dyslipidemia. The patient lives very far from access to a laboratory for monitoring of therapy. **What would be the best option for secondary stroke prevention?**

a) Aspirin 81mg po daily
b) Acenocoumarol 2mg po daily, INR goal 2-3
c) Clopidogrel 75mg daily
d) Rivaroxaban 20mg po daily

Cardioembolic Source Risk

Table 4—*Cardioembolic Sources (Section 4.4)*

Major Risk	Minor or Uncertain Risk
Atrial fibrillation	Mitral valve prolapse
Mitral stenosis	Mitral annular calcification
Prosthetic mechanical valves	PFO
Recent myocardial infarction	Atrial septal aneurysm
Left ventricular thrombus	Calcific aortic stenosis
Atrial myxoma	
Infective endocarditis	
Dilated cardiomyopathies	
Marantic endocarditis	

Chest 2008;630S-669S

Secondary Stroke Prevention in patients who experienced Cardioembolic stroke due to Atrial Fibrillation

- **Anticoagulation (CHADS2 score automatically ≥2)**
  - NOACs or VKA anticoagulant based on the presence of valvular or non-valvular AFIB)

- **How soon after having a cardioembolic stroke can anticoagulation be started?**
  - Within 14 days after the onset of neurological symptoms
  - Delay initiation beyond 14 days If the patient is diagnosed with a high risk for hemorrhagic conversion
    - High risk of hemorrhagic conversion: large infarct, hemorrhagic transformation on initial imaging, uncontrolled hypertension

Secondary Stroke Prevention in patients who experienced Cardioembolic stroke due to Atrial Fibrillation

- For ischemic stroke or TIA with **valvular AFib**, anticoagulation with a VKA (target INR 2.0 to 3.0)

- For ischemic stroke or TIA with **NON-VALVULAR AFIB** :
  - VKA therapy
  - Apixaban
  - Dabigatran
  - Rivaroxaban
    - The selection of an antithrombotic agent should be individualized on the basis of risk factors, cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics, including renal function and time in INR therapeutic range

Secondary Stroke Prevention in patients who experienced Cardioembolic stroke due to Atrial Fibrillation

- For patients who are unable to take oral anticoagulants:
  - Aspirin alone is recommended (Class I; Level of Evidence A).
  - Aspirin + clopidogrel (Class IIb; Level of Evidence B).

- The combination of Oral Anticoagulation (VKA or NOAC) + antiplatelet therapy
  - not recommended for all patients after ischemic stroke or TIA
  - reasonable after acute coronary syndrome or stent placement

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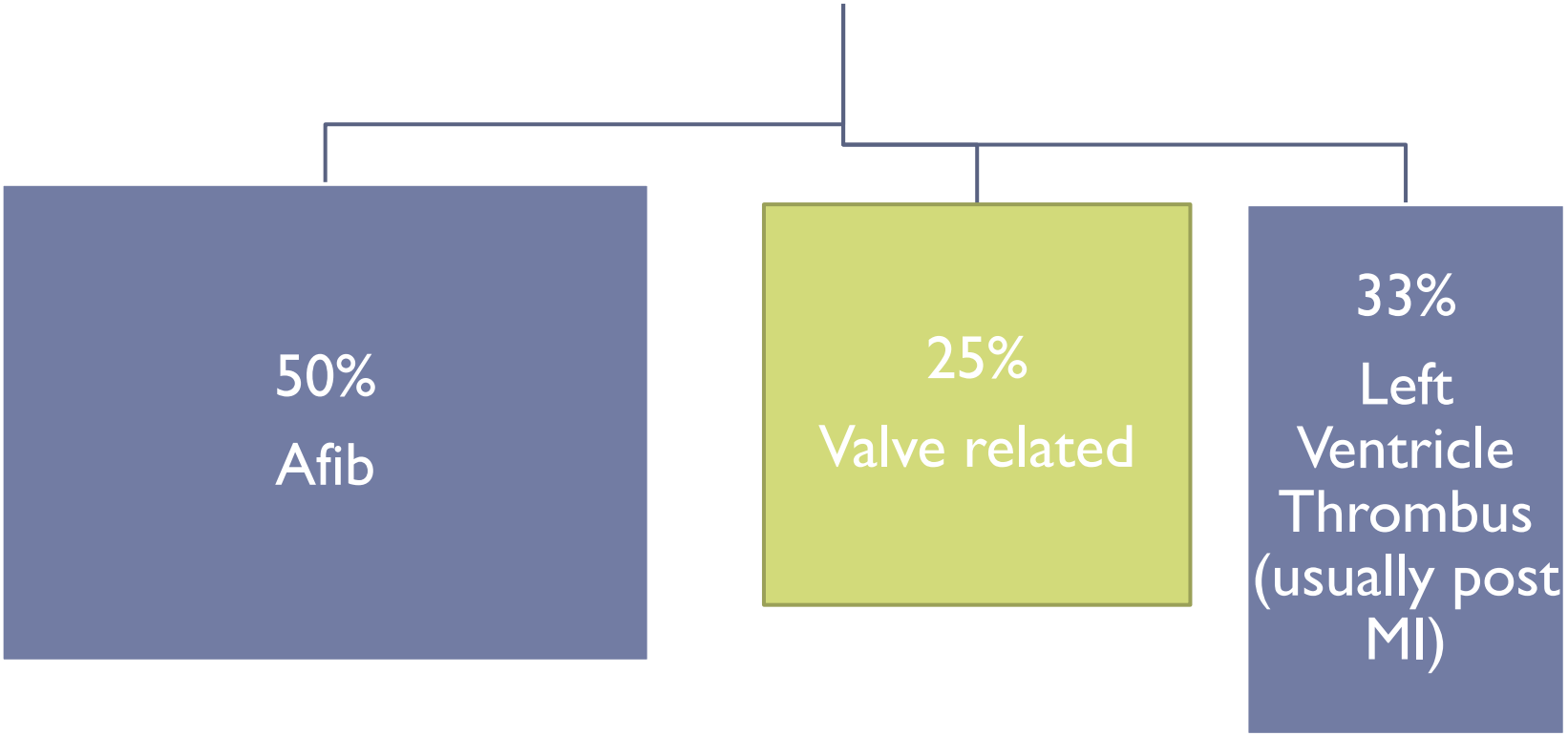
d) Rivaroxaban 20mg po daily

Cardioembolic Stroke make up 20% of IS



Stroke.2006;37:577-617

Secondary Stroke Prevention in patients who experienced Cardioembolic stroke in the presence of prosthetic heart valves

- Patients with a history of ischemic stroke/ TIA who have a mechanical valve replacement:
  - mechanical mitral heart valves, VKA goal INR 2.5 to 3.5
  - mechanical aortic heart valves, VKA goal INR 2 to 3

- Patients with **mechanical prosthetic heart valves who have an ischemic stroke despite therapeutic INR:**
  - Consider adding aspirin 75 mg/d to 100 mg/d to VKA and maintain INR at a target.

Secondary Stroke Prevention in patients who experienced Cardioembolic stroke in the presence of prosthetic heart valves

- Patients with a history of ischemic stroke/ TIA who have a BIOprosthetic valve replacement:
  - **Bioprosthetic aortic or mitral valve**, give 3 to 6 months of anticoagulation **(INR 2-3)** from the time of valve placement.
  - After 3-6 months of AC, stop anticoagulation and continue on long-term aspirin 75 to 100 mg/d

Take Home Message
Antithrombotic Therapy for CVA

- Antithrombotic therapy for secondary prevention of CVA depends on the type of stroke:
  - If atherosclerotic stroke, give antiplatelet
  - If cardio-embolic stroke (stroke associated with atrial fibrillation or valvular heart disease), give anticoagulant
    - Select anticoagulation (NOACs versus VKA)depending on factors such:
      - as renal impairment
      - presence of a valve replacement

Anticoagulation Counseling

Anticoagulation Counseling Tips

- Involve your patient
- Compliance – frequency of medication
- NOACS: Importance of follow up even if no INR checks
- VKA: Importance of checking INR
- Inform the doctor about new medications
- Missed doses
- How to take the medication
- How to store the medication
- In case of bleeding, share with physician time of last dose and renal function

Anticoagulation Counseling Tips

- Dabigatran
  - Do not crush or chew tablets
  - Do not open or sprinkle the capsule
  - Avoid in patients with GERD, history of GI bleed, MI
- Rivaroxaban
  - Take with food
  - You can crush tablets
  - Avoid in history of GI bleed
- Apixaban
  - You can crush tablets

Consider Counseling Initiatives

Anticoagulants

What are anticoagulants?

Anticoagulants are medicines that prevent the blood from clotting as quickly or as effectively as normal.

- It is used to thin the blood so that clots will not form.
- It is used to treat blood clots.

What are some things I need to know or do while I take this drug?

- Tell dentists, surgeons, and other doctors that you use this drug.
- Keep a list of all your drugs (prescription, natural products, vitamins, Over The Counter) with you.
- Talk with the doctor before starting or stopping any drug, including prescription or OTC, natural products, or vitamins.
- Talk with your doctor if you have recently had or will be having a spinal or epidural procedure.

Consider Counseling Initiatives

When do I have to call my doctor or get medical help about right away?

- Allergic reaction, you may feel:
  - rash; itching
  - tightness in the chest or throat
  - swelling of the mouth, face, lips, tongue, or throat
- Signs of bleeding:
  - throwing up or coughing blood that looks red or like coffee grounds (or dark brown)
  - blood in the urine that looks either pink or brown
  - black, red, or tarry stools
  - bruises without a reason or that get bigger
  - any bleeding that is very bad or that you cannot stop like bleeding from the nose, gums or vaginal or menstrual bleeding
- A fall or when you hit your head even if you feel fine
- Stomach pain
- Change in thinking clearly, trouble speaking, change in balance, blurred eyesight.
- Very bad headache, numbness, muscle weakness or paralysis, loss of bladder or bowel control

Helpful Links :
Provider & Patient Education

- http://www.doacresources.org/resources
- http://www.anticoagulationtoolkit.org/
- http://excellence.acforum.org/

Conclusion

- NOACS have provided a significant advancement in oral anticoagulation
  - Appropriate patient selection is mandatory
  - Good renal function is important
  - Screen for unrecognized drug interactions
- SPAF:
  - CHADS2 score < 2, antiplatelet is reasonable
  - CHADS 2 Score ≥2 : give anticoagulation
    - NOACS if non-valvular atrial fibrillation and dose adjust for renal impairment
    - VKA if valvular atrial fibrillation
- VTE:
  - NOACs are first link but contraindicated in renal impairment, no dose adjustments are available for VTE treatment
  - Conventional bridge therapy with(VKA + parenteral anticoagulant) is second line, unless patient cannot get NOACs
- CVA:
  - If atherosclerotic stroke, give antiplatelet
  - If cardio-embolic stroke, give anticoagulant
    - For anticoagulation: select between NOACs and VKA depending on factors such as renal impairment


THANKS!