Risk of VTE and Treatment

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Objectives

Should be able to understand terms associated with VTE

Should be able to triage a patient upon diagnosis

Should be able to determine to risks and benefits to VTE treatments

Should be able to differentiate between conventional and new therapies for VTE

Terms

VTE- venous thrombus embolism

DOAC- direct oral acting anticoagulant

NOAC- novel oral anticoagulant

Vitamin K antagonist- basically warfarin

DVT Classification

Proximal

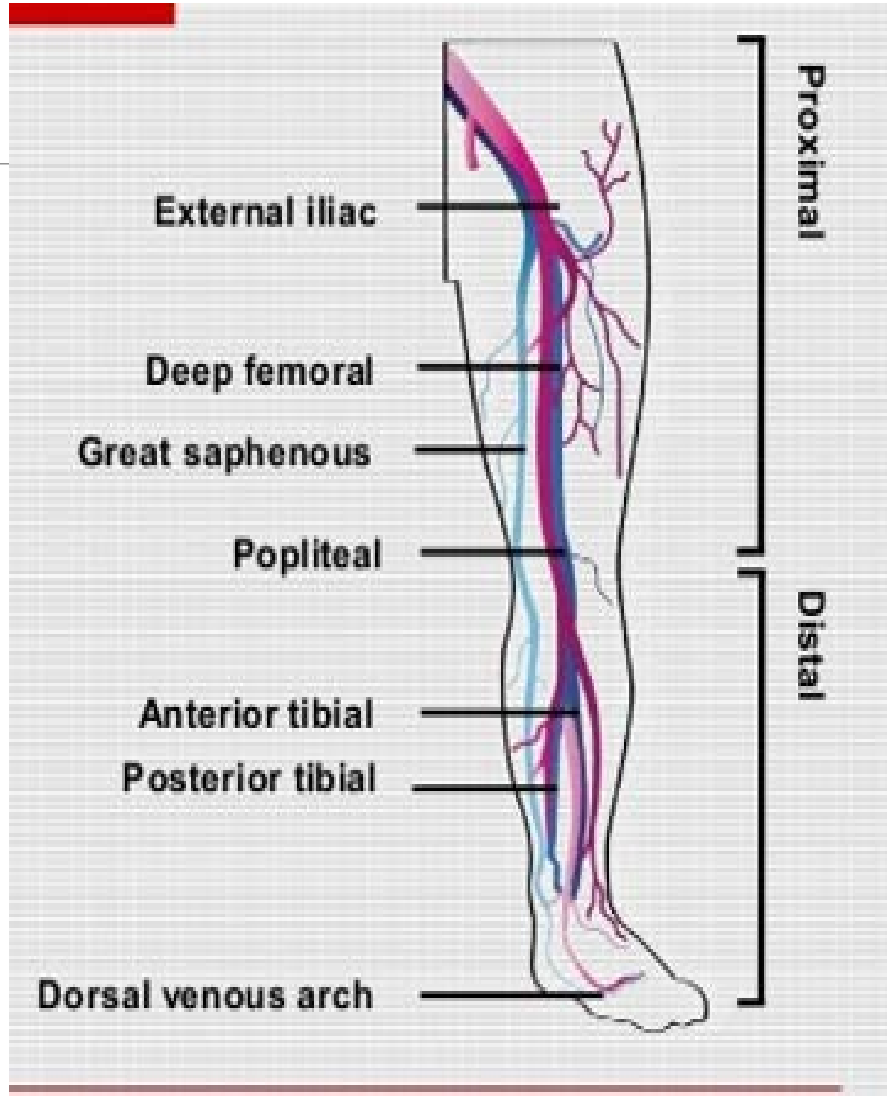
- Above the knee
- Popliteal and femoral veins
- Risk of recurrence greater

Distal- below the knee in calf

- DVT usually starts here

Thrombus may extend to proximal veins

then embolize



Provoked vs. Unprovoked

Unprovoked- No identifiable event

Provoked -cause by a known event

- Surgery
- Hospital Admission
- Estrogen
- Pregnancy

Risk factors

- Reversible- remission
- Irreversible- inheritable thrombophilias

Timing

Initial Anticoagulation- first 10 days

Long-term- finite time up to 12 months

Extended- administered indefinitely

Triage

Observation:

- Social, clinical, safety
- Comorbidities
- Education or compliance
- Financial
- Dosing Transitions
- Bridging

Inpatient if patient:

- Has VTE iliofemoral or above
- DX PE
- High risk of bleeding from treatment
- Comorbidity that requires admission

Risk Factors for Bleeding with AC Therapy

Age > 65

Previous bleed

Cancer

Renal/Liver failure

Thrombocytopenia

Previous stroke

Frequent falls

Diabetes

Anemia

Antiplatelet therapy

Poor anticoagulant control

Comorbidity w/dec. functional capacity

Recent surgery

Alcohol abuse

1. Hull RD, Raskob GE, Rosenbloom D, et al. Heparin for 5 days as compared with 10 days in the initial treatment of proximal venous thrombosis. N Engl J Med 1990; 322:1260.

Estimated absolute risk of major bleeding (%)			
Categorization of risk of bleeding[Δ]	**Low risk[◇] (0 risk factors)**	**Moderate risk[◇] (1 risk factor)**	**High risk[◇] (≥2 risk factors)**
Anticoagulation 0 to 3 months[§]			
Baseline risk (%)	0.6	1.2	4.8
Increased risk (%)	1	2	8
Total risk (%)	1.6[§]	3.2	12.8[¥]
Anticoagulation after first 3 months[‡]			
Baseline risk (%/years)	0.3[†]	0.6	≥2.5
Increased risk (%/years)	0.5	1	≥4
Total risk (%/years)	0.8[**]	1.6[**]	≥6.5

1. *Hull RD, Raskob GE, Rosenbloom D, et al. Heparin for 5 days as compared with 10 days in the initial treatment of proximal venous thrombosis. N Engl J Med 1990; 322:1260.*

Which one of these is not a Factor Xa inhibitor?

A. Xarelto® (rivaroxaban)
B. Pradaxa® (Dabigatran)
C. Savaysa® (Edoxaban)
D. Eliquis® (Apixiban)

B dabigatran (Pradaxa) which is a direct thrombin inhibitor

Medications

Heparin

Low molecular weight heparin (LMWH)

Warfarin (Coumadin®, Jantoven®)

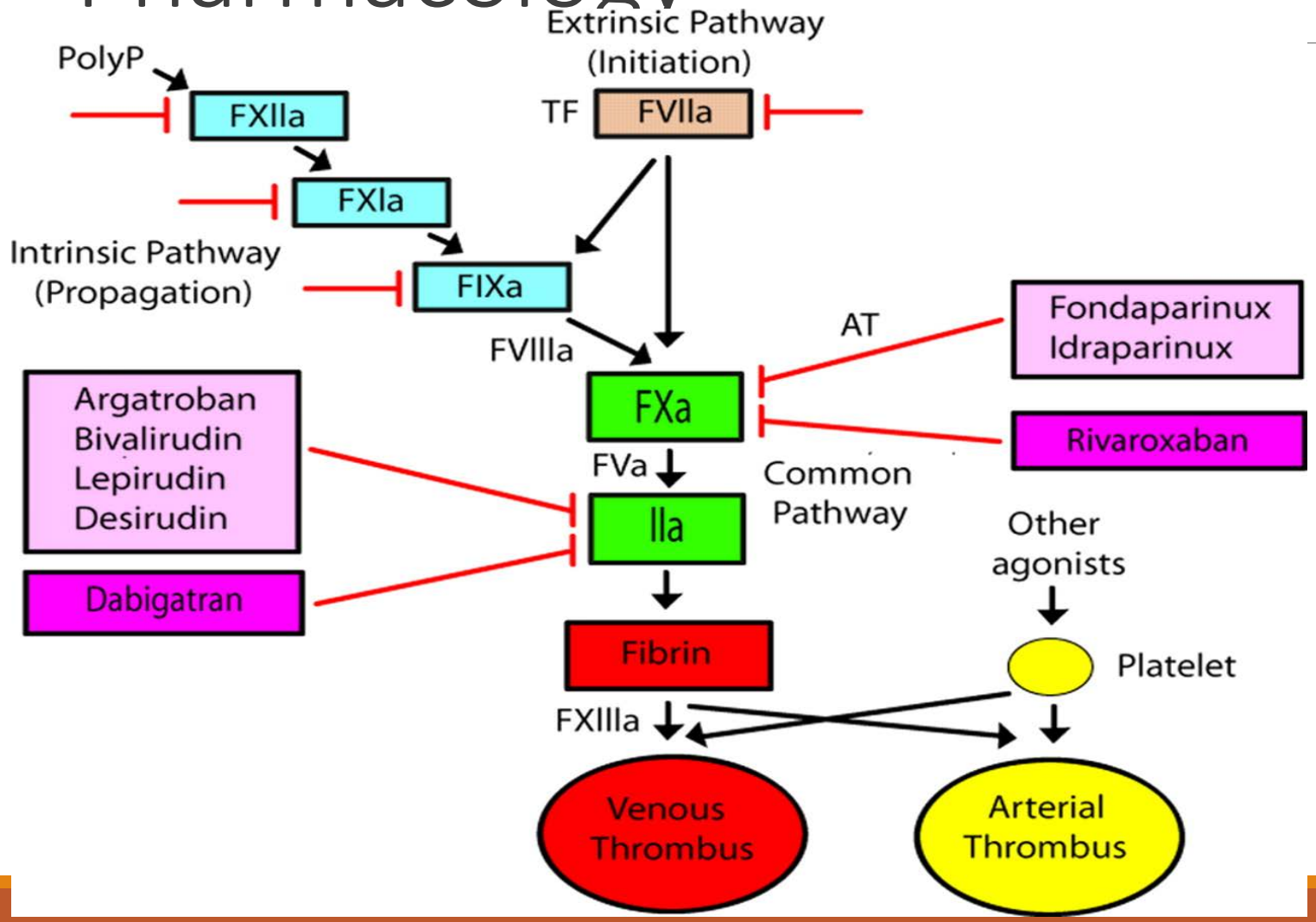
Oral Xa inhibitors

- Rivaroxaban (Xarelto®)
- Apixaban (Eliquis®)
- Edoxaban (Savaysa®)

Direct Thrombin Inhibitor

- Dabigatran (Pradaxa®)

Pharmacology



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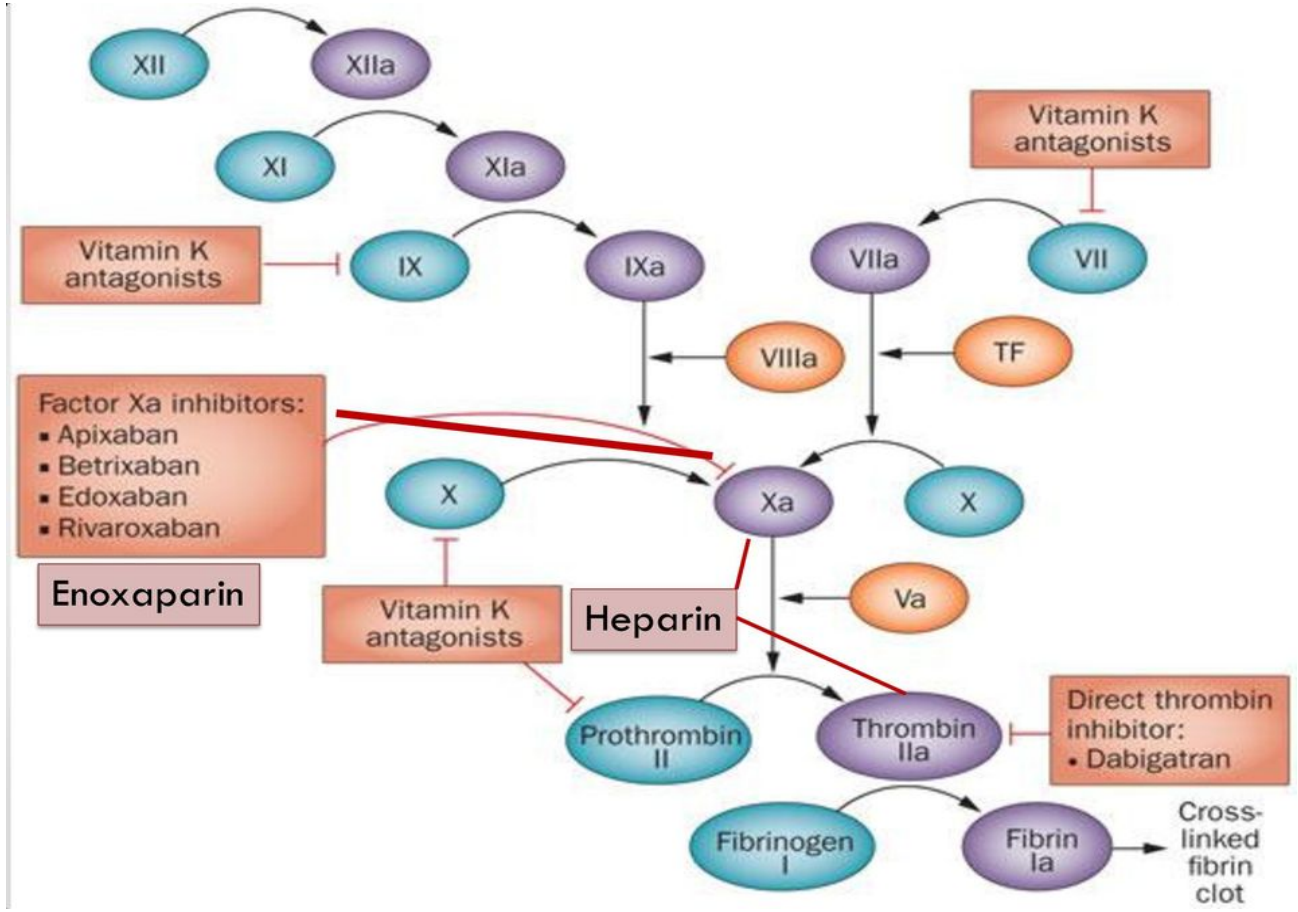
Pharmacology



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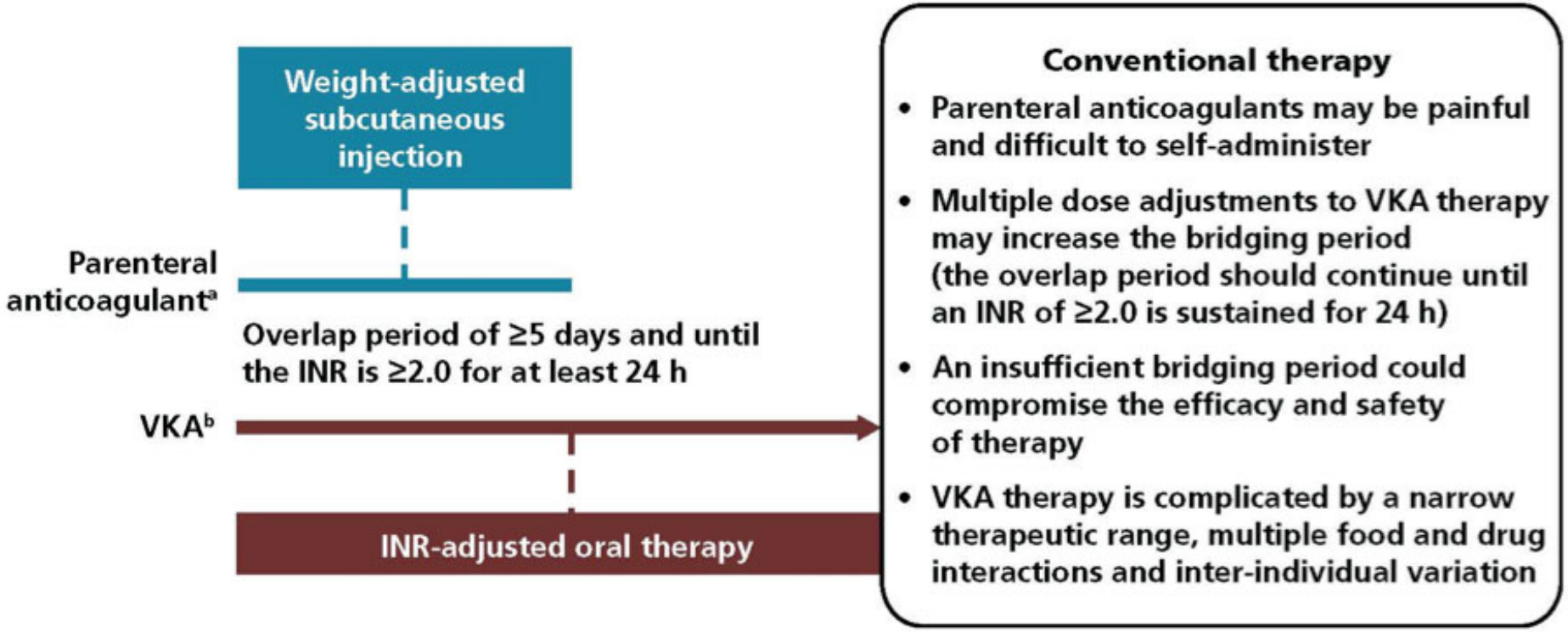
True/False

Heparin may be discontinued once a therapeutic INR is reached, immediately?

Conventional



http://vatspace.com/static/media/images/upload/issue10/a-single-drug-approach-for-the-treatment-and-secondary-prevention-of-vt/Figure1.png?vm=r

False. The patient has to be bridge for at least 5 days with Heparin and have 2 consecutive INR’s above 2

Choice

No head to head studies

New oral anticoagulants (NOAC) compared to bridge-warfarin

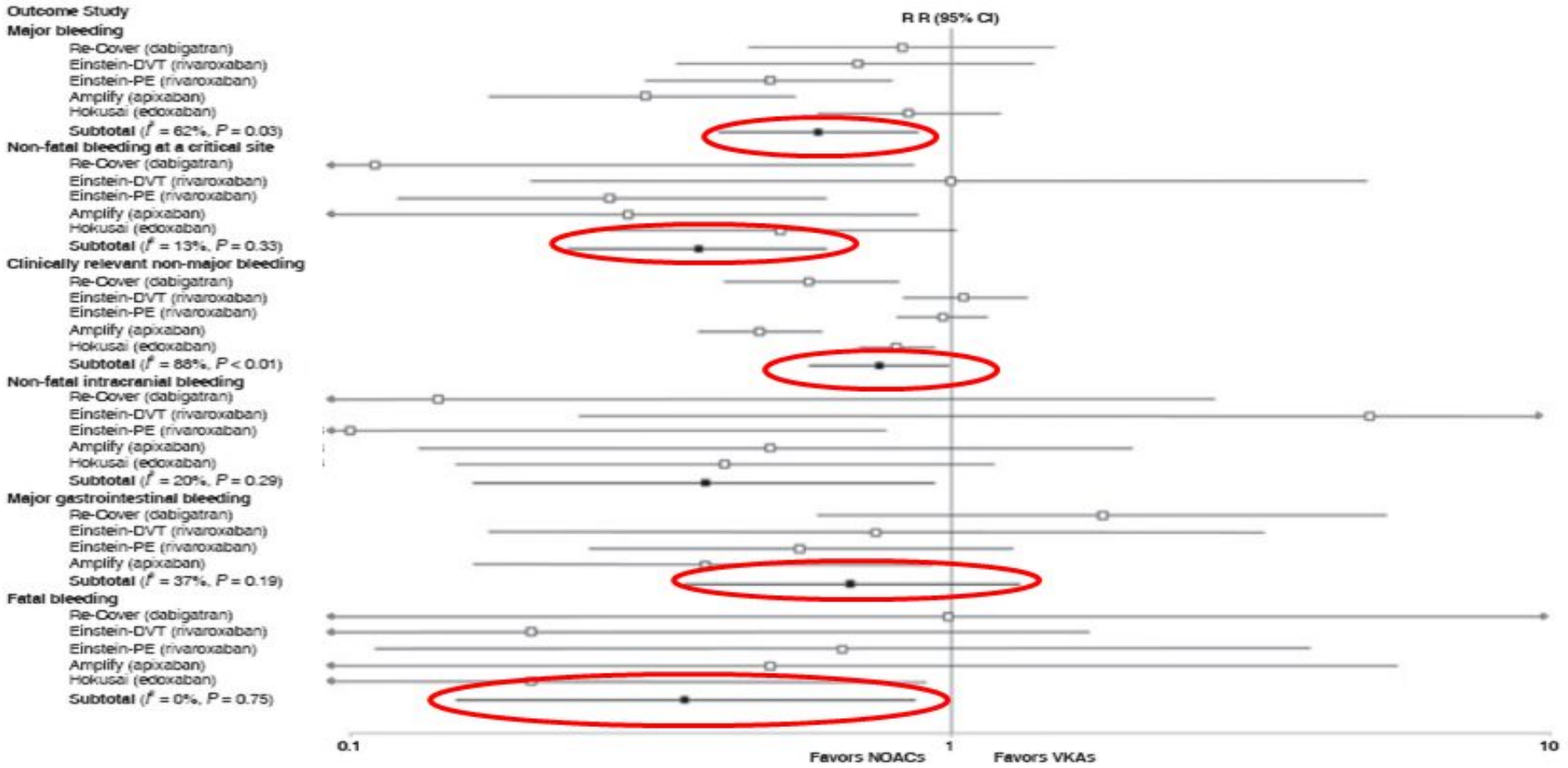
Rivaroxiban and apixaban do Not need parenteral lead-in (Phase III)

Dabigatron and edoxaban only studied with lead-in parenteral therapy

Not considered bridging

Safety of DOACs for treatment of acute VTE is superior to warfarin

meta-analysis of phase 3 trials



J Thromb Haemost 2014;12:320

Pivotal trials

Parameter	Dabigatran (RE-LY)[16,19–21]		Rivaroxaban (ROCKET AF)[15,22,70]	Apixaban (ARISTOTLE)[18]	Edoxaban (ENGAGE AF-TIMI)[17]	
Patients randomized	18,113		14,264	18,201	21,105	
Comparator	**Dose-adjusted warfarin (target INR 2.0–3.0)**					
Doses tested	110 mg bid	150 mg bid	20 mg od[a]	5 mg bid[b]	30 mg od[c]	60 mg od[c]
Patients eligible for reduced dose	NA	NA	2,950 (20.7%)	831 (4.6%)	5,330 (25.3%) at randomization; 7.1% after randomization	
Major bleeding outcomes (DOAC vs warfarin; % per year)						
Major bleeding	2.92 vs 3.61; *P*=0.003	3.40 vs 3.61; *P*=0.41	3.6 vs 3.4; *P*=0.58	2.13 vs 3.09; *P*<0.001	1.61 vs 3.43; *P*<0.001	2.75 vs 3.43; *P*<0.001
Fatal bleeding	0.19 vs 0.33; *P*=0.039	0.23 vs 0.33; *P*=0.15	0.2 vs 0.5; *P*=0.003	NR (34 vs 55 patients)	0.13 vs 0.38; *P*<0.001	0.21 vs 0.38; *P*=0.006
ICH	0.23 vs 0.76; *P*<0.001	0.32 vs 0.76; *P*<0.001	0.5 vs 0.7; *P*=0.02	0.33 vs 0.80; *P*<0.001	0.26 vs 0.85; *P*<0.001	0.39 vs 0.85; *P*<0.001
Major GI bleeding	1.15 vs 1.07; *P*=0.52	1.56 vs 1.07; *P*=0.001	2.00 vs 1.24; *P*<0.0001	0.76 vs 0.86; *P*=0.37	0.82 vs 1.23; *P*<0.001	1.51 vs 1.23; *P*=0.03

https://www.dovepress.com/cr_data/article_fulltext/s109000/109104/img/IJGM_109104_T001.jpg?vm=r

Wrap-Up

Diagnosis

Triage

Risk

Decision

Please come to all day event for in-depth discussion on medications