Updates in the Diagnosis and Management of VTE

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Conflicts of Interest

- I have no actual or potential conflicts of interest in relation to this program or presentation to disclose.

Objectives

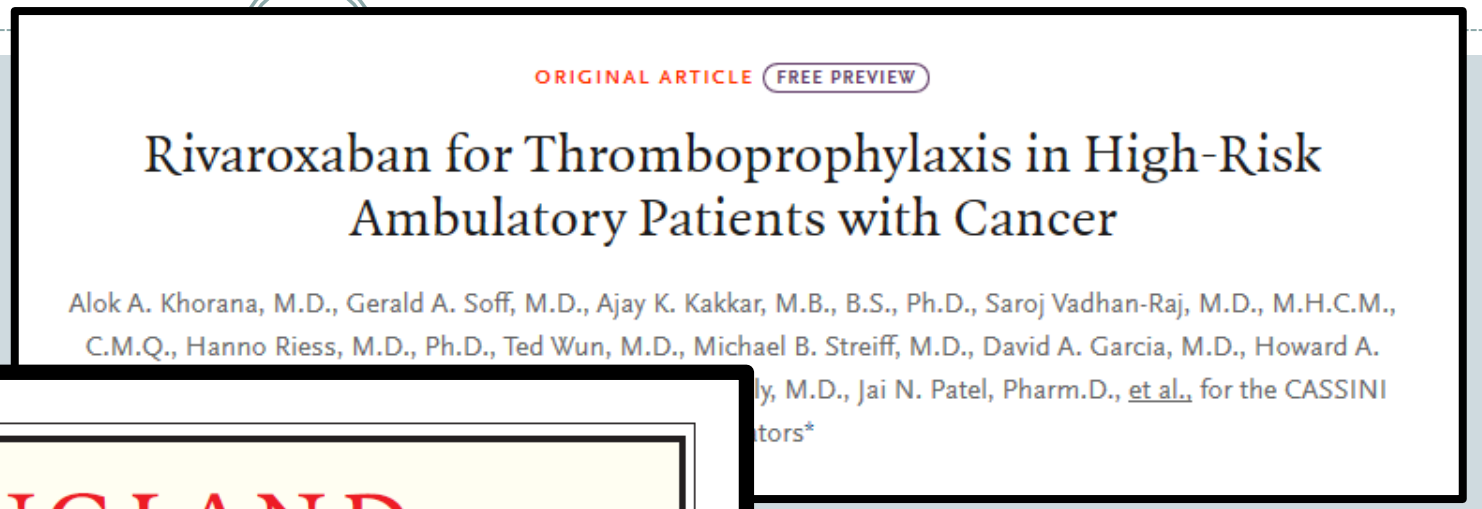
- Summarize the evidence for using DOACs in cancer-associated VTE
- Review updated guidance for HIT
- Present recent data on DOACs in APLS
- Discuss evidence-based approach to PE

Case

A 66 year old man with newly diagnosed pancreatic cancer is on your service getting chemotherapy. Pre chemo CBC : WBC-8.0, Hgb- 9.1 and platelet count -390K. Should he be discharged on VTE prophylaxis?

1. Yes
2. No
3. Whatever Bob says..he is the oldest hospitalist in the room

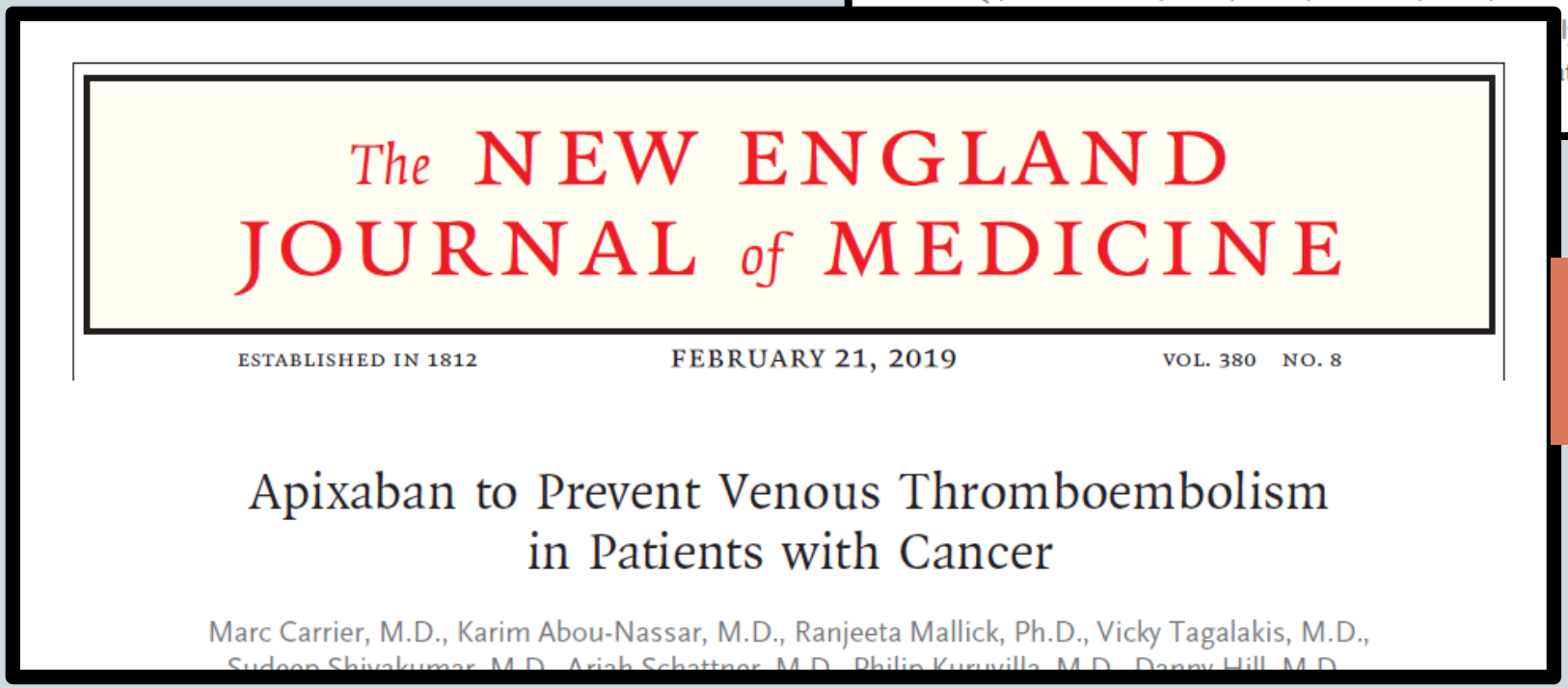
What's New in Cancer-Associated VTE?



ORIGINAL ARTICLE FREE PREVIEW

Rivaroxaban for Thromboprophylaxis in High-Risk Ambulatory Patients with Cancer

Alok A. Khorana, M.D., Gerald A. Soff, M.D., Ajay K. Kakkar, M.B., B.S., Ph.D., Saroj Vadhan-Raj, M.D., M.H.C.M., C.M.Q., Hanno Riess, M.D., Ph.D., Ted Wun, M.D., Michael B. Streiff, M.D., David A. Garcia, M.D., Howard A. ly, M.D., Jai N. Patel, Pharm.D., et al., for the CASSINI tors*



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 21, 2019 VOL. 380 NO. 8

Apixaban to Prevent Venous Thromboembolism in Patients with Cancer

Marc Carrier, M.D., Karim Abou-Nassar, M.D., Ranjeeta Mallick, Ph.D., Vicky Tagalakis, M.D.,

Industry funded studies of cancer patients starting chemo at high risk For VTE

Rascob NEJM 2018; Young AM et al, Journal of Clinical Oncology; Carrier M NEJM 2019

Khorona Risk Score

Patient characteristic	*Risk score*	*Risk of VTE*
Site of cancer		
Very high risk[b]	2	Score ≥ 3 = 7%
High risk	1	
Pre-chemotherapy platelet count >350×10^9/L	1	Score 1–2 = 2%
Hemoglobin < 10 g/dL or use of RBC growth factors	1	
Pre-chemotherapy leukocyte count >11×10^9/L	1	Score 0 = 0.5%
Body mass index ≥ 35 kg/m^2	1	

[a] High risk is defined as a score of 3 or more[5].
[b] Stomach, pancreas, brain.
[c] Lung, lymphoma, gynecologic, bladder, testicular.
RBC = red blood cells.

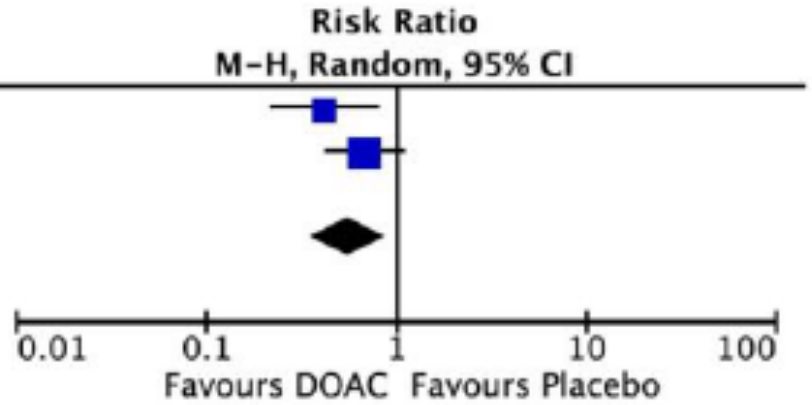
Khorona AA et al. Blood 2008;111:4902–7

a. Risk ratio for overall VTE (during 6-month study period)

Study or Subgroup	DOAC Events	DOAC Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
AVERT	12	291	28	283	39.5%	0.4168 [0.2162, 0.8033]
CASSINI	25	420	37	421	60.5%	0.6773 [0.4153, 1.1045]
Total (95% CI)		**711**		**704**	**100.0%**	**0.5592 [0.3511, 0.8907]**
Total events	37		65			

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 1.35$, df = 1 (P = 0.24); $I^2 = 26\%$

Test for overall effect: Z = 2.45 (P = 0.01)

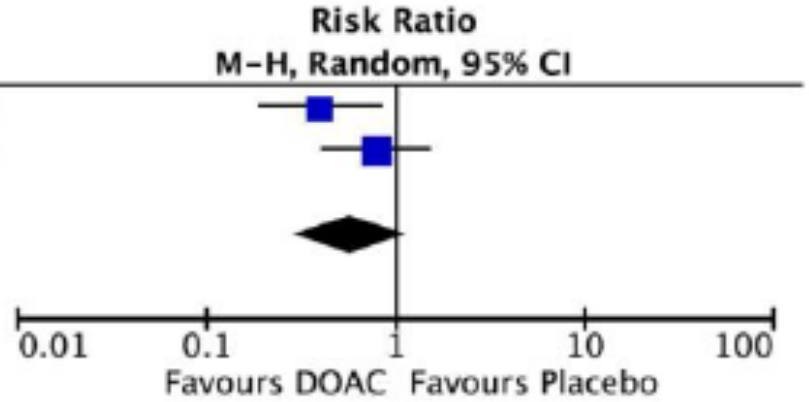


b. Risk ratio for symptomatic VTE (during 6-month study period)

Study or Subgroup	DOAC Events	DOAC Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
AVERT	9	291	22	283	46.3%	0.3978 [0.1864, 0.8491]
CASSINI	15	420	19	421	53.7%	0.7914 [0.4077, 1.5362]
Total (95% CI)		**711**		**704**	**100.0%**	**0.5756 [0.2937, 1.1278]**
Total events	24		41			

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 1.79$, df = 1 (P = 0.18); $I^2 = 44\%$

Test for overall effect: Z = 1.61 (P = 0.11)



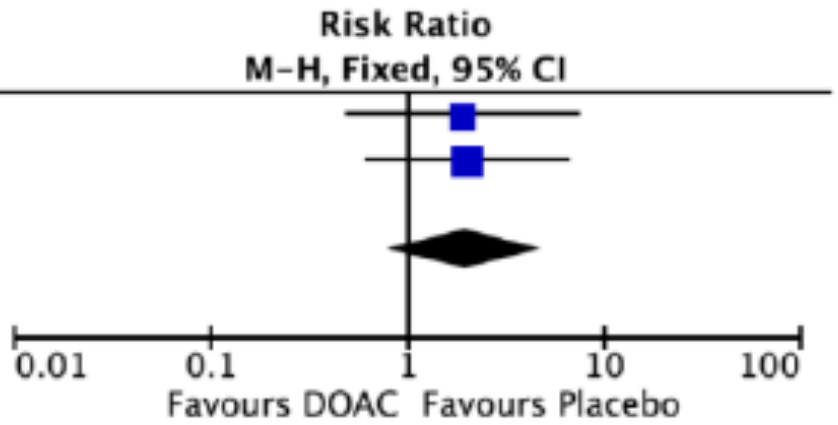
6 month VTE rates DOAC vs placebo: apixaban 4% v 10%;rivaroxaban 3.6 vs 9%

Li A et al Thromb Res 2019

a. Risk ratio for major bleeding (during on-treatment period)

Study or Subgroup	DOAC Events	DOAC Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
AVERT	6	288	3	275	43.4%	1.9097 [0.4824, 7.5608]
CASSINI	8	405	4	404	56.6%	1.9951 [0.6056, 6.5730]
Total (95% CI)		**693**		**679**	**100.0%**	**1.9580 [0.7953, 4.8210]**
Total events	14		7			

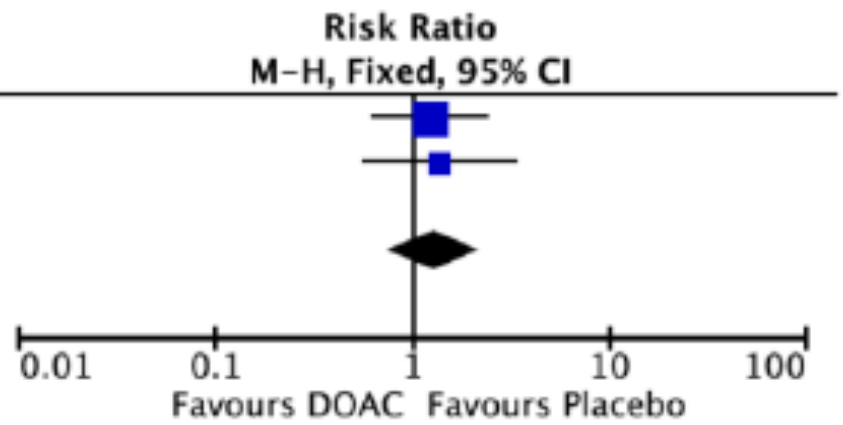
Heterogeneity: $Chi^2 = 0.00$, $df = 1$ ($P = 0.96$); $I^2 = 0\%$
Test for overall effect: $Z = 1.46$ ($P = 0.14$)



b. Risk ratio for clinically relevant non-major bleeding (during on-treatment period)

Study or Subgroup	DOCA Events	DOCA Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
AVERT	18	288	14	275	64.1%	1.2277 [0.6228, 2.4199]
CASSINI	11	405	8	404	35.9%	1.3716 [0.5575, 3.3744]
Total (95% CI)		**693**		**679**	**100.0%**	**1.2793 [0.7442, 2.1992]**
Total events	29		22			

Heterogeneity: $Chi^2 = 0.04$, $df = 1$ ($P = 0.85$); $I^2 = 0\%$
Test for overall effect: $Z = 0.89$ ($P = 0.37$)



Major bleeding rates v placebo : Apixaban 3.5% vs 2%; rivaroxaban 2% vs 1%

Li A et al Thromb Res 2019

What Do the Guidelines Say?

<u>International Society for Thrombosis and Hemostasis</u>

- Suggest DOACs in ambulatory cancer patients receiving chemo with Khorona score ≥2 with low bleeding risk and no DDI

Recent metaanalysis found patients with high-risk Khorana score (3+) derived the largest absolute risk reduction of VTE.

<u>2019 International Clinical Guidelines for the Treatment and Prophylaxis of VTE inPatients with Cancer</u>

- Suggest DOAC (rivaroxaban or apixaban) in ambulatory pts on systemic anticancer therapy at intermediate-to-high risk of VTE, identified by cancer type (ie, atic) or by a validated risk ment model (ie, a Khorana ≥2), AND not actively bleeding or not at a high risk of bleeding
- Not recommended in lung cancer

Wang et al JTH 2019; Farge et al Lancet Onc 2019; Li A et al Thromb Res 2019

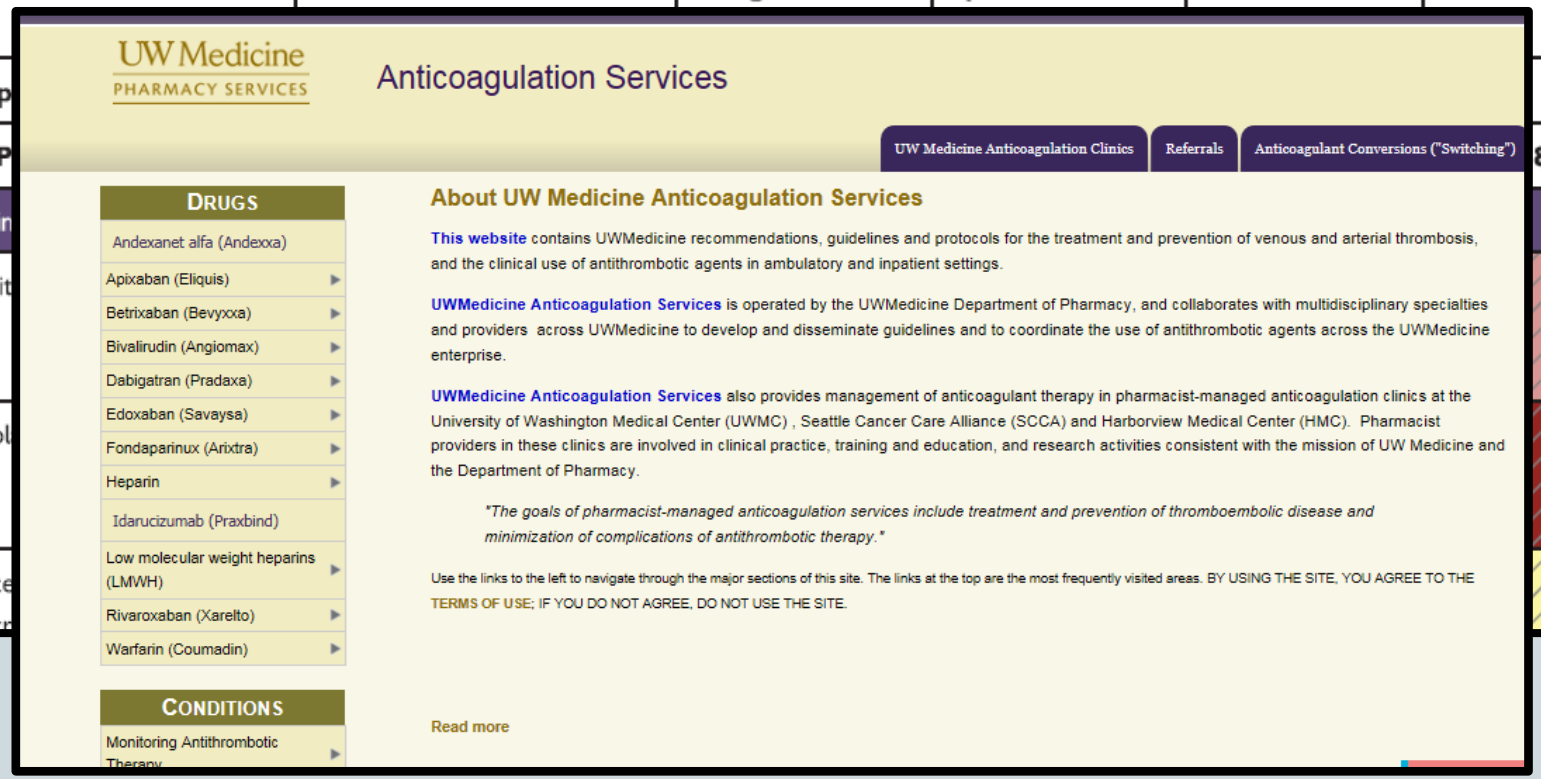
Conclusions DOAC Prophylaxis in Cancer

- Cancer patients starting chemotherapy with a Khorana Score $\geq$ 2 have a substantial risk of VTE (~10% at 6 months)
- Low-dose DOACs can reduce the risk of VTE by more than 50% but there is increased risk of bleeding..mostly in patients with GI or GU malignancy
- Net clinical benefit may be strongest in patients with Khorona risk score ≥3
- Questions remain: CrCl < 50 ml, lung cancer, immunomodulating therapy?

DDI-Anticancer drugs and DOACs

Table 4 Anticipated effects of common anticancer drugs on non-vitamin K antagonist oral anticoagulants plasma levels

	Via[142]	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
P-gp					
CYP					8%)
Antin					
Paclit					
Vinbl					
Doce					



Steffal J et al. European Heart Journal (2018) 39, 1330–1393

Case

A 66 year old man with newly diagnosed pancreatic cancer is on your service receiving chemotherapy. He is to be discharged tomorrow. His WBC is 8.0, Hgb 9,1 and platelet count 390K. What is his risk of VTE AFTER he leaves the hospital?

1. no
2. yes
3. Whatever Bob says…he is the oldest hospitalist in the room

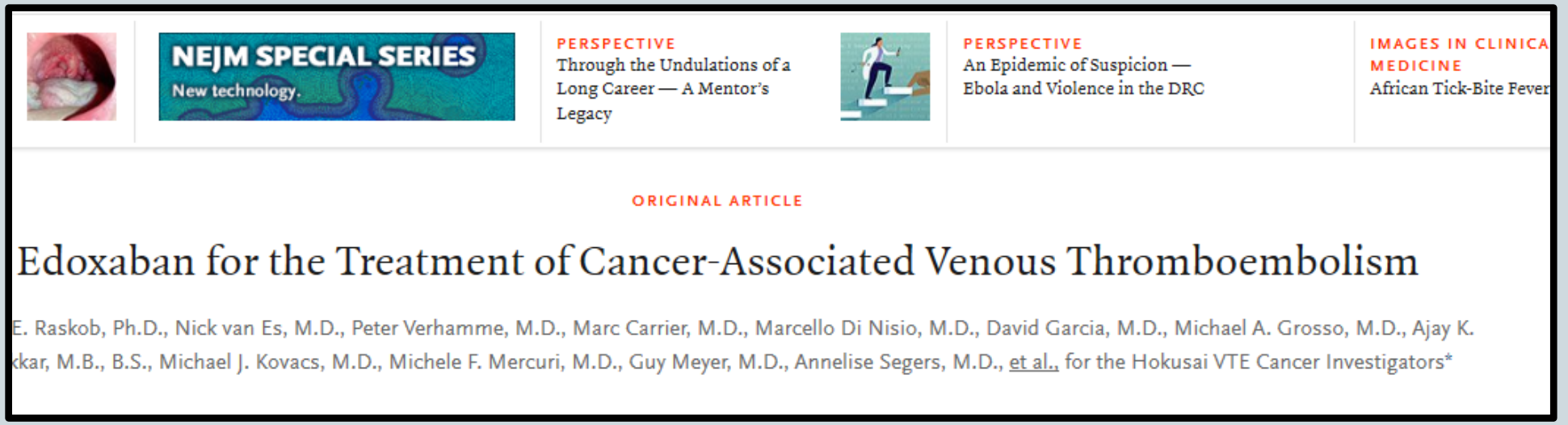
Khorona score =4

Case

A 65 year old man with metastatic lung cancer presents with unilateral lower extremity edema and chest pain. CT PE shows multiple segmental PE. His VS are stable. What anticoagulant regimen do you recommend?

1. LMWH
2. Edoxaban
3. Rivaroxaban
4. Apixaban
5. All of the above…oh wait, that seems like a really bad idea

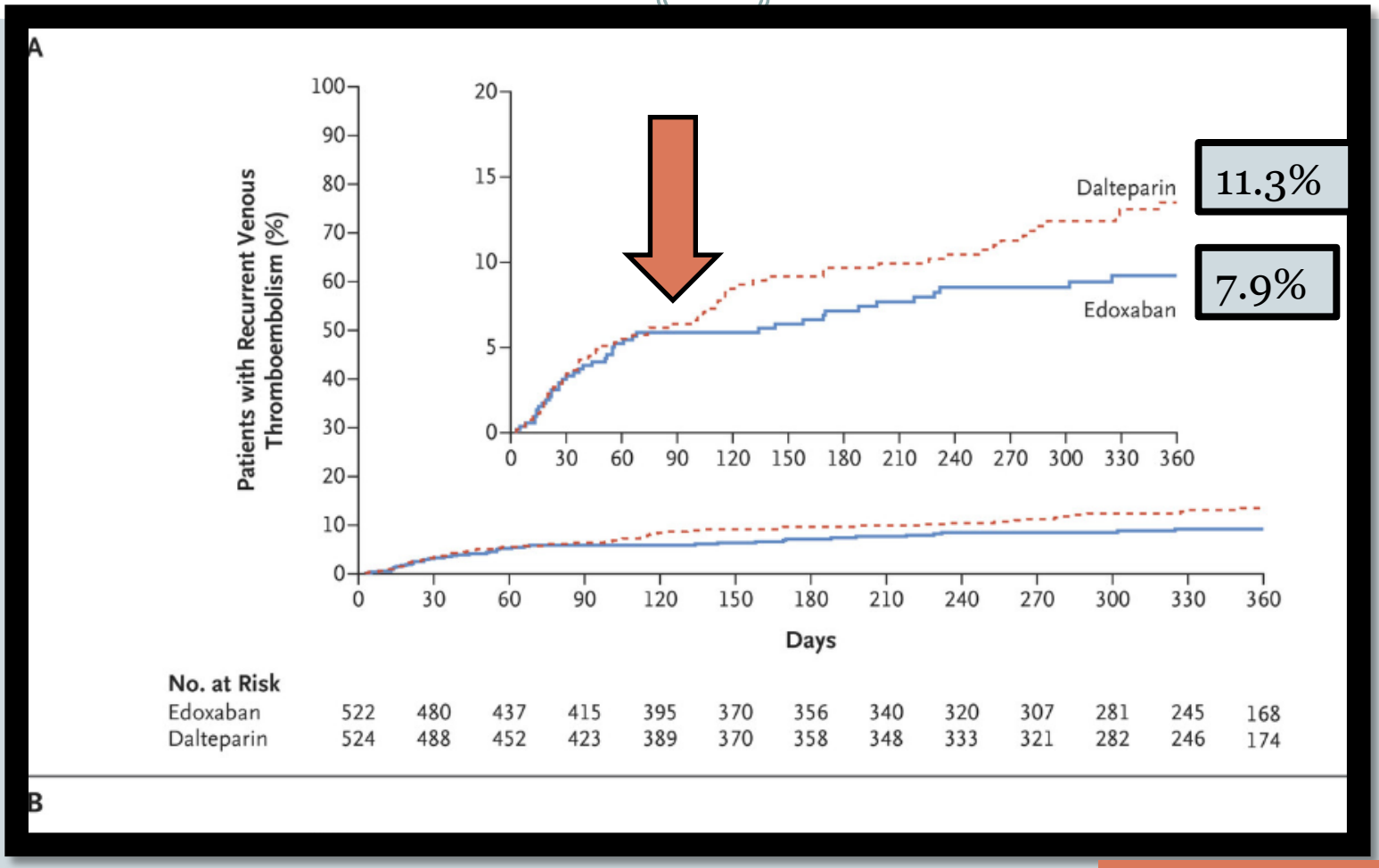
What's New in Cancer-Associated VTE?



~1000 patients
Edoxaban non inferior for composite endpoint of recurrent VTE/ major bleeding

Rascob NEJM 2018;

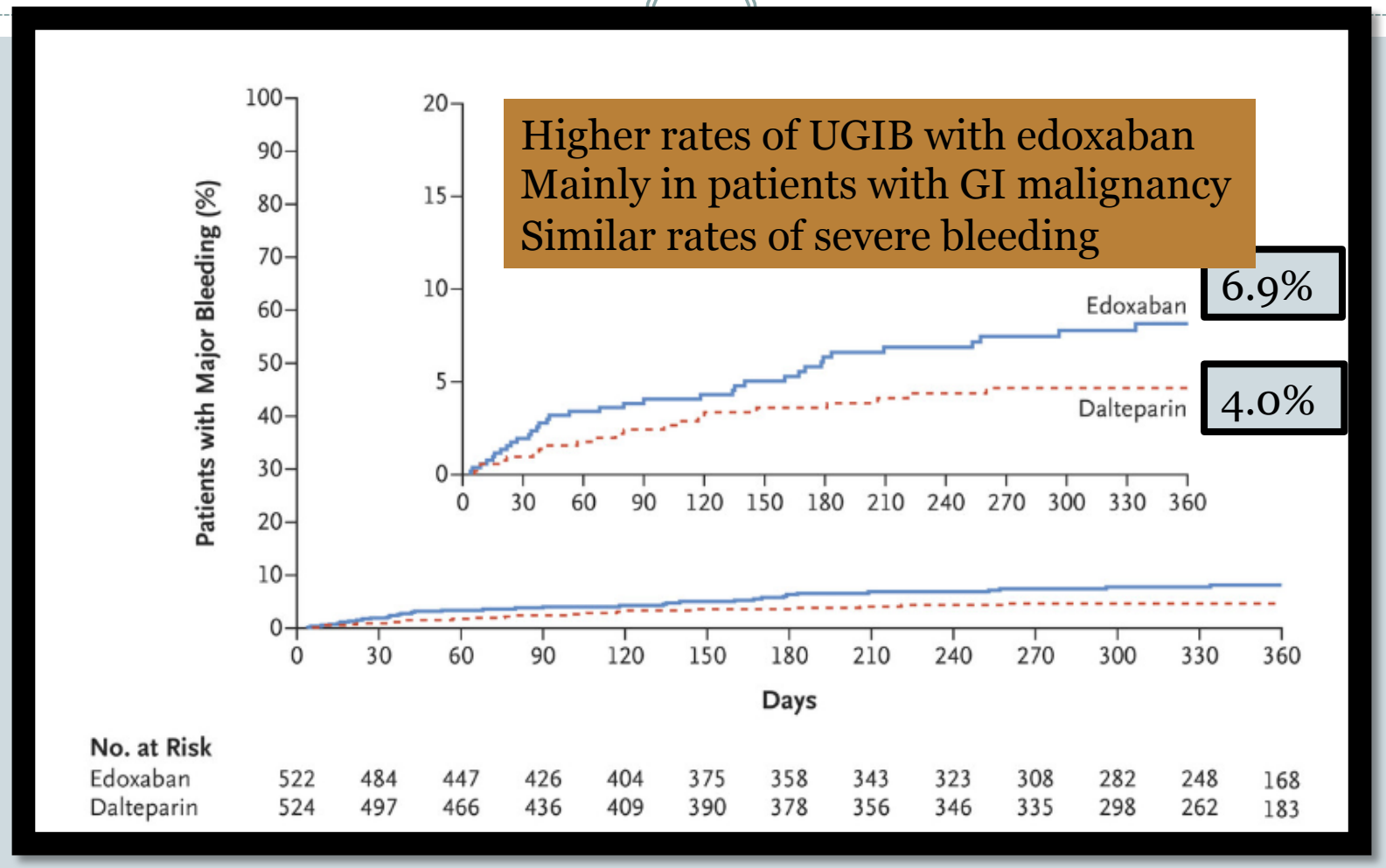
Hokusai- Recurrent VTE



Raskob et al. NEJM 2017

Treatment duration
211 days-edoxaban
184 days-dalteparin

Hokusai- VTE Cancer Major Bleeding



Raskob et al. NEJM 2017

What's New in Cancer-Associated VTE?

~400 patients
rivaroxaban associated with lower risk of recurrent VTE, specifically PE
But more clinically relevant nonmajor bleeding
Excluded cancer of esophagus and GE jxn after interim analysis revealed high bleeding rates

Rascob NEJM 2018; Young AM et al, Journal of Clinical Oncology; Carrier M NEJM 2019

Hokusai- VTE Bleeding

Major bleeding in subjects with and without GI cancer

GI cancer	Edoxaban (n=522)	Dalteparin (n=524)
Yes	18/136 (13.2%)	3/125 (2.4%)
No	14/386 (3.6%)	13/399 (3.3%)

Among patients with GI cancer, edoxaban increased the risk of major bleeding compared with dalteparin

SELECT D-riva vs LMWH for cancer..similar results

Agent	VTE recurrence	Bleeding	ESOPH CA
Riva	4%	4%	36%
LMWH`	11%	6%	11%

Young et al J Clinical Oncology 2018

NCCN Cancer-Associated VTE 2018

NCCN Guidelines® Insights

Cancer-Associated Venous Thromboembolic Disease, Version 2.2018

agent	comments
LMWH	Preferred 2017
edoxaban	with LMWH lead in
rivaroxaban	

Guidelines list urinary or GI tract lesions, pathology, or instrumentation as relative contraindications to DOACs in patients with cancer

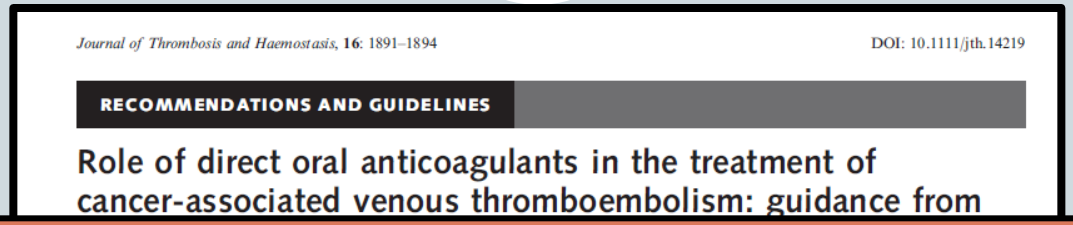
Streiff et al .J Natl Compr Canc Network 2018;16(11):1289–1303

ISTH DOACS in CANCER GUIDEDANCE

- We suggest the use of specific DOAC for active cancer patients with an acute VTE, low risk of bleeding & no drug–drug interactions with current systemic therapy. LMWHs constitute an acceptable alternative.
- Currently,edoxaban and rivaroxaban are the only DOACs that have been compared with LMWH in RCTs in cancer
- Inform patients regarding potential reduction in recurrence but higher bleeding

Khorana et al. Journal of Thrombosis and Haemostasis, 16 : 1891–1894

ISTH DOACS in CANCER GUIDEDANCE



Journal of Thrombosis and Haemostasis, **16**: 1891–1894 DOI: 10.1111/jth.14219

RECOMMENDATIONS AND GUIDELINES

Role of direct oral anticoagulants in the treatment of cancer-associated venous thromboembolism: guidance from

- We suggest the use of LMWHs for cancer patients with acute diagnosis of VTE and a high risk of bleeding (GI cancers with intact primary, cancers at risk of bleeding from the GU tract, bladder, or nephrostomy tubes, active GI mucosal abnormalities such as duodenal ulcers, gastritis, esophagitis, or colitis.)
- Specific DOACs (edoxaban and rivaroxaban) are acceptable alternatives if there are no drug–drug interactions with current systemic therapy.

Khorana et al. Journal of Thrombosis and Haemostasis, 16 : 1891–1894

Conclusions (Treatment Cancer Associated VTE)

- Edoxaban (after 5-day LMWH lead-in) and Rivaroxaban are effective treatments for cancer-associated DVT/PE
  - Preliminary data re: apixaban is encouraging but more evidence would be desirable

CARAVICCIO-1000 patients :apixaban vs LMWH
Results anticipated soon

aware that treatment with a DOAC may increase the risk of bleeding (compared to LMWH)

- Approximately 1 “extra” major bleed caused for every 50 patients treated with DOAC (instead of LMWH) for 6 mos.
- The “number needed to harm” may be lower in patients with GI or GU cancers (more evidence is needed)

Case

A 65 year old man with metastatic lung cancer presents with unilateral lower extremity edema. An ultrasound shows occlusive thrombus in the common femoral, deep femoral and popliteal veins. He has no SOB, CP, and VS are stable. What anticoagulant regimen do you recommend?

1. LMWH
2. Edoxaban
3. Rivaroxaban
4. Apixaban
5. All of the above…oh wait, that seems like a really bad idea

Case

51 year old man with no PMHX presents with acute CP and SOB, BP stable, HR 120s O2 sat 92%, d-dimer 1500, CT PE with bilateral PE in all lobes with RV/LV ratio > 1.0. BNP 370, trop 1.5. He is started on anticoagulation. What next?

1) Call the PERT team

2) Call the what?

3) Admit him to step down for close observation

4) Get an ECHO to guide need for thrombolysis

5) Order a STAT ECHO but then decide to try to get front row tickets to Hamilton instead because they are easier to score than a STAT ECHO for a hemodynamically stable guy

ESC PE Guidelines-Classification of PE

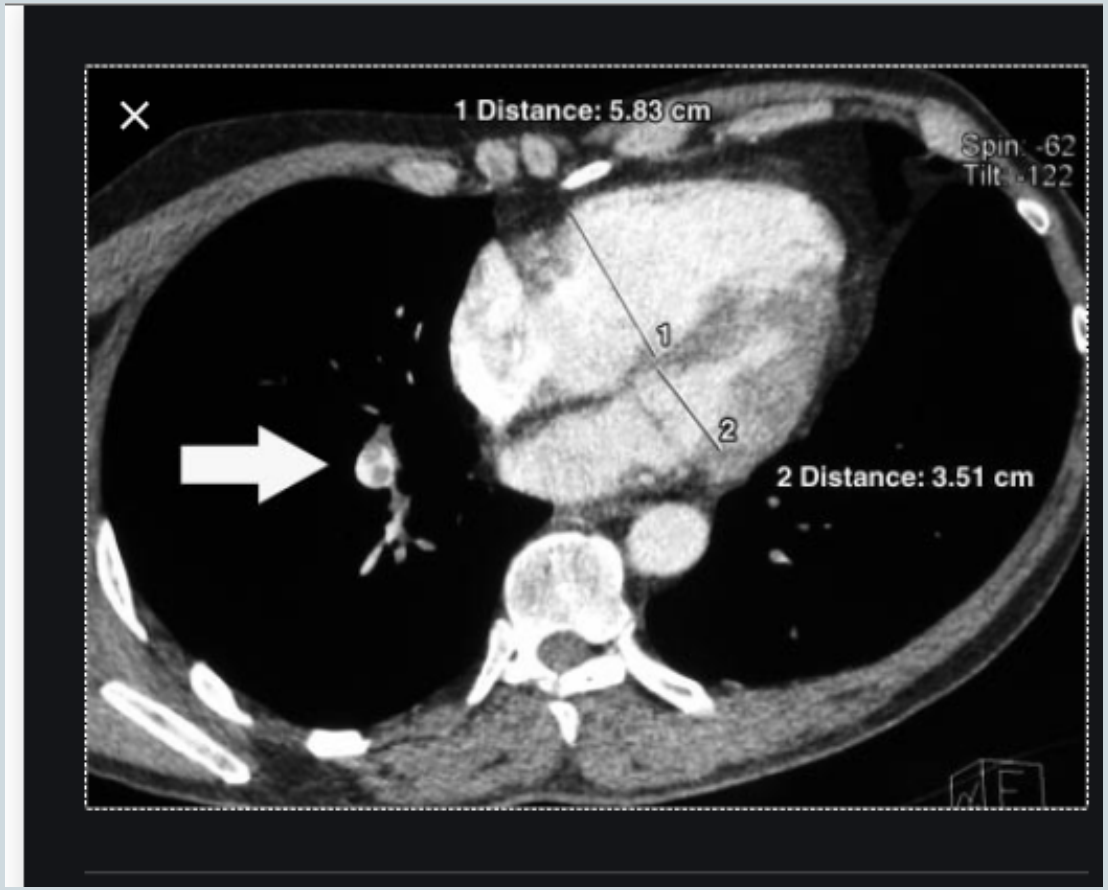
Early mortality risk		Indicators of risk			
		Haemodynamic instability[a]	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥I	RV dysfunction on TTE or CTPA[b]	Elevated cardiac troponin levels[c]
High		+	(+)[d]	+	(+)
Intermediate	Intermediate–high	-	+[e]	+	+
	Intermediate–low	-	+[e]	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

©ESC 2019

Konstantinedes et al. Eur Heart J. 2019;Epub ahead of print.

ESC PE Guidelines- PE Treatment

Parameters	*Points*
Age >80 years	+1
History of cancer	+1
History of cardiopulmonary disease	+1
Systolic BP <90 mm Hg	+1
Heart rate >110 beats/minute	+1
O_2 saturation <90%	+1



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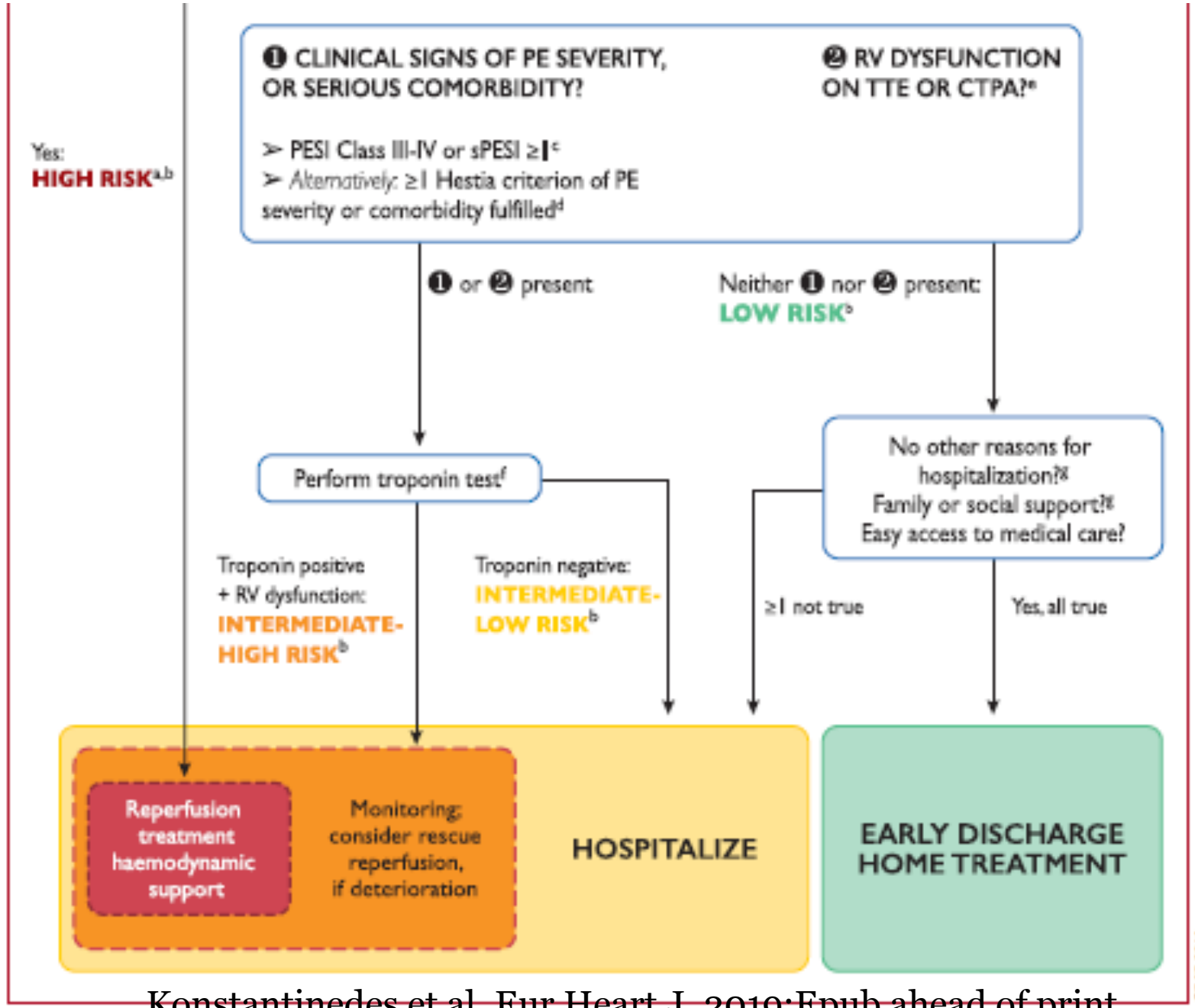

Konstantinedes et al. Eur Heart J. 2019;Epub ahead of print.

ACUTE PE TREATMENT

- Intermediate risk-systemic thrombolysis not routinely recommended
- DOACS first line
- Use LMWH over UFH if using parenteral therapy
- If outpatient confirm able to get the drug and VERY close clinical follow up

Konstantinedes et al. Eur Heart J. 2019;Epub ahead of print.

Case

51 year old man with no PMHX presents with acute CP and SOB, BP stable, HR 120s, O2 sat 92%, d-dimer 1500, CT PE with bilateral PE in all lobes with RV/LV ratio > 1.0 BNP 370, trop 1.5 He is started on anticoagulation. What next?

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5) Order a STAT ECHO but then decide to try to get front row tickets to Hamilton instead because they are easier to score than a STAT ECHO for a hemodynamically stable guy

PESI=1

INTERMEDIATE-HIGH RISK

SIDE BAR-HOW LONG SHOULD HE REMAIN ON ANTICOAGULATION?

ESC PE Guidelines-Duration of Therapy

Estimated risk for long-term recurrence[a]	Risk factor category for index PE[b]	Examples[b]	DURATION OF AC
Low (<3% per year)	Major transient or reversible factors associated with >10-fold increased risk for the index VTE event (compared to patients without the risk factor)	• Surgery with general anaesthesia for >30 min • Confined to bed in hospital (only "bathroom privileges") for ≥3 days due to an acute illness, or acute exacerbation of a chronic illness • Trauma with fractures	≥ 3 months
Intermediate (3–8% per year)	Transient or reversible factors associated with ≤10-fold increased risk for first (index) VTE	• Minor surgery (general anaesthesia for <30 min) • Admission to hospital for <3 days with an acute illness • Oestrogen therapy/contraception • Pregnancy or puerperium • Confined to bed out of hospital for ≥3 days with an acute illness • Leg injury (without fracture) associated with reduced mobility for ≥3 days • Long-haul flight	Suggest indefinite
	Non-malignant persistent risk factors	• Inflammatory bowel disease • Active autoimmune disease	
	No identifiable risk factor		
High (>8% per year)		• Active cancer • One or more previous episodes of VTE in the absence of a major transient or reversible factor • Antiphospholipid antibody syndrome	Recommend indefinite

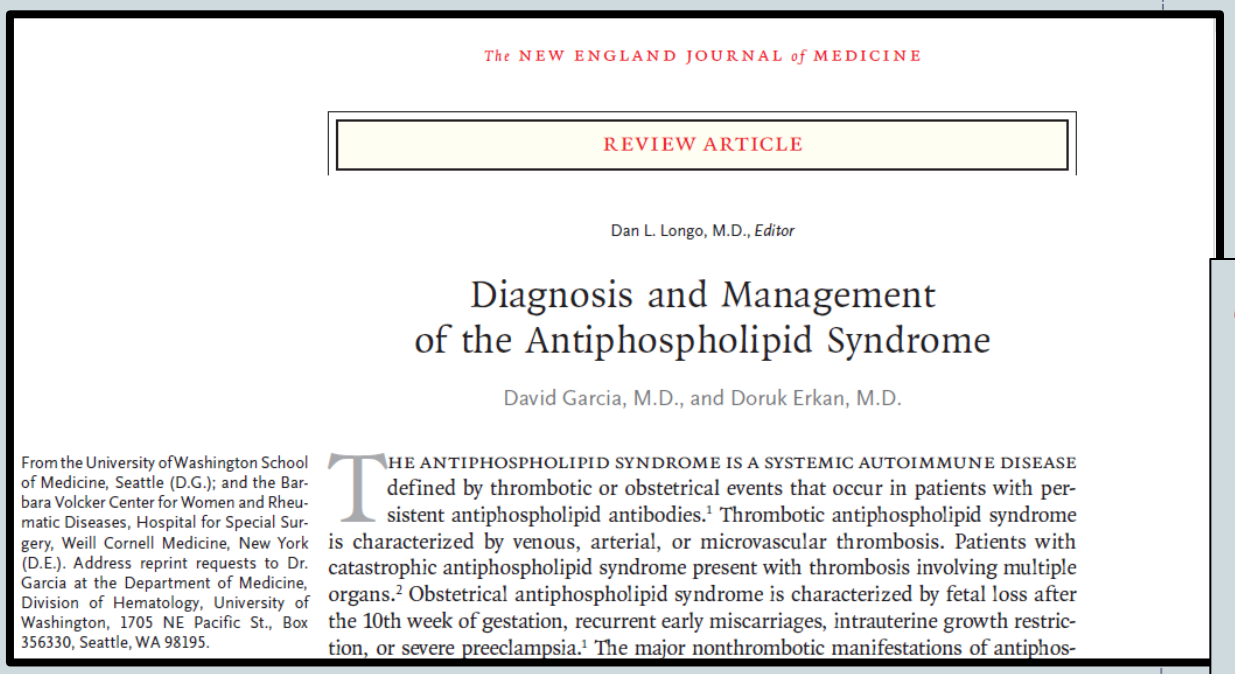
Konstantinedes et al. Eur Heart J. 2019;Epub ahead of print.

Case

A 35 year old woman with lupus presents with unprovoked bilateral pulmonary embolism. Baseline coags are significant for a prolonged aPTT raising concern for antiphospholipid antibody syndrome. What anticoagulation regimen do you recommend?

1) LMWH→warfarin
2) Rivaroxaban VTE dosing
3) IV heparin→ warfarin

Anticoagulation in APS



The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Diagnosis and Management of the Antiphospholipid Syndrome

David Garcia, M.D., and Doruk Erkan, M.D.

From the University of Washington School of Medicine, Seattle (D.G.); and the Barbara Volcker Center for Women and Rheumatic Diseases, Hospital for Special Surgery, Weill Cornell Medicine, New York (D.E.). Address reprint requests to Dr. Garcia at the Department of Medicine, Division of Hematology, University of Washington, 1705 NE Pacific St., Box 356330, Seattle, WA 98195.

THE ANTIPHOSPHOLIPID SYNDROME IS A SYSTEMIC AUTOIMMUNE DISEASE defined by thrombotic or obstetrical events that occur in patients with persistent antiphospholipid antibodies.[1] Thrombotic antiphospholipid syndrome is characterized by venous, arterial, or microvascular thrombosis. Patients with catastrophic antiphospholipid syndrome present with thrombosis involving multiple organs.[2] Obstetrical antiphospholipid syndrome is characterized by fetal loss after the 10th week of gestation, recurrent early miscarriages, intrauterine growth restriction, or severe preeclampsia.[1] The major nonthrombotic manifestations of antiphos-

- Diagnostic criteria
  - Thrombosis
  - Persistently lupus anticoagulant, positive acL, and/or B2gp1 abs (separated by at least 12 weeks)

Garcia et al N Engl J Med 2018;378:2010-21.

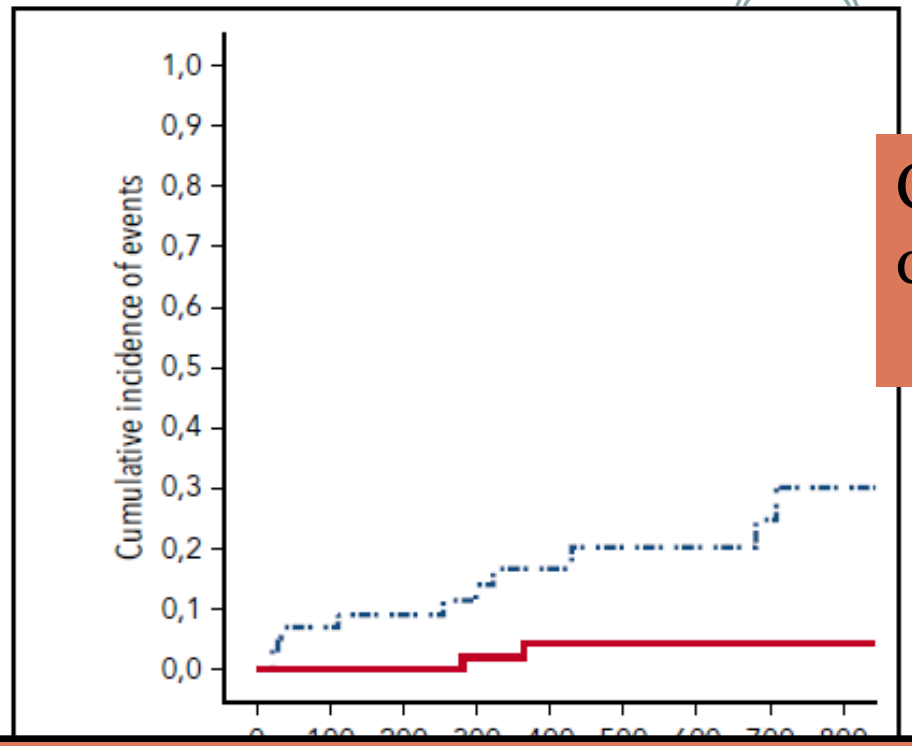
Anticoagulation in APS

Intervention-Rivaroxaban 20 mg QD (15 mg if CrCl 30-50 ml/min) v warfarin (INR 2-3) for SECONDARY prevention in triple positive APS

Primary outcome -Cumulative incidence of TE, major bleeding, vascular death

Pengo et al. Blood. 2018;132(13):1365-1371

TRAPS



Cumulative incidence of death, thromboembolism, major bleeding

rivaroxaban

warfarin

Rivaroxaban in high risk patients with APS was associated with excess of arterial events compared to warfarin

Trial stopped early

ASTRO APS ONGOING

Pengo et al. Blood. 2018;132(13):1365-1371

Antiphospholipid Antibody Syndrome

- WHY- risk of recurrence off AC much higher; at risk for arterial disease, bridge therapy; DOACs generally avoided
- WHO- arterial and venous events, unexpected arterial events, recurrent thrombosis ON anticoagulation, underlying autoimmune d/o, prolonged aPTT
- WHAT-send Lupus anticoagulant, Beta 2 glycoprotein antibodies and anticardiolipin antibodies (IgG & Ig M)
- WHEN-LAC-don't do it on anticoagulation; antibodies you can send anytime
- IF POSITIVE-
  - must repeat in 12 weeks-high rate of transient positivity
  - LAC most predicative of 1st and recurrent VTE, triple positives at highest risk

Case

A 35 year old woman with lupus presents with unprovoked bilateral pulmonary embolism. Baseline coags are significant for a prolonged aPTT raising concern for antiphospholipid antibody syndrome. What anticoagulation regimen do you recommend?

1) LMWH→warfarin
2) Rivaroxaban VTE dosing
3) IV heparin→ warfarin

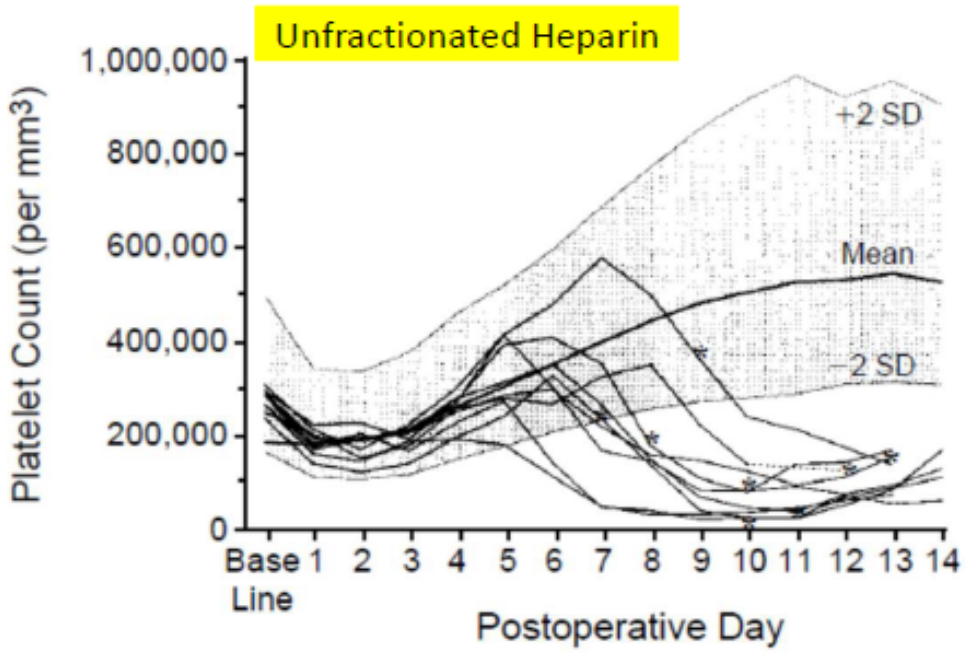
CASE

A 65 year old man with COPD is admitted with community acquired pneumonia to the ICU. He is intubated, receives antibiotics and therapy for COPD. He is extubated on HD#5. He is transferred to the your service on HD#6 and you notice his platelet count is now 65K. His renal and liver function are normal. PLT count was 200K on admission. He has been on 5000 u SQ UFH TID. You hold heparin and send a HIT assay which results as positive. You:

1. DC heparin and start argatroban
2. DC heparin and start fondaparinux
3. DC heparin and start rivaroxaban
4. You say out loud to no one in particular “WHY the heck are we still using UFH? “

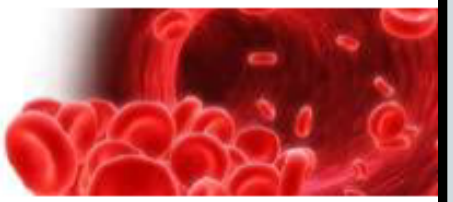
The Clinical-Pathologic Syndrome of Heparin-induced Thrombocytopenia

- Exposure to UFH/LMWH for 5 or more days
- Platelet drop of 50% or more
- Moderate thrombocytopenia (20-100,000/µL)
- Thrombosis (venous>arterial)
  - Skin lesions (plaques, necrosis)
  - Systemic inflammatory response syndrome
  - DIC



Anticoagulation FORUM

Arepally GM. Blood 2017; Warkentin TE et al. NEJM 1995



Management of Suspected Heparin-induced Thrombocytopenia

- Step 1: Assess pre-test probability
- Step 2: If intermediate or high risk, eliminate exposure and initiate alternative AC
- Step 3: Send HIT assay
- Step 4: Follow up on HIT assay results

Table 1. 4T Scoring System for Evaluating the Pretest Probability of Heparin-Induced Thrombocytopenia.*

Variable	Score		
	2	1	0
Acute thrombocytopenia	Platelet count decrease of >50% and nadir ≥20,000/mm^3	Platelet count decrease of 30–50% or nadir 10,000–19,000/mm^3	Platelet count decrease of <30% or nadir ≤10,000/mm^3
Timing of onset	Day 5–10, or day 1 if recent heparin exposure	>Day 10 or unclear exposure	≤Day 4 with no recent heparin exposure
Thrombosis	New thrombosis or anaphylactoid reaction after heparin bolus	Progressive or recurrent thrombosis	None
Other cause of thrombocytopenia	None	Possible	Definite
Total score	6–8, indicating high score	4 or 5, indicating intermediate score	0–3, indicating low score

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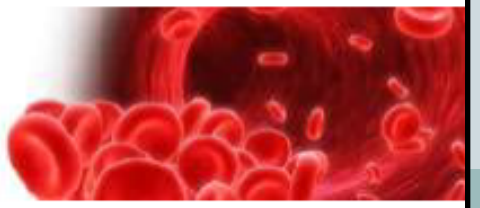
Greinacher A N Engl J Med 2015;
Lo GK et al. J Thromb Haemost 2006



	Score = 2	Score = 1	Score = 0
Thrombocytopenia Compare the highest platelet count within the sequence of declining platelet counts with the lowest count to determine the % of platelet fall. **(Select only 1 option)**	○ > 50% platelet fall AND nadir of ≥ 20 AND no surgery within preceding 3 days	○ > 50% platelet fall BUT surgery within preceding 3 days OR ○ any combination of platelet fall and nadir that does not fit criteria for Score 2 or Score 0 (eg, 30-50% platelet fall or nadir 10-19)	○ < 30% platelet fall ○ any platelet fall with nadir < 10
Timing (of platelet count fall or thrombosis*) Day 0 = first day of most recent heparin exposure **(Select only 1 option)**	○ platelet fall day 5-10 after start of heparin ○ platelet fall within 1 day of start of heparin AND exposure to heparin within past 5-30 days	○ consistent with platelet fall days 5-10 but not clear (eg, missing counts) ○ platelet fall within 1 day of start of heparin AND exposure to heparin in past 31-100 days ○ platelet fall after day 10	○ platelet fall ≤ day 4 without exposure to heparin in past 100 days
Thrombosis (or other clinical sequelae) **(Select only 1 option)**	○ confirmed new thrombosis (venous or arterial) ○ skin necrosis at injection site ○ anaphylactoid reaction to IV heparin bolus ○ adrenal hemorrhage	○ recurrent venous thrombosis in a patient receiving therapeutic anticoagulants ○ suspected thrombosis (awaiting confirmation with imaging) ○ erythematous skin lesions at heparin injection sites	○ thrombosis suspected
oTher cause for Thrombocytopenia** **(Select only 1 option)**	○ no alternative explanation for platelet fall is evident	**Possible other cause is evident:** ○ sepsis without proven microbial source ○ thrombocytopenia associated with initiation of ventilator ○ other	**Probable other cause present:** ○ within 72 h of surgery ○ confirmed bacteremia/ fungemia ○ chemotherapy or radiation within past 20 days ○ DIC due to non-HIT cause ○ posttransfusion purpura (PTP) ○ platelet count < 20 AND given a drug implicated in causing D-ITP (see list) ○ non-necrotizing skin lesions at LMWH injection site (presumes DTH) ○ other

Drugs implicated in drug-induced immune thrombocytopenia (D-ITP)

Relatively Common: glycoprotein IIb/IIIa antagonists (abciximab, eptifibatide, tirofiban); quinine, quinidine, sulfa antibiotics, carbamazepine, vancomycin
Less Common: actinomycin, amitriptyline, amoxicillin/piperacillin/nafcillin, cephalosporins (cefazolin, ceftazidime, ceftriaxone), celecoxib, ciprofloxacin, esomeprazole, fexofenadine, fentanyl, fucidic acid, furosemide, gold salts, levofloxacin, metronidazole, naproxen, oxaliplatin, phenytoin, propranolol, propoxyphene, ranitidine, rifampin, suramin, trimethoprim. Note: This is a partial list.

0-3 LOW
4-5 INT
6-8 HIGH

Linkins L et al. CHEST 2012

CASE

A 65 year old man with COPD is admitted with community acquired pneumonia to the ICU. He is intubated, receives antibiotics and therapy for COPD. He is extubated on HD#5. He is transferred to the your service on HD#6 and you notice his platelet count is now 65K. His renal and liver function are normal. PLT count was 200K on admission. He has been on 5000 u SQ UFH TID. You hold heparin and send a HIT assay which results as positive.

4t'S SCORE=4-5

CLINICAL GUIDELINES

blood advances

American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia

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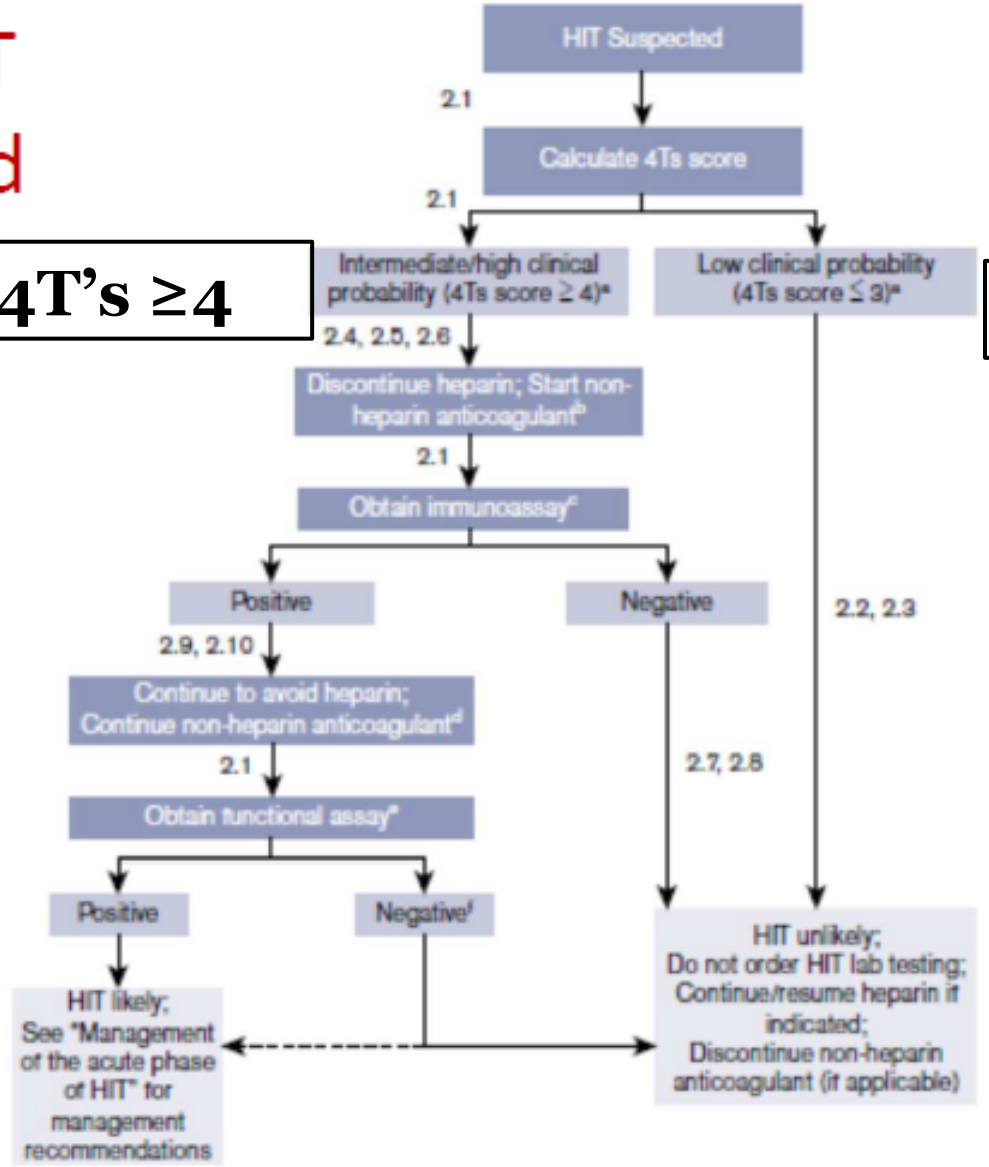
2018 ASH HIT Diagnosis and Treatment Algorithm

4T's ≥4

4T's ≤3



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Cuker A et al. Blood Advances 2018

Important Treatment Recommendations of ASH HIT Guideline

- In acute phase HITT or HIT, the panel *recommends* therapeutic dose alternative AC with parenteral DTI, fondaparinux or direct oral anticoagulant
  - In critically ill patients, bivalirudin or argatroban may be preferable
  - In patients with life- or limb-threatening thromboembolism, parenteral alternative AC may be preferred
  - In stable patients at low risk of bleeding, fondaparinux or DOACs are reasonable options
  - Of DOACs, most published experience with rivaroxaban
    - In HITT, prefer 15 mg BID X 3 weeks then 20 mg daily
    - In HIT, prefer 15 mg BID until platelet recovery then 20 mg daily
- Panel *recommends* against use of IVC filters

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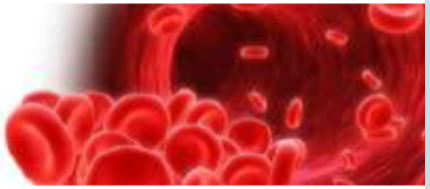

Important Treatment Recommendations of ASH HIT Guideline

- HIT without thrombosis: The panel *recommends* therapeutic AC until platelet count recovery at a minimum
  - Panel *suggests* against continuing AC ≥ 3 months unless delayed platelet recovery in setting of ongoing HIT
- HIT with thrombosis: Therapeutic AC for 3 to 6 months (no recommendation from panel on this patient group)
- The panel *recommends* against initiation of VKA before platelet count recovery
- The panel *suggests* treatment with a DOAC rather than a VKA

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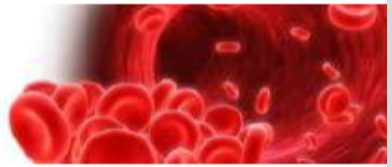
Cuker A et al. Blood Advances 2018



CASE

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1. DC heparin and start argatroban
2. DC heparin and start fondaparinux
3. DC heparin and start rivaroxaban
4. You say out loud to no one in particular “WHY the heck are we still using UFH? “

Thromboembolism & Anticoagulation Workshop

- Approach to subsegmental PE, calf vein DVT and superficial vein thrombosis
- Determine duration of anticoagulation for VTE
- Review options for secondary prevention of VTE
- Manage anticoagulation in recurrent VTE
- Choose appropriate DOAC for VTE
- Role of thrombophilia work up

Questions?