Updates in the Diagnosis and Management of VTE
Tracy Minichiello, MD
Chief Anticoagulation and Thrombosis Services
San Francisco, VA Medical Center
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?

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. Kupchick, M.D., Jai N. Patel, Pharm.D., et al., for the CASSINI Investigators

The NEW ENGLAND JOURNAL of MEDICINE

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., Sudome Shinkuma, M.D., Arik Schattner, M.D., Philip Kunavikorn, M.D., Danny Hill, 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

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Risk score</th>
<th>Risk of VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site of cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very high risk(^b)</td>
<td>2</td>
<td>Score ≥ 3 = 7%</td>
</tr>
<tr>
<td>High risk</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pre-chemotherapy platelet count &gt;350×10⁹/L</td>
<td>1</td>
<td>Score 1–2 = 2%</td>
</tr>
<tr>
<td>Hemoglobin &lt; 10 g/dL or use of RBC growth factors</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pre-chemotherapy leukocyte count &gt;11×10⁹/L</td>
<td>1</td>
<td>Score 0 = 0.5%</td>
</tr>
<tr>
<td>Body mass index ≥ 35 kg/m²</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

\(^{a}\) 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.
6 month VTE rates DOAC vs placebo: apixaban 4% v 10%; rivaroxaban 3.6 vs 9%

Li A et al Thromb Res 2019
Major bleeding rates vs placebo: Apixaban 3.5% vs 2%; rivaroxaban 2% vs 1%  

Li A et al Thromb Res 2019
What Do the Guidelines Say?

International Society for Thrombosis and Hemostasis

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

2019 International Clinical Guidelines for the Treatment and Prophylaxis of VTE in Patients with Cancer

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

- Not recommended in lung cancer

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

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 $\geq 3$
- Questions remain: CrCl $< 50$ ml, lung cancer, immunomodulating therapy?
## Table 4

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Via&lt;sup&gt;142&lt;/sup&gt;</th>
<th>Dabigatran</th>
<th>Apixaban</th>
<th>Edoxaban</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-gp inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYP3A4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYP2C19</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other CYPs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dabigatran</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apixaban</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edoxaban</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

### Anticoagulation Services

**About UW Medicine Anticoagulation Services**

This website contains UWMedicine recommendations, guidelines and protocols for the treatment and prevention of venous and arterial thrombosis, and the clinical use of antithrombotic agents in ambulatory and hospital settings.

**UWMedicine Anticoagulation Services** is spearheaded by the UWMedicine Department of Pharmacy, and collaborates with multidisciplinary specialties and providers across UWMedicine to develop and disseminate guidelines and to coordinate the use of antithrombotic agents across the UWMedicine enterprise.

**UWMedicine Anticoagulation Services** also provides management of anticoagulant therapy in pharmacist-managed anticoagulation clinics at the University of Washington Medical Center (UWMC), Seattle Cancer Care Alliance (SCCA) and Harborview Medical Center (HMC). Pharmacist providers in these clinics are involved in clinical practice, training and education, and research activities consistent with the mission of UW Medicine and the Department of Pharmacy.

"The goals of pharmacist-managed anticoagulation services include treatment and prevention of thrombotic disease and minimization of complications of antithrombotic therapy."

Use the links in the left to navigate through the major sections of this site. The links in the top are the most frequently visited areas. BY USING THE SITE, YOU AGREE TO THE TERMS OF USE. IF YOU DO NOT AGREE, DO NOT USE THE SITE.

---

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
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?

Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism

E. Raskob, Ph.D., Nick van Es, M.D., Peter Verhamme, M.D., Marc Carrier, M.D., Marcello Di Nisio, M.D., David Garcia, M.D., Michael A. Grosso, M.D., Ajay K. Kark, M.B., B.S., Michael J. Kovacs, M.D., Michele F. Mercuri, M.D., Guy Meyer, M.D., Annelise Segers, M.D., et al., for the Hokusai VTE Cancer Investigators

~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

Higher rates of UGIB with edoxaban
Mainly in patients with GI malignancy
Similar rates of severe bleeding

Raskob et al. NEJM 2017
What’s New in Cancer-Associated VTE?

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

~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
Hokusai- VTE Bleeding

<table>
<thead>
<tr>
<th>GI cancer</th>
<th>Edoxaban (n=522)</th>
<th>Dalteparin (n=524)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>18/136 (13.2%)</td>
<td>3/125 (2.4%)</td>
</tr>
<tr>
<td>No</td>
<td>14/386 (3.6%)</td>
<td>13/399 (3.3%)</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Agent</th>
<th>VTE recurrence</th>
<th>Bleeding</th>
<th>ESOPH CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riva</td>
<td>4%</td>
<td>4%</td>
<td>36%</td>
</tr>
<tr>
<td>LMWH</td>
<td>11%</td>
<td>6%</td>
<td>11%</td>
</tr>
</tbody>
</table>

Young et al J Clinical Oncology 2018
**NCCN Guidelines® Insights**

Cancer-Associated Venous Thromboembolic Disease, Version 2.2018

<table>
<thead>
<tr>
<th>agent</th>
<th>comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>LMWH</td>
<td>Preferred 2017</td>
</tr>
<tr>
<td>edoxaban</td>
<td>with LMWH lead in</td>
</tr>
<tr>
<td>rivaroxaban</td>
<td></td>
</tr>
<tr>
<td>apixaban</td>
<td>Limited to those with compelling reason to avoid LMWH</td>
</tr>
</tbody>
</table>

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

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.
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.
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**

- Patients with acute cancer-associated VTE should be 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
<table>
<thead>
<tr>
<th>Early mortality risk</th>
<th>Indicators of risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Haemodynamic instability&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>High</td>
<td>+</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Intermediate–high</td>
</tr>
<tr>
<td></td>
<td>Intermediate–low</td>
</tr>
<tr>
<td>Low</td>
<td>-</td>
</tr>
</tbody>
</table>

<sup>a</sup> Haemodynamic instability: RV pressure > 16 mmHg, PCWP > 15 mmHg, RV pressure > 60 mmHg, or RV pressure > 150 mmHg and PCWP > 9 mmHg.

<sup>b</sup> RV dysfunction: RVF on echo, RV dysfunction on CTPA, RV pressure > 15 mmHg on CTPA, or RV pressure > 40 mmHg on TTE.

<sup>c</sup> Elevated cardiac troponin levels: cTnI > 0.03 ng/mL or cTnT > 0.10 ng/mL.

<sup>d</sup> RV dysfunction on TTE or CTPA: RV pressure > 15 mmHg on TTE or RV pressure > 60 mmHg on CTPA.

<sup>e</sup> RV dysfunction on TTE or CTPA: RV pressure > 15 mmHg on TTE or RV pressure > 40 mmHg on CTPA.
### ESC PE Guidelines - PE Treatment

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;80 years</td>
<td>+1</td>
</tr>
<tr>
<td>History of cancer</td>
<td>+1</td>
</tr>
<tr>
<td>History of cardiopulmonary disease</td>
<td>+1</td>
</tr>
<tr>
<td>Systolic BP &lt;90 mm Hg</td>
<td>+1</td>
</tr>
<tr>
<td>Heart rate &gt;110 beats/minute</td>
<td>+1</td>
</tr>
<tr>
<td>O$_2$ saturation &lt;90%</td>
<td>+1</td>
</tr>
</tbody>
</table>
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..consider use of HESTIA criteria
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

PESI=1
INTERMEDIATE-HIGH RISK

SIDE BAR-HOW LONG SHOULD HE REMAIN ON ANTICOAGULATION?
### ESC PE Guidelines - Duration of Therapy

<table>
<thead>
<tr>
<th>Estimated risk for long-term recurrence&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Risk factor category for index PE&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Examples&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
</table>
| 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 |
| 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 |
| 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 |

<sup>a</sup> Estimated risk for long-term recurrence: Low (<3% per year), Intermediate (3–8% per year), High (>8% per year).

<sup>b</sup> Risk factor category for index PE: Major transient or reversible factors, Transient or reversible factors, Non-malignant persistent risk factors, No identifiable risk factor.

Suggest indefinite

Recommend indefinite

DO NOT USE LOW DOSE DOAC FOR SECONDARY PREVENTION IF:
>120 kg
Recurrent VTE on anticoagulation
Concurrent AFIB
Cancer associated VTE
APLS

Treating 1,000 patient-years with extended anticoagulation following acute VTE may result in:

**DOAC**

- ~5 (95% CI, 1 to 9) fewer deaths
- ~4 (95% CI, 1 to 6) fewer VTE-related deaths
- ~70 (95% CI, 41 to 99) fewer VTE recurrence
- ~3 (95% CI, -2 to 8) more major bleeding
- ~67 (95% CI, 39 to 94) net clinical benefit (absence of VTE recurrence or major bleeding)

**VKA**

- ~78 (95% CI, 40 to 117) fewer VTE recurrence
- ~14 (95% CI, 02 to 29) more major bleeding
- ~63 (95% CI, 20 to 107) net clinical benefit (absence of VTE recurrence or major bleeding)
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

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

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

Trial stopped early.
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
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

Unfractionated Heparin

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>
<thead>
<tr>
<th>Variable</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute thrombocytopenia</td>
<td>2</td>
</tr>
<tr>
<td>Platelet count decrease of &gt;50% and nadir &gt;20,000/mm³</td>
<td></td>
</tr>
<tr>
<td>Timing of onset</td>
<td></td>
</tr>
<tr>
<td>Day 5–10, or day 1 if recent heparin exposure</td>
<td></td>
</tr>
<tr>
<td>Thrombosis</td>
<td></td>
</tr>
<tr>
<td>New thrombosis or anaphylactoid reaction after heparin bolus</td>
<td></td>
</tr>
<tr>
<td>Other cause of thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Progressive or recurrent thrombosis</td>
<td>Possible</td>
</tr>
<tr>
<td>Definite</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total score</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>6–8, indicating high score</td>
<td>4 or 5, indicating intermediate score</td>
</tr>
<tr>
<td>0–3, indicating low score</td>
<td></td>
</tr>
</tbody>
</table>

Greinacher A N Engl J Med 2015;
<table>
<thead>
<tr>
<th>Score = 2</th>
<th>Score = 1</th>
<th>Score = 0</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thrombocytopenia</strong>&lt;br&gt;Compare the highest platelet count within the sequence of declining platelet counts with the lowest count to determine the % of platelet fall.&lt;br&gt;(Select only 1 option)</td>
<td><strong>Thrombocytopenia</strong>&lt;br&gt;Compare the highest platelet count within the sequence of declining platelet counts with the lowest count to determine the % of platelet fall.&lt;br&gt;(Select only 1 option)</td>
<td><strong>Thrombocytopenia</strong>&lt;br&gt;Compare the highest platelet count within the sequence of declining platelet counts with the lowest count to determine the % of platelet fall.&lt;br&gt;(Select only 1 option)</td>
</tr>
<tr>
<td>- o &gt; 50% platelet fall AND nadir of ≥ 20 AND no surgery within preceding 3 days</td>
<td>- o &gt; 50% platelet fall BUT surgery within preceding 3 days OR&lt;br&gt;any combination of platelet fall and nadir that does not fit criteria for Score 2 or Score 0&lt;br&gt;(eg, 30-50% platelet fall or nadir 10-19)</td>
<td>- o &lt; 30% platelet fall&lt;br&gt;any platelet fall with nadir &lt; 10</td>
</tr>
<tr>
<td>*<em>Timing (of platelet count fall or thrombosis</em>)**&lt;br&gt;Day 0 = first day of most recent heparin exposure&lt;br&gt;(Select only 1 option)</td>
<td>*<em>Timing (of platelet count fall or thrombosis</em>)**&lt;br&gt;Day 0 = first day of most recent heparin exposure&lt;br&gt;(Select only 1 option)</td>
<td>*<em>Timing (of platelet count fall or thrombosis</em>)**&lt;br&gt;Day 0 = first day of most recent heparin exposure&lt;br&gt;(Select only 1 option)</td>
</tr>
<tr>
<td>- o platelet fall day 5-10 after start of heparin&lt;br&gt;- o platelet fall within 1 day of start of heparin AND exposure to heparin within past 5-30 days</td>
<td>- o consistent with platelet fall days 5-10 but not clear (eg, missing counts)&lt;br&gt;- o platelet fall within 1 day of start of heparin AND exposure to heparin in past 31-100 days&lt;br&gt;- o platelet fall after day 10</td>
<td>- o platelet fall ≤ day 4 without exposure to heparin in past 100 days</td>
</tr>
<tr>
<td><strong>Thrombosis (or other clinical sequelae)</strong>&lt;br&gt;(Select only 1 option)</td>
<td><strong>Thrombosis (or other clinical sequelae)</strong>&lt;br&gt;(Select only 1 option)</td>
<td><strong>Thrombosis (or other clinical sequelae)</strong>&lt;br&gt;(Select only 1 option)</td>
</tr>
<tr>
<td>- o confirmed new thrombosis (venous or arterial)&lt;br&gt;- o skin necrosis at injection site&lt;br&gt;- o anaphylactoid reaction to IV heparin bolus&lt;br&gt;- o adrenal hemorrhage</td>
<td>- o recurrent venous thrombosis in a patient receiving therapeutic anticoagulants&lt;br&gt;- o suspected thrombosis (awaiting confirmation with imaging)&lt;br&gt;- o erythematous skin lesions at heparin injection sites</td>
<td>- o thrombosis suspected</td>
</tr>
</tbody>
</table>

**oTher cause for Thrombocytopenia**<br>(Select only 1 option)<br>- o no alternative explanation for platelet fall is evident<br>- o possible other cause is evident:<br>  - sepsis without proven microbial source<br>  - thrombocytopenia associated with initiation of ventilator<br>  - other<br>- o probable other cause present:<br>  - within 72 h of surgery<br>  - confirmed bacteremia/fungemia<br>  - chemotherapy or radiation within past 20 days<br>  - DIC due to non-HIT cause<br>  - posttransfusion purpura (PTP)<br>  - platelet count < 20 AND given a drug implicated in causing D-ITP (see list)<br>  - non-nectroizing skin lesions at LMWH injection site (presumes OTH)<br>  - other

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

*Relatively Common*: glycoprotein IIb/IIIa antagonists (abxiximab, eptifibatide, tirofiban); quinine, quinidine, sulfa antibiotics, carbamazepine, vancocycin

*Less Common*: actinomycin, amitryptiline, amoxicillin/piperacillin/nafillin, cephalosporins (cefaolin, cefazidine, ceftriaxone), celecoxib, ciprofloxacin, esomeprazole, levoIeunadine, fentanyl, fucidic acid, furoseneide, gold salts, levofloxacin, metronidazole, naproxen, oxaliplatin, phenytion, propranolol, propoxyphene, ranitidine, rifampicin, suramin, trimethoprim. Note: This is a partial list.
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
American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia

Adam Cuker,1,2 Gwethami M. Arepally,3 Beng H. Chong,4 Douglas B. Cines,1,2 Andreas Greinacher,5 Yves Gruel,6 Lori A. Linkins,7 Stephen B. Rodner,8 Sixten Selleng,9 Theodore E. Warkentin,7,10 Ashleigh Wex,11 Reem A. Mustafa,12,13 Rebecca L. Morgan,12 and Nancy Santesso12

1Department of Medicine and 2Department of Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; 3Department of Medicine, Duke University Medical Center, Durham, NC; 4Department of Haematology, University of New South Wales, Sydney, NSW, Australia; 5Institute of Immunology and Transfusion Medicine, University of Greifswald, Greifswald, Germany; 6Department of Haematology-Haemostasis, Trousseau Hospital, Tours, France; 7Department of Medicine, McMaster University, Hamilton, ON, Canada; 8New York, NY; 9Department of Anaesthesiology, University of Greifswald, Greifswald, Germany; 10Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada; 11Columbus, OH; 12Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada; and 13Department of Medicine, University of Missouri–Kansas City, Kansas City, MO

American Society of Hematology (ASH) 2018 VTE Guidelines: HIT

27 November 2018 • Volume 2, Number 22
2018 ASH HIT Diagnosis and Treatment Algorithm

4T’s ≥4

4T’s ≤3

Cuker A et al. Blood Advances 2018
Important Treatment Recommendations of ASH HIT Guideline

• In acute phase HIT or HITT, 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

Anticoagulation FORUM

Cuker A et al. Blood Advances 2018
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

Cuker A et al. Blood Advances 2018
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?”
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?

Tracy Minichiello, MD