Isolated Distal DVT: Selecting the Best Management Strategies

Tuesday, March 19, 2019, 12:00 PM ET

Guest Speaker: Dr. Natalie Evans, MD, MS
Cleveland Clinic

AC Forum Moderators:
Sara Vazquez, PharmD, BCPS, CACP
Diane Wirth, ANP, CACP
Presenters

Natalie S. Evans, MD, MS
Medical Director, Non-Invasive Vascular Laboratory
Staff Physician
Section of Vascular Medicine
Cleveland Clinic

Sara Vazquez, PharmD
Clinical Pharmacist
University of Utah Health
Salt Lake City, UT

Diane Wirth, ANP, CACP
Manager Heart Failure Program
Grady Memorial Hospital
Atlanta, GA
Hot Off the Press
Order Sets for CAD/PAD and VTE
Prophylaxis for Medically Ill Patients

Diane Wirth ANP-BC
Promoting Clinical Application
Clinical Order Sets

- Order sets standardize the clinical decision process
- Incorporate the latest evidence-based best practice to clinical workflow
- Improves patient outcomes and reduces adverse events
- Can be integrated into EMR systems
VTE Prophylaxis for Hospitalized Medically Ill Patients

• New FDA approval for extended prophylaxis for subset of medically ill patients- APEX trial- paradigm shift
• Risk stratification of hospital patients for appropriate prophylaxis
• Bleeding risk assessment
Risk Stratifying VTE Prophylaxis for the Medically Ill Patient

**VTE Risk Assessment**

See appendices for risk assessment tools (IMPROVE, Padua, Caprini) to assist with VTE risk assessment.

- High or moderate risk of VTE
- Low risk of VTE

If the patient is low risk for VTE per your hospital’s Risk Assessment Model and is not anticipated to experience severe immobility, then no VTE prophylaxis (pharmacological or mechanical) is necessary. Reassess your patients’ VTE risk status as clinically indicated.

**LOW VTE RISK BASED ON RISK ASSESSMENT SCORES**

- Improve 4 Score: 0-1
- Improve 7 Score: 0-1
- Padua Score: 0-3
- Caprini Score: 0-1

**HIGH OR MODERATE VTE RISK BASED ON RISK ASSESSMENT SCORES**

- Improve 4 Score ≥2
- Improve 7 Score: ≥2
- Padua Score: ≥4
- Caprini Score: ≥2

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**Bleeding Risk Assessment**

**IMPROVE Bleeding Risk Factor**

- Moderate renal failure (GFR 30-59) 1 point
- Sex: Male vs Female 1 point
- Age: 40 – 84 1.5 points
- Current cancer 2 points
- Rheumatic diseases 2 points
- CV catheter 2 points
- ICU / CCU stay 2.5 points
- Severe renal failure (GFR < 30 ml/min) 2.5 points
- Hepatic failure (INR > 1.5) 2.5 points
- Age ≥ 85 3.5 points
- Admission platelets < 50 x 10^9 4 points
- Bleeding prior 3 months 4 points
- Gastro-duodenal ulcer 4.5 points

**Total Score**

Scores ≥ 7 indicate higher bleeding risk and caution with pharmacologic prophylaxis. Reassess candidacy for anticoagulant or mechanical prophylaxis as clinically indicated.
Gathering Information to Guide Your Decision

<table>
<thead>
<tr>
<th>Baseline Information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASSESSMENTS</strong></td>
</tr>
<tr>
<td>✅ 8PTT ________</td>
</tr>
<tr>
<td>✅ Prothrombin time (PT) ______________</td>
</tr>
<tr>
<td>✅ HGB ________</td>
</tr>
<tr>
<td>✅ PLTS ________</td>
</tr>
<tr>
<td>✅ ALT ________</td>
</tr>
<tr>
<td>✅ AST ________</td>
</tr>
<tr>
<td><strong>RENAL FUNCTION</strong></td>
</tr>
<tr>
<td>✅ Calculate estimated CrCl using the Cockcroft-Gault equation</td>
</tr>
</tbody>
</table>
| \[
(\frac{[72 \times \text{serum creatinine}]}{[\text{actual weight} \times \text{Age}]}) \times 0.85 \text{ if female}
\] |
| ✅ Age: ____________ |
| ✅ Actual body weight: ____________ (kg) |
| ✅ Gender: ____________ |
| ✅ Serum Creatinine: ____________ (mg/dL) |
| *Monitor renal functioning during hospital stay |
| ✅ Estimated CrCl: ____________ (mL/minute) |

**SECTION X: PATIENT CRITERIA FOR USE OF BETRIXABAN IN-HOUSE AND FOR EXTENDED PROPHYLAXIS**

- No invasive procedures are planned in the next 30 days
- No contraindications to anticoagulant prophylaxis
- Creatinine clearance > 30 ml/min
- Not taking concomitant therapy with a strong PGP inhibitor
- Non-pregnant or breastfeeding
- Not currently on dual antiplatelet therapy (DAPT)
- Confirmation of insurance coverage of betrixaban for duration of prophylactic regimen and hospitalized with acute NYHA Class III/IV heart failure, respiratory failure, acute infectious disease or rheumatic illness or ischemic stroke with lower extremity paresis, and severe immobility (bed or chair bound 100% of the day) for at least 1 day and moderate immobility (bed or chair bound 50% of day with bathroom privileges) for at least 4 days

AND ONE OF THE FOLLOWING:

- Age ≥75
- Age 60-74 and two additional VTE risk factor
- Age 40-59 and a prior VTE or active cancer and one additional risk factor below

**RISK FACTORS**

- Previous VTE or superficial vein thrombosis
- History of NYHA Class III or IV HF
- Concomitant acute infection
- Obesity (BMI >35)
- History of cancer
- Inherited or acquired thrombophilia
- Current use of erythropoiesis-stimulating agent
- Hormone therapy
# Prophylaxis options

## VTE Prophylaxis Options (Select One):

- [ ] Oral
- [ ] Parenteral
  - For CrCl > 30ml/min
    - Dalteparin 5000 u SC once daily
    - Enoxaparin 40 mg SC once daily
    - Fondaparinux 2.5 mg SC once daily
  - For CrCl 15-29 ml/min
    - Enoxaparin 30 mg SC once daily
  - For CrCl < 15 ml/min
    - Unfractionated heparin 5000 u SC  bid  tid
- [ ] Mechanical prophylaxis

## Betrixaban VTE Prophylaxis Options (Select One):

- Betrixaban 160 mg PO on day one, then 80 mg daily for 35-42 days (CrCl >30ml/min)

## Adjusted Dosing

- Betrixaban 80 mg PO on day one, then 40 mg daily for 35-42 days renal dosing (CrCl 15-30ml/min) or taking strong PGP inhibitor
### Appendixes: VTE Risk Assessments

**IMPROVE: 7-ELEMENT IN-HOSPITAL RISK MODEL**

<table>
<thead>
<tr>
<th>VTE Risk Factors</th>
<th>3 POINTS</th>
<th>2 POINTS</th>
<th>1 POINT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous VTE</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>□</td>
<td>□</td>
<td></td>
</tr>
<tr>
<td>Lower limb paralysis</td>
<td>□</td>
<td>□</td>
<td></td>
</tr>
<tr>
<td>Current cancer</td>
<td>□</td>
<td>□</td>
<td></td>
</tr>
<tr>
<td>Age &gt; 60 years</td>
<td>□</td>
<td>□</td>
<td></td>
</tr>
<tr>
<td>Immobilization ≥ 7 days</td>
<td>□</td>
<td>□</td>
<td></td>
</tr>
<tr>
<td>ICU / CCU stay</td>
<td>□</td>
<td>□</td>
<td></td>
</tr>
</tbody>
</table>

**IMPROVE 7 VTE Score:**
Scores 0-6 are low risk with no indication for prophylaxis
Scores ≥ 7 are high risk and warrant prophylaxis

**IMPROVE: 4-ELEMENT IN-HOSPITAL RISK MODEL**

<table>
<thead>
<tr>
<th>VTE Risk Factors</th>
<th>3 POINTS</th>
<th>2 POINTS</th>
<th>1 POINT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous VTE</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>□</td>
<td>□</td>
<td></td>
</tr>
<tr>
<td>Current cancer</td>
<td>□</td>
<td>□</td>
<td></td>
</tr>
<tr>
<td>Age &gt; 60 years</td>
<td>□</td>
<td>□</td>
<td></td>
</tr>
</tbody>
</table>

**IMPROVE 4 VTE Score:**
Scores 0-2 are low risk with no indication for prophylaxis
Scores ≥ 2 are high risk and warrant prophylaxis

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**Appendixes: VTE Risk Assessments Continued**

**CAPRINI SCORE**
Below depicts the different weighted points for the risk factors included in the Caprini Score:

<table>
<thead>
<tr>
<th>5 POINTS</th>
<th>2 POINTS</th>
<th>1 POINT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke (in the previous month)</td>
<td>Elective arthroplasty</td>
<td></td>
</tr>
<tr>
<td>Fracture of the hip, pelvis, or leg</td>
<td>Acute spinal cord injury (in the last month)</td>
<td></td>
</tr>
<tr>
<td>Age ≥ 75 years</td>
<td>Anticardiolipin antibodies</td>
<td></td>
</tr>
<tr>
<td>Prior episode of VTE</td>
<td>High homocysteine in the blood</td>
<td></td>
</tr>
<tr>
<td>Positive family history for VTE</td>
<td>Heparin induced thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td>Prothrombin 20210A</td>
<td>Other congenital or acquired thrombophilia</td>
<td></td>
</tr>
<tr>
<td>Factor V Leiden</td>
<td>Lupus anticoagulants</td>
<td></td>
</tr>
</tbody>
</table>

**CAPRINI SCORE Continued**

<table>
<thead>
<tr>
<th>2 POINTS</th>
<th>1 POINT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: 61 – 74 years</td>
<td>Cancer</td>
</tr>
<tr>
<td>Arthroscopic surgery</td>
<td>Wrester cast</td>
</tr>
<tr>
<td>Lacerotomy lasting more than 45 minutes</td>
<td>Bed bound for more than 72 hours</td>
</tr>
<tr>
<td>General surgery lasting more than 45 minutes</td>
<td>Central venous access</td>
</tr>
<tr>
<td>Age ≥ 60 years</td>
<td>Sepsis (in the previous month)</td>
</tr>
<tr>
<td>BMI &gt; 25 kg/m²</td>
<td>Serious lung disease such as pneumonia (in the previous month)</td>
</tr>
<tr>
<td>Minor surgery</td>
<td>Abnormal pulmonary function test</td>
</tr>
<tr>
<td>Extensive in the lower extremities</td>
<td>Acute myocardial infarction</td>
</tr>
<tr>
<td>Varicose veins</td>
<td>Congestive heart failure (in the previous month)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Bed rest</td>
</tr>
<tr>
<td>Post-partum</td>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>Oral contraceptive</td>
<td>Unexplained or recurrent abortion</td>
</tr>
</tbody>
</table>

**Note:** The Caprini score is calculated by adding the scores of all factors present in the patient.
The Caprini score is interpreted in the following way:
Total score of 0-1: Low risk of VTE
Total score of ≥ 2: High/moderate risk of VTE
Compass Trial

• Evaluated whether rivaroxaban alone or in combination with aspirin would be more effective than aspirin alone for secondary cardiovascular prevention.

• Safety- Major bleeding

• Outcome
  • Rivaroxaban is indicated, in combination with aspirin, to reduce the risk of major cardiovascular events (cardiovascular [CV] death, myocardial infarction [MI], and stroke) in patients with chronic CAD or PAD (1).
Safe initiation of DOAC for patients with CAD/PAD already on guideline directed therapy

**Eligibility Continued**

**INCLUSION CRITERIA CONTINUED**

**HIGH-RISK FEATURES**

Subjects with CAD must also meet at least one of the following criteria:

- Age ≥65, or
- Age <65 and other high-risk features
  - Documented atherosclerosis or revascularization involving at least 2 vascular beds, OR
  - At least 2 additional risk factors:
    - Current or recent smoker (quit within 1 year)
    - Diabetes mellitus
    - Renal dysfunction with estimated glomerular filtration rate <60 ml/min
    - History of symptomatic heart failure
    - Non-lacunar ischemic stroke ≥1 month ago

**PERIPHERAL ARTERY DISEASE (PAD), SELECT AT LEAST 1**

- Previous PAD revascularization (e.g., aorto-femoral bypass surgery, limb bypass surgery, or percutaneous transluminal angioplasty revascularization of the iliac, or infrainguinal arteries), or
- Previous limb or foot amputation for arterial vascular disease, or
- History of intermittent claudication and one or more of the following:
  - An ankle-brachial index (ABI) < 0.90, or
  - Significant peripheral artery stenosis (≥50%) documented by angiography, or by duplex ultrasound, or
  - Significant carotid artery disease (previous carotid revascularization or asymptomatic carotid artery stenosis ≥50%)

*Note: Patients with severe heart failure (ejection fraction <30% or New York Heart Association class III or IV) were not included in the COMPASS randomized trial.*

**USE NOT RECOMMENDED**

The following criteria indicate scenarios where rivaroxaban + aspirin should NOT be used as a secondary cardiovascular prevention strategy:

- Active pathological bleeding
- Advanced chronic kidney disease (estimated CrCl <15 ml per minute)
- Mechanical heart valves
- Other indication for anticoagulation (e.g., atrial fibrillation or venous thromboembolism) or antiplatelet medication (e.g., cilostazole)
- Current need for dual antiplatelet therapy (DAPT): aspirin plus P2Y12 antiplatelet medicine (clopidogrel, prasugrel, or ticagrelor)
- Pregnancy/breastfeeding
- Severe hypersensitivity reaction to rivaroxaban or aspirin (e.g., anaphylactic reactions)
- Any stroke within 1 month
- Systemic treatment with strong inhibitors of both CYP 3A4 and p-glycoprotein or strong inducers of CYP 3A4

**USE WITH CAUTION**

The following criteria indicate scenarios where use of rivaroxaban + aspirin should be done after carefully considering risks and benefits:

- Any history of pathologic bleeding
- High risk of pathologic bleeding
- History of hemorrhagic or lacunar stroke (>1 month)

Reassess candidacy for anticoagulant prophylaxis as clinically indicated or with any medication changes.
Factors Influencing DOAC Use

**Factors Influencing Drug Selection**

Renal and liver characteristics are necessary to determine appropriateness of anticoagulation therapy.

**RENEAL FUNCTION**

- Calculate estimated CrCl using the Cockcroft-Gault formula based on the following:
  \[
  \frac{[(140 - \text{Age}) \times \text{actual weight in kg}]}{(72 \times \text{serum creatinine})} \times 0.85 \text{ if female}
  \]

- **Age:**
- **Actual body weight:**
- **Gender:**
- **Serum creatinine:**
- **Estimated CrCl:**

**RENEAL IMPAIRMENT**

- **AVOID** use in patients with an estimated CrCl < 15 ml/min

**LIVER FUNCTION**

- Liver disease: [ ] No [ ] Yes: Child Pugh Grade:

**DOAC Drug Interactions and Dose Adjustments**

**BODY WEIGHT**

- Overweight (Weight >120 kg or BMI over 40): use with caution
- Underweight (Weight <50 kg): use with caution

*Note: few patients with BMI >35 were included in the COMPASS trial*

**CONCOMITANT MEDICATION**

**PHARMACODYNAMIC DRUG INTERACTIONS**

- **AVOID** or minimize concomitant use of antplatelets (e.g. *dual antiplatelet therapy* [DAPT]), and/or NSAIDs whenever possible
- **AVOID** or minimize concomitant use of other forms of aspirin (e.g. Excedrin, Alka-Seltzer, acetylsalicylic acid [ASA])
- **AVOID** or minimize concomitant use of other drugs that impair hemostasis (e.g. enoxaparin, warfarin, fibrinolytic therapy, SSRIs, SNRIs) to reduce the risk of bleeding

[Anticoagulation Forum logo]
Initiation Guidance, What You Need to do

Orders
- Rivaroxaban 2.5 mg PO twice daily
- Aspirin 81 mg PO once daily

AND

Be sure to discontinue any P2Y12 antiplatelet therapy when initiating rivaroxaban + aspirin therapy

Lab Orders
- Baseline CBC
- Baseline serum creatinine (to calculate Cockcroft Gault formula)
- Baseline INR (to calculate Child Pugh score)
- Baseline liver function tests (to calculate Child Pugh score)
- Other (specify):

MANAGED CARE
- Complete prior authorization paperwork if required by payer (https://www.covermymeds.com)

SHARED DECISION-MAKING DISCUSSION

Note: If drug costs are a barrier to filling prescriptions for medication, refer patient to appropriate resources.

Select all that have been discussed with patient:
- Bleeding risk/reversal agents
- Dosing regimen options (e.g. once vs. twice daily)
- Lifestyle factors of drug (e.g. diet, blood draws, activities)
- Out-of-pocket medication cost discussed with patient
- Other (specify):

Patient Education

Provide applicable education materials/instructions to the patient as per policy/procedure (1, 6).

The following topics are important to include within patient education:
- Follow-up appointments for blood work
- Follow-up contact information:
- Safety net phone number to call if any barriers or issues after discharge:
- Medication management, including starting/stopping new medication, missed doses and dose change (dose de-escalation or switch to oral therapy at appropriate date/time)
- Importance of medication adherence
- Expected duration of anticoagulation therapy
- Drug/diet considerations (if any)
- Bleeding and bruising risks
- When to seek medical attention (e.g. warning signs for bleeding, symptoms of VTE)
- Written education materials for patient/family/caregivers to review after discharge
- Medication reconciliation completed
- Patient education documented per health system policy

Anticoagulation FORUM
Isolated Distal DVT: Selecting the Best Management Strategies

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Diane Wirth, ANP, CACP
Disclosures

Natalie Evans, MD, MS

• Consultant for Janssen Pharmaceuticals Inc. (modest)
Objectives

• Which isolated distal deep vein thrombosis (IDDVT) should be anticoagulated?
• If no anticoagulation, how should IDDVT be managed?
• Which anticoagulant should we use?
• How long should we treat?
• What about patients with cancer and IDDVT?
Spelled it out since I hadn’t for the first time

Natalie Evans, 3/17/2019
Case 1

- 19-year-old woman presents to ED with persistent left knee and calf pain 13 days after surgery
- History of multiple ACL reconstruction surgeries
- Normal vitals; healing knee incisions; left ankle and calf swelling
- Normal creatinine, hemoglobin, and platelets
- Venous duplex: peroneal and gastrocnemius DVT
Case 2

• 59-year-old man with lumbar spine surgery 3 days prior ready for hospital discharge
• Denies leg symptoms; is ambulatory
• Normal vital signs, no leg swelling or tenderness
• Stage 3 CKD, hemoglobin 11.8 mg/dL, platelets normal
• Screening ultrasound performed per neurosurgery service protocol shows peroneal DVT at mid-calf
Definition

• Distal = calf deep vein thrombosis
  • Posterior tibial, peroneal veins
  • Anterior tibial veins
    • Thrombosis is rare
• Calf muscle veins
  • Soleal veins, draining to posterior tibial and peroneal
  • Gastrocnemial veins, draining to popliteal vein
  • Significance of thrombosis in these veins unclear, but generally treated the same as the true deep veins of the calf
Implications of IDDVT

• Symptomatic DVT typically begins in the calf
• Without anticoagulation, calf DVTs progress or extend to proximal veins
• Untreated proximal DVT may cause pulmonary embolism (PE) in up to half of cases
• 10% of patients with PE die within first hour
• Post-thrombotic syndrome may develop

Kearon, Circulation 2003;107:I22
Why not treat all DVT?

• Case fatality rate of major bleeding is 2-3 times that of recurrent VTE

• VTE treatment trials cannot account for individual bleeding risk

• Meta-analysis: symptomatic VTE on anticoagulation
  • Case fatality rate of recurrent VTE after first 3 months of treatment: 3.6%
  • Case fatality rate of major bleeding during first 3 months of anticoagulation: 11.3%

Carrier, Ann Int Med 2010;152:578
Epidemiology of IDDVT

• Isolated distal DVT is common
  • Prevalence is highly variable given diagnostic methods used, population studied, etc.
  • Among inpatients, IDDVT accounts for about 20% of diagnosed DVTs
  • In studies of whole-leg ultrasound, IDDVT accounts for about half of diagnosed DVTs
  • In some outpatient studies, IDDVT makes up 60-70% of diagnosed DVT

• Diagnosis of IDDVT is operator-dependent

Treatment paradigm for IDDVT

- Severity of symptoms
- Need for anticoagulation
- Thrombus extension risk
# Thrombus propagation

## Risk factors for IDDVT extension warranting anticoagulation

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive D-dimer</td>
<td></td>
</tr>
<tr>
<td>Extensive thrombosis or close to proximal veins (&gt; 5 cm length; involving multiple veins; &gt; 7 mm in diameter)</td>
<td></td>
</tr>
<tr>
<td>No reversible provoking factor for DVT</td>
<td></td>
</tr>
<tr>
<td>Active cancer</td>
<td></td>
</tr>
<tr>
<td>History of VTE</td>
<td></td>
</tr>
<tr>
<td>Inpatient status</td>
<td></td>
</tr>
</tbody>
</table>

Kearon, Chest 2012;141:e419S
Basis for treatment recommendation for IDDVT

- Trial of 51 patients with IDDVT randomized to 5 days of heparin overlapping with warfarin vs. heparin alone
- 22/23 warfarin patients free from recurrence at one year compared with 19/28 in no-warfarin group

Lagerstedt, Lancet 1985;2:515
ACT trial

• Feasibility study of open-label, randomized, controlled trial of IDDVT

• 70 patients randomized to 3 months of anticoagulation versus no anticoagulation, with repeat ultrasound at 7 and 21 days

• Primary outcome: composite proximal propagation, PE, VTE death, major bleeding
  • 11.4% of non-treated group vs. 0% of treated group
  • Not statistically significantly different
  • No major bleeds

Horner, Chest 2014;146:1468
CALTHRO trial

• Examined symptomatic patients with negative proximal ultrasound and high pretest probability or positive D-dimer

• All got whole-leg ultrasound at enrollment, results of which were kept blinded until outcome/study completion

• All got repeat proximal ultrasound at 5-7 days
  • If propagation to proximal, anticoagulation initiated
  • If no propagation, observed

Palareti, Thromb Haemost 2010;104:1063
CALTHRO trial

Isolated distal DVT
N=65
- 22/65 (34%) had involvement of >1 vein
- 2/65 had proximal extension at 5-7 days
- 5 events at 3 months, including 2 detected at d. 5-7

No DVT
N=359
- 3 events at 3 months, including 1 detected at d. 5-7

Excluding events detected at 5-7 days, difference barely significant
CACTUS trial

- Multicenter, double-blind trial of symptomatic calf DVT followed for 3 months
- Excluded patients with cancer or previous VTE
- Randomized to nadroparin versus placebo for 6 weeks; all got compression stockings
- Primary efficacy outcome: composite of extension to proximal veins, contralateral proximal DVT, symptomatic PE at day 42
- Primary safety outcome: major or clinically relevant non-major bleeding at day 42

Righini, Lancet Haemotol 2016;3:e556
## CACTUS results

<table>
<thead>
<tr>
<th></th>
<th>Nadroprin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>122</td>
<td>130</td>
</tr>
<tr>
<td>VTE at day 42</td>
<td>4/122 (3%)</td>
<td>7/130 (5%)</td>
</tr>
<tr>
<td>Bleeding at day 42</td>
<td>5/122 (4%)</td>
<td>0/130</td>
</tr>
</tbody>
</table>

No difference

Significant difference

One patient developed heparin-induced thrombocytopenia

Limitation: study met only half the pre-specified sample size
Pooled estimates of CALTHRO/CACTUS

• VTE rate (proximal DVT, PE) of untreated IDDVT at 3 months approximately 10%
• Authors argue that rate is not negligible
• D-dimer and pre-test probability may help determine who is at low risk for extension

Sartori, Lancet Haemotol 2017;4:e156
Does anticoagulation reduce pain?

- Post hoc analysis of CACTUS trial
- 130 patients on nadroparin, 122 on placebo asked to rate leg pain using visual analog scale
- No difference at 1 week or at 6 weeks
- Limitations: post hoc analysis, small study size

Righini, J Thromb Haemost 2019;17:507
Anticoagulant choice

• Isolated distal DVT not studied in major anticoagulant trials

• Current guidelines suggest direct oral anticoagulants over vitamin K antagonist for VTE (Grade 2B)

• For patients with cancer, low-molecular-weight heparin suggested over VKA or DOAC (Grade 2C)

• Intensity of anticoagulation for IDDVT needs further research

Kearon, Chest 2016;149:315
Duration of anticoagulation

Table 3: Crude rates of recurrent VTE after stopping anticoagulant treatment according to location of initial VTE, length of treatment, and months of follow-up after stopping treatment—all participants

<table>
<thead>
<tr>
<th>Length of treatment (months)</th>
<th>Months after stopping treatment</th>
<th>Recurrent episodes of VTE per 100 patient years (95% CI) (events/patient years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pulmonary embolism</td>
</tr>
<tr>
<td>1 or 1.5</td>
<td>≤6</td>
<td>21.9 (15.6 to 30.6) (34/155)</td>
</tr>
<tr>
<td></td>
<td>7-24</td>
<td>11.8 (9.1 to 15.2) (59/500)</td>
</tr>
<tr>
<td></td>
<td>0-24</td>
<td>11.3 (7.9 to 16.0) (31/275)</td>
</tr>
<tr>
<td>3</td>
<td>≤6</td>
<td>10.2 (6.4 to 16.2) (18/176)</td>
</tr>
<tr>
<td></td>
<td>7-24</td>
<td>8.9 (6.6 to 11.9) (44/495)</td>
</tr>
<tr>
<td></td>
<td>0-24</td>
<td>10.7 (5.6 to 20.5) (9/84)</td>
</tr>
</tbody>
</table>

DVT = deep vein thrombosis; NA = not applicable; VTE = venous thromboembolism.

Boutitie, BMJ 2011;342:d3036
DM7  Corrected spelling of research name:
https://www.bmj.com/content/342/bmj.d3036

Florent Boutitie, statistical investigator
Debi McGill, 3/5/2019
Duration of anticoagulation

• Guidelines recommend duration of 3 months compared with longer regimen (Grade 1B)

• Guidelines suggest 3 months compared with shorter regimen (Grade 2C)
Bleeding risk of DOACs

• 12 RCTs involving 102,607 patients
• DOACs associated with lower rates of major, fatal, clinically relevant non-major, and total bleeding compared with VKAs
• No increased risk of major GI bleeding in DOACs compared with warfarin
• Real-world data also suggests the observed bleeding rate is lower than experienced using warfarin

Blood 2014;124:2450   NEJM 2013;368:1272
Bleeding Risk of DOACs

• DOACs versus VKA

• Meta-analysis of 100,000 patients
  • Fatal bleeding: RR 0.53 (95% CI 0.43-0.64)
  • Case-fatality rate: 7.6 vs. 11.0%

• Retrospective matched cohort of 59,000 patients
  • 3.3% major bleeding in first 90 days
  • 1.7% all-cause mortality
  • Bleeding similar to warfarin; HR 0.92 (95% CI 0.82-1.03)

Non-anticoagulation management strategies

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (95% CI)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent major bleeding</td>
<td>2.7 (1.6-4.6)</td>
<td>2</td>
</tr>
<tr>
<td>Serum creatinine &gt; 1.2 mg/dl</td>
<td>2.1 (1.7-2.8)</td>
<td>1.5</td>
</tr>
<tr>
<td>Anemia</td>
<td>2.1 (1.7-2.7)</td>
<td>1.5</td>
</tr>
<tr>
<td>Cancer</td>
<td>1.7 (1.4-2.2)</td>
<td>1</td>
</tr>
<tr>
<td>Clinically overt PE</td>
<td>1.7 (1.4-2.2)</td>
<td>1</td>
</tr>
<tr>
<td>Age &gt; 75 years</td>
<td>1.7 (1.3-2.1)</td>
<td>1</td>
</tr>
</tbody>
</table>

PE: pulmonary embolism; CI: confidence interval

Incidence of bleeding in patients with score 1-4: 2.6%; in patients with score > 4: 7.3%

Ruiz-Gimenez, Thromb Haemost 2008;100:26
Serial ultrasound

• When and how often to perform are unknown
• Guidelines suggest 5-7 days after initial diagnosis, and 5-7 days after that
• If propagation to proximal veins, anticoagulation
  • If patient cannot be anticoagulated, vena cava filter
• If propagation below the knee, anticoagulation generally recommended

Kearon, Chest 2012;141:e419S
Cancer and IDDVT

• Unclear how to manage cancer patients with IDDVT with respect to duration of anticoagulation

• Residual vein obstruction (RVO) has been cited inconsistently as a risk factor for recurrent VTE

• 153 patients with cancer-associated IDDVT

• Those with RVO had double the recurrence rate after anticoagulation stopped

• Limitations: post hoc analysis, patients treated for variable length

Dentali, J Thromb Thrombolysis 2018;46:404
Case 1

• Patient with risk factors for propagation
  • Symptoms
  • Thrombus in multiple veins
  • Continued immobilization

• Recent surgery but otherwise low risk for bleeding
• Apixaban started and patient discharged from hospital
Case 2

• Low risk for propagation
  • Asymptomatic
  • Reversible risk factor
  • Thrombus isolated to one vein

• Recent spine surgery, chronic kidney disease increase risk for bleeding

• Patient lives close to medical center

• Serial ultrasound strategy pursued
Summary

• IDDVT is common but prevalence varies by population

• Sparse data make optimal management unclear

• Anticoagulation typically used for patients who are symptomatic, have extensive IDDVT, or have risk factors for propagation

• More research needed into optimal intensity and duration of anticoagulation