MANAGEMENT OF ACUTE DEEP VEIN THROMBOSIS – UPDATE

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MANAGEMENT OF ACUTE DEEP VEIN THROMBOSIS

Caveat

- The following deep vein thrombosis is in regards to the lower extremity only

References

- Malaysian CPG on Management of Venous Thromboembolism July 2003
DVT ≠ PE
Deep vein thrombosis precedes and may coexist with pulmonary embolism.

Conditions are NOT the same nor interchangeable.
Differences

+ DVT has a significantly lower mortality rate than PE

+ PE is more likely to recur (60%) than DVT (20%) alone.
MANAGEMENT OF ACUTE DEEP VEIN THROMBOSIS

- Conceptual Similarities
  - Most symptomatic PE have DVT
  - Most clinical trials on anticoagulation group DVT alone, DVT & PE and PE alone together
  - Similar risk of PE in proximal DVT and after 1st PE
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- Diagnosis of DVT of lower Extremity
  - Risk Stratify Patients for Likelihood of DVT
    - **Wells Score**  Wells PS et al JAMA 2006 Jan 11;295(2):199-207
Wells Criteria

- Confirmed Malignancy (+1)
- Bed bound > 3 days or Major surgery within 1 mth (+1)
- Calf diameter difference > 3 cm (+1)
- Presence of collateral superficial veins (+1)
- Entire leg swollen (+1)
- Localized tenderness along deep vein system (+1)
- Greater pitting edema in symptomatic leg (+1)
- Paralysis, paresis or cast immobilization of lower limb (+1)
- Previous documented DVT (+1)
- Alternative diagnosis to DVT likely? (-2)
<table>
<thead>
<tr>
<th>Risk</th>
<th>Wells Score</th>
<th>Probability of DVT</th>
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<tbody>
<tr>
<td>Low</td>
<td>0 – 1</td>
<td>5%</td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td>17%</td>
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<tr>
<td>High</td>
<td>2 &amp; more</td>
<td>53%</td>
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Low PTP

High/Mod Sensitive D-dimer\textsuperscript{c,a}

- Negative
  - No DVT\textsuperscript{b}
  - Proximal US\textsuperscript{c} (See Figure 5)
    - Negative
    - Positive
      - No DVT\textsuperscript{b}
      - Treat\textsuperscript{d}

- Positive

Proximal US\textsuperscript{c,a}

- Negative
- Positive

Whole-leg US\textsuperscript{c} (See Figure 5)

- Negative
- Positive

- No DVT\textsuperscript{b}
- Treat\textsuperscript{d}
D-dimer Tests

- Moderately sensitive: whole blood or latex semi-quantitative; sensitivity ~ 85%
- Highly sensitive: ELISA-based or quantitative latex or immunoturbidimetric; sensitivity ~ 95%
If D-dimer is negative in a patient with low pre-test probability for DVT, no further testing is recommended (Grade 1B)

If D-dimer is positive in a patient with low pre-test probability for DVT, check with compression ultrasound of the proximal leg veins rather than whole leg ultrasound (Grade 2C) or venography (Grade 1B)
ACCP recommended compression ultrasound of the proximal leg veins rather than whole leg ultrasound in low pretest probability because -

- Whole leg U/S identifies isolated calf vein DVT in low pretest probability where there is a low chance of propagating proximally and becoming a dangerous clot
- Identifying and treating likely-harmless calf vein DVTs carries an excess risk of serious bleeding from anticoagulation.
If Highly sensitive D-dimer is Negative in a patient with moderate pre-test probability for DVT of the leg, no further testing is to be pursued (Grade 1B)

If Highly sensitive D-dimer is Positive in a patient with moderate pre-test probability for DVT of the leg, compression ultrasound of proximal leg or whole leg (Grade 1B)
If whole leg U/S is Negative – No further testing is recommended. \textbf{Repeat} compression U/S in one week.

- After 1 week: U/S still negative \implies D/C
- : U/S positive \implies \textbf{Treat for DVT}

If whole leg U/S is Positive:

- For proximal DVT \implies \textbf{Treat for DVT}
- For isolated distal calf vein \implies \textbf{Serial U/S} (Grade 2C)
Figure Legend:

Recommendations for evaluation of suspected first lower extremity DVT: patients with high pretest probability (PTP) for DVT. Where there are preferred strategies, these are indicated by boldface print; less preferred strategies are indicated by italicizing/shading. Venography is not generally indicated in the figure, as it is not routinely used. aGrade 1B vs no testing and vs venography. bGrade 1B for treating DVT vs confirmatory venography. cGrade 1B vs no further testing; Grade 2B vs venography. dGrade 1B vs further testing. eGrade 2B for repeat proximal US, highly sensitive D-dimer or whole-leg US over venography. fGrade 2B for repeat proximal US over venography. gGrade 2B for no further testing over venography if whole-leg US is negative (see also Figure 5). See Figure 1 legend for expansion of abbreviation.
If patient has high pre-test probability, check with:

- Whole leg ultrasound

For negative whole leg ultrasound; no further testing is suggested (Grade 2B)

For positive whole leg ultrasound → Treat DVT
D-dimer as a stand alone test to rule out DVT is NEVER used in high pre-test probability patients. (Grade 1B)
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Risk Stratification Not Done

Proximal US\(^a\)
Whole-leg US\(^a\)
(See Figure 5)

Mod/High Sensitivity D-dimer\(^e\)

Negative

Repeat Proximal US in 1 week\(^c, b\)
Whole-leg US\(^c, b\)
(See Figure 5)

Mod/High Sensitivity D-dimer\(^c, b\)
Venography\(^d\)
(See Figure 13)

Positive

Treat\(^d\)

No DVT\(^d\)
Treat\(^d\)
No DVT\(^d\)
Repeat Proximal US in 1 week\(^c\)
Whole-leg US\(^c\)
(See Figure 5)

Negative

Positive

No DVT\(^d\)
Treat\(^d\)
If risk stratification is not done, the ACCP recommendation is to check compression ultrasound of the proximal leg veins or whole-leg ultrasound, rather than D-dimer, as the initial test (Grade 2B).

Whenever ultrasound is impractical or the test result cannot be trusted (e.g., obesity or leg casting limit visualization), CT venography or magnetic resonance venography (or direct thrombus imaging) should be considered.
Patients with confirmed Proximal Leg DVT:

- Patients with acute proximal leg DVT who will receive warfarin should initially be treated with heparin (low molecular weight or unfractionated, subcutaneous or intravenous) or fondaparinux (Grade 1B). Two randomized trials showed the benefit of this approach over no heparin.
- Continued for at least 5 days and until the INR is 2.0 or greater for 24 hours (Grade 1B). If the INR becomes supratherapeutic (>3.0) before 5 days, the heparin/fondaparinux should be stopped.
Patients with high clinical suspicion for DVT
  Treat immediately pending results.

Of intermediate suspicion
  Allow upto 4 hours for test results before treating.

Of low suspicion
  Allow upto 24 hours for test results before treating. (Grade 2C)
Majority of Isolated Distal Leg DVTs Do Not Merit Diagnosis or Treatment

- Especially those without popliteal or more proximal vein thrombosis
- 75% will never extend proximally or embolize, and anticoagulation is therefore unnecessary and potentially harmful in these cases.
- 15% of untreated distal DVTs will extend proximally.
- Proximal extension occurs within 2 weeks esp with risk factors

Therefore, the ideal approach to diagnosis and management of Isolated distal DVTs is unclear.
ACCP suggests low-molecular weight heparin or fondaparinux, rather than unfractionated heparin, as first-line treatment for acute DVT (Grade 2B/2C).

ACCP suggests daily rather than twice-daily administration of LMWH (Grade 2C).

ACCP suggests people with acute DVT do not need a period of bed rest, and should walk as soon as feasible to reduce the risk of post-thrombotic syndrome (Grade 2C).
Starting and Managing Warfarin/Coumadin for Initial Treatment of DVT

+ Start patients on warfarin 10 mg daily for 2 days, then dose by INR. There is no need to treat with heparin for several days before starting warfarin therapy (Grade 2C)

+ Use a target INR of 2.5 (range 2.0 – 3.0).

+ INR should be allowed to fluctuate up to 0.5 below or above therapeutic range (e.g., an INR of 1.5 to 3.5 for DVT/PE) without any change in dose — just recheck INR in 1-2 weeks. There is no need to bridge with heparin in this situation. (Grade 2C)
Antiplatelet drugs like aspirin and clopidogrel (Plavix) significantly increase the risk for major bleeding when taken with Coumadin. Aspirin or Plavix should only be added to warfarin when there is a clear or highly likely benefit: patients with acute coronary syndrome, mechanical valves, or recent bypass surgery or coronary artery stents. NSAIDs also increase bleeding risk when taken with coumadin, and should be avoided. (Grade 2C)
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- For **INRs up to 10**, if there is no evidence of bleeding, don’t give vitamin K or plasma products. **Just hold warfarin and re-check INR frequently.** (Grade 2B)
- For **INRs greater than 10** without evidence of bleeding, give oral vitamin K (Grade 2C)
- For patients with **major bleeding** while taking warfarin at any dose, rapidly reverse the coagulopathy using **four-factor prothrombin complex** (i.e., factors II, VII, IX and X ) (NOT fresh frozen plasma, they recommend) and **vitamin K : 5 or 10 mg given IV by slow injection.** (Grade 2C)
When treatment period is over stop warfarin – no need to taper dosage. (Grade 2C)
Indications for infrarenal IVC filters

- Therapeutic (Documented Thromboembolic Disease)
  - Patients with evidence of pulmonary embolus or IVC, iliac, or femoral-popliteal deep vein thrombosis (DVT) and one or more of the following:
    - Absolute or relative contraindication to anticoagulation
    - Complication of anticoagulation
    - Failure of anticoagulation
      - Recurrent PE despite adequate therapy
      - Inability to achieve/maintain adequate anticoagulation
      - Propagation/progression of DVT on therapeutic anticoagulation
  - Massive pulmonary embolism with residual deep venous thrombus in a patient at risk for further PE
  - Free-floating iliofemoral or inferior vena cava thrombus
  - Severe cardiopulmonary disease and DVT (e.g., cor pulmonale with pulmonary hypertension)
### The ACCP Grading System and Initiatives Toward Uniform Grading Across Guideline Panels

#### Grading Recommendations

<table>
<thead>
<tr>
<th>Grade of Recommendation/Description</th>
<th>Benefit vs Risk and Burdens</th>
<th>Methodological Quality of Supporting Evidence</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A/strong recommendation, high-quality evidence</td>
<td>Benefits clearly outweigh risk and burdens, or vice versa</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
<td>Strong recommendation, can apply to most patients in most circumstances without reservation</td>
</tr>
<tr>
<td>1B/strong recommendation, moderate quality evidence</td>
<td>Benefits clearly outweigh risk and burdens, or vice versa</td>
<td>RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies</td>
<td>Strong recommendation, can apply to most patients in most circumstances without reservation</td>
</tr>
<tr>
<td>1C/strong recommendation, low-quality or very low-quality evidence</td>
<td>Benefits clearly outweigh risk and burdens, or vice versa</td>
<td>Observational studies or case series</td>
<td>Strong recommendation but may change when higher quality evidence becomes available</td>
</tr>
<tr>
<td>2A/weak recommendation, high-quality evidence</td>
<td>Benefits closely balanced with risks and burden</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
<td>Weak recommendation, best action may differ depending on circumstances or patients’ or societal values</td>
</tr>
<tr>
<td>2B/weak recommendation, moderate-quality evidence</td>
<td>Benefits closely balanced with risks and burden</td>
<td>RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies</td>
<td>Weak recommendation, best action may differ depending on circumstances or patients’ or societal values</td>
</tr>
<tr>
<td>2C/weak recommendation, low-quality or very low-quality evidence</td>
<td>Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced</td>
<td>Observational studies or case series</td>
<td>Very weak recommendations; other alternatives may be equally reasonable</td>
</tr>
</tbody>
</table>
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THANK YOU