Antithrombotic Therapy for Venous Thromboembolic Disease*

American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition)

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This chapter about treatment for venous thromboembolic disease is part of the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Grade 1 recommendations are strong and indicate that the benefits do or do not outweigh risks, burden, and costs. Grade 2 suggests that individual patient values may lead to different choices (for a full understanding of the grading, see "Grades of Recommendation" chapter). Among the key recommendations in this chapter are the following: for patients with objectively confirmed deep vein thrombosis (DVT) or pulmonary embolism (PE), we recommend anticoagulant therapy with subcutaneous (SC) low-molecular-weight heparin (LMWH), monitored IV, or SC unfractionated heparin (UFH), unmonitored weight-based SC UFH, or SC fondaparinux (all Grade 1A). For patients with a high clinical suspicion of DVT or PE, we recommend treatment with anticoagulants while awaiting the outcome of diagnostic tests (Grade 1C). For patients with confirmed PE, we recommend early evaluation of the risks to benefits of thrombolytic therapy (Grade 1C); for those with hemodynamic compromise, we recommend short-course thrombolytic therapy (Grade 1B); and for those with nonmassive PE, we recommend against the use of thrombolytic therapy (Grade 1B). In acute DVT or PE, we recommend initial treatment with LMWH, UFH or fondaparinux for at least 5 days rather than a shorter period (Grade 1C); and initiation of vitamin K antagonists (VKAs) together with LMWH, UFH, or fondaparinux on the first treatment day, and discontinuation of these heparin preparations when the international normalized ratio (INR) is ≥ 2.0 for at least 24 h (Grade 1A). For patients with DVT or PE secondary to a transient (reversible) risk factor, we recommend treatment with a VKA for 3 months over treatment for shorter periods (Grade 1A). For patients with unprovoked DVT or PE, we recommend treatment with a VKA for at least 3 months (Grade 1A), and that all patients are then evaluated for the risks to benefits of indefinite therapy (Grade 1C). We recommend indefinite anticoagulant therapy for patients with a first unprovoked proximal DVT or PE and a low risk of bleeding when this is consistent with the patient's preference (Grade 1A), and for most patients with a second unprovoked DVT (Grade 1A). We recommend that the dose of VKA be adjusted to maintain a target INR of 2.5 (INR range, 2.0 to 3.0) for all treatment durations (Grade 1A). We recommend at least 3 months of treatment with LMWH for patients with VTE and cancer (Grade 1A), followed by treatment with LMWH or VKA as long as the cancer is active (Grade 1C). For prevention of postthrombotic syndrome (PTS) after proximal DVT, we recommend use of an elastic compression stocking (Grade 1A). For DVT of the upper extremity, we recommend similar treatment as for DVT of the leg (Grade 1C). Selected patients with lower-extremity (Grade 2B) and upper-extremity (Grade 2C). DVT may be considered for thrombus removal, generally using catheter-based thrombolytic techniques. For extensive superficial vein thrombosis, we recommend treatment with prophylactic or intermediate doses of LMWH or intermediate doses of UFH for 4 weeks (Grade 1B).

(CHEST 2008; 133:454S–545S)

Key words: cancer; chronic thromboembolic pulmonary hypertension; deep vein thrombosis; fondaparinux; low-molecular-weight heparin; plasminogen activator; pulmonary embolism; thrombectomy; thrombolytic therapy; thrombophlebitis; unfractionated heparin; vena caval filter; venous thromboembolism; vitamin K antagonist

Abbreviations: APTT = activated partial thromboplastin time; CDT = catheter-directed thrombolysis; CI = confidence interval; CTPH = chronic thromboembolic pulmonary hypertension; DVT = deep venous thrombosis; INR = international normalized ratio; IPC = intermittent pneumatic compression; IVC = inferior vena cava; LMWH = low-molecular-weight heparin; MPFF = micronized purified flavonoid fraction; NSAID = nonsteroidal antiinflammatory drug; OR = odds ratio; PE = pulmonary embolism; PTS = postthrombotic (phlebitic) syndrome; QOL = quality of life; RCT = randomized controlled trial; RR = relative risk; rt-PA = recombinant tissue plasminogen activator; SC = subcutaneous; SVC = superior vena cava; SVT = superficial venous thrombosis; tPA = tissue plasminogen activator; UEDVT = upper-extremity deep vein thrombosis; UFH = unfractionated heparin; VKA = vitamin K antagonist; VTE = venous thromboembolism

Summary of Recommendations

1.1 Initial Anticoagulation of Acute DVT of the Leg

1.1.1. For patients with objectively confirmed DVT, we recommend short-term treatment with SC LMWH (Grade 1A), **IV UFH** (Grade 1A), **monitored SC UFH** (Grade 1A), **fixed-dose SC UFH** (Grade 1A), **or SC fondaparinux** (Grade 1A) **rather than no such short-term treatment.**

1.1.2. For patients with a high clinical suspicion of DVT, we recommend treatment with anticoagulants while awaiting the outcome of diagnostic tests (Grade 1C).

1.1.3. In patients with acute DVT, we recommend initial treatment with LMWH, UFH, or fondaparinux for at least 5 days and until the INR is ≥ 2.0 for 24 h (Grade 1C).

1.1.4. In patients with acute DVT, we recommend initiation of VKA together with LMWH, UFH, or fondaparinux on the first treatment day rather than delayed initiation of VKA (Grade 1A).

1.2 IV UFH for the Initial Treatment of DVT

1.2.1. In patients with acute DVT, if IV UFH is chosen, we recommend that after an initial IV bolus (80 U/kg or 5,000 U), it be administered by continuous infusion (initially at a dose of 18 U/kg/h or 1,300 U/h) with dose adjustment to achieve and maintain an activated partial thromboplastin time (APTT) prolongation that corresponds to plasma heparin levels of 0.3 to 0.7 IU/mL anti-Xa activity by the amidolytic assay rather than administration as IV boluses throughout treatment, or administration without coagulation monitoring (Grade 1C).

1.3 SC UFH Compared With IV Heparin for the Initial Treatment of DVT

1.3.1. In patients with acute DVT, if monitored SC UFH is chosen, we recommend an initial dose of 17,500 U, or a weight-adjusted dose of about 250 U/kg bid, with dose adjustment to achieve and maintain an APTT prolongation that corresponds to plasma heparin levels of 0.3 to 0.7 IU/mL anti-Xa activity when measured 6 h after injection rather than starting with a smaller initial dose (see also Section 1.5) [Grade 1C].

1.3.2. In patients with acute DVT, if fixed-dose, unmonitored SC UFH is chosen, we recommend an initial dose of 333 U/Kg followed by 250 U/kg bid rather than non–weight-based dosing (see also Section 1.5) [Grade 1C].

1.4 LMWH for the Initial Treatment of DVT

1.4.1. In patients with acute DVT, we recommend initial treatment with LMWH SC once or twice daily, as an outpatient if possible (Grade 1C), **or as an inpatient if necessary** (Grade 1A), **rather than treatment with IV UFH.**

1.4.2. In patients with acute DVT treated with LMWH, we recommend against routine monitoring with anti-factor Xa level measurements (Grade 1A).

1.4.3. In patients with acute DVT and severe renal failure, we suggest UFH over LMWH (Grade 2C).

1.9 Catheter-Directed Thrombolysis for Acute DVT

1.9.1. In selected patients with extensive acute proximal DVT (*eg*, iliofemoral DVT, symptoms for < 14 days, good functional status, life expectancy of ≥ 1 year) who have a low risk of bleeding, we suggest that catheter-directed thrombolysis (CDT) may be used to reduce acute symptoms and post-thrombotic morbidity if appropriate expertise and resources are available (Grade 2B).

1.9.2. After successful CDT in patients with acute DVT, we suggest correction of underlying venous lesions using balloon angioplasty and stents (Grade 2C).

1.9.3. We suggest pharmacomechanical thrombolysis (*eg*, with inclusion of thrombus fragmentation and/or aspiration) in preference to CDT alone to shorten treatment time if appropriate expertise and resources are available (Grade 2C).

1.9.4. After successful CDT in patients with acute DVT, we recommend the same intensity and duration of anticoagulant therapy as for comparable patients who do not undergo CDT (Grade 1C).

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Manuscript accepted December 20, 2007.

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DOI: 10.1378/chest.08-0658