

Chapter 5. Future Research

Q1. What are the efficacy and safety of LMWH compared with UFH for the treatment of DVT?

Q2. What are the efficacy and safety of LMWH compared with UFH for treatment of PE?

- ! Studies need to address the relative risks and benefits of the different LMWH preparations that are available to determine whether they are interchangeable.
- ! Studies need to determine the optimal dosing regimens for LMWH (e.g., once/day vs. twice/day).
- ! Studies need to include evaluation of LMWH in subpopulations of patients with VTE (e.g., PE with or without concomitant DVT, patients with massive PE after initial stabilization, patients with thrombophilic conditions).

Q3a. What are the efficacy and safety of outpatient versus inpatient treatment of DVT with LMWH or UFH?

Q3b. What is the cost-effectiveness of outpatient versus inpatient treatment of DVT with LMWH or UFH?

- ! High quality trials are needed that are designed as equivalency studies to confirm that LMWH as an outpatient is as efficacious and safe as UFH in the hospital.
- ! Additional studies need to evaluate the use of outpatient treatment among a less restricted group of patients, or specifically in subgroups such as patients with malignancies or hereditary thrombophilias.
- ! Studies should examine the efficacy and safety of LMWH as an outpatient for stable patients with PE.
- ! Studies should evaluate the efficacy and safety of LMWH as an outpatient for treatment of symptomatic calf vein thrombosis.

Q4. What is the optimal duration of treatment for DVT and PE?

- ! Randomized studies are needed to determine the optimal duration of therapy for PE.
- ! Randomized studies of VTE treatment duration are needed in patients with malignancies, in patients with thrombophilia, and in children.
- ! Studies should evaluate the use of low-dose warfarin for long duration prophylaxis, to see if safety may be improved without sacrificing efficacy.

Q5. How accurate are clinical prediction rules used for the diagnosis of DVT or PE?

- ! Studies need to further refine the clinical prediction rules to optimize their performance characteristics.
- ! Studies should test the addition of laboratory testing to clinical prediction rules. This addition should also be evaluated with cost-effectiveness analyses.
- ! Further research is needed to identify the optimal role for clinical prediction rules. Are they to be used to aid in interpretation of radiological tests or can they supplant further testing?
- ! Further research needs to look at the most effective way to apply these prediction rules in general practice.

Q6a. What are the test characteristics of ultrasonography for diagnosis of DVT?

Q6b. Are calf vein thromboses adequately identified with ultrasound?

- ! Studies are needed to clarify the role of ultrasonography for diagnosis of upper extremity DVT; identification of one successful high quality study suggests that this topic needs further study.
- ! Studies need to incorporate discussion whether calf vein thromboses even need to be identified, when evaluating the sensitivity and specificity of testing modalities.

Q7. What are the test characteristics of helical CT, MRI, and MRA for diagnosis of PE relative to V/Q scanning and/or standard angiography?

- ! This question would benefit from more prospective studies of high quality in which helical CT is directly compared with pulmonary arteriography for detecting PE.
- ! Future studies of MRI/MRA need to be standardized in terms of speed, image acquisition (number and time), number of breath holds, presence or absence of cardiac gating and dose of contrast to yield more precise estimates of test characteristics.
- ! The feasibility of MRI/MRA in patients with symptomatic PE (with tachypnea and tachycardia) needs to be studied.
- ! Results of studies of these testing modalities should be reported with positive and negative predictive values stratified by location of the thrombus (lobar, segmental, subsegmental).
- ! Beyond determination of sensitivity and specificity, further studies are needed that examine the role of CT and MRI/MRA within existing clinical diagnostic strategies.

Q8. What are the test characteristics of D-dimer for diagnosis of VTE?

! Because many of the available D-dimer assays yield continuous rather than dichotomous results, studies of this test need to report the results with ROC curves. This will allow clinicians to appreciate how the choice of an optimal cutoff depends on how the test is to be employed, and will more easily allow comparisons of different assays and comparisons across populations of patients.

! Research is needed to address the issue that D-dimer levels may be abnormal in patients with calf vein thrombosis for whom the clinical significance is uncertain.

! The role of D-dimer measurement as a screening tool in asymptomatic post-operative patients is unknown.

! Studies are needed to determine the usefulness of D-dimer measurement in patients with comorbid illnesses.

! A systematic review is currently being completed by a group of investigators at the University of Virginia School of Medicine. At the time of this writing, complete results were not available for our review.