Suspected Lower Extremity Deep Vein Thrombosis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Fowkes FJ, Price JF, Fowkes FG. Incidence of diagnosed deep vein thrombosis in the general population: systematic review. *Eur J Vasc Endovasc Surg* 2003; 25(1):1-5.	Review/Other-Dx	9 studies	Systematic review including meta-analysis to determine the incidence of DVT in the general population. Results from all studies of adequate quality were pooled together.	Weighted mean incidence of first DVT in the whole general population was 5.04 (95% CI: 4.70, 5.38) per 10,000 person years. Incidence was similar in males and females and increased with age from about 2-3 per 10,000 person years at ages 30-49 to 20 per 10,000 person years at ages 70-79. Around 40% of cases of DVT were idiopathic.	4
2. Hamper UM, DeJong MR, Scoutt LM. Ultrasound evaluation of the lower extremity veins. *Radiol Clin North Am* 2007; 45(3):525-547, ix.	Review/Other-Dx	N/A	Review role of duplex US and color Doppler US for the evaluation of patients suspected of harboring a thrombus in their lower extremity veins. Article reviews the clinical presentation and differential diagnoses, technique, and diagnostic criteria for acute and chronic DVT.	Venous US has become the standard primary imaging technique for the initial evaluation of patients for whom there is clinical suspicion of DVT of the lower extremity veins over the past 2 decades.	4
3. Kearon C. Natural history of venous thromboembolism. *Circulation* 2003; 107(23 Suppl 1):I22-30.	Review/Other-Dx	N/A	Review the natural history of venous thromboembolism.	Although acute venous thromboembolism usually presents with either leg or pulmonary symptoms, most patients have thrombosis at both sites at the time of diagnosis.	4
4. White RH. The epidemiology of venous thromboembolism. *Circulation* 2003; 107(23 Suppl 1):I4-8.	Review/Other-Dx	N/A	Review epidemiology of venous thromboembolism.	Approximately one third of patients with symptomatic venous thromboembolism manifest PE, while two-thirds manifest DVT alone.	4
5. Goodacre S, Sampson F, Stevenson M, et al. Measurement of the clinical and cost-effectiveness of non-invasive diagnostic testing strategies for deep vein thrombosis. *Health Technol Assess* 2006; 10(15):1-168, iii-iv.	Review/Other-Dx	N/A	To estimate the diagnostic accuracy of noninvasive tests for proximal DVT and isolated calf DVT, in patients with clinically suspected DVT or high-risk asymptomatic patients, and identify factors associated with variation in diagnostic performance. Also to identify practical diagnostic algorithms for DVT, and estimate the diagnostic accuracy, clinical effectiveness and cost-effectiveness of each.	In patients with clinically suspected DVT, D-dimer has 91% sensitivity and 55% specificity for DVT. US has 94% sensitivity for proximal DVT, 64% sensitivity for distal DVT and 94% specificity. CT has 95% sensitivity for all DVT (proximal and distal combined) and 97% specificity. MRI has 92% sensitivity for all DVT and 95% specificity. Diagnostic algorithms based on a combination of Wells score, D-dimer and US (with repeat if negative) are feasible at most UK hospitals and are among the most cost-effective.	4
6. Gottlieb RH, Voci SL, Syed L, et al. Randomized prospective study comparing routine versus selective use of sonography of the complete calf in patients with suspected deep venous thrombosis. *AJR* 2003; 180(1):241-245.	Observational-Dx	235 patients - complete calf protocol group: 261 patients - incomplete calf protocol group	Randomized prospective study comparing routine vs selective use of US of the complete calf in patients with suspected DVT.	No adverse outcomes (0.0%; 97.5% one-sided CI, 0.6%-1.6%) in complete calf protocol group. Two adverse outcomes in incomplete calf protocol group (0.8%; 95% CI, 0.1%-2.7%). No significant difference in adverse outcomes in two groups.	3

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7. Righini M, Le Gal G, Aujesky D, et al. Complete venous ultrasound in outpatients with suspected pulmonary embolism. *J Thromb Haemost* 2009; 7(3):406-412.	Observational-Dx	855 consecutive outpatients	To assess whether performing an additional distal vein US would increase the diagnostic yield of the test. Data of outpatients included in a multicenter randomized controlled trial were analyzed.	US was positive in 21% of patients, of whom 10% (53/541) had proximal DVT and 11% (59/541) isolated distal DVT. Of the 59 patients with distal DVT, 21 (36%) had no PE. The diagnostic performance of distal US for the diagnosis of pulmonary was as follows: sensitivity 22% [95% CI, 17-29]; specificity 94% (95% CI, 91-96); positive likelihood ratio 3.9 (95% CI, 2.4-6.4). Distal US has limited diagnostic performance, and its additional use only modestly increases the yield of US in patients with suspected PE.	2
8. Nielsen HK, Husted SE, Krusell LR, et al. Anticoagulant therapy in deep venous thrombosis. A randomized controlled study. *Thromb Res* 1994; 73(3-4):215-226.	Experimental-Tx	90 patients	Randomized controlled study to evaluate the efficacy of anticoagulant therapy vs no anticoagulant therapy treatment in DVT patients actively mobilized from day of admission.	Study showed no effect of anticoagulant therapy on DVT progression in actively mobilized patients when compared to a non-anticoagulant treated group. However, the patient population of the study is relatively small with wide CIs for differences between groups. Large scale placebo-controlled study needed.	1
9. Goldhaber SZ, Bounameaux H. Pulmonary embolism and deep vein thrombosis. *Lancet* 2012; 379(9828):1835-1846.	Review/Other-Dx	N/A	To discuss PE and DVT of the legs.	No results stated in abstract.	4
10. Beyer J, Schellong S. Deep vein thrombosis: Current diagnostic strategy. *Eur J Intern Med* 2005; 16(4):238-246.	Review/Other-Dx	N/A	Review diagnostic strategies used in diagnosing DVT with emphasis on diagnostic strategies for clinicians in hospitals and general practitioners using practical approaches.	Gold standard for detecting DVT is venography, but invasivity, radiation, contrast media, and painful injection in pedal veins are limiting factors for initial and repeat exams. Venography is now replaceable in most cases since the introduction of DVT scores, D-dimer testing and venous US.	4
11. Wells PS. Integrated strategies for the diagnosis of venous thromboembolism. *J Thromb Haemost* 2007; 5 Suppl 1:41-50.	Review/Other-Dx	N/A	Review integrated strategies for the diagnosis of DVT and PE.	Combination of clinical assessment, D-dimer and imaging enables safe PE rule out protocols without imaging, an ability to suspect false positive imaging results, and more accurate determination of true positive imaging. These integration strategies result in safer, more convenient and cost-effective care for patients.	4

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12. Wells PS, Owen C, Doucette S, Fergusson D, Tran H. Does this patient have deep vein thrombosis? *JAMA* 2006; 295(2):199-207.	Review/Other-Dx	14 studies (8,239 patients); 2 reviewers	To systematically review trials that determined the prevalence of DVT using clinical prediction rules either with or without D-dimer, for the diagnosis of DVT. Studies that prospectively enrolled consecutive, unselected outpatients with suspected DVT and applied clinical prediction rules before D-dimer testing or diagnostic imaging were included.	Prevalence of DVT in low, moderate, and high clinical probability groups was 5.0% (95% CI, 4.0%-8.0%), 17% (95% CI, 13%-23%), and 53% (95% CI, 44%-61%), respectively. Overall prevalence of DVT was 19% (95% CI, 16%-23%). For all studies, the sensitivity, specificity, and negative likelihood ratios of D-dimer testing in the low probability group were 88% (95% CI, 81%-92%), 72% (95% CI, 65%-78%), and 0.18% (95% CI, 0.12-0.18); in the moderate probability group: 90% (95% CI, 80%-95%), 58% (95% CI, 49%-67%), and 0.19% (95% CI, 0.11-0.32); and in the high probability group: 92% (95% CI, 85%-96%), 45% (95% CI, 37%-52%), and 0.16% (95% CI, 0.09-0.30). Diagnostic accuracy for DVT improves when clinical probability is estimated before diagnostic tests.	4
13. Kaufman JA, Kinney TB, Streiff MB, et al. Guidelines for the use of retrievable and convertible vena cava filters: report from the Society of Interventional Radiology multidisciplinary consensus conference. *Surg Obes Relat Dis* 2006; 2(2):200-212.	Review/Other-Dx	N/A	To provide guidelines for the clinical application of nonpermanent vena cava filters.	N/A	4
14. Prandoni P, Prins MH, Lensing AW, et al. Residual thrombosis on ultrasonography to guide the duration of anticoagulation in patients with deep venous thrombosis: a randomized trial. *Ann Intern Med* 2009; 150(9):577-585.	Experimental-Tx	538 consecutive outpatients	Parallel, randomized multicenter trial to assess whether tailoring the duration of anticoagulation on the basis of the persistence of residual thrombi on US reduces the rate of recurrent venous thromboembolism compared with the administration of conventional fixed-duration treatment in adults with proximal DVT.	Overall, 46 (17.2%) of 268 patients allocated to fixed-duration anticoagulation and 32 (11.9%) of 270 patients allocated to flexible-duration anticoagulation developed recurrent venous thromboembolism. For patients with unprovoked DVT, the adjusted HR was 0.61 (CI, 0.36 to 1.02) and 0.81 (CI, 0.32 to 2.06) for those with secondary DVT. Major bleeding occurred in 2 (0.7%) patients in the fixed-duration group and 4 (1.5%) patients in the flexible-duration group (P=0.67).	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
15. Lockhart ME, Sheldon HI, Robbin ML. Augmentation in lower extremity sonography for the detection of deep venous thrombosis. *AJR* 2005; 184(2):419-422.	Observational-Dx	1,980 patients (3,956 lower extremities)	To evaluate the value of venous flow augmentation with duplex US in the evaluation of DVT of the lower extremities. Data collected from patients who were prospectively evaluated for DVT by duplex US during a 12-month interval.	Augmentation component of the lower extremity US rarely provides additional information in the diagnosis of DVT. No DVT were discovered with augmentation. Factors such as the lack of usefulness and patient discomfort may justify removal of augmentation from the routine study. However, augmentation should still be applied as a diagnostic tool in difficult or uncertain cases.	3
16. Murphy TP, Cronan JJ. Evolution of deep venous thrombosis: a prospective evaluation with US. *Radiology* 1990; 177(2):543-548.	Observational-Dx	46 patients	To observe prospectively the early evolution of DVT by duplex US during the initial 6 months after thrombosis to assess the persistence of venous abnormalities.	Isolated popliteal DVT was found to be more likely to revert to normal at duplex compression US than thrombosis involving both the femoral and popliteal systems (P<.05). Increased venous diameter was a sign of acute clot (P<.005). Clot echogenicity did not help to enable distinction of acute DVT and chronic DVT. At compression US, 10/21 patients (48%) who initially had occlusive thrombosis had persistent abnormalities that mimicked findings consistent with acute DVT.	3
17. AbuRahma AF, Saiedy S, Robinson PA, Boland JP, Cottrell DJt, Stuart C. Role of venous duplex imaging of the lower extremities in patients with fever of unknown origin. *Surgery* 1997; 121(4):366-371.	Review/Other-Dx	114 duplex exams; 89 patients	To evaluate the role of venous duplex imaging of the lower extremity in evaluating a large series of patients with FUO.	A total of 114 duplex examinations, gathered during a 2-year period, were analyzed. The 89 patients had a mean age of 58 years. Infections were the most common cause of FUO (57/89, 64%), and unknown causes constituted 19%. There were 7 cases of DVT (8%), 5 (6%) of whom met the criteria for probable cause of FUO. The overall cost of venous duplex imaging examinations was $51,300 ($450 x 114 tests), with an average cost of $10,260 for each case of DVT detected as probable cause of FUO.	4

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18. Mourad O, Palda V, Detsky AS. A comprehensive evidence-based approach to fever of unknown origin. *Arch Intern Med* 2003; 163(5):545-551.	Review/Other-Dx	N/A	To perform a systematic review to develop evidence-based recommendations for the diagnostic workup of FUO.	The prevalence of FUO in hospitalized patients is reported to be 2.9%. Eleven studies indicate that the spectrum of disease includes "no diagnosis" (19%), infections (28%), inflammatory diseases (21%), and malignancies (17%). DVT (3%) and temporal arteritis in the elderly (16%-17%) were important considerations. Four good natural history studies indicate that most patients with undiagnosed FUO recover spontaneously (51%-100%). One fair-quality study suggested a high specificity (99%) for the diagnosis of endocarditis in FUO by applying the Duke criteria. One fair-quality study showed that computed tomographic scanning of the abdomen had a diagnostic yield of 19%. Ten studies of nuclear imaging revealed that technetium was the most promising isotope, showing a high specificity (94%), albeit low sensitivity (40%-75%) (2 fair-quality studies). Two fair-quality studies showed liver biopsy to have a high diagnostic yield (14%-17%), but with risk of harm (0.009%-0.12% death). Empiric bone marrow cultures showed a low diagnostic yield of 0% to 2% (2 fair-quality articles).	4
19. Carpenter JP, Holland GA, Baum RA, Owen RS, Carpenter JT, Cope C. Magnetic resonance venography for the detection of deep venous thrombosis: comparison with contrast venography and duplex Doppler ultrasonography. *J Vasc Surg* 1993; 18(5):734-741.	Observational-Dx	85	Prospective, blinded study to determine whether MRV could accurately demonstrate DVT when compared with duplex scanning and contrast venography.	Compared to contrast venography, MRV had sensitivity of 100%, specificity of 96%, PPV of 90%, and NPV of 100%. Duplex scanning had sensitivity of 100%, specificity of 96%, PPV of 94%, and NPV of 100%. Study concludes that MRV is an accurate noninvasive venographic technique for the detection of DVT.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
20. Evans AJ, Sostman HD, Knelson MH, et al. 1992 ARRS Executive Council Award. Detection of deep venous thrombosis: prospective comparison of MR imaging with contrast venography. *AJR* 1993; 161(1):131-139.	Observational-Dx	61 consecutive patients	Prospective, blinded study to compare MRI with contrast venography (gold standard) to determine the efficacy of MRI in patients with clinically suspected DVT.	DVT in the pelvis - sensitivity of MRI was 100% (9/9); specificity was 95% (52/55). Thigh - sensitivity (16/16) and specificity (43/43) were both 100%. Calf - sensitivity was 87% (13/15) and specificity was 97% (36/37). No statistically significant difference between MRI and contrast venography in the detection of DVT. MRI is at least as sensitive and specific as contrast venography in the detection of DVT.	2
21. Evans AJ, Sostman HD, Witty LA, et al. Detection of deep venous thrombosis: prospective comparison of MR imaging and sonography. *J Magn Reson Imaging* 1996; 6(1):44-51.	Observational-Dx	75 patients	Prospectively compare MRI with US in the detection of DVT in patients with clinically suspected DVT.	Sensitivity of MRI was 100%; the specificity was 100% and accuracy was 96%. Sensitivity of US was 77%; the specificity was 98% and the accuracy was 83%. MRI is more sensitive (P=.02) and accurate (P<.01) than US. No difference in the specificity of MRI and that of US (P=.31).	2
22. Sampson FC, Goodacre SW, Thomas SM, van Beek EJ. The accuracy of MRI in diagnosis of suspected deep vein thrombosis: systematic review and meta-analysis. *Eur Radiol* 2007; 17(1):175-181.	Review/Other-Dx	14 articles	Systematic review of literature and meta-analysis to estimate the diagnostic accuracy of MRI for DVT.	Pooled estimate of sensitivity was 91.5% (95% CI: 87.5%-94.5%) and the pooled estimate of specificity was 94.8% (95% CI: 92.6%-96.5%). Sensitivity for proximal DVT was higher than sensitivity for distal DVT (93.9% vs 62.1%). Individual studies reported sensitivity ranging from zero to 100%, while specificity ranged from 43% to 100%. MRI has equivalent sensitivity and specificity to US for diagnosis of DVT, but has been evaluated in many fewer studies, using a variety of different techniques.	4
23. Thomas SM, Goodacre SW, Sampson FC, van Beek EJ. Diagnostic value of CT for deep vein thrombosis: results of a systematic review and meta-analysis. *Clin Radiol* 2008; 63(3):299-304.	Review/Other-Dx	13 studies	Systematic review and meta-analysis to estimate the sensitivity and specificity of CT for the diagnosis of DVT in patients with suspected DVT and PE.	Sensitivity ranged from 71%-100%, specificity ranged from 93%-100%. Pooled estimate of sensitivity was 95.9% (95% CI 93%-97.8%) and the pooled estimate of specificity was 95.2% (93.6%-96.5%). CT has a similar sensitivity and specificity to US in patients with suspected PE where investigation of suspected DVT is required. Inadequate research to determine the diagnostic accuracy of CT in patients with suspected DVT alone.	4

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24. Spritzer CE, Arata MA, Freed KS. Isolated pelvic deep venous thrombosis: relative frequency as detected with MR imaging. *Radiology* 2001; 219(2):521-525.	Review/Other-Dx	769 MRIs	To determine the relative frequency of DVT isolated to the pelvic veins, as demonstrated with MRI.	DVT was identified in 167 (21.7%) of the 769 MRIs. 34 (20.4%) of the 167 studies demonstrated DVT isolated to the pelvic veins.	4
25. Cramer SC, Rordorf G, Maki JH, et al. Increased pelvic vein thrombi in cryptogenic stroke: results of the Paradoxical Emboli from Large Veins in Ischemic Stroke (PELVIS) study. *Stroke* 2004; 35(1):46-50.	Observational-Dx	95 patients	The Paradoxical Emboli From Large Veins in Ischemic Stroke (PELVIS) study hypothesized that patients with cryptogenic stroke have an increased prevalence of pelvic DVT.	The 95 patients who met entry criteria were scanned. Their mean+/-SD age was 46+/-10 years, and time from stroke onset to pelvic MRV scan was 49+/-16 hours. Compared with those with stroke of determined origin (n=49), patients with cryptogenic stroke (n=46) were significantly younger, had a higher prevalence of patent foramen ovale (61% vs 19%), and had less atherosclerosis risk factors. Cryptogenic patients had more MRV scans with a high probability for pelvic DVT (20%) than patients with stroke of determined origin (4%, P<0.03), with most having an appearance of a chronic DVT.	2
26. Loud PA, Katz DS, Klippenstein DL, Shah RD, Grossman ZD. Combined CT venography and pulmonary angiography in suspected thromboembolic disease: diagnostic accuracy for deep venous evaluation. *AJR* 2000; 174(1):61-65.	Observational-Dx	71 consecutive patients	Report findings of combined CT venography and pulmonary angiography in patients with suspected PE and compare CT venous findings (interpreted prospectively) with lower extremity venous US.	DVT revealed by CT venous phase images in 19 patients, 12 of whom had PE. CT and US findings correlated exactly in the femoropopliteal deep venous system. CT venous phase images revealed pelvic extension of DVT in 6 patients and isolated vena cava thrombus in one patient. CT venous phase imaging at time of CT pulmonary angiography is comparable with venous US in the evaluation of femoropopliteal DVT.	3

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27. Hunsaker AR, Zou KH, Poh AC, et al. Routine pelvic and lower extremity CT venography in patients undergoing pulmonary CT angiography. *AJR* 2008; 190(2):322-326.	Observational-Dx	829 patients	To assess the utility of performing routine pelvic and lower extremity CT venography along with pulmonary CT angiography in all patients evaluated for PE.	Venous thromboembolism, PE, and DVT occurred in 152 (18.3%), 124 (15.0%), and 61 (7.3%) of 829 patients, respectively. Between the high-risk and low-risk groups, prevalence of venous thromboembolism was 114 (25.6%) of 446 and 38 (9.9%) of 383 patients, respectively (P<0.001); prevalence of PE was 92 (20.6%) of 446 and 32 (8.3%) of 383 patients, respectively (P<0.001). Isolated DVT was found in 28 (3.4%) of 829 patients. The incremental value of CT venography for the entire cohort was 3.4%, 0.72% in the low-risk group (6/829) and 2.6% (22/829) in the high-risk group. For outcome variable venous thromboembolism, malignancy and previous venous thromboembolism were statistically significant (P=0.04 and P<0.001, respectively); for PE, malignancy and previous venous thromboembolism were statistically significant (P=0.03 and P=0.005, respectively); for DVT, only previous venous thromboembolism was statistically significant (P<0.001).	3
28. American College of Radiology. Manual on Contrast Media. Available at: http://www.acr.org/~/link.aspx?_id=29C40D1FE0EC4E5EAB6861BD213793E5&_z=z.	Review/Other-Dx	N/A	Guidance document on contrast media to assist radiologists in recognizing and managing risks associated with the use of contrast media.	N/A	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

CI = Confidence interval

CT = Computed tomography

DVT = Deep vein thrombosis

FUO = Fever of unknown origin

HR = Hazard ratio

MRI = Magnetic resonance imaging

MRV = Magnetic resonance venography

PE = Pulmonary embolism

SD = Standard deviation

US = Ultrasound