Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. White RH. The epidemiology of venous thromboembolism. *Circulation* 2003; 107(23 Suppl 1):I4-8.	Review/Other-Tx	N/A	To review the epidemiology of VTE including incidence rates in the United States.	VTE occurs for the first time in approximately 100 persons per 100,000 each year in the United States, and rises exponentially from <5 cases per 100,000 persons <15 years old to approximately 500 cases (0.5%) per 100,000 persons at age 80 years. Approximately one third of patients with symptomatic VTE manifest PE, whereas two thirds manifest DVT alone. Despite anticoagulant therapy, VTE recurs frequently in the first few months after the initial event, with a recurrence rate of approximately 7% at 6 months. Death occurs in approximately 6% of DVT cases and 12% of PE cases within 1 month of diagnosis. The time of year may affect the occurrence of VTE, with a higher incidence in the winter than in the summer. One major risk factor for VTE is ethnicity, with a significantly higher incidence among Caucasians and African Americans than among Hispanic persons and Asian-Pacific Islanders. Overall, approximately 25% to 50% of patient with first-time VTE have an idiopathic condition, without a readily identifiable risk factor. Early mortality after VTE is strongly associated with presentation as PE, advanced age, cancer, and underlying cardiovascular disease.	4

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
2. Anderson FA, Jr., Spencer FA. Risk factors for venous thromboembolism. *Circulation* 2003; 107(23 Suppl 1):I9-16.	Review/Other-Tx	N/A	To summarize the strength of the evidence regarding specific risk factors for VTE and provides a guide for identifying patients who could benefit from VTE prophylaxis. This article also identifies population groups whose apparent risk for VTE is too low to justify preventive treatment.	VTE is overlooked as a major public health problem and viewed as a complication of hospitalization for another illness rather than as a specific disease entity. However, recent trials in patients hospitalized with a wide variety of acute medical illnesses have demonstrated a risk of VTE in medical patients comparable with that seen after major general surgery. In addition, epidemiologic studies have shown that between one quarter and one half of all clinically recognized symptomatic VTEs occur in individuals who are neither hospitalized nor recovering from a major illness. This expanding understanding of the population at risk challenges physicians to carefully examine risk factors for VTE to identify high-risk patients who could benefit from prophylaxis.	4
3. Kearon C, Kahn SR, Agnelli G, Goldhaber S, Raskob GE, Comerota AJ. Antithrombotic therapy for venous thromboembolic disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008; 133(6 Suppl):454S-545S.	Review/Other-Tx	N/A	To provide recommendations on treatment for venous thromboembolic disease as part of the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition).	No results stated in abstract.	4
4. Kahn SR. The post-thrombotic syndrome: progress and pitfalls. *Br J Haematol* 2006; 134(4):357-365.	Review/Other-Tx	N/A	To review the current understanding of the clinical presentation, pathophysiology, diagnosis, risk factors, epidemiology and management of PTS.	The PTS develops in up to one half of patients after symptomatic DVT and is the most common complication of DVT. Typical features of PTS include chronic pain, swelling, heaviness, oedema and skin changes in the affected limb. In severe cases, venous ulcers may develop. The frequency of PTS is likely to be reduced by preventing DVT with the use of effective thromboprophylaxis in high-risk patients and settings and by minimizing the risk of ipsilateral DVT recurrence. Use of compression stockings for 2 years after DVT appears to reduce the incidence and severity of PTS but issues remain regarding their use and effectiveness.	4

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
5. Delis KT, Bountouroglou D, Mansfield AO. Venous claudication in iliofemoral thrombosis: long-term effects on venous hemodynamics, clinical status, and quality of life. *Ann Surg* 2004; 239(1):118-126.	Observational-Tx	39 patients	To evaluate the long-term impact of iliofemoral thrombosis on walking capacity, venous hemodynamic status, CEAP class, venous clinical severity, and quality of life, and determined the prevalence of venous claudication.	A total of 81% of limbs with iliofemoral thrombosis had superficial and deep reflux and 19% superficial reflux; reflux in control limbs was 29.7% (P<0.001) and 27% (P>0.2), respectively; 43.6% (17/39; 95% CI, 27%-60%) of patients developed venous claudication ipsilateral to iliofemoral thrombosis (initial claudication distance: 130 m, range 105-268 m), compelling 15.4% (6/39; 95% CI, 3.5%-27%) to discontinue treadmill (absolute claudication distance: 241 m, range 137-298 m). Limbs with prior iliofemoral thrombosis had a lower outflow fraction (37%, range 32.2%-43%; P<0.001), abnormally higher venous filling index (3.8 mL/s, range 2.5-5.7 mL/s; P<0.001), and residual volume fraction (45%, range 32.5%-51.5%; P=0.006), and clinical impairment in CEAP and Venous Clinical Severity Scoring systems (P<0.0001). Patients with iliofemoral thrombosis had impaired physical functioning (P=0.02) and role (P=0.033), general health (P=0.001), social function (P=0.047), and mental health (P=0.043).	2

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
6. Kahn SR, Shrier I, Julian JA, et al. Determinants and time course of the postthrombotic syndrome after acute deep venous thrombosis. *Ann Intern Med* 2008; 149(10):698-707.	Observational-Tx	387 patients	To determine the frequency, time course and predictors of the PTS after acute DVT.	At all study intervals, about 30% of patients had mild (score, 5 to 9), 10% had moderate (score, 10 to 14), and 3% had severe (score >14 or ulcer) PTS. Greater post-thrombotic severity category at the 1-month visit strongly predicted higher mean post-thrombotic scores throughout 24 months of follow-up (1.97, 5.03, and 7.00 increase in Villalta score for mild, moderate, and severe 1-month severity categories, respectively, vs none; P<0.001). Additional predictors of higher scores over time were venous thrombosis of the common femoral or iliac vein (2.23 increase in score vs distal [calf] venous thrombosis; P<0.001), higher body mass index (0.14 increase in score per kg/m(2); P<0.001), previous ipsilateral venous thrombosis (1.78 increase in score; P=0.001), older age (0.30 increase in score per 10-year age increase; P=0.011), and female sex (0.79 increase in score; P=0.020).	2
7. Barritt DW, Jordan SC. Anticoagulant drugs in the treatment of pulmonary embolism. A controlled trial. *Lancet* 1960; 1(7138):1309-1312.	Observational-Tx	73 patients	To measure the effect of anti-coagulants in patients who have had one PE, both on the course of the first embolism and on the risk of further attacks.	In patients who have already had PE the subsequent course of the disease is affected by the regime of anticoagulant therapy used: the mortality of PE is reduced. Deaths from PE are likely to outnumber the deaths that may be attributed to treatment. Heparin and nicoumalone reduce the risk of death from that embolism.	2

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
8. Alpert JS, Smith R, Carlson J, Ockene IS, Dexter L, Dalen JE. Mortality in patients treated for pulmonary embolism. *JAMA* 1976; 236(13):1477-1480.	Review/Other-Tx	144 consecutive patients	The hospital course of patients with PE demonstrated by pulmonary angiography was reviewed to determine the mortality of patients with treated PE.	12 patients (8%) died of PE, and 8 died of causes other than PE; 124 (86%) survived. PE was the primary cause of death in only 4/12 patients who died of PE. PE contributed to the death of 8 other patients, each of whom had associated potentially lethal disease, particularly heart disease. The most important factor affecting mortality was shock due to acute right ventricular failure secondary to massive PE (mortality, 32%). Mortality was not related to magnitude of PE per se; the mortality of patients with massive PE without shock (6%) was the same as that for patients with submassive PE (5%). Patients with PE who survive long enough to have the diagnosis established and appropriate prophylactic therapy begun have an excellent prognosis, unless they have associated severe medical disease.	4
9. Kernohan RJ, Todd C. Heparin therapy in thromboembolic disease. *Lancet* 1966; 1(7438):621-623.	Review/Other-Tx	67 patients	To assess the effects of intensive heparin therapy in the treatment of venous thrombosis and PE.	Abstract not available.	4
10. Brandjes DP, Heijboer H, Buller HR, de Rijk M, Jagt H, ten Cate JW. Acenocoumarol and heparin compared with acenocoumarol alone in the initial treatment of proximal-vein thrombosis. *N Engl J Med* 1992; 327(21):1485-1489.	Experimental-Tx	120 patients	A randomized, double-blind study to compare the efficacy and safety of continuous intravenous heparin plus acenocoumarol with the efficacy and safety of acenocoumarol alone in the initial treatment of outpatients with proximal-vein thrombosis.	The study was terminated early by the Data Safety and Monitoring Committee because of an excess of symptomatic events in the group that received acenocoumarol alone (in 12/60 patients [20%], as compared with 4/60 patients [6.7%] in the combined-therapy group by intention-to-treat analysis; P=0.058). Asymptomatic extension of venous thrombosis was observed in 39.6% of the patients in the acenocoumarol group and in 8.2% of patients treated with heparin plus acenocoumarol (P<0.001). Major bleeding complications were infrequent and comparable in the two groups.	1

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
11. Gallus A, Jackaman J, Tillett J, Mills W, Wycherley A. Safety and efficacy of warfarin started early after submassive venous thrombosis or pulmonary embolism. *Lancet* 1986; 2(8519):1293-1296.	Experimental-Tx	266 patients	To conduct an open, randomized comparison of two anticoagulant regimens which differ in the timing of warfarin therapy (and therefore have different durations of initial heparin treatment).	Two anticoagulant regimens, similar except for the timing of warfarin therapy, were compared in patients with clinically submassive VTE. Warfarin was begun after 7 days of continuous intravenous heparin infusion in group L (127 patients) or within 3 days (average 1 day) of starting heparin in group S (139 patients), with similar outcomes. The frequency of symptomatic VTE recurrence during the hospital stay was 4.7% in group L and 3.6% in group S, and that of symptomless new perfusion defects 8.5% in group L and 3.9% in group S. On routine iodine-125-fibrinogen leg scanning of patients presenting with distal thrombosis (in the calf, popliteal, or distal femoral veins) 3.6% of group S but no group L patients had symptomless proximal extension. The incidence of bleeding was similar with both regimens. Outpatient follow-up showed no excess recurrent VTE in either treatment group. Early warfarin treatment significantly shortened hospital stay by an average of 3.9 days (30%) in patients admitted solely because of VTE.	1
12. Hull RD, Raskob GE, Rosenbloom D, et al. Heparin for 5 days as compared with 10 days in the initial treatment of proximal venous thrombosis. *N Engl J Med* 1990; 322(18):1260-1264.	Experimental-Tx	199 patients	To perform a randomized, double-blind trial comparing a shorter course of continuous intravenous heparin (5 days, with warfarin sodium begun on the first day) with the conventional 10-day course of heparin (with warfarin sodium begun on the fifth day) in the initial treatment of 199 patients with acute proximal venous thrombosis documented by venography.	The frequency of objectively documented recurrent VTE was low and essentially the same in the two groups (7.1% in the short-course group vs 7.0% in the long-course group). Because the observed difference between the groups was 0.1% in favor of the long-course group, it is unlikely ($P<0.05$) that a true difference in favor of this group would be greater than 7.5%; the difference could be as much as 7.3% in favor of the short-course group. Major bleeding episodes were infrequent, and the rate was similar in both groups.	1

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
13. Kahn SR, Ginsberg JS. The post-thrombotic syndrome: current knowledge, controversies, and directions for future research. *Blood Rev* 2002; 16(3):155-165.	Review/Other-Tx	N/A	To critically review the evidence on the epidemiology, pathophysiology, diagnosis, prevention and treatment of PTS, and to discuss the impact of PTS on healthcare costs and quality of life.	About 20%-50% of patients develop PTS within 1-2 years of symptomatic DVT, and severe PTS, which can include venous ulcers, occurs in 5%-10% of cases. Although there is no gold standard for the diagnosis of PTS, the presence of typical clinical features in a patient with previous DVT provides strong supporting evidence. Objective evidence of venous valvular incompetence helps to confirm the diagnosis in symptomatic patients. Preventing ipsilateral recurrence of DVT, by ensuring an adequate duration and intensity of anticoagulation for the initial DVT and by prescribing situational thromboprophylaxis after discontinuation of oral anticoagulants, is likely to reduce the risk of developing PTS. There is no proven role for thrombolysis of the initial DVT to prevent PTS. Daily use of graduated compression stockings after DVT may reduce the risk of PTS, and may prevent worsening of established PTS.	4
14. Prandoni P, Lensing AW, Prins MH, et al. Below-knee elastic compression stockings to prevent the post-thrombotic syndrome: a randomized, controlled trial. *Ann Intern Med* 2004; 141(4):249-256.	Experimental-Tx	180 consecutive patients	To evaluate the efficacy of compression elastic stockings for prevention of the PTS in patients with proximal DVT.	Post-thrombotic sequelae developed in 44/90 controls (severe in 10) and in 23/90 patients wearing elastic stockings (severe in 3). All but 1 event developed in the first 2 years. The cumulative incidence of the PTS in the control group vs the elastic stockings group was 40.0% (95% CI, 29.9% to 50.1%) vs 21.1% (CI, 12.7% to 29.5%) after 6 months, 46.7% (CI, 36.4% to 57.0%) vs 22.2% (CI, 13.8% to 30.7%) after 1 year, and 49.1% (CI, 38.7% to 59.4%) vs 24.5% (CI, 15.6% to 33.4%) after 2 years. After adjustment for baseline characteristics, the hazard ratio for the PTS in the elastic stockings group compared with controls was 0.49 (CI, 0.29 to 0.84; P=0.011).	1

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

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15. Comerota AJ, Aldridge SC. Thrombolytic therapy for deep venous thrombosis: a clinical review. *Can J Surg* 1993; 36(4):359-364.	Review/Other-Tx	13 studies	A clinical review of data from 13 studies comparing anticoagulant therapy with thrombolytic therapy for DVT.	Data from 13 studies comparing anticoagulant therapy with thrombolytic therapy for DVT in 591 patients have shown that, among those treated with heparin, 4% had significant or complete lysis, 14% had partial lysis and 82% failed to improve or worsened. Of those receiving lytic therapy, 45% had significant or complete lysis, 18% had partial lysis and 37% failed to improve or worsened. Long-term follow-up of randomized patients has shown that those with successful lysis had a lower incidence of PTS and improved long-term venous function. The failure rate of systemic lytic therapy among patients suffering iliofemoral venous thrombosis is high; therefore, CDT has been adopted with increasing success. Thrombolytic therapy, delivered systemically using catheter-directed techniques, should be considered as an important alternative in the treatment of patients with DVT.	4
16. Schweizer J, Kirch W, Koch R, et al. Short- and long-term results after thrombolytic treatment of deep venous thrombosis. *J Am Coll Cardiol* 2000; 36(4):1336-1343.	Experimental-Tx	250 patients	To assess the short- and long-term efficacy of different thrombolytic therapy regimens in patients with leg or pelvic DVT.	Systemic thrombolytic therapy significantly reduced the number of closed vein segments after 12 months in patients with acute DVT compared with conventional treatment ($P<0.05$). PTS also occurred with less frequency in systemically treated patients vs controls ($P<0.001$). High-dose thrombolysis led to better rates of complete recanalization after 7 days ($P<0.01$) than locoregional lysis. However, 12 patients receiving thrombolysis (9 systemic, 3 local) suffered major bleeding complications; 9 patients on systemic treatment developed pulmonary emboli.	1

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

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17. Mewissen MW, Seabrook GR, Meissner MH, Cynamon J, Labropoulos N, Haughton SH. Catheter-directed thrombolysis for lower extremity deep venous thrombosis: report of a national multicenter registry. *Radiology* 1999; 211(1):39-49.	Observational-Tx	303 limbs of 287 patients	To evaluate CDT for treatment of symptomatic lower extremity DVT.	Iliofemoral DVT (n=221 [71%]) and femoral-popliteal DVT (n=79 [25%]) were treated with urokinase infusions (mean, 7.8 million i.u.) for a mean of 53.4 hours. After thrombolysis, 99 iliac and 5 femoral vein lesions were treated with stents. Grade III (complete) lysis was achieved in 96 (31%) infusions; grade II (50%-99% lysis), in 162 (52%); and grade I (<50% lysis), in 54 (17%). For acute thrombosis, grade III lysis occurred in 34% of cases of acute and in 19% of cases of chronic DVT (P<.01). Major bleeding complications occurred in 54 (11%) patients, most often at the puncture site. Six patients (1%) developed pulmonary emboli. Two deaths (< 1%) were attributed to PE and intracranial hemorrhage. At 1 year, the primary patency rate was 60%. Lysis grade was predictive of 1-year patency rate (grade III, 79%; grade II, 58%; grade I, 32%; P<.001).	2
18. Kim HS, Patra A, Paxton BE, Khan J, Streiff MB. Adjunctive percutaneous mechanical thrombectomy for lower-extremity deep vein thrombosis: clinical and economic outcomes. *J Vasc Interv Radiol* 2006; 17(7):1099-1104.	Observational-Tx	37 patients	To assess the clinical and economic benefits of CDT alone vs CDT with rheolytic PMT for lower-extremity DVT.	26 limbs in 23 patients received CDT with urokinase, whereas 19 limbs in 14 patients were treated with CDT plus PMT. Mean treatment duration for CDT was 56.5 +/- 27.4 hours, compared with 30.3 +/- 17.8 hours for CDT plus PMT (P=.001). Mean urokinase dose for CDT was 6.70 +/- 5.9 million U compared with 2.95 +/- 1.82 million U for CDT plus PMT (P=.011). Urokinase CDT achieved complete clot lysis in 80.7% of limbs (n=21) compared with 84.2% of limbs (n=16) treated with CDT plus PMT (P=.764). The incidences of major bleeding (CDT, 7.7%; CDT plus PMT, 5.3%; P=.749) and PE (CDT, 3.8%; CDT plus PMT, 5.3%; P=.818) were similar. The mean urokinase and PMT device cost for CDT alone was $10,127 compared with $5,128 for CDT plus PMT (P=.026).	2

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

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19. Lin PH, Zhou W, Dardik A, et al. Catheter-direct thrombolysis versus pharmacomechanical thrombectomy for treatment of symptomatic lower extremity deep venous thrombosis. *Am J Surg* 2006; 192(6):782-788.	Observational-Tx	93 patients	To compare the treatment outcome in patients with symptomatic DVT who underwent either CDT or PMT intervention.	A total of 93 patients who underwent 98 catheter-directed interventions for DVT were included in the study. Among them, CDT or PMT was performed in 46 (47%) and 52 (53%) procedures, respectively. In the CDT group, complete or partial thrombus removal was accomplished in 32 (70%) and 14 (30%) cases, respectively. In the PMT cohort, complete or partial thrombus removal was accomplished in 39 (75%) and 13 (25%) cases, respectively. Venous balloon angioplasty and/or stenting in the CDT or PMT groups was necessary in 36 (78%) and 43 (82%), respectively (difference not significant). Patients in the CDT groups underwent a mean of 2.5 venograms during the hospital course, in contrast to 0.4 venograms per patient in PMT cohorts (P<.001). Immediate (<24 hours) improvement in clinical symptoms in CDT and PMT groups was achieved in 33 (72%) and 42 (81%) cases, respectively (not significant). Significant reductions in the intensive care unit and hospital lengths of stay was noted in the PMT group (0.6 and 4.6 days) when compared to the CDT group (2.4 and 8.4 days). During follow-up visits, the primary patency rates at 1 year of CDT and PMT groups were 64% and 68%, respectively (not significant). Hospital cost analysis showed significant cost reduction in the PMT group compared to the CDT group (P<.01).	2

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

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20. Enden T, Haig Y, Klow NE, et al. Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the CaVenT study): a randomised controlled trial. *Lancet* 2012; 379(9810):31-38.	Experimental-Tx	209 patients	To examine whether additional treatment with CDT using alteplase reduced development of PTS.	209 patients were randomly assigned to treatment groups (108 control, 101 CDT). At completion of 24 months' follow-up, data for clinical status were available for 189 patients (90%; 99 control, 90 CDT). At 24 months, 37 (41.1%, 95% CI, 31.5-51.4) patients allocated additional CDT presented with PTS compared with 55 (55.6%, 95% CI, 45.7-65.0) in the control group (P=0.047). The difference in PTS corresponds to an absolute risk reduction of 14.4% (95% CI, 0.2-27.9), and the number needed to treat was 7 (95% CI, 4-502). Iliofemoral patency after 6 months was reported in 58 patients (65.9%, 95% CI, 55.5-75.0) on CDT vs 45 (47.4%, 37.6-57.3) on control (P=0.012). 20 bleeding complications related to CDT included 3 major and 5 clinically relevant bleeds.	1
21. Vedantham S. Interventional approaches to deep vein thrombosis. *Am J Hematol* 2012; 87 Suppl 1:S113-118.	Review/Other-Tx	N/A	To outline the risks, benefits, and uncertainties surrounding endovascular DVT therapies, describe clinical situations in which endovascular treatment options should reasonably be considered, and update the reader on new outcome data that pertains to catheter-based DVT interventions.	Endovascular thrombolytic therapy is reasonable to perform for selected patients with DVT causing acute limb-threatening circulatory compromise, acute inferior vena cava occlusion, or acute iliofemoral DVT for the purposes of limb salvage and relief of presenting DVT symptoms, and appears likely to prevent PTS in patients with proximal DVT. A multicenter randomized trial, the ATTRACT Study, is currently underway in the United States to determine whether pharmacomechanical CDT is sufficiently safe and effective to be recommended for routine use in proximal DVT patients. Selected patients with established moderate-to-severe PTS in association with an occluded iliac vein or a refluxing saphenous vein may also be amenable to endovascular intervention to reduce venous hypertension, alleviate symptoms, and improve limb function and quality of life. Pending the results of further studies, an individualized approach to patient selection for interventional DVT therapies is recommended.	4

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

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22. Casey ET, Murad MH, Zumaeta-Garcia M, et al. Treatment of acute iliofemoral deep vein thrombosis. *J Vasc Surg* 2012; 55(5):1463-1473.	Review/Other-Tx	15 studies	A systematic review and meta-analysis to compare the efficacy of three available treatments for acute iliofemoral DVT: systemic anticoagulation, surgical thrombectomy, and CDT.	When compared to systemic anticoagulation, thrombectomy was associated with a statistically significant reduction in the risk of developing PTS (RR, 0.67; 95% CI, 0.52-0.87), venous reflux (RR, 0.68; 95% CI, 0.46-0.99), and a trend for reduction in the risk of venous obstruction (RR, 0.84; 95% CI, 0.60-1.19). When compared to systemic anticoagulation, pharmacologic CDT was associated with statistically significant reduction in the risk of PTS (RR, 0.19; 95% CI, 0.07-0.48), venous obstruction (RR, 0.38; 95% CI, 0.18-0.37), and a trend for reduction in the risk of venous reflux (RR, 0.39; 95% CI, 0.16-1.00). Overall, the quality of evidence was low; downgraded due to the observational nature of the majority of studies, lack of comparability of study cohorts at baseline, loss to follow-up, imprecision, and indirectness of outcomes (surrogacy). There were insufficient data to compare the outcomes of thrombectomy to CDT.	4
23. Meissner MH, Gloviczki P, Comerota AJ, et al. Early thrombus removal strategies for acute deep venous thrombosis: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. *J Vasc Surg* 2012; 55(5):1449-1462.	Review/Other-Tx	N/A	A committee of experts in venous disease was charged by the Society for Vascular Surgery and the American Venous Forum to develop evidence-based practice guidelines for early thrombus removal strategies, including catheter-directed pharmacologic thrombolysis, pharmacomechanical thrombolysis, and surgical thrombectomy.	On the basis of the best evidence currently available, it is recommended against routine use of the term “proximal venous thrombosis” in favor of more precise characterization of thrombi as involving the iliofemoral or femoropopliteal venous segments (Grade 1A). The authors suggest the use of early thrombus removal strategies in ambulatory patients with good functional capacity and a first episode of iliofemoral DVT of <14 days in duration (Grade 2C) and strongly recommend their use in patients with limb-threatening ischemia due to iliofemoral venous outflow obstruction (Grade 1A). Pharmacomechanical strategies over catheter-directed pharmacologic thrombolysis alone are advised if resources are available and that surgical thrombectomy be considered if thrombolytic therapy is contraindicated (Grade 2C).	4

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
24. Vedantham S, Thorpe PE, Cardella JF, et al. Quality improvement guidelines for the treatment of lower extremity deep vein thrombosis with use of endovascular thrombus removal. *J Vasc Interv Radiol* 2006; 17(3):435-447; quiz 448.	Review/Other-Tx	N/A	Guidelines written to be used in quality improvement programs to assess the endovascular treatment of lower extremity DVT.	The use of endovascular methods to treat lower extremity DVT is feasible and has shown potential to speed symptomatic relief and prevent PTS related disability. The quality improvement guidelines presented here are intended to improve the interventionalist's ability to coordinate the patient selection process, to perform these procedures in the safest possible manner, and to obtain the best clinical results.	4
25. Enden T, Klow NE, Sandvik L, et al. Catheter-directed thrombolysis vs. anticoagulant therapy alone in deep vein thrombosis: results of an open randomized, controlled trial reporting on short-term patency. *J Thromb Haemost* 2009; 7(8):1268-1275.	Experimental-Tx	103 patients	To assess short-term efficacy of additional CDT compared with standard treatment alone.	103 patients (64 men, mean age 52 years) were allocated additional CDT (n=50) or standard treatment alone (n=53). After CDT, grade III (complete) lysis was achieved in 24 and grade II (50%-90%) lysis in 20 patients. One patient suffered major bleeding and two had clinically relevant bleeding related to the CDT procedure. After 6 months, iliofemoral patency was found in 32 (64.0%) in the CDT group vs 19 (35.8%) controls, corresponding to an absolute RR of 28.2% (95% CI, 9.7%-46.7%; P=0.004). Venous obstruction was found in 10 (20.0%) in the CDT group vs 26 (49.1%) controls; absolute RR 29.1% (95% CI, 20.0%-38.0%; P=0.004). Femoral venous insufficiency did not differ between the two groups.	1

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

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26. Weaver FA, Meacham PW, Adkins RB, Dean RH. Phlegmasia cerulea dolens: therapeutic considerations. *South Med J* 1988; 81(3):306-312.	Review/Other-Tx	16 cases of PCD	To review 16 cases of PCD treated during the past 15 years.	Malignant disease was the most common underlying condition (7 patients). Venous gangrene was present in 7 extremities. Three treatment methods were used alone or in combination-intravenous heparin, venous thrombectomy, and thrombolytic therapy. Heparin was used initially in 13 patients; it yielded a successful result in 7 (53%) patients, none of whom had venous gangrene. Venous thrombectomy was done in 6 patients; in 3 it was the primary procedure, in 2 it followed failure of heparin, and in one it followed failure of both heparin and thrombolytic therapy. Venous thrombectomy was successful in 3 (50%) patients, one of whom had early venous gangrene. Thrombolytic therapy was used on one occasion in conjunction with both heparin and venous thrombectomy, without benefit. Five patients died, all with venous gangrene, 3 after heparin only, 1 after heparin and venous thrombectomy, and 1 after all 3 treatment methods. Review of the 38 cases reported in the recent literature shows comparable results. These data suggest that nongangrenous forms of PCD respond well to systemic anticoagulation. Combination therapy using venous thrombectomy and heparin is indicated for severe ischemia, early venous gangrene, or failure of PCD to improve after 6 to 12 hours of heparin therapy. Phlegmasia cerulea dolens with venous gangrene is the lethal form of the entity and responds poorly to established therapy.	4

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
27. Hood DB, Weaver FA, Modrall JG, Yellin AE. Advances in the treatment of phlegmasia cerulea dolens. *Am J Surg* 1993; 166(2):206-210.	Review/Other-Tx	12 patients	To assess the use of venous thrombectomy and the use of thrombolytic therapy rather than thrombectomy for clinical progression and advanced cases of PCD.	PCD is a potentially lethal but treatable disease. Most patients, when diagnosed early, respond to bedrest, extremity elevation, fluid resuscitation, and systemic anticoagulation. If there is no response to these measures within 12 hours, thrombolytic therapy with catheter-based delivery should be instituted. If there is a contraindication to thrombolytic therapy, venous thrombectomy should be undertaken. For patients whose condition is far advanced at presentation, thrombolytic therapy or venous thrombectomy should be considered as part of the initial therapeutic plan.	4
28. Vedantham S, Goldhaber SZ, Kahn SR, et al. Rationale and design of the ATTRACT Study: a multicenter randomized trial to evaluate pharmacomechanical catheter-directed thrombolysis for the prevention of postthrombotic syndrome in patients with proximal deep vein thrombosis. *Am Heart J* 2013; 165(4):523-530 e523.	Review/Other-Tx	N/A	To describe the rationale for the ATTRACT Study which is an ongoing NIH sponsored, Phase III, multicenter, randomized, open-label, assessor-blinded, parallel two-arm, controlled clinical trial to determine if the initial use of pharmacomechanical CDT along with the standard DVT therapy reduces the proportion of patients who develop PTS during 24 months of follow-up compared with standard DVT therapy alone in patients with symptomatic acute proximal DVT.	N/A	4

Radiologic Management of Iliofemoral Venous Thrombosis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
29. Meissner MH, Eklof B, Smith PC, et al. Secondary chronic venous disorders. *J Vasc Surg* 2007; 46 Suppl S:68S-83S.	Review/Other-Tx	N/A	To review the diagnosis and treatment for secondary chronic venous disorders.	The diagnostic evaluation of secondary chronic venous disorders is similar to primary chronic venous disorders and is based upon duplex ultrasound. However, the definition of hemodynamically significant venous stenosis remains obscure and there are no reliable tests to confirm the presence of such lesions. Diagnosis depends more on anatomic rather than hemodynamic criteria, and intravenous ultrasound is superior to venography in estimating the morphological degree and extent of iliac vein stenosis. The fundamental role of compression in the treatment of chronic venous disorders is well recognized. Compliance with compression is essential to heal ulcers and minimize recurrence. The efficacy of various adjuncts to ulcer treatment, including complex wound dressings and medications have been variable. Although superficial venous surgery has not been demonstrated to improve ulcer healing rates, it does decrease ulcer recurrence. Deep venous valve reconstruction is performed in only a few specialized centers, and the results are better for primary than for secondary chronic venous disorders. Treatment of incompetent perforating veins remains controversial. Although artificial venous valves are promising, most early experimental models have failed. With respect to venous obstruction, iliocaval angioplasty and stenting has emerged as the primary treatment for proximal iliofemoral venous obstruction with surgical bypass assuming a secondary role.	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

CDT = Catheter-directed thrombolysis

CI = Confidence interval

DVT = Deep vein thrombosis

PE = Pulmonary embolism

PMT = Percutaneous mechanical thrombectomy

PTS = Post-thrombotic syndrome

RR = Relative risk

VTE = Venous thromboembolism