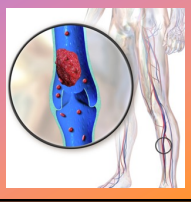
DEEP VEIN THROMBOSIS (DVT)

Clinical Presentation, Diagnosing, Treatment, and More

Lisa Yager MSN, CRNP, A-GPCNP-C



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DEEP VEIN THROMBOSIS (DVT)

- Venous thrombosis within a vessel of the deep system
- Usually related to injury or sluggish blood flow return
- Most present in the lower leg, thigh, or pelvis
- May occur in the upper extremities, brain, liver, kidney, or intestines (mesenteric) (Cleveland Clinic, 2022)
- Untreated DVT may lead to life-threatening outcomes
  - Pulmonary Embolism
- Accurate diagnosis is essential to help prevent fatal outcomes (Bauer & Hulaman, 2022)

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INCIDENCE

DVT/VTE is a major cause of morbidity and mortality, which can be prevented

- Estimated incidence of VTE (venous thromboembolism) is 1 per 1,000 people annually
  - DVT accounts for 2/3 of VTE events
- Pulmonary Embolism (PE) most serious complication
  - accounts for 1/3 of VTE events
- Much of the morbidity of DVT results from post-thrombotic syndrome (PTS)
  - Occurs in approximately 50% of patients with 2 years of DVT diagnosis
  - Symptoms include leg pain, swelling, venous ulcer (severe cases)

(Stone et al., 2017)

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MORTALITY RATE

- Patients with DVT that goes undiagnosed/untreated have a mortality rate of >3 %
- Patients with undiagnosed/untreated PE have a 10 X greater risk of mortality

Anticoagulation is the mainstay of therapy to help prevent PE and thrombosis recurrence and to ultimately decrease mortality rate

(Stone et al., 2017)

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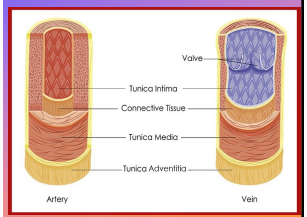
Veins are made of 3 layers:

- *Tunica adventitia*
  - Outermost layer
  - Thickest layer
  - Loose connective tissue that forms external elastic membrane
  - Fuses with surrounding tissue
- *Tunica media*
  - Middle layer
  - Smooth muscle fibers, elastic fibers, and collagen
  - Helps vessel expand and contract
- *Tunica intima*
  - Inner most layer
  - Thinnest of 3 layers
  - Composed of connective tissue and internal elastic membrane
  - Helps keep toxins out and prevent blood clots

ANATOMY AND FUNCTION OF VEINS



Cleveland Clinic, 2022

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ANATOMY AND FUNCTION (CONT)

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- Veins have valves
  - Allow for blood flow toward heart/forward direction
  - Purpose is to prevent back-flow of blood
- Thin-walled vessels
  - Less elasticity compared to arteries
  - Can accommodate large blood volumes
    - Approximately 75% of blood
  - Low pressure
- Venous blood flow/return is aided by contraction of muscles

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PATHOPHYSIOLOGY OF DVT DEVELOPMENT/ FORMATION

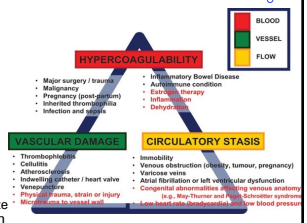
Virchow's Triad be used to recognize 3 main contributing factors in the formation of thrombosis

- Venous stasis/blood flow turbulence
- Damage to vessel wall/vascular injury
- Hypercoagulability (Stone et al., 2017)

Triggers of venous thrombosis is often multifactorial

Different parts of Virchow's triad can contribute but all result in early thrombus interaction with the endothelium

- Stimulation of cytokine production -> leukocyte adhesion to endothelium -> formation of venous thrombosis (Sheikh, Kudaravalli & Hotwagner, 2022)



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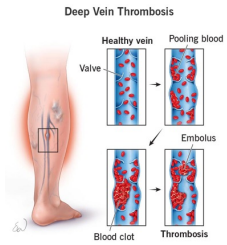
PATHOPHYSIOLOGY (CONT)

- Thrombus tends to occurs in areas of decreased or mechanically altered blood flow



- Valves help promote blood flow through venous system, but are also potential locations of venous stasis and hypoxia
  - Hypercoagulable microenvironments (at valves) – may be r/t decrease in certain **antithrombotic proteins** that are expression on the venous valves
    - Thrombomodulin
    - Endothelial protein C receptor
  - Hypoxia promotes the expression of certain **pro-coagulants**
    - P-selectin (adhesion molecule)
    - Tissue factor (primary cause for thrombus)

(Stone et al., 2017)

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COMPONENTS OF THROMBUS

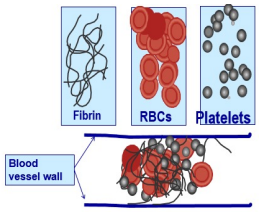
INNER LAYER

Platelet rich white thrombus

OUTER LAYER

Red blood cells

Fibrin (intertwined)



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CLINICAL PRESENTATION

DVT should suspected in patients who present with leg:

- Swelling/edema
- Pain
- Warmth
- Erythema of extremity (Bauer & Huisman, 2022)

Symptoms are typically unilateral

- Can be bilateral

Symptoms may only be in calf for those with distal DVT

Proximal DVT patients may have calf/whole leg swelling along with symptoms

Iliac vein thrombosis should be suspected in patients who present with gross swelling of the proximal part leg/buttock pain

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CLINICAL PRESENTATION (CONT)

Thrombus that involves the iliac bifurcation, pelvic veins, or vena cava usually produce bilateral lower extremity swelling (Patel, 2019)

Symptoms may be mild or severe

Some patients may be asymptomatic

Leg pain occurs in 50% of patient; where tenderness is noted in approximately 75% of patients (Patel, 2019)

If tenderness is present, usually confined to calf muscle or along the course of deep vein of medial thigh (Patel, 2019)

Warmth and erythema of skin may be present over area of thrombus (Patel, 2019)

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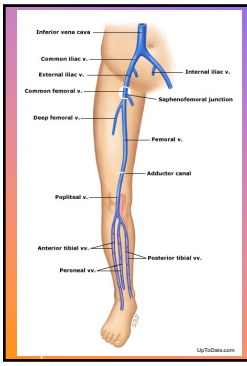

PHYSICAL EXAMINATION

Physical exam on patient with suspected DVT should include:

- Examining legs, abdomen, and pelvis
- Look for dilated superficial veins
- Unilateral edema/swelling (noting difference in calf circumference)
- Unilateral tenderness, warmth, erythema (may be bilateral too)
- Pain and tenderness along the course of major veins/deep veins (refer to image)
- Findings of local mass/inguinal mass – signs of malignancy (Bauer & Huisman, 2022)

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RISK FACTORS

- History of immobility (illness, prolonged hospitalization, injury)
- Recent surgery or trauma (typically within past 12 weeks of symptom onset)
- Prior history of DVT/VTE
- Family history of DVT/VTE
- Obesity
- Hormone replacement/oral contraceptives
- Pregnancy/postpartum
- Malignancy or suspected malignancy
- History of stroke with residual immobility/hemiplegia
- Heart failure/CHF
- Age > 65 yo
- Inflammatory Bowel Disease (IBD)

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OTHER RISKS – HYPERCOAGULABLE STATES

- Factor V Leiden (most common)
- Prothrombin gene mutation
- Protein deficiency (natural proteins that prevent clotting)
  - Protein C
  - Protein S
  - Antithrombin
- Elevated or dysfunctional fibrinogen
- Elevated levels of other factors
  - Factor VIII
  - Factor IX
  - Factor XI

(Cleveland Clinic, 2022)

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DIAGNOSING

Patients with suspected first DVT (no prior history)

- Recommend clinical assessment along with pretest probability (PTP) – Wells and Modified Wells score
  - Low PTP (0 or less) – should have D-dimer performed
  - D-dimer should not be done if it is expected to be high (recent surgery/trauma)

(Bauer & Huisman, 2022)

Table 2 Modified Wells score. The modified Wells score is a score out of 9 based on risk factors such as recent surgery and malignancy as well as findings on clinical examination.

MODIFIED WELLS SCORE[5]	
RISK FACTOR	POINTS
Active cancer (patient receiving treatment for cancer within the previous 6 months or currently receiving palliative treatment)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recently bedridden for 3 days or more, or **major surgery** within the previous 12 weeks requiring general or regional anaesthesia	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than that on the asymptomatic side (measured 10 cm below tibial tuberosity)	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented deep-vein thrombosis	1
Alternative diagnosis at least as likely as DVT	-2
	Score > or = 2 DVT likel score < 2 DVT unlikely

* Alternative diagnosis - Baker's cyst, cellulitis, muscle damage, inguinal lymphadenopathy, etc.)
0 or less - Low probability
1-2 Moderate probability
3-8 High probability

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DIAGNOSING (CONT)

Patients with 1st time suspected LE DVT

Low PTP and normal D-dimer (<500 ng/mL)
- Require no further testing

Low PTP and positive D-dimer level (≥500 ng/mL)
- Should undergo whole leg ultrasonography (US)
  - Positive US/identification of DVT requires treatment
  - Negative US/no identification of DVT requires no further testing/treatment

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DIAGNOSING (CONT)

Patient with 1st time suspected LE DVT with moderate PTP
- Consider getting high-sensitivity D-dimer (not if recent surgery/trauma)
  - Alternative – proceed directly to US w/o D-dimer (often influenced by availability of US)
    - Beneficial for Dx of other factors such as Baker's cyst)
  - Normal D-dimer – (<500ng/mL) does not need any further testing
  - Positive D-dimer - (≥500 ng/mL); whole leg US/venous duplex should be performed

Patients with 1st suspected LE DVT with high PTP
- Go straight to whole leg US/Venous duplex

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ULTRASOUND/VENOUS DUPLEX

NEGATIVE ULTRASOUND	POSITIVE ULTRASOUND
No further testing needed	Should be treated
May repeat in 1-7 days if patient still symptomatic	If iliac thrombus suspected, include iliac in US
	If non-diagnostic – go to CT Venogram

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D-DIMER – KEEP IN MIND

Not typically used as outpatient test	Can be non-specific	Should not be used as stand-alone test in those with suspected DVT
Levels may be elevated in those with malignancy, sepsis, recent trauma/surgery, pregnancy, renal failure	Values tend to rise with age	Should be use in conjunction with assessment, PTP, and US

Bauer & Hukman, 2022

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TREATMENT

- Anticoagulation is the mainstay of treatment
- Purpose is to prevent recurrent thrombosis, embolization, and death
- Risks are highest during first 3-6 months following diagnosis

(Hull & Lip, 2023)

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INITIAL ANTICOAGULATION

Anticoagulation immediately following diagnosis (usually within first 10 days)

- Often may need initial management while decide on long-term anticoagulation
- Options include
  - Low molecular weight heparin (LMWH) – enoxaparin, dalteparin, tinzaparin, and nadroparin
    - Out/in- patient 1mg/kg/dose SC q 12 hours
    - Alternative in-patient dose 1.5 mg/kg/dose SC daily
    - May administer until start of DOAC (typically less than 5 days)
    - Use for those who will be starting Warfarin – give for >5 days and overlap with start of Warfarin until INR is therapeutic (2-3)
    - Preferred for patient with active cancer, pregnant, those starting Warfarin, and patient who have malabsorption/vomiting
  - Heparin (inpatient)
    - Initial dosing 80 units/kg (max. 10,000 units)
    - Then infusion of 18 units/kg/hr (max. 2000 units/hr)

*Dosing may need to be adjusted for those with renal failure

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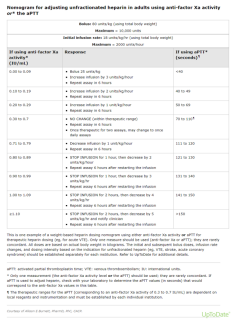
HEPARIN INFUSION



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LONG-TERM ANTICOAGULATION

- Usually 3-6 months – up to 12 months
- Direct factor Xa and thrombin inhibitors great choices of anticoagulation
  - Quick onset
  - Peak efficacy is 1-4 hours after ingestion

(Lip & Hull, 2024)

- Rivaroxaban and apixaban
  - Can be initial therapy without the need for LMWH
  - Therapy should not be delayed while deciding which anticoagulant will be started
  - LMWH can be used until agent is decided and started

(Lip & Hull, 2024)

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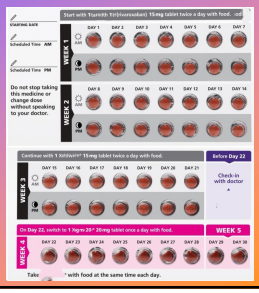
INITIAL DOSING OF DOAC

RIVAROXABAN

- Initial dosing is 15 mg twice a day for first 3 weeks
- Then 20 mg daily (in the evening)
- Option of a starter kit



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INITIAL DOSING OF DOAC

APIXABAN

- Initial dosing is 10 mg twice a day for first week
- Then 5 mg twice a day
- Option of a starter kit

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ORAL DIRECT THROMBIN INHIBITOR

Dabigatran

- Similar efficacy to warfarin
- Not commonly used
- Dosing is 150 mg twice daily after initial therapy of 5-10 days of parental anticoagulation with Heparin or short course LMWH

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WARFARIN (VITAMIN K ANTAGONIST)

- Preferred agent for those who do not have access to factor Xa or direct thrombin inhibitors
- Those with severe renal disease
- Those whose anticoagulation needs to be closely monitored
  - Start same day (day 1) or within first 5 days of starting LMWH/UFH at a dose of 5mg/day (or range 2-10 mg/day)
  - INR is monitored daily until within therapeutic range (2-3; target 2.5) for 2 consecutive days
  - Once therapeutic x 2 consecutive days – Heparin/LMWH may be discontinued (premature cessation may result in inadequate protection against recurrent thrombosis)

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Suggested protocol for initiating warfarin therapy

Days of warfarin treatment	INR <1.5	INR 1.5 to 1.9	INR 2.0 to 3.0	INR >3.0
Suggested initial dose for days 1 and 2				
Normal adult	5 mg*	n/a	n/a	n/a
Frail adult, malnourished, elderly, liver disease	2.5 mg*	n/a	n/a	n/a
Dosing for day 3 and beyond				
Day 3	5 to 10 mg	2.5 to 5 mg	0 to 2.5 mg	No dose
Day 4	10 mg	5 to 7.5 mg	0 to 5 mg	No dose
Day 5	10 mg	7.5 to 10 mg	0 to 5 mg	No dose
Day 6	7.5 to 12.5 mg	5 to 10 mg	0 to 7.5 mg	No dose

In this protocol, which is provided for guidance only, suggested doses of warfarin after day 2 are given as ranges. The clinician must judge the rapidity and magnitude of INR changes for the individual patient and make dosage adjustments accordingly. An algorithm for monitoring and adjustment of maintenance warfarin is presented separately. Refer to UpToDate topics on use of warfarin and table on suggested protocol for adjustment of maintenance warfarin.

n/a: not applicable.

* This table assumes that the patient has started with an INR in the normal range.

Refer to text for details concerning the source for this protocol and relevant references.

Hull & Lip, 2023

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SUGGESTED WARFARIN INITIATION

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DURATION OF TREATMENT

Individualize based on presence of provoked vs unprovoked episode/event, risk factors, and risk of recurrence and bleeding

- Most patients (provoked/unprovoked) should receive minimum of 3 months anticoagulation for lower limb/distal DVT
- Select populations, anticoagulation should extend 6-12 months

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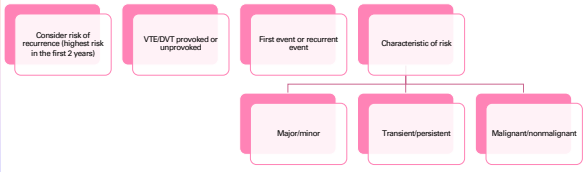
WHEN CONSIDERING EXTENDED ANTICOAGULATION



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WHEN CONSIDERING EXTENDED ANTICOAGULATION

- Consider risk of recurrence (highest recurrence in first 2 years)
- VTE/DVT provoked or unprovoked
- First or recurrent event
- Characteristic of risk
  - Transient/persistent
  - Major/minor
  - Malignant/nonmalignant (15-20% higher recurrence rate/year for those with active cancer)
- Recurrent proximal DVT (without identifiable risk factors and low risk of bleeding)
- Symptomatic PE (without identifiable risk factors and low risk of bleeding)

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CHARACTERIZING RISK FACTORS

Terms, definitions, and characterizing risk factors for indefinite anticoagulation

Term	Definition and examples
No identifiable risk factor (unprovoked)	VTE where no identifiable provoking event or risk factor is evident
Identifiable risk factor (provoked)	VTE caused by a known event or risk factor (eg, surgery, hospital admission, estrogen)
Transient risk factor	Risk factors for VTE that are reversible • **Major risk factors (ie, transient factors that favor limited-duration anticoagulation):** • Major surgery >30 minutes, hospitalization or confined to bed with "bathroom privileges" for ≥3 days due to acute illness, CS, trauma with fractures, estrogen therapy, pregnancy or puerperium • **Minor risk factors (ie, transient factors that favor continuing anticoagulation):** • Minor surgery <30 minutes, hospitalization <3 days, reduced mobility at home ≥3 days due to acute illness, lower extremity injury without fracture with reduced mobility ≥3 days, long-haul flight
Persistent risk factor	Risk factors that persist over a prolonged period of time • Examples include irreversible conditions such as active malignancy, obesity, active inflammatory bowel disease, active autoimmune disease, continued hormonal therapy, nephrotic syndrome, recurrent long-haul flights
Proximal DVT of lower extremity	VTE that is in the popliteal, femoral, or iliac veins
Distal DVT of lower extremity	VTE that is without a proximal component and confined to the calf veins (peroneal, posterior, anterior tibial, and muscular veins)
Pulmonary embolism	Thrombus in the main, segmental, or subsegmental branches of the pulmonary artery
Initial anticoagulation	Anticoagulant therapy that is administered immediately following a diagnosis of VTE
Anticoagulation following initial phase	Anticoagulant therapy that is typically administered for a finite time period (ie, scheduled stop date, typically 3 months)
Extended anticoagulation	Anticoagulant therapy that is administered beyond the typical 3 months but with a scheduled stop date (eg, 6 to 12 months)
Indefinite anticoagulation	Anticoagulant therapy that is administered beyond the typical 3 months but without a scheduled stop date
DOACs	Also known as newer/novel oral anticoagulants (NOAs), non-vitamin K antagonist oral anticoagulants (NOACs), and target-specific oral anticoagulants (TOACs, TSOACs)

VTE: venous thromboembolism; CS: cesarean section; DVT: deep venous thrombosis; DOACs: direct oral anticoagulants.

Lip, Hull, & Garcia, 2023

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PULMONARY EMBOLISM

Patients with incident of PE carry a long- lasting risk of recurrence

Anticoagulation is mainstay of PE treatment during in-hospital and after hospital phase

- Prevent extension of thrombus
- Prevent recurrence of VTE
- At least 3 months of treatment

- Extended therapy may be needed (6-12 months)
- DOACs reduce recurrent VTE by approx. 80-90% with a 2-6 % risk of non-major bleeding (Chopard et al., 2022)

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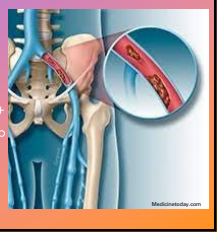
ILIOFEMORAL DVT

- 25% of all DVTs
- Increased risk of embolic and post-thrombotic complications
- Despite treatment with anticoagulant and compression – 50% will develop post-thrombotic syndrome (PTS)
  - Venous claudication
  - Edema
  - Skin damage/ulcerations
  - Risk of recurrent DVT
  - Venous hypertension
  - Valve incompetence
- Early thrombus removal with thrombolysis or thrombectomy can help restore venous patency and preserve valve function

(Foley, Waldo, & Armstrong, 2015)



Medicinetoday.com

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SURGICAL TREATMENT OF DVT

Benefits: improve swelling, decrease risk of post-thrombotic syndrome, can be done in acute and chronic period (up to a few months)

- Thrombolysis
  - Lytic catheter placement – left overnight in affected extremity
  - Patient brought back next day for any addition treatment
  - High risk of bleeding, patients need to stay in ICU while undergoing lysis therapy
- Thrombectomy
  - Mechanical or suction thrombectomy removal of clot
  - Angioplasty and stenting performed during same procedure
  - No required need for ICU stay

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INDICATIONS FOR THROMBOLYSIS AND THROMBECTOMY

- Patients with vascular compromise
- When anticoagulants are contraindicated
- Iliofemoral DVT associated with severe swelling/vascular compromise of affected extremity
- IVC filters is recommended for those patients who have iliofemoral DVT and anticoagulants are contraindicated

(Foley, Waldo, & Armstrong, 2015)

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MANAGEMENT OF CHRONIC DVT

- May require long-term use of anticoagulation
  - Unprovoked DVT/PE
  - DVT/PE associated with chronic risk factor (hypercoagulable, cancer, immobility)
- Wearing compression/support stockings
  - 20-30 mmHg strength
- Thrombolysis/Thrombectomy
  - Patient/provider dependent

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POST-THROMBOTIC SYNDROME

- Effects 20-50% of patients within first 2 years of DVT diagnosis
- Caused by damage to the valves/veins which leads to sluggish venous return and increased venous pressure
- Signs/Symptoms can be mild – severe
  - Pain
  - Swelling
  - Cramping
  - itching
  - Redness/discoloration
  - Thickening of skin/hyperplasia
  - Feeling of heaviness/fatigue
  - New spider veins/varicosities
  - paresthesia

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MANAGING POST-THROMBOTIC SYNDROME

- Compression therapy
  - Compression stockings 20-30 mmHg
  - Pneumatic compression pump
- Lifestyle changes
  - Elevate legs at/above heart level when sitting or lying
  - Maintain a healthy or ideal body weight
  - Use of good moisturizer for skin
- Exercise
  - Leg muscles; calf muscle is the pump to return blood to the heart
  - Walking

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COLLABORATION WITH OTHER HEALTHCARE PROVIDERS

Collaboration with other providers such as Hematologist and Vascular Surgery may be needed to provide the best care

- Hematology – hypercoagulable panel work-up
  - Inherited hypercoagulable states
    - Most common factor V Leiden mutation and prothrombin gene mutation (50-60% of cases)
    - Protein S deficiency
    - Antithrombin deficiency

(Bauer & Lip, 2023)

- Vascular Surgery consult
  - Follow-up testing (venous US/MRV/CT venogram)
  - Work-up for May-Thurner Syndrome/iliac vein compression/stenosis
  - Eval for surgical intervention

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THANK YOU

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