SVM APP Course Handouts Table of Contents
Saturday, March 16, 2024

* Handout not included in packet

The Pregnant VTE

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Disclosure

No financial or any other conflict of interest with regard to this presentation

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VTE in Pregnancy

Incidence: 1.2 **per 1,000 deliveries** (5x to 10x)

Incidence: Antepartum (0.6) **=** **Postpartum** (0.6)

Risk is Greatest in the first 6 weeks **postpartum, and** persists until 12 weeks

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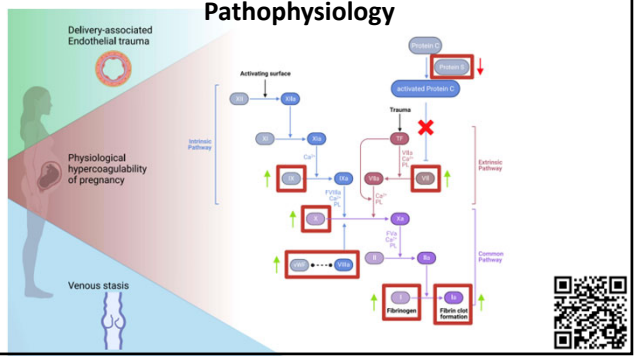
Pathophysiology



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VTE in Pregnancy

Prophylaxis

Treatment

Duration?

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32F | G1P0 | EGA 30w | L CFV DVT

Ambulatory | VSS | No Phlegmasia

a) Subcutaneous UFH

b) Rivaroxaban 10 mg/day

c) Apixaban 10 mg BID

d) LMWH 1mg/kg BID, with anti-Xa monitoring

e) LMWH 1mg/kg BID, without anti-Xa monitoring

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Agent	OK in Pregnancy?	Crosses Placenta?	Comments
LMWH	YES	No	✓ LMWH is preferred over UFH (? lower risk of HIT)
UFH	YES	No	✓ LMWH is preferred over UFH
Fondaparinux	Not preferred	Reported crosses in small amounts	✓ Very limited clinical experience
Warfarin	NO	Yes	✓ Potential for teratogenicity, pregnancy loss, fetal bleeding, neurodevelopmental deficits
DTI (Dabigatran)	NO	Likely Yes	✓ Reproductive effects in humans are unknown
Xai (Apixaban) (Rivaroxaban) (Edoxaban)	NO	Likely Yes	✓ Reproductive effects in humans are unknown

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Table 2. Incidence of side effects related to low molecular weight heparins in pregnancy

	Therapeutic dose	Prophylactic dose	Any dose
Antepartum bleeding	0% to 0.57%	0.42%	0% to 0.43%
Postpartum bleeding	1.15% to 5.6%	0.92%	0.94% to 1.6%
Wound hematoma	1.39%	0%	0.5% to 0.61%
Major skin reaction/allergy	1.15%	0.96%	0.5% to 1.8%
Osteoporosis	0%	0.26%	0.04% to 0.2%
HIT	0%	0%	0%

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32F | G1P0 | EGA 34w | L CFV DVT

Ambulatory | VSS | No Phlegmasia

LMWH | EDD in 4w | Prefers Vaginal Delivery

a) Await spontaneous labor, then stop LMWH

b) Schedule/Induce delivery, stop LMWH 24 hours prior

c) Schedule elective CS, stop LMWH 24 hours prior

d) Repeat VDUS and stop LMWH if no DVT

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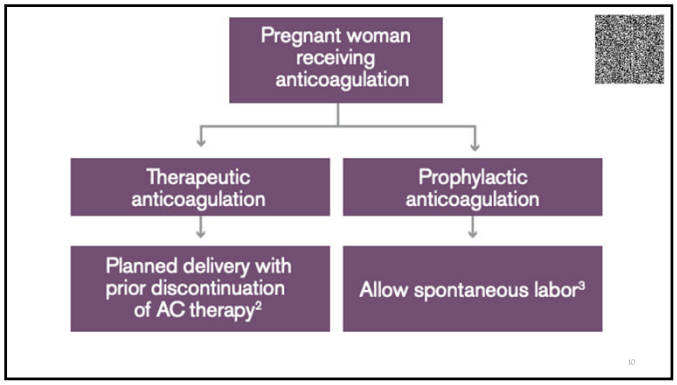

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32F | G1P0| L CFV DVT

Ambulatory | VSS | No Phlegmasia

LMWH | EDD in 4w | Prefers Vaginal Delivery

Uncomplicated Delivery at 40w | Planning for Breast Feeding

Which one should be avoided?

(a) Fondaparinux (b) Warfarin

(c) Rivaroxaban (e) LMWH

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Table 6 – Anticoagulants Considered Safe in the Context of Breastfeeding

Drugs to use	Drug Levels in Breast Milk
UFH[1]	Undetectable
LMWH[1]	Detectable (low) but not orally absorbed
Warfarin[1]	Undetectable
Acenocoumarol[1]	Undetectable
Danaparoid	Undetectable
Fondaparinux	Data Unavailable; unlikely to be orally absorbed

[1] *The agents with greatest experience in this patient population and the best evidence for safety were warfarin, acenocoumarol, LMWH, and UFH.*

Table 7 – Anticoagulants Considered Unsafe in the Context of Breastfeeding

Drugs not to use	Drug Levels in Breast Milk
Rivaroxaban	Detectable (low)
Other DOACs[2]	Data Unavailable

[2] *It is possible that DOACs are safe, but until further evidence and experience are available, clinicians should avoid prescribing these agents to women who are breastfeeding.*

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34F | G2P1| EGA 8w

Extremely concerned about getting another DVT

What would you recommend?

(a) No prophylaxis needed

(b) Get a VDUS and Rx only if positive for DVT

(c) Antepartum prophylaxis only

(d) Postpartum prophylaxis only

(e) Antepartum and postpartum prophylaxis

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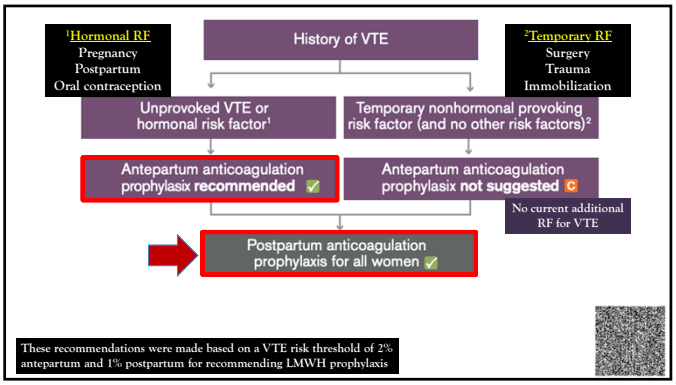

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Antepartum risks of recurrent VTE

- Without prophylaxis: **4.2%** (95% CI, 0.3% to 6.0%)
- With prophylaxis provided: **0.9%** (95% CI, 0.5% to 1.8%)

Postpartum risks of recurrent VTE

- Without prophylaxis: **6.5%** (95% CI, 4.3% to 9.7%)
- With prophylaxis provided: **1.8%** (95% CI, 1.2% to 2.7%)

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24F | G1P0 | EGA 30w

No Personal Hx of VTE | +Fam Hx of VTE

(a) No prophylaxis needed

(b) Get a VDUS and Rx only if positive for DVT

(c) Antepartum prophylaxis only

(d) Postpartum prophylaxis only

(e) Antepartum and postpartum prophylaxis

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24F | G1P0 | EGA 30w

No Personal Hx of VTE | +Fam Hx of VTE

Patient has Heterozygous FVL

(a) No prophylaxis needed

(b) Get a VDUS and Rx only if positive for DVT

(c) Antepartum prophylaxis only

(d) Postpartum prophylaxis only

(e) Antepartum and postpartum prophylaxis

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24F | G1P0 | EGA 30w

No Personal Hx of VTE | +Fam Hx of VTE

Patient has Protein C Deficiency

(a) No prophylaxis needed

(b) Get a VDUS and Rx only if positive for DVT

(c) Antepartum prophylaxis only

(d) Postpartum prophylaxis only

(e) Antepartum and postpartum prophylaxis

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24F | G1P0 | EGA 30w

No Personal Hx of VTE | +Fam Hx of VTE

Patient has Homozygous PTG mutation

(a) No prophylaxis needed

(b) Get a VDUS and Rx only if positive for DVT

(c) Antepartum prophylaxis only

(d) Postpartum prophylaxis only

(e) Antepartum and postpartum prophylaxis

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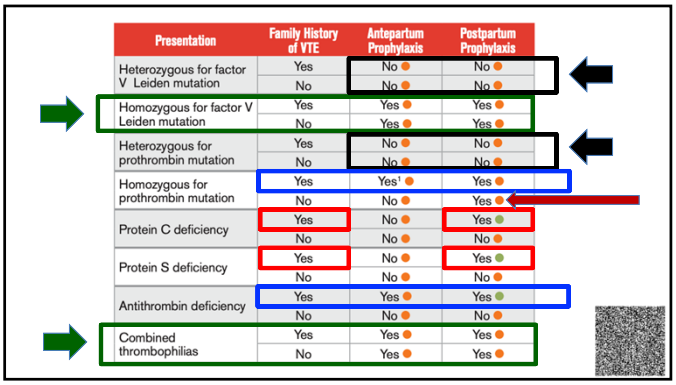

Presentation	Family History of VTE	Antepartum Prophylaxis	Postpartum Prophylaxis
Heterozygous for factor V Leiden mutation	Yes	No	No
	No	No	No
Homozygous for factor V Leiden mutation	Yes	Yes	Yes
	No	Yes	Yes
Heterozygous for prothrombin mutation	Yes	No	No
	No	No	No
Homozygous for prothrombin mutation	Yes	Yes[1]	Yes
	No	No	Yes
Protein C deficiency	Yes	No	Yes
	No	No	No
Protein S deficiency	Yes	No	Yes
	No	No	No
Antithrombin deficiency	Yes	Yes	Yes
	No	No	No
Combined thrombophilias	Yes	Yes	Yes
	No	Yes	Yes

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24F | G1P0 | EGA 30w

No Personal Hx of VTE | +Fam Hx of VTE

Patient has Homozygous PTG mutation

a) Await spontaneous labor, then stop LMWH

b) Schedule/Induce delivery, stop LMWH 24 hours prior

c) Schedule elective CS, stop LMWH 24 hours prior

d) Repeat VDUS and stop LMWH if no DVT

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CLINICAL GUIDELINES
blood advances
American Society of Hematology 2018 guidelines for management of venous thromboembolism: venous thromboembolism in the context of pregnancy
Thrombosis Research
Management of venous thromboembolism in pregnancy
BMC Cardiovascular Disorders
RESEARCH ARTICLE
Open Access
Critical appraisal of international guidelines for the prevention and treatment of pregnancy-associated venous thromboembolism: a systematic review
Prevention and management of venous thromboembolism in pregnancy: cutting through the practice variation
Leslie Skeith

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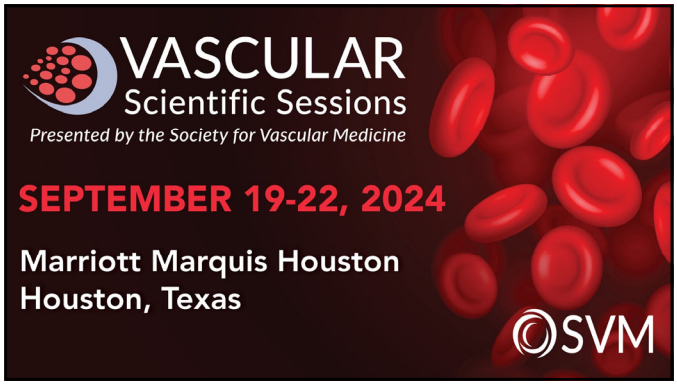
VASCULAR
Scientific Sessions
Presented by the Society for Vascular Medicine
SEPTEMBER 19-22, 2024
Marriott Marquis Houston
Houston, Texas
SVM

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Calf Vein Thrombus or DVT?

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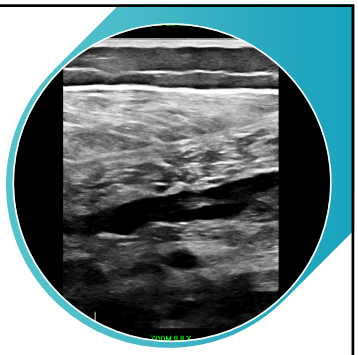
System Medical Director – Vascular Medicine & Vascular Labs - OhioHealth Heart and Vascular

President – Syntropic Core lab

Adjunct Clinical Professor of Medicine – Ohio University HCOM



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Disclosures

- Consultant/Advisor/ DSMB/ CEC -
  - Abbott, Auxetics, Diachii Sankyo, Koya Medical, Medtronic, NAMSA, Penumbra, Philips, PERC, Surmodics, USA Therm, VB Devices
- Board of Trustee
  - The VIVA Foundation
  - American Vein and Lymphatic Society
  - Intersocietal Accreditation Council | Vascular Testing
- President
  - Syntropic Core Lab

2

Are all calf vein DVTs created equally?

55 yr old male
2021 - Right peroneal and soleal DVT + Calf GSV SVT after hammer toe surgery+ 6 hour car ride
2022 – Idiopathic left PTV DVT and GSV calf SVT and perforator thrombosis

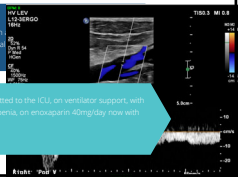
62 year old male with foam sclerotherapy induced thrombosis of the gastrocnemius vein 5 days after endovenous thermal ablation of the GSV and foam sclerotherapy of the tributary veins for C6 disease

35-year-old with gastrocnemius DVT after a Ski accident and ACL tear. Calf is tender.

27 year old female with extending into the distal

42 year old woman undergoing chemotherapy for ovarian cancer presenting with bilateral calf DVTs in the PTVs.

69 year old male admitted to the ICU, on ventilator support, with anemia, thrombocytopenia, on enoxaparin 40mg/day now with PTV DVT



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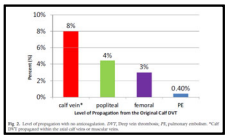
Controversies

- Anatomical – Calf veins are DVT not superficial thrombosis!
  - Only 17% of physicians correctly identified calf veins as deep veins [1]
- Not Clinically relevant ("Calf vein DVT need not be treated")

Propagation [2]



VTE Recurrence [3]

[1] Zieler, et al. Vasc Endovasc Surg. 2002;36:367-75
[2] Masuda EM, et al. J Vasc Surg. 2012;55:550.
[3] Lagerstedt CI, et al. Lancet. 1985;2:515

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Clinical Post thrombotic Syndrome

- 58% of patients reported moderate symptoms
- 5% reported severe symptoms
- 23% had 1-2 physician visits for symptoms
- 23% had >2 visits for symptoms
- 34% had class C4-C6 (CEAP) changes (6-10y)

- Saarinen J. *J Cardiovasc Surg.* 2002;43:687-91
- Saarinen J. *J Vasc Surg* 2002;36:959-964

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Pulmonary Embolism

- Vignette
  - 53 yr old seen 2 weeks after ED visit for mild calf pain
  - Noted small PTV DVT
  - Recommended to see PCP in 2-3 days
  - 10+ hour trip from Myrtle Beach to Columbus
  - "What about my SOB"?
  - Calf clots don't cause PE
- PE and tibial vessel DVT - 29%
  Kistner, et al. Am J Surg. 1972;124:169-172
- CVT and resp Sx - 35% PE
  Passman, et al. J Vasc Surg. 1997;25:39-45
- CVT with high probability V/Q - 56%
  Kazmers, et al. Am Surg. 1999;65:1124-1128
- PE - isolated calf DVT 25.4%
  - Soleal vein DVT was most common

  Wei, et al. Int Angiol. 2013;32:465-70

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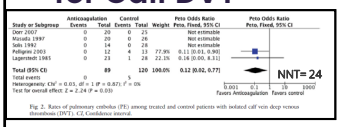
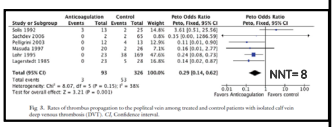
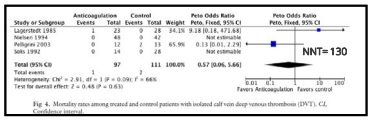
Meta-Analysis of Anticoagulation for Calf DVT







De Martino RR, et al. *J Vasc Surg.* 2013;56:228.

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Risks From Anticoagulation

- Spencer, et al. *J Thromb Thrombolysis.* 2012;33:211-7

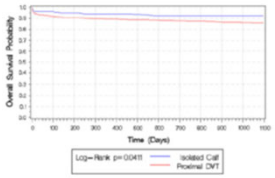

Fig. 3 Cumulative rate of survival without major bleeding stratified by DVT location (isolated calf vs. proximal)

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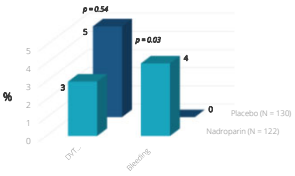
Contemporary Studies: CACTUS Trial

- Study Design: randomized, placebo-controlled European trial comparing 6 weeks of therapeutic-dose LMWH vs. placebo in 600 patients with a symptomatic isolated calf DVT.
- Primary Outcome: composite measure of extension of calf DVT to proximal veins, contralateral proximal DVT, and symptomatic pulmonary embolism at 42 days.
- Safety Outcome: major or clinically relevant non-major bleeding at 42 days.



Righini M, et al. *Lancet Haematol.* 2016;3:e556.

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Isolated Calf DVT: 2016 CHEST Guidelines

- In patients with acute isolated distal DVT of the leg and (i) without severe symptoms or risk factors for extension, we suggest serial imaging of the deep veins for 2 weeks over anticoagulation (Grade 2C) or (ii) with severe symptoms or risk factors for extension (see text), we suggest anticoagulation over serial imaging of the deep veins (Grade 2C).

Kearon C, et al. *CHEST.* 2016;149:315.

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Isolated Calf DVT: 2016 CHEST Guidelines

- In patients with acute isolated distal DVT of the leg who are managed with anticoagulation, we recommend using the same anticoagulation as for patients with acute proximal DVT (Grade 1B).
- In patients with acute isolated distal DVT of the leg who are managed with anticoagulation, we recommend using the same anticoagulation as for patients with acute proximal DVT (Grade 1B).

Kearon C, et al. *CHEST.* 2016;149:315.

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Practical Clinical Considerations

- Therapeutic anticoagulation for calf DVT could increase the risk of operative bleeding in surgical patients.
  - [1] Hematoma or hemarthrosis after surgery
- "It's difficult to get patients back in for another ultrasound."
  - It's also difficult to get patients to take anticoagulation, especially injectable agents
- "Shouldn't the novel oral anticoagulants make the argument for treatment easier?"
  - May reduce but not eliminate the bleeding risk

[1] Schneider T, et al. *Am J Knee Surgery.* 1998;11:95.

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Take-Home Points

- Anticoagulate if:
  1. Patient is high risk for proximal DVT progression or PE AND/OR
  2. Symptomatic AND
  3. Low risk for bleeding
- Surveillance imaging for 2 weeks (unclear frequency) and treat if proximal extension
- Cost-effectiveness is unclear
  1. If contraindications to AC
  2. Patient resistance to AC
  3. Asymptomatic, incidental finding

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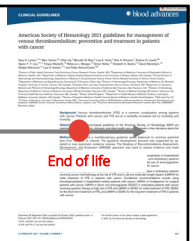
ASH CLINICAL PRACTICE GUIDELINES
VENOUS THROMBOEMBOLISM (VTE)



VTE in Cancer Anticoagulation Summary

Initial treatment (within first week of diagnosis)	Short-term treatment (3 to 6 mos. from diagnosis)	Long-term treatment (> 6 mos. from diagnosis)	End of life
Recommendation 20 DOAC *or* LMWH	Recommendation 23 DOAC *over* LMWH	Recommendation 32, 33 *Long-term, indefinite anticoagulation* rather than short-term treatment	Discontinue anticoagulant therapy

Blood Adv. 2021 Feb 23;5(4):927-974.

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Real Life Management

- 55 yr old male
  2021 - Right peroneal and soleal DVT + Calf GSV SVT after hammer toe surgery+ 6 hour car ride
  2022 – Idiopathic left PTV DVT and GSV calf SVT and perforator thrombosis
- 62 year old male with foam sclerotherapy induced thrombosis of the gastrocnemius vein 5 days after endovenous thermal ablation of the GSV and foam sclerotherapy of the tributary veins for C6 disease
- 35-year-old with gastrocnemius DVT after a Ski accident and ACL tear. Calf is tender.
- 27 year old female with an idiopathic DVT of the TP trunk extending into the distal popliteal vein vein
- 42 year old woman undergoing chemotherapy for ovarian cancer presenting with bilateral calf DVTs in the PTVs.
- 69 year old male admitted to the ICU, on ventilator support, with anemia, thrombocytopenia, on enoxaparin 40mg/day now with PTV DVT

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Conclusions

- Calf vein DVT represents a unique clinical setting and may be heterogenous
  - They may represent the beginning of a process – with immediate and long-term consequences
  - They may also represent what is left – from a proximal DVT
  - They may be a final event for some patients
  - They may be caused by propagation of SVT, via perforator thrombus (NOT STUDIED WELL)
- Clinical complications may be long-term
- Anticoagulation is well tolerated in an otherwise "healthy" population
- Patients without appropriate follow-up represent a significant risk
- NOT INDICATION FOR AN IVC FILTER

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Obesity and Thrombosis

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Director, Vascular Medicine
University Hospitals Harrington Heart & Vascular Institute
Cleveland, OH

1

Objectives

- Identify the epidemiology of obesity and thrombosis
- Discuss management considerations
- Identify the impact of obesity on VTE management

2

Case

- 68 yo man presents for pre-op eval. Has planned surgery for colon cancer at the hepatic flexure. Patient and CR surgeon are concerned about his VTE risk given h/o idiopathic right popliteal DVT 13 years ago. Treated with warfarin for many years then stopped bc he was tired of the monitoring.
- PMH: HTN, OA, obesity (BMI 48; 150 Kg), DVT as noted
- FH: no VTE SH: nonsmoker, ret engineer
- OE: clinically well, CV reg, Lungs CTA, Ext 1+ edema RLE gaiter area with associated LDS and hemosiderin staining, DP 2+ bil
- How do you risk stratify him for VTE?
- What prophylaxis is recommended?

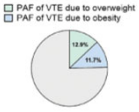
3

Obesity and VTE Epidemiology

The Risk of Incident Venous Thromboembolism Attributed to Overweight and Obesity: The Tromsø Study

Tobias Frischmuth[1,2] Brigitte G. Tandel[1] Sigrid K. Brækkan[1,2] John-Bjarne Hansen[1,2] Vânia M. Morelli[1,2]

BMI (kg/m²)	Prevalence in VTE (%)	PAF % (95% CI)
Overall VTE		
<25	29.4	
25-30	45.3	12.9 (6.6-19.0)
≥30	25.3	11.7 (8.5-14.9)
Overweight and obesity		24.6 (16.6-32.9)



Thromb Haemost 2024;124:239-249.

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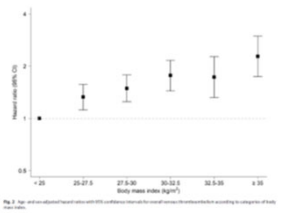
The Risk of Incident Venous Thromboembolism Attributed to Overweight and Obesity: The Tromsø Study

Tobias Frischmuth[1,2] Brigitte G. Tandel[1] Sigrid K. Brækkan[1,2] John-Bjarne Hansen[1,2] Vânia M. Morelli[1,2]

Table 2 Characteristics of venous thromboembolism (VTE) events ($n = 1,051$) in the Tromsø Study (1994–2020)

Characteristics	Value
Age at VTE	69 ± 13
Sex (men)	49.3 (518)
Deep vein thrombosis	55.2 (580)
Pulmonary embolism	44.8 (471)
Unprovoked VTE	41.6 (437)
Provoked VTE	58.4 (614)
Major surgery	14.8 (155)
Trauma	9.2 (97)
Acute medical conditions	12.2 (128)
Cancer	24.7 (260)
Immobilization	21.1 (222)
Others	4.0 (42)



Thromb Haemost 2024;124:239-249.

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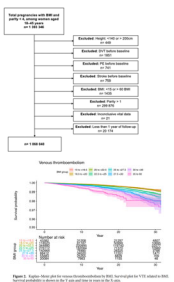
Prepregnancy overweight and obesity and long-term risk of venous thromboembolism in women

Ahmad Mahmood[1], Katarina Gloe Sandblad[1,2], Christina E. Lundberg[1], Gustaf Hellstrand[1], Per Olof Hansson[1,3], Martin Adiels[4] & Annika Rosengren[1,2,5]

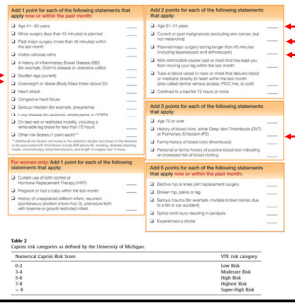


Variable	All	15 ≤ BMI < 18.5	18.5 ≤ BMI < 20	20 ≤ BMI < 22.5	22.5 ≤ BMI < 25	25 ≤ BMI < 27.5	27.5 ≤ BMI < 30	30 ≤ BMI < 35	35 ≤ BMI < 60	p
n	1,068,040	43,382	118,523	344,880	276,112	140,964	68,412	55,683	20,084	
Median follow up, years (IQR)	12.9 (5.9–21.2)	19.6 (8.6–27.3)	17.3 (7.7–26.4)	14.7 (6.7–24.6)	12.3 (5.8–20.2)	11.1 (5.2–18.4)	10.1 (4.7–17.2)	9.0 (4.1–15.3)	7.7 (3.7–12.9)	<0.001
Venous thromboembolism (VTE)										
Crude events	3997	181	413	1166	1002	558	305	264	108	<0.001
Event rate per 100,000 years (95% CI)	26.5 (25.7–27.3)	23.1 (19.9–26.7)	20.6 (18.7–22.7)	22.1 (20.9–23.4)	26.8 (25.2–28.5)	32.1 (28.5–34.9)	38.8 (34.5–43.4)	45.7 (40.3–51.5)	41.1 (30.2–73.8)	<0.001
Age at diagnosis, years	40.1 ± 9.5	40.1 ± 9.7	41.1 ± 9.8	41.0 ± 9.4	40.3 ± 9.6	38.9 ± 9.2	40.4 ± 9.8	37.8 ± 9.0	35.7 ± 7.5	<0.001
Pulmonary embolism (PE)										
Crude Events	2549	108	265	755	641	341	204	166	69	<0.001
Event rate per 100,000 years (95% CI)	16.9 (16.2–17.6)	13.8 (11.3–16.6)	13.2 (11.7–14.9)	14.5 (13.5–15.4)	17.1 (15.8–18.5)	19.6 (17.6–21.8)	25.9 (22.5–29.7)	29.7 (24.5–35.4)	30.0 (19.3–49.4)	<0.001
Age at diagnosis, years ± SD	40.9 ± 9.7	41.5 ± 10.3	41.8 ± 9.9	41.8 ± 9.4	40.9 ± 10.1	40.5 ± 9.1	41.1 ± 9.9	38.3 ± 9.0	34.7 ± 7.8	<0.001
Deep venous thrombosis (DVT)										
Crude events	1765	83	179	507	435	261	126	126	48	<0.001
Event rate per 100,000 years (95% CI)	11.7 (11.2–12.3)	10.6 (8.4–13.1)	8.9 (7.7–10.3)	9.6 (8.8–10.5)	11.6 (10.6–12.8)	15.0 (13.2–17.0)	16.0 (13.3–19.0)	21.8 (18.1–25.9)	27.1 (20.0–36.0)	<0.001
Age at diagnosis, years ± SD	39.4 ± 9.2	38.9 ± 9.0	40.7 ± 9.6	39.9 ± 9.2	40.0 ± 9.3	37.5 ± 9.2	40.1 ± 9.8	37.5 ± 8.8	37.3 ± 7.0	<0.001

Sci Reports 2023;13:14597

6

VTE Risk Assessment



Padua Risk-Assessment Model[a]

Risk Factor	Score
Active cancer[b]	3
Previous venous thromboembolism (excluding superficial thrombosis)	3
Reduced mobility[c]	3
History of thrombophilic condition	3
Recent (≤1 mo) trauma or surgery	2
Age of ≥70 yr	1
Heart or respiratory failure	1
Acute myocardial infarction or ischemic stroke	1
Acute infection or rheumatologic disorder	1
Obesity (body mass index of ≥30 kg/m²)	1
Hormone replacement therapy	1

[a] A total score of ≥4 indicates a high risk of VTE. Adapted, with permission, from reference 8.
[b] Patients with local or distant metastases or in whom chemotherapy or radiotherapy had been performed in the previous six months.
[c] Bedrest with bathroom privileges for at least three days.

7

Prophylaxis

- How do you risk stratify him for VTE?
  - Both Caprini risk score and Padua risk score = high risk
- What prophylaxis is recommended? = pharmacomechanical prophylaxis

Table 2 Dosing recommendations for prophylactic doses of parenteral anticoagulants in morbidly obese patients (BMI ≥ 40 kg/m²) with normal renal function (CrCl > 30 ml/min.) [5, 10, 29, 30, 33]

Medication	Recommended dosing regimen
Enoxaparin [29, 30, 33]	Enoxaparin 40 mg subcutaneously twice daily
Unfractionated heparin [33]	7500 units subcutaneously three times daily
Fondaparinux	Consider using enoxaparin if not contraindicated. If unable to substitute, use standard fondaparinux 2.5 mg subcutaneously daily
Other LMWHs (dalteparin, tinzaparin, nadroparin) [5, 10]	Consider using enoxaparin instead. If unable to substitute, consider increasing total daily dose by 25–30 %

- Given the malignancy – this should be continued 28 days after surgery/dc

J Thromb Thrombolysis 2016;41:475-481.

8

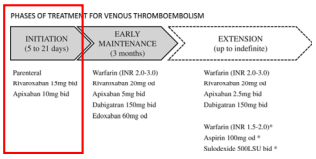
Case

- + LMWH prophylaxis but SCDs compliance was poor.
- Didn't have coverage for extended LMWH prophylaxis.
- 3 weeks post-op developed right leg pain and swelling with DOE climbing a flight of stairs
- OE: BP 100/60; Tachypneic RR 24, 4L O2 requirement, CV rate 120, Ext 2+ edema with calf and ankle tenderness
- ED eval: right femoral, popliteal and PT DVT; CT with bil segmental and subsegmental PE; RV:LV 1.5; troponin 356; BNP 760 and ECHO demonstrated flattening of the septum, RVSP 45 mmHg est, moderate RV dysfunction
- PESI: 148 = very high risk

9

Case

- What initial therapy is indicated?



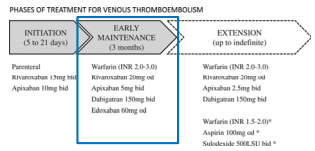
- LMWH or UFH until stable

Circulation 2015;132:1856-1859.

10

Case

- What therapy would you recommend at discharge?



Circulation 2015;132:1856-1859.

11

Journal of Thrombosis and Haemostasis, **14**: 1308–1313 DOI: 10.1111/jth.13323

RECOMMENDATIONS AND GUIDELINES

Use of the direct oral anticoagulants in obese patients: guidance from the SSC of the ISTH

K. MARTIN,* J. BEYER-WESTENDORF,† B. L. DAVIDSON,‡ M. V. HUISMAN,§ P. M. SANDSET¶ and S. MOLL*

Guidance statements

1 We recommend appropriate standard dosing of the DOACs in patients with a BMI less than or equal to 40 kg m^{-2} and weight less than or equal to 120 kg for VTE treatment, VTE prevention, and prevention of ischemic stroke and systemic arterial embolism in non-valvular AF.

2 We suggest that DOACs should not be used in patients with a BMI of > 40 kg m^{-2} or a weight of > 120 kg, because there are limited clinical data available for patients at the extreme of weight, and the available PK/PD evidence suggests that decreased drug half-lives occur with increasing weight, which raises concerns about underdosing in the population at the extreme of weight.

3 If DOACs are used in a patient with a BMI of > 40 kg m^{-2} or a weight of > 120 kg, we suggest checking a drug-specific peak and trough level (anti-FXa for apixaban, edoxaban, and rivaroxaban; ecarin time or dilute thrombin time with appropriate calibrators for dabigatran; or mass spectrometry drug level for any of the DOACs). If the level falls within the expected range, continuation of the DOAC seems reasonable. However, if the drug-specific level is found to be below the expected range (Table S1) [17,24,26–29], we suggest changing to a VKA rather than adjusting the dose of the DOAC.

12

Obesity - Newly Published Guidelines

Use of direct oral anticoagulants in patients with obesity for treatment and prevention of venous thromboembolism: Updated communication from the ISTH SSC Subcommittee on Control of Anticoagulation

	Phase 3 Studies Comparing DOACs with VKA in VTE		Phase 4 Studies Comparing DOAC with VKA in VTE (Including Retrospective and Prospective Studies and Meta-analyses)	
	BMI >35 or BW >120 kg	BMI >40	BMI >35 or BW >120 kg	BMI >40
Apixaban	X	X	Similar outcomes[2]	Similar outcomes[3,4]
Dabigatran	X	X	X	X
Edoxaban	X	X	X	X
Rivaroxaban	Similar outcomes[5]	X	Similar outcomes[6,8–10]	Similar outcomes[8,9]
Pooled DOAC	Similar outcomes[11]	X	Similar outcomes [12–14]	Similar outcomes[12]

Summary Guidance Statements for use of DOACs in Patients with Obesity

1) Consistent with the 2016 ISTH SSC recommendations, we conclude that the use of any DOAC is appropriate for patients with BMI up to 40 kg/m^2 or weight 120 kg. For patients with BMI >40 kg/m^2 or weight >120 kg, we recommend that the individual DOACs should be used as follows:

2) For treatment of VTE, we suggest that standard doses of rivaroxaban or apixaban are among appropriate anticoagulant options regardless of high BMI and weight. Fewer supportive data exist for apixaban than rivaroxaban. VKA, weight-based LMWH (per manufacturers' recommendations), and fondaparinux are also options.

J Thromb Haemost 2021;19:1874-1882.

13

Real life results of direct-acting oral anticoagulants recommended-dose in obese vs normal-weight patients with venous thromboembolism

José Antonio Rueda-Camino[a,b,*], Raquel Barba[a,b], Sonia Otálora[c], Alessandra Bura-Riviere[d], Adriana Visoná[c], Isabelle Mahé[d,e], Alicia Alda-Lozano[b], Joaquín Alfonso Megido[f], Nazaret Pacheco-Gómez[f], Rachel P. Rosovsky[g], Manuel Monreal[c,h], the RIETE Investigators[i]

Table 3
Comparisons of clinical outcomes during anticoagulation and after discontinuation between patients with normal body weight vs. those with obesity.

	BMI ≥ 30 kg/m^2		BMI 18.5–24.9 kg/m^2		Hazard ratio (95 % CI)*
	N	Events per 100 patient-years	N	Events per 100 patient-years	
Patients, N	2085		2670		
Recurrent PE	20	1.10 (0.71–1.71)	11	0.84 (0.46–1.52)	1.33 (0.64–2.73)
Recurrent DVT	11	0.61 (0.34–1.10)	17	1.30 (0.81–2.09)	0.48 (0.23–1.00)
Recurrent VTE	31	1.71 (1.20–2.43)	28	2.14 (1.48–3.09)	0.83 (0.49–1.34)
Major bleeding	26	1.41 (0.96–2.12)	23	1.76 (1.17–2.65)	0.91 (0.52–1.59)
Gastrointestinal	12	0.67 (0.38–1.18)	9	0.69 (0.36–1.33)	1.04 (0.44–2.46)
Intracranial	5	0.28 (0.12–0.67)	7	0.54 (0.26–1.13)	0.57 (0.19–1.66)
Death	53	2.93 (2.23–3.81)	72	5.42 (4.32–6.86)	0.56 (0.39–0.79)
Main causes of death					
Fatal PE	2	0.11 (0.03–0.44)	3	0.22 (0.07–0.70)	0.53 (0.09–3.19)
Fatal bleeding	2	0.11 (0.03–0.44)	2	0.15 (0.04–0.61)	0.79 (0.11–5.67)
Disseminated cancer	11	0.60 (0.33–1.09)	18	1.36 (0.86–2.16)	0.42 (0.20–0.89)
Sepsis or multiorgan failure	10	0.55 (0.30–1.02)	11	0.82 (0.46–1.50)	0.74 (0.31–1.74)
Acute respiratory failure	8	0.44 (0.22–0.88)	10	0.75 (0.41–1.41)	0.62 (0.25–1.52)
Sudden unexpected death	2	0.11 (0.03–0.44)	1	0.08 (0.01–0.54)	1.70 (0.15–18.8)

Abbreviations: BMI: body mass index; CI: confidence interval; DVT: deep vein thrombosis; kg/m^2: kilograms per metre squared; N: number of patients; vs: versus; VTE: venous thromboembolism.
* Death is computed as a competing risk event for all types of recurrence and bleeding.

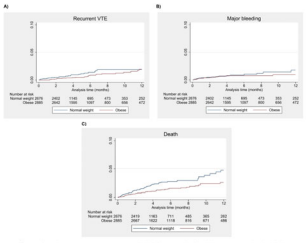


Fig. 2. Kaplan Meier curves: 2A. Recurrent VTE. 2B. Major bleeding. 2C. Death. Abbreviations: VTE: venous thromboembolism.

Thromb Res 2024;233:165-172.

14

Retrospective, multicenter analysis of the safety and effectiveness of direct oral anticoagulants for the treatment of venous thromboembolism in obesity

Jeffrey D. Sperry[1] · Aletha Loeb[2] · Melissa J. Smith[3] · Tessa B. Brighton[4] · Julie A. Ehret[5] · Joli D. Fermo[6] · Morgan E. Gentili[6] · Jason W. Lancaster[7] · Jennifer N. Mazur[8] · Katherine Spezzano[9] · Jennifer A. Szwak[10]

Table 1 Baseline characteristics of high and low body mass index (BMI) groups

Characteristic	BMI ≥ 40 kg/m^2 (n = 165)	BMI < 40 kg/m^2 (n = 320)	*p*-value
BMI, median (Q1, Q3)	44.4 (42.1, 49.6)	28.9 (24.8, 33.5)	< 0.001
BMI ≥ 50 kg/m^2, n (%)	38 (23)	-	
BMI ≥ 60 kg/m^2, n (%)	8 (4.8)	-	
Weight, median (Q1, Q3), kg	129 (114, 147)	84 (71.8, 97)	< 0.001
Weight > 150 kg, n (%)	32 (19.4)	-	
Age, median (Q1, Q3), years	57 (46, 66)	63 (51, 72)	< 0.001
Comorbidities			
Active cancer, n (%)	29 (17.6)	33 (10.3)	0.031
Stroke, n (%)	12 (7.3)	54 (16.9)	0.006
Hypercoagulable states, n (%)	8 (4.8)	37 (11.6)	0.03
Active COVID infection, n (%)	6 (6.3)	26 (8.1)	0.093
Liver disease, n (%)	9 (5.5)	24 (7.5)	0.522
ESRD, n (%)	7 (4.2)	16 (5)	0.825
Serum creatinine on discharge, median (Q1, Q3), mg/dL	0.9 (0.7, 1.2)	0.8 (0.7, 1.1)	0.002
Baseline INR, median (Q1, Q3)	1.1 (1.0, 1.2)	1.1 (1.0, 1.3)	0.224
Indication for anticoagulation			0.111
PE, n (%)	107 (64.8)	182 (56.9)	
DVT, n (%)	27 (16.4)	78 (24.4)	
PE & DVT, n (%)	30 (18.2)	58 (18.1)	
Not reported, n (%)	1 (0.6)	2 (0.6)	
Provoked VTE, n (%)	79 (47.9)	182 (56.9)	0.071
DOAC prescribed			†
Apixaban, n (%)	127 (77.0)	246 (76.9)	
Rivaroxaban, n (%)	38 (23.0)	73 (22.8)	
Dabigatran, n (%)	0 (0)	1 (0.3)	
Edoxaban, n (%)	0 (0)	0 (0)	
Concomitant medications			
Aspirin, n (%)	38 (23)	95 (29.7)	0.142
NSAIDs, n (%)	14 (8.5)	43 (13.4)	0.154
P-gp inhibitor, n (%)	14 (8.5)	11 (3.4)	0.028
P2Y12 agent, n (%)	4 (2.4)	9 (2.8)	1

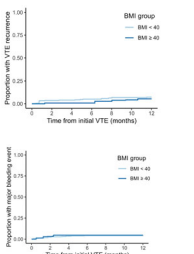


Table 2 Selected primary and secondary outcomes displayed by BMI group, including statistical results from the propensity score analysis

	BMI ≥ 40 kg/m^2 (n = 165)	BMI < 40 kg/m^2 (n = 320)	Propensity Score Analysis
VTE Recurrence, n (%)	5 (3.0)	13 (4.1)	Adjusted OR: 0.66 (95% CI: 0.18–2.09)
Major Bleeding Event, n (%)	5 (3.0)	15 (4.7)	Adjusted OR: 1.19 (95% CI: 0.36–3.92)
Any Bleeding Event, n (%)	21 (12.7)	47 (14.7)	-

J Thromb Thrombolysis 2024;epub; doi.org/10.1007/s11239-024-02955-6

15

Case

- Cancer was early stage
- Complete surgical resection
- Treated with rivaroxaban – does well

- At 6 months follow up -?discussions regarding AC
  - Can he/should he stop given the current situational event?
  - If he continues – what dose?

DOAC, data are insufficient to provide evidence-based guidance regarding DOAC dose reduction for obese patients after the initial 6 months of full dose for extended treatment of VTE.

J Thromb Haemost 2021;19:1874-1882.

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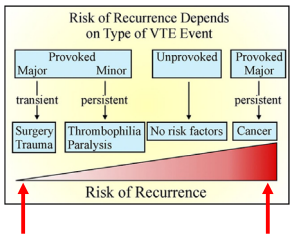
VTE Recurrence



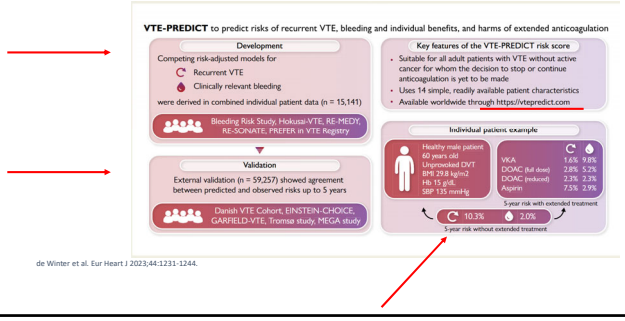
- Clinical features associated with increased risk for VTE and recurrence
  - Age
  - Gender
  - Some thrombophilia
  - Provoked events vs. idiopathic events
  - Biomarkers
  - Patient co-morbidities – IBD, CTD, immobility, obesity, smoking, cancer

Many recurrent risk predictions scores/models – HERDOO2, DASH, Vienna risk model, VTE-Predict

Prins, et al. Blood Adv 2018;2:788-796

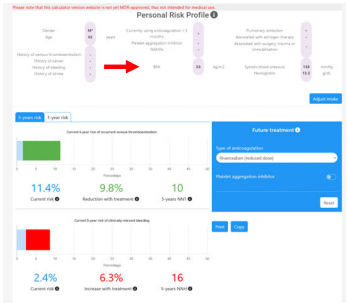
17

VTE-PREDICT



de Winter et al. Eur Heart J 2023;44:1231-1244.

18



19

Case

- Seen again in pre-op eval for bariatric surgery
- Questions for the consult: does he need bridging? Should we use our regular prophylaxis strategy or does he need more? Shouldn't he have testing for all these blood clots?
- 5-years since his last DVT/PE
- Remains on rivaroxaban 20 mg daily

- Does he need bridging pre-op?
- How long should you hold the rivaroxaban?

20

Case

- Should we use our regular prophylaxis strategy or does he need more?

- Shouldn't he have testing for all these blood clots?

- What will be the plan post-op?

21

Use of direct oral anticoagulants in patients with obesity for treatment and prevention of venous thromboembolism: Updated communication from the ISTH SSC Subcommittee on Control of Anticoagulation

TABLE 2 Expected impact of bariatric surgery procedures on absorption of DOACs

DOAC	Site of Absorption in Gastrointestinal Tract	Surgical Intervention and Anticipated Effect on Absorption		
		Gastric Banding	Partial/Sleeve Gastrectomy	RYGB
Apixaban	Primarily upper GI tract, with possible limited absorption in the colon; absorption decreased by when delivered to the distal small bowel compared with oral administration[44]	Unlikely affected	Unlikely affected	Possibly reduced
Dabigatran	Lower stomach and proximal small intestine[41,42,44]	Possibly reduced	Possibly reduced	Possibly reduced
Edoxaban	Proximal small intestine, dependent on acidic environment[43,44]	Possibly reduced	Possibly reduced	Possibly reduced
Rivaroxaban	Largely stomach, some small intestine, but absorption reduced when released distal to stomach[41,45]	Possibly reduced	Possibly reduced	Possibly reduced

6). We suggest not to use DOAC for treatment or prevention of VTE in the acute setting after bariatric surgery (because of concerns of decreased absorption), and instead, to initiate such patients on parenteral anticoagulation in the early postsurgical phase. We suggest that switching to VKA or DOAC may be considered after at least 4 weeks of parenteral treatment, and if so, suggest obtaining a DOAC trough level to check for drug absorption and bioavailability.

J Thromb Haemost 2021;19:1874-1882.

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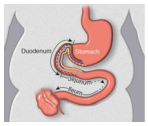
Effect of major gastrointestinal tract surgery on the absorption and efficacy of direct acting oral anticoagulants (DOACs)

- Site of absorption is variable for the available drugs
- Transit time and surface availability affects absorption
- Following GI surgery – most literature recommended LMWH/VKA use



- Rivaroxaban needs to pass through the stomach for adequate absorption
  - Not for delivery by J-tube
- Apixaban absorb mostly in stomach - ? distal small bowel and proximal colon
- Edoxaban less well studied. Dissolves in the stomach, absorption in the proximal small bowel
- Dabigatran – likely should be avoided in patients with small bowel resection or bypass

Hakeam HA, et al. J Thromb Thrombolysis 2017;43:343-351.

23

GI Surgery Considerations

1. We recommend using vitamin K antagonists, rather than DOACs, in patients who require full-dose anticoagulation after bariatric surgery, as VKAs can be monitored with the INR. We recommend against using DOACs, because published data describing DOAC absorption, PK/PD and clinical efficacy and safety are too sparse, and there is no PK/PD model to predict DOAC drug disposition and action in patients after bariatric surgery.
2. If DOACs are used in a patient after bariatric surgery, we suggest checking a drug-specific peak and trough level. If the level falls within the expected published ranges [45], continuation of the DOAC seems reasonable. However, if the drug-specific level is found to be below or above the expected range, we suggest changing to a VKA rather than adjusting the dose of the DOAC. As food intake and weight may change in the weeks and months after the surgery, repeat DOAC drug level testing may be indicated at certain intervals.

Martin KA et al. Am J Med 2017;130:517-524.

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Conclusions

- Obesity is increasing world wide
- The influence of obesity on VTE risk, peri-operative prophylaxis and treatment strategies in VTE need to be recognized
- Obesity can and likely should influence many anticoagulation strategies
- There is increasing data and scientific recommendations for use of the DOACs (rivaroxaban and apixaban) in the obese population with BMI > 40
- After bariatric surgery (GI surgery) the impact on DOAC absorption should be recognized and VKA and LMWH may be preferred

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University Hospitals Harrington Heart & Vascular Institute Cleveland | Ohio

Advanced Treatment of Acute PE – Who and How?

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1

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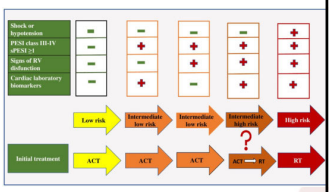
Intermediate-Risk PE

- Normotensive
- Right ventricular dysfunction is present
- Increased risk of adverse outcomes
- Mortality 15-20%
  - A subset may suddenly develop hypotension, shock, and sudden death



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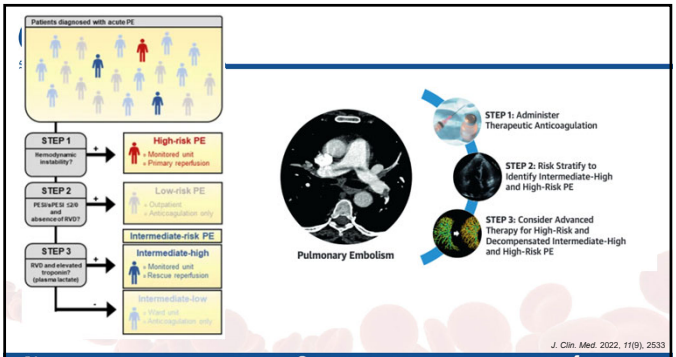

J. Clin. Med. 2022, 11(9), 2533

3

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Risk Stratification

Early mortality risk		Indicators of risk			
		Haemodynamic instability[a]	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥1	RV dysfunction on TTE or CTPA[b]	Elevated cardiac troponin levels[c]
High		+	(+)[d]	+	(+)
Intermediate	Intermediate–high	-	+[e]	+	+
	Intermediate–low	-	+[e]	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

Konstantinides SV. ESC Guidelines. Eur Heart J. 2020 Jan 21;41(4):543-603.

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4

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Table 1. Original and Simplified Pulmonary Embolism Severity Index (PESI)

Variable	Score: Original PESI[a]	Score: Simplified PESI[b]
Age >80 y	Age in years	1
Male sex	+10	
History of cancer	+30	1
History of heart failure	+10	1[c]
History of chronic lung disease	+10	
Pulse ≥110 beats/min	+20	1
Systolic blood pressure <100 mm Hg	+30	1
Respiratory rate ≥30 breaths/min	+20	
Temperature <36°C	+20	
Altered mental status	+60	
Arterial oxyhemoglobin saturation level <90%	+20	1

Normotensive patients with acute pulmonary embolism

Modified FAST score:

Heart rate ≥ 100 bpm 2 points | Syncope 1.5 points | Elevated troponin 1.5 points

<3 points: Low-risk for adverse in-hospital outcome

≥3 points: intermediate-high risk for adverse in-hospital outcome

The present study validated the modified FAST score as a simple tool for rapid risk stratification of normotensive patients with pulmonary embolism

Table 1. *Modified Bova score*

Predictor variable	Points
Systolic blood pressure < 100 mmHg	2
Cardiac troponin I > 0.04 ng/ml	2
Right ventricular dysfunction	2
Heart rate ≥ 110 beats/min	1

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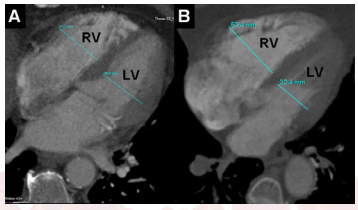
RV/LV ≥0.9 ratio is independent predictor of adverse outcomes



Piazza G. J Am Coll Cardiol. 2020 Nov 3;76(18):2117-2127

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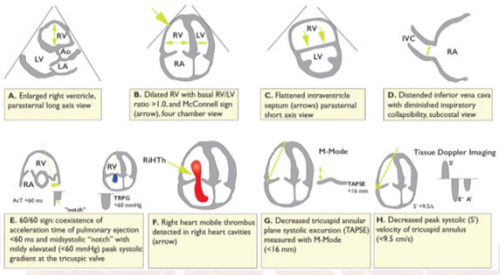
Echocardiographic Predictors of Risk in PE



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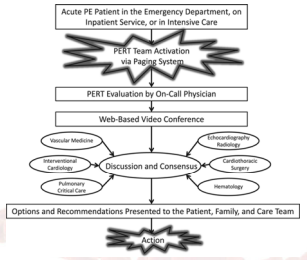

6.8 Recommendations for multidisciplinary pulmonary embolism teams

Recommendation	Class[a]	Level[b]
Set-up of a multidisciplinary team and a programme for the management of high- and (in selected cases) intermediate-risk PE should be considered, depending on the resources and expertise available in each hospital.	IIa	C

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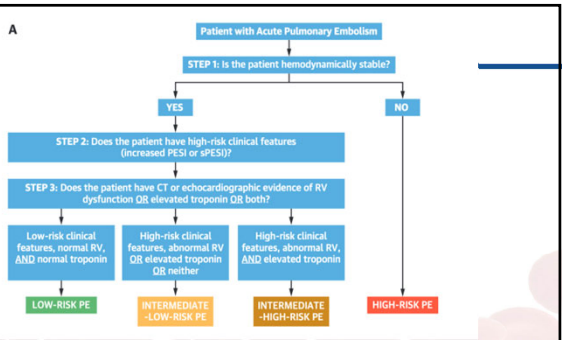

Piazza G. J Am Coll Cardiol. 2020 Nov 3;76(18):2117-2127

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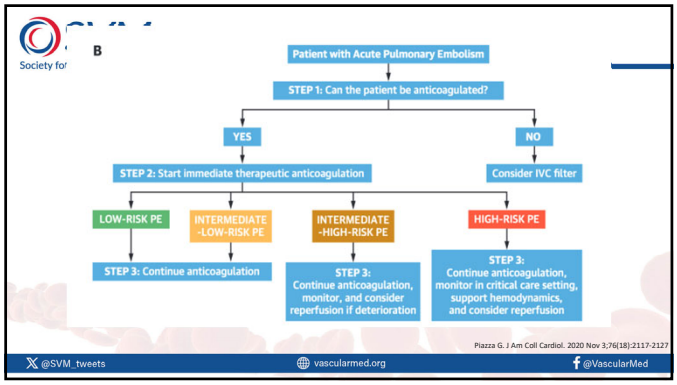
B
Patient with Acute Pulmonary Embolism
STEP 1: Can the patient be anticoagulated?
YES
NO
STEP 2: Start immediate therapeutic anticoagulation
Consider IVC filter
LOW-RISK PE
INTERMEDIATE -LOW-RISK PE
INTERMEDIATE -HIGH-RISK PE
HIGH-RISK PE
STEP 3: Continue anticoagulation
STEP 3: Continue anticoagulation, monitor, and consider reperfusion if deterioration
STEP 3: Continue anticoagulation, monitor in critical care setting, support hemodynamics, and consider reperfusion
Piazza G. J Am Coll Cardiol. 2020 Nov 3;76(18):2117-2127
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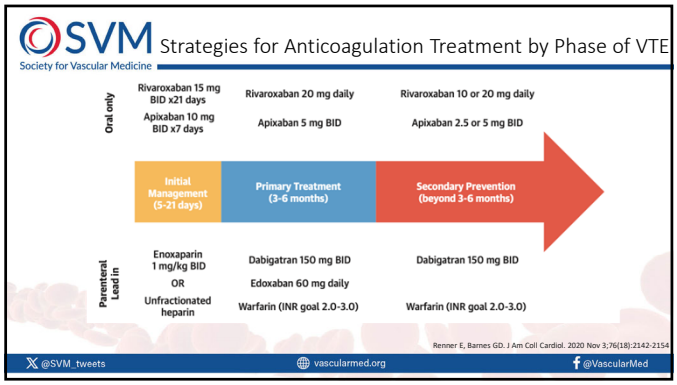
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Strategies for Anticoagulation Treatment by Phase of VTE
Oral only
Rivaroxaban 15 mg BID x21 days
Apixaban 10 mg BID x7 days
Rivaroxaban 20 mg daily
Apixaban 5 mg BID
Rivaroxaban 10 or 20 mg daily
Apixaban 2.5 or 5 mg BID
Initial Management (5-21 days)
Primary Treatment (3-6 months)
Secondary Prevention (beyond 3-6 months)
Parenteral Lead in
Enoxaparin 1 mg/kg BID
OR
Unfractionated heparin
Dabigatran 150 mg BID
Edoxaban 60 mg daily
Warfarin (INR goal 2.0-3.0)
Dabigatran 150 mg BID
Warfarin (INR goal 2.0-3.0)
Renner E, Barnes GD. J Am Coll Cardiol. 2020 Nov 3;76(18):2142-2154
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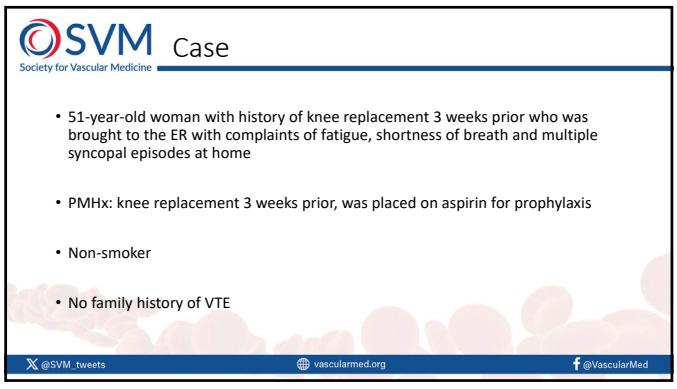
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Case
• 51-year-old woman with history of knee replacement 3 weeks prior who was brought to the ER with complaints of fatigue, shortness of breath and multiple syncopal episodes at home
• PMHx: knee replacement 3 weeks prior, was placed on aspirin for prophylaxis
• Non-smoker
• No family history of VTE
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Vitals and Labs

- Appears lethargic and with cyanotic lips
- Vitals:
  - HR: 120-130s
  - BP: 110/64 mmHg
  - O2 Sat: 70% → required non-rebreather 15L
- Labs:
  - hsTrop: 636
  - BNP: 1653
  - Lactate: 3.5

13

- *How would you risk stratify this patient?*
- *Which factors elevate her risk?*

14

Risk Stratification

- Factors that reflect higher risk
  - Syncope
  - Altered mental status
  - Tachycardia
  - Oxygen requirement
  - Elevated troponin and BNP
  - Elevated lactate
- PESI Score: 125 points – Class V – very high risk
- BOVA score: 5 points – stage III – high risk

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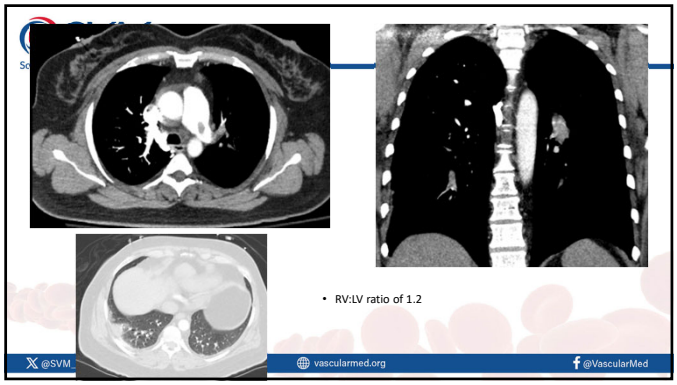
• RV:LV ratio of 1.2
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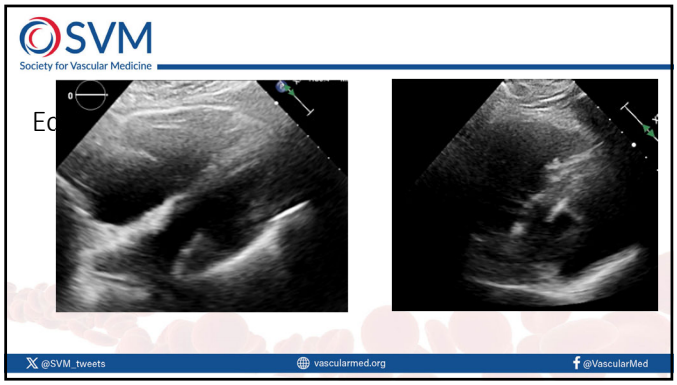
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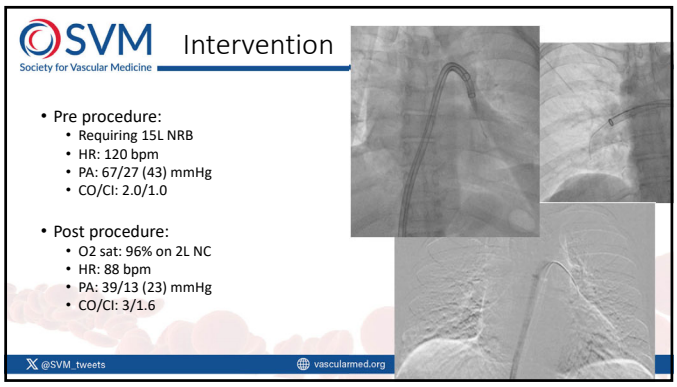
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Intervention
• Pre procedure:
• Requiring 15L NRB
• HR: 120 bpm
• PA: 67/27 (43) mmHg
• CO/CI: 2.0/1.0
• Post procedure:
• O2 sat: 96% on 2L NC
• HR: 88 bpm
• PA: 39/13 (23) mmHg
• CO/CI: 3/1.6
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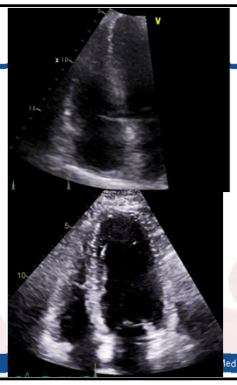
- POD 1 Echocardiogram
  - Improved RV size and function
  - On 2L NC
- POD 3 discharged home on Apixaban
  - Off oxygen
- 1 month follow up echo with normal RV size and function



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Take Home Points

- Patients with intermediate- and high-risk PE represent the populations at highest risk for early mortality
- Risk stratification tools, imaging, and multidisciplinary expertise are key in identifying best management approach in a case-by-case basis
- Selection of advanced therapies depends on assessment of the patient's risk of adverse outcomes

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Consultant Case Files: The Swollen Limb

Alexandra Solomon, MD, RPVI

March 16th, 2024

1

Disclosures

- None, but any are welcome!

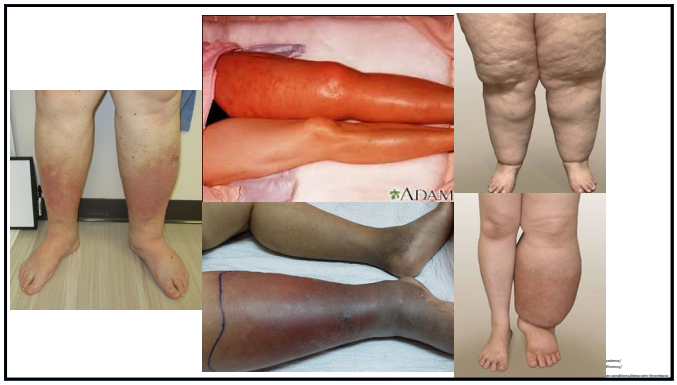
2

Learning Objectives

At the end of this session, participants will be able to:

1. Devise a differential diagnosis for limb edema.
2. Complete a comprehensive diagnostic workup.
3. Outline the basics of limb edema management.

3



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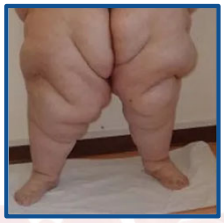
Our Patient

- 50 yo woman
- Bilateral leg swelling for many years
- Progressively worsening
- Legs feel like “cement” or “quicksand”
- Diuretics and elevation do not help
- Severely impacting quality of life



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Differential Diagnosis of Lower Extremity Edema

- Cardiac
  - heart failure, pulmonary hypertension
- Vascular
  - Arterial vasodilation, venous insufficiency, venous obstruction (intrinsic or extrinsic)
- Lymphedema
- Lipedema
- Renal failure/nephrotic syndrome
- Liver disease
- Thyroid disease
- Malignancy
- Musculoskeletal
- Trauma/injury
- Nutritional
- Infectious – cellulitis, filariasis
- Iatrogenic
- Pregnancy/hormonal
- Other – idiopathic, CRPS, etc.
- Medication-related
  - Dihydropyridine calcium channel blockers, vasodilators, steroids, hormone replacement, gabapentin, pregabalin, antineoplastic agents, anti-parkinson medications, MAOIs, trazodone, NSAIDs, PPIs, etc.

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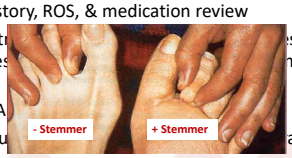
Clinical Evaluation of Lower Extremity Edema

- Comprehensive history, ROS, & medication review
- **Physical Exam:** dist…s, evidence of phlebitis, tenderne…onary evaluation
  - **Stemmer sign**



- **Labs**: CBC, CMP, UA
- **Imaging:** venous du…am, CT/MR

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Return to Patient Case

- O2-dependent due to a paralyzed LEFT hemidiaphragm
- HFpEF – does not follow with cardiology
- Diabetes complicated by gastroparesis and nephrotic syndrome
- Hypothyroidism and anemia
- Previously saw 3 vascular specialists:
  1. Venous insufficiency and needed procedure
  2. No procedure recommended
  3. Weight loss advised
- **Medications:** torsemide, levothyroxine

Recent Laboratory Results:
- Hgb 9.1
- Creatinine 2.1 w/ eGFR 28
- Albumin 2.9
- TFTs wnl

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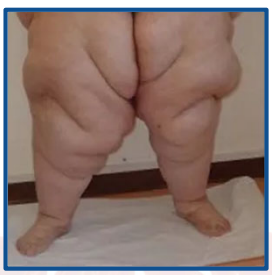
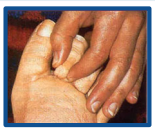
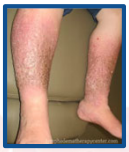
Physical Exam

- BMI 62
- T 98.4
- BP 129/78 mmHg
- HR 72 bpm
- SpO2 95% 2L NC O2
- Cardiopulmonary exam limited due to body habitus







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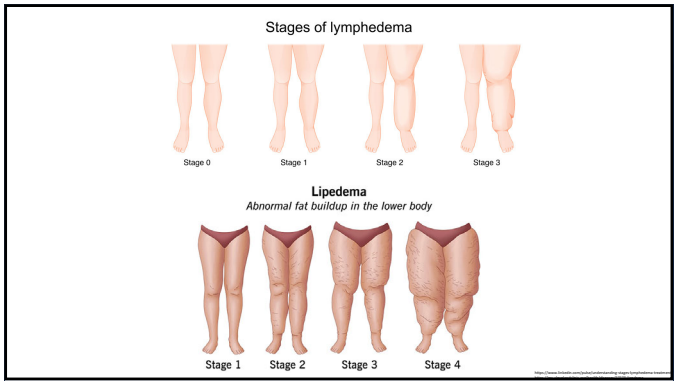

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Patient Case Wrap-Up

- Venous duplex US negative for DVT
- **Lipolymphedema**
  - Advanced lipedema → lymphatic obstruction and accumulation of lymphatic fluid
- & Nephrotic Syndrome
- & Malnutrition/hypoalbuminemia
- & Heart failure
- & Hypothyroidism (controlled)

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"Patients can have as many diseases as they damn well please."

Dr. John B. Hickam

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Basics of Lower Extremity Edema Management

- Elevation
- Low-salt diet
- Diligent skin care
- Comfortable footwear
- Regular physical activity
- Compression therapy (30 mmHg)
- Optimize other medical conditions

- **Lymphedema:** manual lymphatic drainage and pneumatic compression pump
- **Lymphedema/Lipedema:** Weight loss (?GLP-1 RA)
- **Advanced Therapies:** excision, liposuction, LNT, LVA

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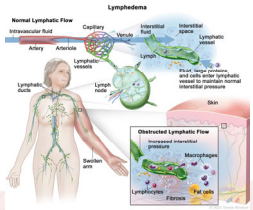
A Quick Word on Diuretics & Lymphedema

- Diuretics remove water
- Lymphedema is **NOT** a water problem
- Lymphatic fluid is protein-rich
- Diuretics do **NOT** improve the swelling from lymphedema



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Take Home Points

- Lower extremity edema has many possible etiologies (and often multiple at once)
  - Don't forget to review that medication list!
- Lymphedema is caused by an abnormality of lymphatic drainage, leading to a build up of protein-rich fluid in the interstitium. Stemmer sign is positive.
- Lipedema affects women and is caused by an abnormal deposition of adipose tissue in the legs. Stemmer sign is negative (initially).
- Diuretics do not treat swelling due to lymphedema or lipedema!
- Conservative management of leg edema includes compression, elevation, diligent skin care, low-salt diet, physical activity, and weight loss.

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Thank you!

Alexandra Lauren Solomon, MD, RPVI
alsolomon181@gmail.com

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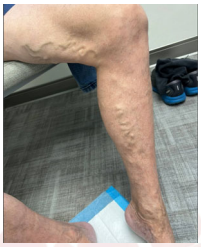
Consultant Case Files: Venous Insufficiency

Katherine Hays DNP, ACNP-BC, FSVM
OhioHealth Heart and Vascular
Columbus OH

1

History:

- 68 yo male, retired roofer with LEFT only varicose veins
- PMH: BPH, history of colon CA in remission, history of SVT
- PSH: colon resection
- Meds: Flomax, ASA



2

Venous Claudication? Arterial Claudication? Or Pseudoclaudication?

- Heaviness
- Aching
- Swelling
- Throbbing
- Itching

- When do symptoms occur? Day/night, when walking/with prolonged standing
- What helps relieve the symptoms? Elevation, NSAIDS
- Have they tried compression? If so, did compression help

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Other Pertinent History:

- History of prior vein or arterial surgeries/procedures?
- Family history of venous disease?
- Personal or family history of thromboembolic events?
- History of venous hemorrhage
- History of venous ulcer

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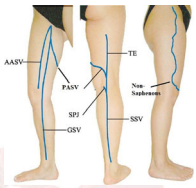
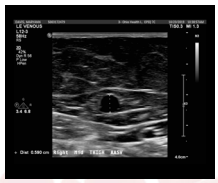
Anatomy – Superficial System





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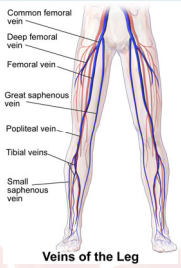
Anatomy - Deep System

- Reflux
- Obstruction
  - Post thrombotic changes
  - May Thurner



Veins of the Leg

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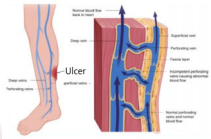
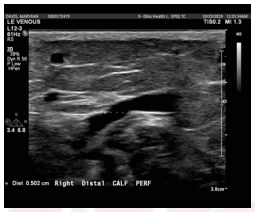
Anatomy - Perforators





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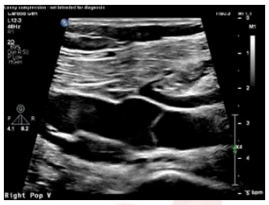
Venous Homeostasis

- Normal Central Pump
- Pressure gradient between the veins and the right atrium
- Intact venous valves
- Normal muscle pumps



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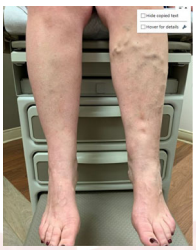
Physical Exam

- Location of Swelling
  - Bilateral, L>R (iliofemoral or iliocaval compression)
  - Above the knees, generalized? (systemic, cardiac)
  - BLE and left arm (thoracic outlet)
- Size and Distribution of Varicosities
  - Saphenous vs Non-saphenous
  - Large in diameter



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Revised CEAP Classification

CEAP classification	
Clinical classification	
C0	No visible or palpable signs of disease
C1	Telangiectasias or reticular veins
C2	Varicose veins
C3	Edema
C4a	Pigmentation or eczema
C4b	Lipodermatosclerosis or atrophic blanche
C5	Healed venous ulcer
C6	Active venous ulcer
S	Symptomatic, including ache, pain, tightness, skin irritation, heaviness, muscle cramps, and other complaints attributable to venous dysfunction
A	Asymptomatic
Etiologic classification	
Ec	Congenital
Ep	Primary
Es	Secondary (post-thrombotic)
En	No venous cause identified
Anatomic classification	
As	Superficial veins
Ap	Perforator veins
Ad	Deep veins
An	No venous location identified
Pathophysiologic	
Pr	Reflux
Po	Obstruction
Pr, o	Reflux and obstruction
Pn	No venous pathophysiology identifiable

Fluoroscopy-Guided Endovenous Sclerotherapy Using a Microcatheter Prior to Endovenous Laser Ablation: Comparison between Liquid and Foam Sclerotherapy for Varicose Tributaries - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/CEAP-Classification-for-Chronic-Venous-Disease_tbl1_264203524 [accessed 21 Feb, 2024]

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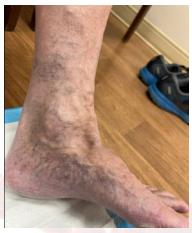
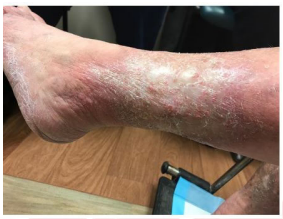
Corona Phlebectatica



Atrophie Blanche



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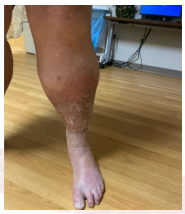
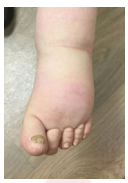
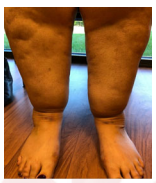
Lipodermatosclerosis (LDS)
Venous Eczema



Lymphedema vs lipedema





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VCSS (Venous Clinical Severity Score)

Attribute	Absent = 0	Mild = 1	Moderate = 2	Severe = 3
Pain	None	Occasional, not restricting activity or requiring analgesics	Daily, moderate activity limitation, occasional analgesics	Daily, severe limiting activities or requiring regular use of analgesics
Varicose veins*	None	Few, scattered; branch VV's	Multiple; GS varicose veins confined to calf or thigh	Extensive; thigh *and* calf or GS *and* TS distribution
Venous edema†	None	Evening ankle edema only	Afternoon edema, above ankle	Morning edema above ankle *and* requiring activity change, elevation
Skin pigmentation‡	None or focal, low intensity (tan)	Diffuse, but limited in area, and old (brown)	Diffuse over most of gaiter distribution (lower 1/3) or recent pigmentation (purple)	Wider distribution (above lower 1/3) *and* recent pigmentation
Inflammation	None	Mild cellulitis, limited to marginal area around ulcer	Moderate cellulitis, involves most of gaiter area (lower 1/3)	Severe cellulitis (lower 1/3 and above) or significant venous eczema
Induration	None	Focal, circummalleolar (< 5 cm)	Medial or lateral, less than lower third of leg	Entire lower third of leg or more
No. of active ulcers	0	1	2	> 2
Active ulceration, duration	None	< 3 mo	> 3 mo < 1 y	Not healed > 1 y
Active ulcer, size§	None	< 2-cm diameter	2- to 6-cm diameter	> 6-cm diameter
Compressive therapy	Not used or not compliant	Intermittent use of stockings	Wears elastic stockings most days	Full compliance: stockings + elevation

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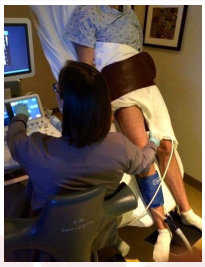
Diagnosis

Venous Insufficiency Study

- Chronic DVT or SVT
- Deep Reflux
- Superficial Reflux
- Pelvic collaterals
- Pulsatile Flow
- Normal Studies



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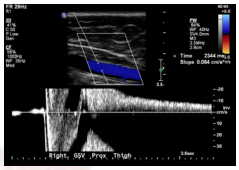
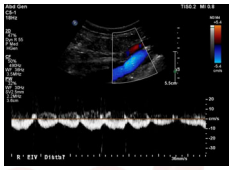
Reflux



Venous Pulsatility



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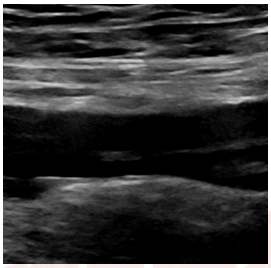
Chronic post-thrombotic changes



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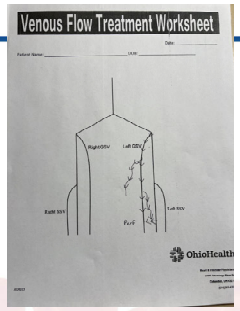
- No deep or superficial thrombosis
- Superficial reflux from the saphenofemoral junction to distal calf
- Refluxing tributaries
- Refluxing distal calf perforator



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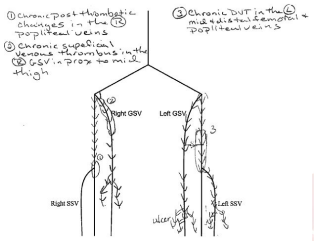
- Chronic deep and superficial post thrombotic changes
- Deep and superficial reflux
- Proximal Obstruction?



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Requirements for treatment

- Conservative Therapy
  - Compression 20-30 mmHg for 3 months
  - Weight loss
  - Exercise
  - Elevation
- Unless venous hemorrhage or ulcer
- Good time to evaluate symptom response

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Venous Duplex requirements:

- Axial reflux involving either saphenofemoral junction or saphenopopliteal junction
- Perforators
  - To be pathologic must have diameter ≥3.5mm with a reflux time ≥500ms
  - AND be under a healed or active ulcer (LDS)
- May have to work with RVTs to find where reflux is coming from
- Remember to think about proximal obstruction

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Procedural Options

- Surgical Stripping and Ligation
  - Junction >1 cm
  - Target vein too superficial
- Catheter Based:
  - Target vein must be amenable to catheter
  - Thermal: RadioFrequency, Laser
  - Non-Thermal: Venoseal
  - MOCA (mechanochemical)
- Non-Catheter:
  - Varithena
  - Physician Compounded Sclerotherapy
  - Phlebectomy

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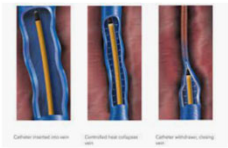
Thermal Ablation

RFA(Radiofrequency)/EVLA(Laser)

- EHIT (Endovenous Heat Induced Thrombosis)
- Pain, Numbness, bruising or hyperesthesias
- Spontaneous thrombosis of veins
- Palpable "cord"
- Tugging sensation at groin, bend of knee
- Skin staining



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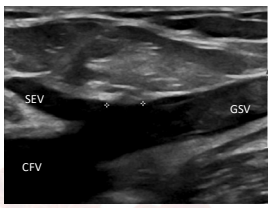
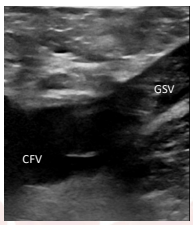
Terminates before SEV



EHIT (Endovascular Heat Induced Thrombosis)



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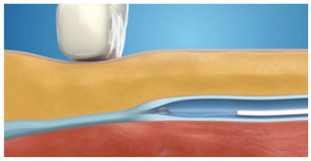
Non-Thermal

Venoseal (Cyanoacrylate)

- Allergic reaction
- Permanent implant
- Spontaneous thrombosis of superficial vein
- Palpable "cord"
- Thrombosis of CFV (rare)
  - Usually due to adjunctive foam



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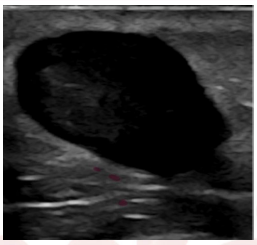
Chemical Ablation

Varithena Microfoam Ablation or Physician Compounded Sclerotherapy

- FIT (foam induced thrombosis)
- Thrombophlebitis of treated vein
- Trapped coagulum
- Skin necrosis or skin injury at insertion site



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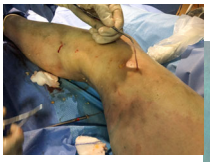
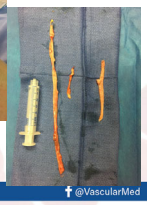
Phlebectomy (Foam Assisted)

- Uses foam sclerotherapy in target vein
- Trapped coagulum
- Wound site infections
- Pain, numbness
- Skin staining
- Bleeding (rare)





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Best Treatment Options for this patient:

1) Venoseal with phlebectomy
   - Not likely covered by insurance but lowest thrombotic risk given history
2) RFA with phlebectomy
   - Better thermal option than laser
   - Prophylaxis with DOAC
3) RFA with sclerotherapy
   - Large cord will take several months to resolve
4) Varithena
   - Highest thrombotic risk
   - Not preferred for saphenous veins still in the fascia

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Typical Ulcers: Neuropathic, Venous, Arterial and Mixed Etiology

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Vascular Medicine NP
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Keys to Ulcer Identification

Medical History	Pain	Location
Wound Appearance	Surrounding Skin	Vascular Exam

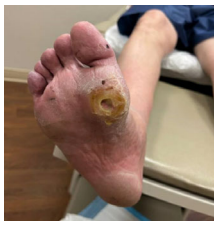
2

Neuropathic Ulcers

- Ulcers which form as a result of neuropathy (loss of sensation), peripheral or central
- Most common: diabetic ulcers due to diabetic neuropathy
- History: Diabetes, peripheral neuropathy
- Pain: not painful or paresthesia present
- Location: Typically occur at pressure points on bony prominences (heel, hallux, phalanx)
- Often begin as callus formation which goes unnoticed due to the neuropathy

3

- Wound Appearance: black, grey or yellow
- Surrounding Skin: often have callus, pale, reticular pattern, Charcot Foot, Hammer Toe
- Vascular Exam: Pulses usually present, ABI non-compressible,



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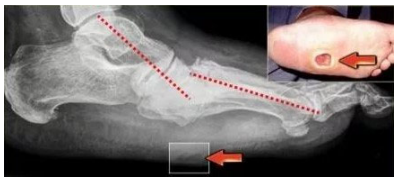
Charcot Foot Ulcer



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Arterial Ulcers

- Occur as the result of decreased arterial blood flow or embolism (thrombotic or athero-embolic)
- Can be large or small vessel disease
- History: HLD, HTN, Smoker, Age>45, claudication, slow progression
- Pain: moderate to severe, claudication, increases with elevation, decreases with dependency
- Location: lateral malleolus, anterior tibial, bony prominences

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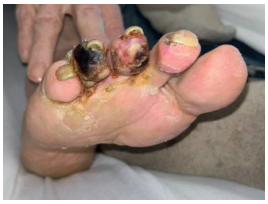
- Wound Appearance: well demarcated, punched out, pale or white base
- Surrounding Skin: dry eschar, pale or cyanotic, cool, Hair loss, shiny/thin, dependent rubor
- Vascular Exam: poor or absent pulses, Abnormal ABI, dependent rubor, pallor with elevation, poor capillary refill



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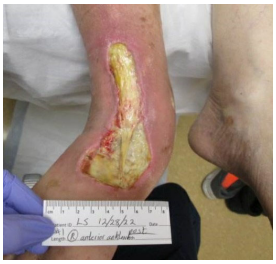

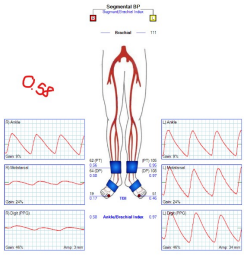

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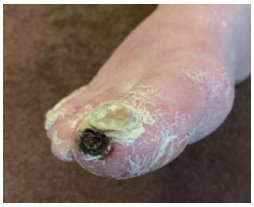

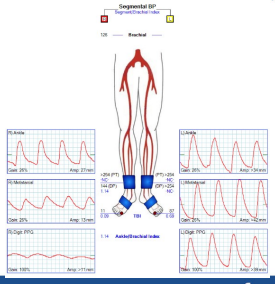

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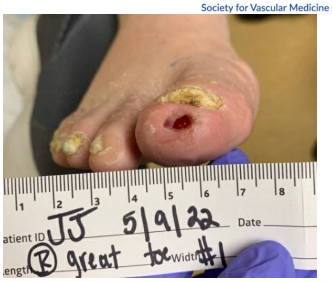
- Chronic total occlusion of a heavily calcified distal right anterior tibial artery
- Status post recanalization using rotational atherectomy, and prolonged balloon angioplasty



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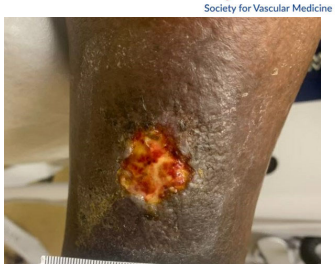
Venous Ulcers

- Occur due to the chronic inflammation and pressure generated by long term swelling
- May be the result of venous insufficiency or chronic venous hypertension
- History: rapid onset, edema, trauma, thrombophlebitis
- Pain: mild to moderate, increases with dependency, decreased with elevation
- Location: medial/lateral ankle, lower calf



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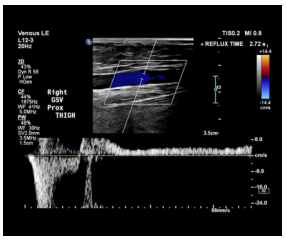
- Appearance: irregular border, base with granulation tissue, exudative, weeping
- Surrounding skin: hyperpigmentation, hyperkeratotic borders, edema, stasis dermatitis
- Vascular Exam: pulses likely normal, ABI normal, abnormal venous insufficiency study



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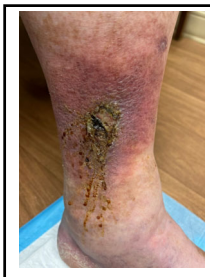
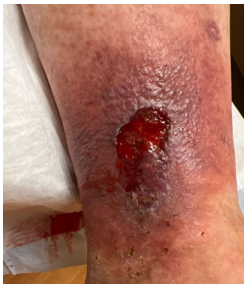


Initial Consultation

Post-Debridement



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Mixed Etiology

- Considered when there are multiple contributing factors: venous, arterial, lymphedema, infection
- Determined by physical exam findings and testing

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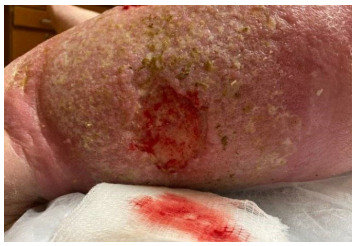
Phlebolymphedema



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Consultant Case Files: Hypercoagulable States

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System Medical Director – Vascular Medicine & Vascular Labs - OhioHealth Heart and Vascular

President – Syntropic Core lab

Adjunct Clinical Professor of Medicine – Ohio University HCOM

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Disclosures

- **Consultant/Advisor/ DSMB/ CEC -**
  - Abbott, Auxetics, Boston Scientific, Diachii Sankyo, Koya Medical, Medtronic, NAMSA, Penumbra, Philips, PERC, Surmodics, USA Therm, VB Devices
- **Board of Trustee**
  - The VIVA Foundation
  - American Vein and Lymphatic Society
  - Intersocietal Accreditation Council | Vascular Testing
- **President**
  - Syntropic Core Lab

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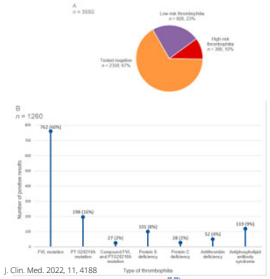
Thrombophilia: Prevalence

Thrombophilia	General Population (%)	Patients with 1st VTE (%)	Family History of Thrombosis (%)
Factor V Leiden	3-7	20	50
Prothrombin Gene Mutation	1-3	6	18
Antiphospholipid Antibodies	0-7	5-15	?
Protein C Deficiency	0.2-0.4	3	6-8
Antithrombin Deficiency	0.02	1	4-8
Protein S Deficiency	?	1-2	3-13
Elevated Factor VIII	11	25	

Rosendaal FR. *Semin Hematol.* 1997;34:171.



J. Clin. Med. 2022, 11, 4188

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Classifying Major Thrombophilias

Table 1. Thrombophilia Classification

Thrombophilia	Arterial/Venous Thrombosis	Inherited/Acquired	Relative Risk of Initial Thrombosis
Factor V Leiden	Venous	Inherited	↑ Heterozygous ↑↑ Homozygous
Prothrombin gene mutation	Venous	Inherited	↑ Heterozygous ↑↑ Homozygous
Protein C deficiency	Venous	Inherited	↑↑
Protein S deficiency	Venous	Inherited	↑↑
Antithrombin deficiency	Venous	Inherited	↑↑
Hyperhomocysteinemia	Arterial/venous	Rarely inherited/most often acquired	↑ If mild to moderate ↑↑ If severe
Antiphospholipid antibodies	Arterial/venous	Acquired	↑↑

Piazza G. Circulation. 2014;130:283.

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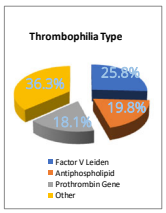
Thrombophilia Testing in the Real World: RIETE

- N = 21,367 consecutive patients with symptomatic VTE.
- Thrombophilia testing was performed in 21%.
- Thrombophilia was detected in 32%.
- The rate of thrombophilia was similar in patients with idiopathic VTE and those with provoked events.



Roldan V, et al. *Thromb Res*. 2009;124:174.

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Journal of Thrombosis and Haemostasis, 6: 1474–1477 DOI: 10.1111/j.1538-7836.2008.03055.x

ORIGINAL ARTICLE

Testing for inherited thrombophilia does not reduce the recurrence of venous thrombosis

- Multiple Environmental and Genetic Assessment of risk factors for venous thrombosis (MEGA) study
- 5051 patients (18-70 years) screened
- 197 Recurrences; 324 No recurrences (Controls)

Journal of Thrombosis and Haemostasis, 6: 1474–1477

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MEGA study

Table 2 Incidence of thrombophilia tests in cases and controls, and odds ratios for recurrent venous thrombosis in tested vs. non-tested patients

Subgroups	% tested: Cases	% tested: Controls	Odds ratios for recurrence (tested vs. non-tested)*
All	35	30	1.2 (0.8–1.8)
Quartiles of age (in years)			
18.3–40.1 (n = 130)	51	39	1.9 (0.8–4.6)
40.1–50.9 (n = 130)	39	35	1.1 (0.4–2.5)
51.1–60.9 (n = 131)	26	29	0.9 (0.4–2.2)
61.0–69.8 (n = 130)	24	18	1.0 (0.4–2.9)
Sex			
Men	31	26	1.1 (0.6–2.0)
Women	41	35	1.4 (0.7–2.9)
Risk factors for first venous thrombosis			
Surgery/trauma/immobilization	23	21	1.2 (0.5–3.1)
OCP/HRT	60	32	3.4 (1.3–8.6)
Non/idiopathic	30	33	0.8 (0.5–1.6)
Family history of venous thrombosis			
Present	47	39	1.5 (0.7–3.1)
Absent	29	26	1.1 (0.7–1.9)
Thrombophilia†			
Present	33	33	0.8 (0.3–2.6)
Absent	36	29	1.3 (0.8–2.1)

OCP, oral contraceptive pill; HRT, hormone replacement therapy. *Adjusted for sex, age, year of first thrombotic event, presence of clinical risk factor that provoked the first thrombotic event, and positive family history, whenever applicable. †Either factor V Leiden mutation or prothrombin 20210A mutation.

OCP/HRT – Could not be explained

Journal of Thrombosis and Haemostasis, 6: 1474–1477

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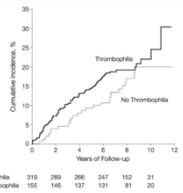
The Leiden Thrombophilia Study

- 474 patients followed prospectively for 7.3 years
- Annual risk 2.6%
- Recurrence 19.3% (Men) vs. 7.4% (women); HR 2.7

Figure 2. Cumulative Incidence of Recurrent Thrombotic Events



Patients with and without thrombophilia during the period from the end of the initial anticoagulation period (90 days) until January 1, 2000. The crude hazard ratio of thrombophilia compared with no thrombophilia was 1.3 (95% confidence interval, 0.8–2.0); the hazard ratio adjusted for age, sex, and oral anticoagulation as a time-dependent covariate was 1.4 (95% confidence interval, 0.9–2.2).

JAMA. 2005;293:2352-2361

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The Leiden Thrombophilia Study

- Prothrombotic abnormalities do not appear to play an important role in the risk of a recurrent thrombotic event.
- Testing for prothrombotic defects has little consequence with respect to prophylactic strategies.

Table 4. Recurrence Rates for Prothrombotic Laboratory Abnormalities in 474 Patients

Abnormality	No. of Recurrences	Incidence Rate (95% CI)*	Hazard Ratio (95% CI)†	Hazard Ratio (95% CI)‡
Factor V Leiden	20	30 (18–46)	1.2 (0.7–1.9)	1.3 (0.8–2.1)
Prothrombin G20210A	4	19 (5–48)	0.7 (0.3–2.0)	0.7 (0.3–2.0)
Anticoagulant deficiency§	8	45 (19–88)	1.8 (0.9–3.7)	1.8 (0.9–3.8)
High factor¶				
VIII (>166 IU/dL)	23	29 (18–43)	1.1 (0.7–1.8)	1.3 (0.8–2.1)
IX (>129 U/dL)	13	21 (11–36)	0.9 (0.5–1.7)	1.2 (0.6–2.1)
XI (>121 U/dL)	11	16 (8–29)	0.6 (0.3–1.1)	0.6 (0.3–1.1)
Hyperfibrinogenemia‖	22	38 (24–58)	1.6 (1.0–2.6)	1.7 (1.1–2.8)
Hyperhomocysteinemia#	14	23 (13–39)	0.9 (0.5–1.6)	0.9 (0.5–1.6)

JAMA. 2005;293:2352-2361

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Influence on therapy

	Total	No Influence on Therapy
	n = 3550	*n* = 3050 (85.9)
Negative thrombophilia work-up, *n* (%)	2358 (66)	2171 (71)
Hereditary low-risk thrombophilia, *n* (%)	826 (23)	675 (22)
Hereditary high-risk thrombophilia, *n* (%)	247 (6.3)	157 (5.1)
Antiphospholipid antibody syndrome, *n* (%)	119 (3.4)	47 (1.5)

J. Clin. Med. 2022, 11, 4188

Table 4. Influence of the type of thrombophilia on therapy.

Type of Thrombophilia	OR (95% CI)
Heterozygous factor V Leiden mutation	1 (ref)
Antiphospholipid antibody syndrome	8.26 (5.40–12.62)
Antithrombin < 70%	5.15 (2.84–9.34)
Homozygous factor V Leiden mutation	3.93 (2.10–7.34)
Protein S < 59%	1.99 (1.21–3.27)
Heterozygous prothrombin 20210G>A mutation	1.89 (1.24–2.90)
Homozygous prothrombin 20210G>A mutation	2.79 (0.25–31.07)
Protein C < 69%	2.17 (0.88–5.33)

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APLA and DOAC

	RAPS [79]	TRAPS [7,82]	ASTRO-APS [7,83]
Chief Investigator	H. Cohen	V. Pengo	S. Woller
Study design	Phase 2/3 RCT	Phase 3 RCT	Phase 2/3 RCT
No. of patients	116	536	200
APS subgroups	Previous VTE, target INR of 2.5; no thrombosis > 3 months; patients with arterial thrombosis excluded	Triple-positive thrombotic APS; arterial, venous and/or biopsy-proven microthrombosis	Thrombotic APS, VTE or arterial, target INR of 2.3, 3.0 or 3.5; no thrombosis > 6 months; definite, likely or historical APS
Intervention	Rivaroxaban 20 mg once daily versus warfarin target INR of 2.5	Rivaroxaban 20 mg once daily versus warfarin target INR of 2.5	Apixaban 2.5 mg or 5 mg twice daily versus warfarin target INR of 2.5
Primary outcome(s)	Thrombin generation – endogenous thrombin potential	Thrombosis – arterial or venous, major bleeding or death (composite)	Thrombosis - arterial and/or venous, bleeding
Duration of recruitment	Jun 2013 to November 2014	December 2014 to January 2018	February 15 to December 2019
Status	Completed and results published	Terminated January 2018 (see text)	Ongoing: protocol modified after potential safety signal (see text)

Journal of Thrombosis and Hemostasis, v16 n6 (June 2018): 1028-1039

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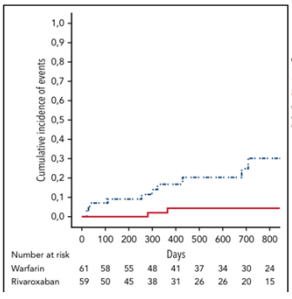

CLINICAL TRIALS AND OBSERVATIONS

Rivaroxaban vs warfarin in high-risk patients with antiphospholipid syndrome

Vittorio Pengo,[1] Gentian Denas,[1] Giacomo Zoppellaro,[1] Seena Padayattil Jose,[1] Ariela Hoxha,[2] Amelia Ruffatti,[2] Laura Andreoli,[3] Angela Tincani,[3] Caterina Canci,[4] Domenico Prisco,[4] Tiziana Fierro,[5] Paolo Gresele,[5] Arturo Cafolla,[6] Valeria De Micheli,[7] Angelo Ghirarduzzi,[8] Alberto Tosetto,[9] Anna Falanga,[10] Ida Martinelli,[11] Sophie Testa,[12] Doris Barcellona,[13] Maria Gerosa,[14] and Alessandra Banzato[1]

Discussion

The aim of the present trial was to evaluate whether a direct oral anticoagulant, rivaroxaban, was noninferior to warfarin in terms of efficacy and safety in high-risk patients with thrombotic APS. However, the trial was stopped prematurely for an excess of events in the rivaroxaban arm. Thromboembolic events, all in

Blood 2018; 132 (13): 1365-1371

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So Why Test?

- Choice of therapy
- Duration of therapy
- Value for family members especially for daughters going on BCPs etc, especially in families with high prevalence of VTE

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Clinical manifestation (Phenotype)- an important aspect in decision making

	AC	Hypercoag Testing	Comments
Situational with transient risks	3 months	No	
Situational with continued risks (acceptable bleeding risk)	Long term	No	
Idiopathic calf DVT or large SVT	3 months	No	Consider ASA 81 after that
Idiopathic large PE or DVT	Long term	Limited	APLA – consider warfarin
Cerebral, portal, retinal vein, mesenteric, renal	Likely long term unless situational	Poor correlation	Consider, APLA, Jak 2, PNH
New VTE while on prophylactic DOACs (and compliant)		Yes	
Patient's insistence		Yes	
When it does not make sense. Example – VTE after a out-patient arthroscopic knee surgery or other minor procedures		Yes	
VTE + Family Hx	Likely long term	Yes	

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Basics

- Don't forget basics – Hammer and Nail
  - Ex - Mild Covid infection 8 weeks prior to VTE Dx → admitted with PE →"Covid induced" → Missed family Hx- **3 family members with VTE!!**
- EVERY PATIENT - Age and gender appropriate cancer screening
- APLA testing - anticardiolipin Ab, Beta 2 glycoprotein -1 Ab, Lupus anticoagulant

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Conclusions

- Hypercoagulable testing not necessary in most cases
- Good history, cancer screening, phenotype assessments are key to proper care of these patients

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16

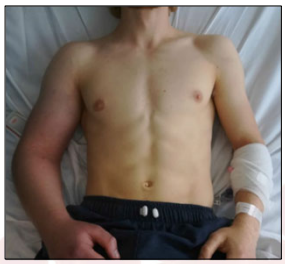
Consultant Case Files: Venous Compression Syndromes

Aaron W. Aday, MD, MSc, RPVI, FSVM
Assistant Professor of Medicine
Vanderbilt University Medical Center

1

Case #1

- 22yo otherwise healthy man with 1 week of right arm swelling and achiness (dominant arm)
- Progressively worsening
- Pitcher for college baseball team, training for new season



Gani A et al. *BMJ Case Rep* 2021;14(2):e240165

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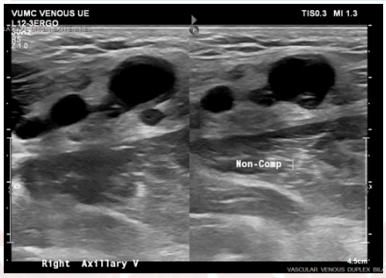
Case #1



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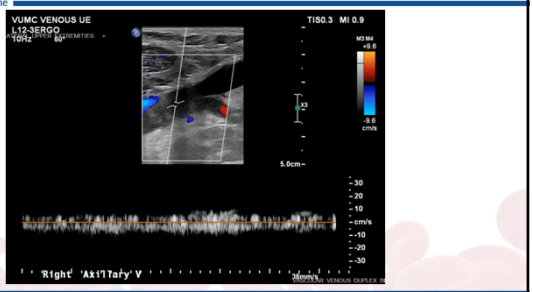
Case #1



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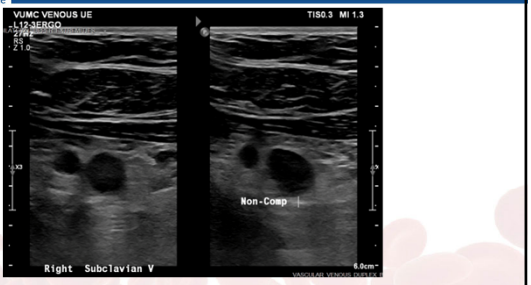
Case #1



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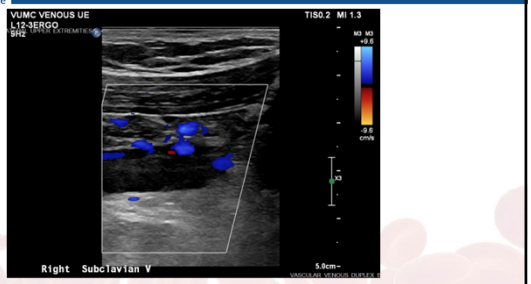
Case #1



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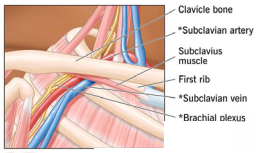
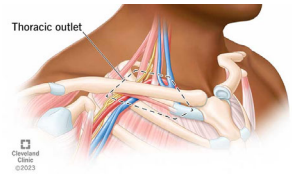
Thoracic Outlet Syndrome





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Thoracic Outlet Syndrome

Table 1. Types of thoracic outlet syndrome (TOS).

Types of TOS	Neurogenic *Most common form of TOS*	Venous *Involvement of the subclavian vein*	Arterial *Involvement of the subclavian artery*
Sex	More common in females (3.5:1)	More common in males	Females/males equally
Typical age	20–40 years	20–30 years	20–30 years
Risk factors	• Repetitive movements • Previous trauma	• Strenuous work using arms • Athletics	• Vigorous arm activity • Trauma
Symptoms	• Pain down arm, forearm, ring finger, and little finger • Tingling/numbness at night • Arm/hand weakness • Arm/hand swelling • Loss of dexterity • Cold intolerance • Headache	• Pain in affected arm often associated with strenuous work • Arm/hand swelling • Veins of shoulder and chest appear more visible • Hand/arm appears blue in color • Blood clot (DVT) may develop	• Pain at rest • Pain with arm activity • Hand appears white in color • Hand/arm cool • Decreased pulse • Aneurysm of subclavian artery may be present • Thrombosis (blood clot) may develop
Lab studies	None	Coagulation studies if DVT develops	Coagulation studies if blood clot develops
Imaging studies	Chest X-ray	Chest X-ray Ultrasound Venography or angiography	Chest X-ray Ultrasound Angiography

Grunebach G et al. *Vasc Med* 2015;20(5):493-495

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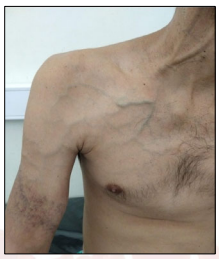
Shoulder/Chest Wall Venous Exam



https://radiopaedia.org/articles/1825

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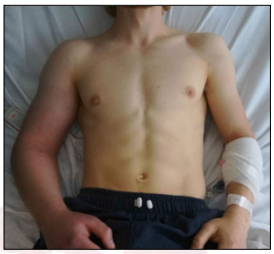
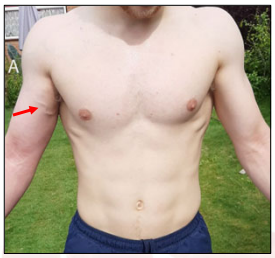
Paget-Schrötter syndrome





Gani A et al. *BMJ Case Rep* 2021;14(2):e240165

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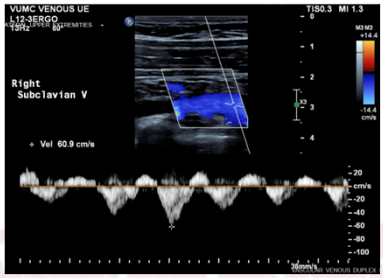
Venous Thoracic Outlet Syndrome



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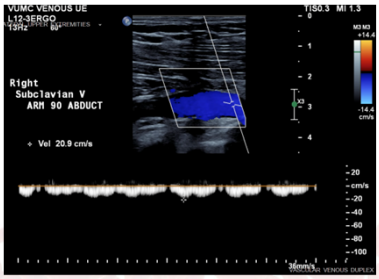
Venous Thoracic Outlet Syndrome



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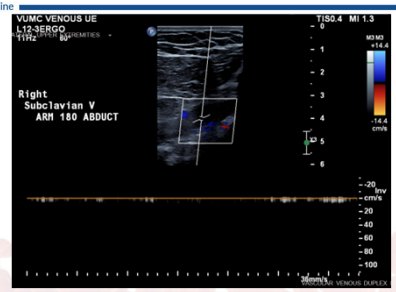
Venous Thoracic Outlet Syndrome



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Venous TOS Treatment

- Anticoagulation
- Thrombectomy/thrombolysis in some cases
- Surgical decompression
- Venous reconstruction
- Venoplasty/stenting
- Long-term management of post-thrombotic syndrome

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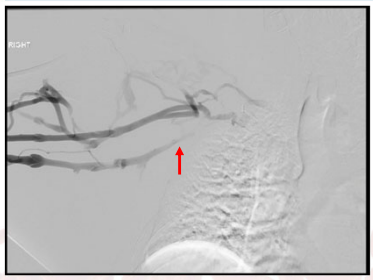
Venous TOS Treatment



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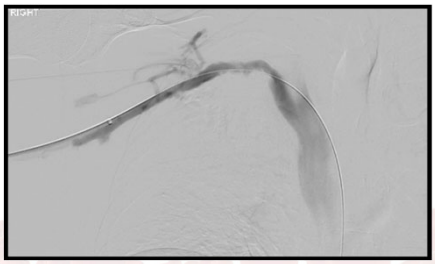
Venous TOS Treatment



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Case #2

- 29yo healthy woman
- Left leg pain and swelling after transcontinental flight
- Recently start OCP
- Difficulty ambulating→ED

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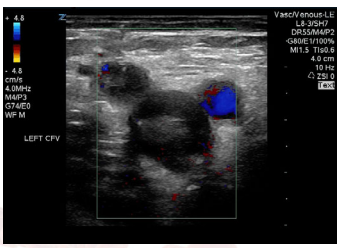
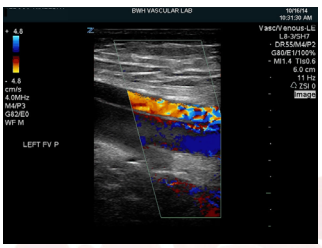
Case #2



Left common femoral vein



Left femoral vein

18

Iliofemoral DVT

Table 1. Anatomic Variants Associated With Increased Risk of Iliofemoral DVT

May-Thurner syndrome
Tumor compression
Vertebral body bone spurs
Congenital IVC/femoral vein anomalies
Retroperitoneal fibrosis
Postpartum uterus
Radiation changes

DVT indicates deep vein thrombosis; and IVC, inferior vena cava.

Aday AW *et al*., *Circulation* 2016;133:1209-1216.

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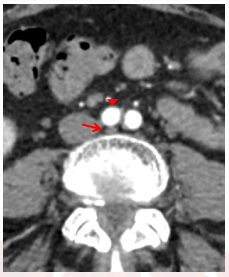
May-Thurner syndrome



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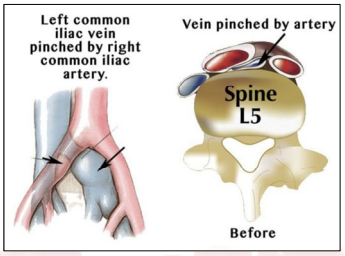
May-Thurner syndrome



https://www.gethealthyveins.com/2021/01/13/may-thurner-syndrome-an-unknown-vascular-condition

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May-Thurner syndrome

Presentation
- Asymptomatic (anatomy only)
- Iliofemoral DVT
- Asymmetric venous insufficiency (spider, reticular, varicose veins)
- Severe post-thrombotic syndrome
- Recurrent limb DVT despite appropriate therapy
- Pelvic congestion symptoms

Treatment
- Nothing
- Conservative therapy (e.g. compression)
- Anticoagulation
- Thrombolysis/thrombectomy
- Venoplasty/stenting

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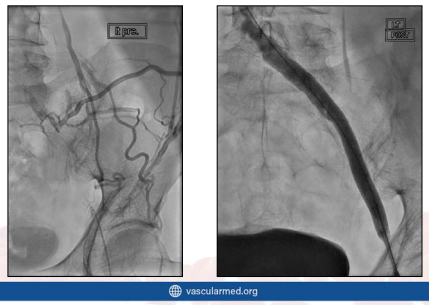
May-Thurner syndrome



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Case #3

- 30yo healthy women with chronic abdominal pain
- Dull, constant pain
- No change with food or defecation.
- Seems to worsen in on feet for extended period
- Notices fullness and heaviness in her pelvic region that doesn't change with menstruation
- Extensive GI workup unrevealing

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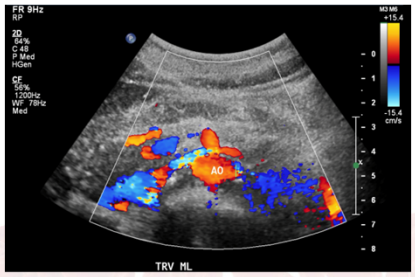
Case #3



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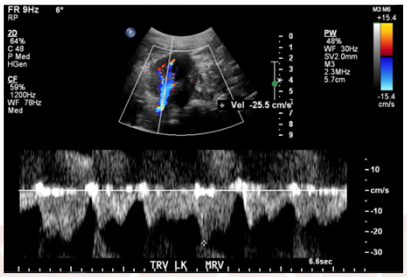
Case #3



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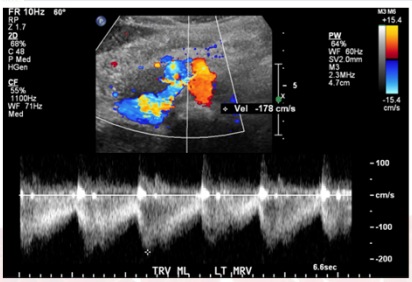
Case #3



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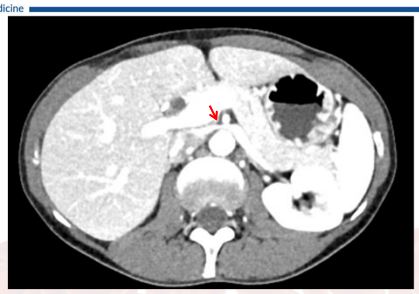
Case #3



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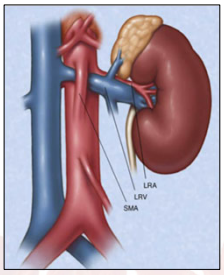
Nutcracker Syndrome



Reed NR et al. *J Vasc Surg* 2009;49(2):386-394

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Nutcracker Syndrome

Presentation
- Typically 20-30s
- Asymptomatic (nutcracker phenomenon)
- Hematuria
- Abdominal/flank pain
- Orthostatic worsening
- Pelvic congestion
- Varicocele

Workup
- Rule out more common diagnoses
- Duplex ultrasound
- CT/MR
- Invasive angiography

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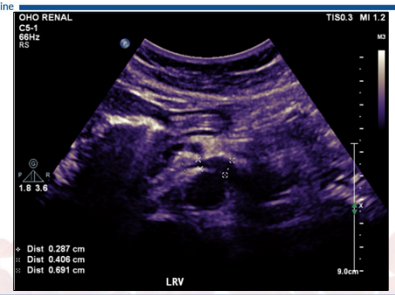
Nutcracker Syndrome



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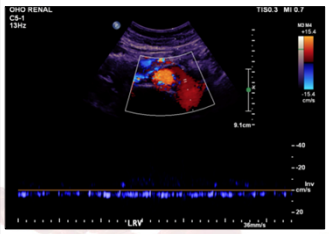
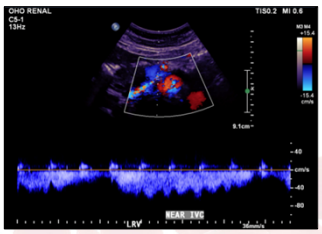
Nutcracker Syndrome





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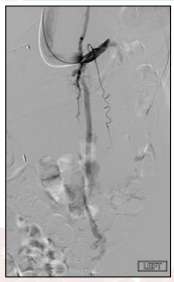
Nutcracker Syndrome



PRESSURE MEASUREMENTS:
Right atrial pressure: 3 mmHg
Free hepatic pressure: 8 mmHg
Wedged hepatic pressure: 11 mmHg

Suprarenal IVC: 4 mmHg
Infrarenal IVC: 7 mmHg
Left renal vein: 13 mmHg.

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Nutcracker Syndrome Treatment

- Observation
- Stenting
- Surgical reconstruction/transposition
- Treatment of pelvic congestion

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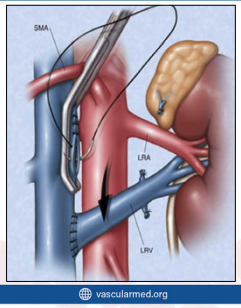
Nutcracker Syndrome Treatment



Reed NR et al. *J Vasc Surg* 2009;49(2):386-394

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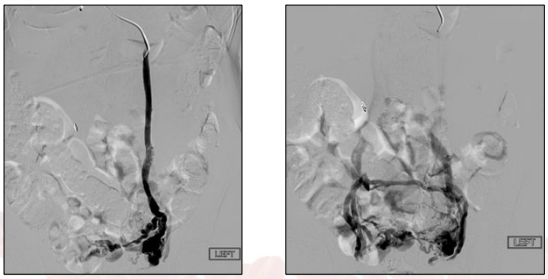
Nutcracker Syndrome Treatment



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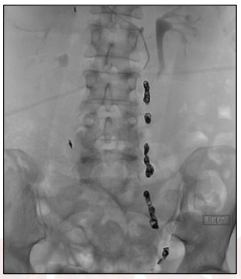
Nutcracker Syndrome Treatment



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Questions?

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