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

* Handout not included in packet

The Pregnant VTE

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1

Disclosure

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

2

VTE in Pregnancy

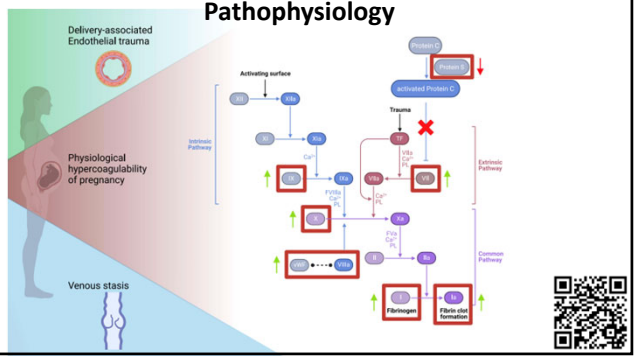
Incidence: 1.2 **per 1,000 deliveries** (5x to 10x)

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

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

3

Pathophysiology



4

VTE in Pregnancy

Prophylaxis

Treatment

Duration?

5

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

6

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

7

7

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%

8

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

Ambulatory | VSS | No Phlegmasia

LMWH | EDD in 4w | Prefers Vaginal Delivery

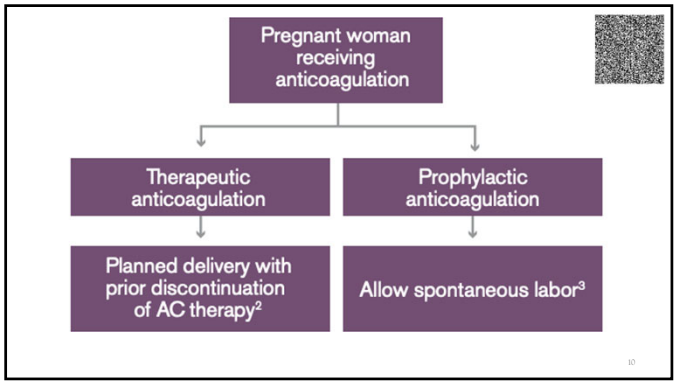
a) Await spontaneous labor, then stop LMWH

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

9



10

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

11

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.*

12

34F | G2P1| EGA 8w

Extremely concerned about getting another DVT

What would you recommend?

(a) No prophylaxis needed

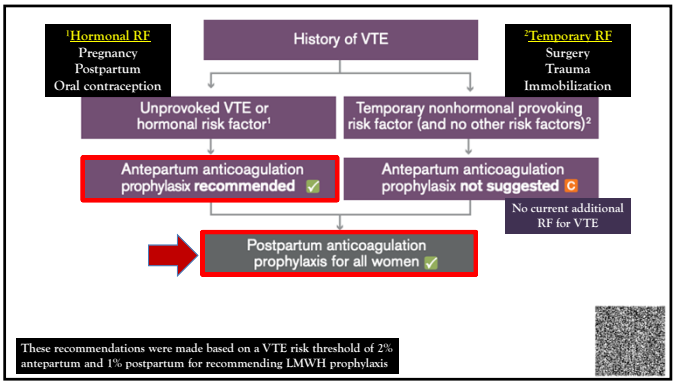
(b) Get a VDUS and Rx only if positive for DVT

(c) Antepartum prophylaxis only

(d) Postpartum prophylaxis only

(e) Antepartum and postpartum prophylaxis

13



14

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%)

15

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

16

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

17

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

18

24F | G1P0 | EGA 30w

No Personal Hx of VTE | +Fam Hx of VTE

Patient has Homozygous PTG mutation

(a) No prophylaxis needed

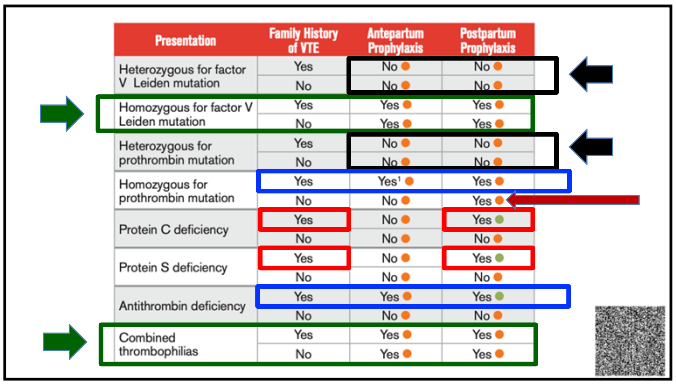
(b) Get a VDUS and Rx only if positive for DVT

(c) Antepartum prophylaxis only

(d) Postpartum prophylaxis only

(e) Antepartum and postpartum prophylaxis

19



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

20

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

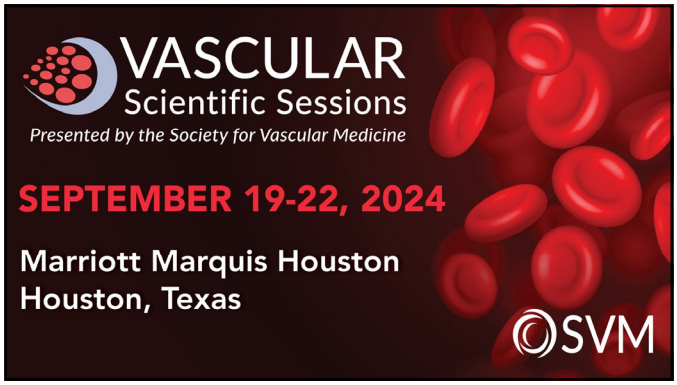
c) Schedule elective CS, stop LMWH 24 hours prior

d) Repeat VDUS and stop LMWH if no DVT

21


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

22


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

23

Calf Vein Thrombus or DVT?

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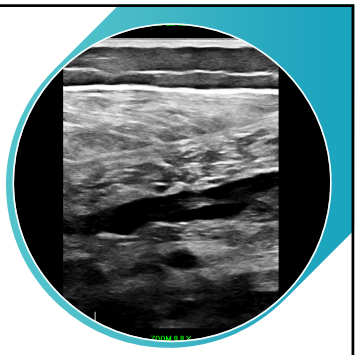
System Medical Director – Vascular Medicine & Vascular Labs - OhioHealth Heart and Vascular

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

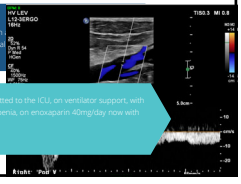
62 year old male with foam sclerotherapy induced thrombosis of the gastrocnemius vein 5 days after endovenous thermal ablation of the GSV and foam sclerotherapy of the tributary veins for C6 disease

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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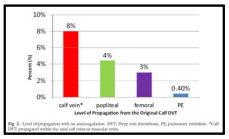
Controversies

- 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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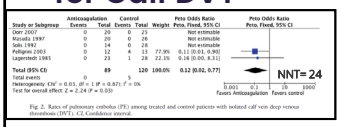
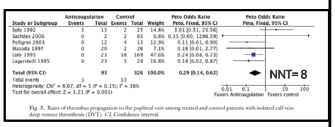
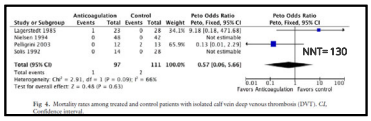
6

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

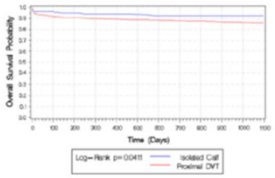

Fig. 3 Cumulative rate of survival without major bleeding stratified by DVT location (isolated calf vs. proximal)

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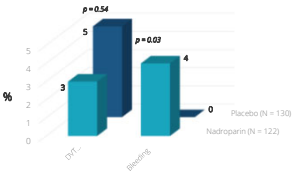
8

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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10

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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11

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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12

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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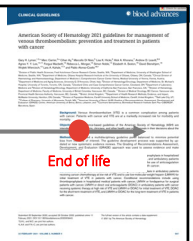
13

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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14

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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15

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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16

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?

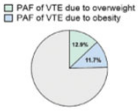
3

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.

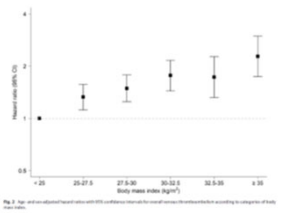
4

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)

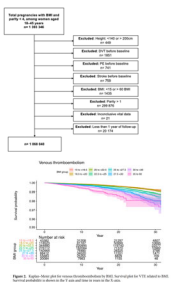


Thromb Haemost 2024;124:239-249.

5

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]

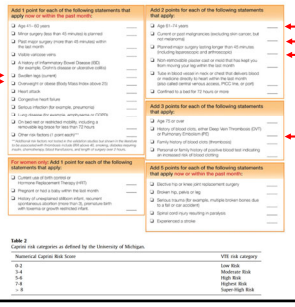


Variable	All	15 ≤ BMI < 18.5	18.5 ≤ BMI < 20	20 ≤ BMI < 22.5	22.5 ≤ BMI < 25	25 ≤ BMI < 27.5	27.5 ≤ BMI < 30	30 ≤ BMI < 35	35 ≤ BMI < 60	p
n	1,068,040	43,382	118,523	344,880	276,112	140,964	68,412	55,683	20,084	
Median follow up, years (IQR)	12.9 (5.9–21.2)	19.6 (8.6–27.3)	17.3 (7.7–26.4)	14.7 (6.7–24.6)	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

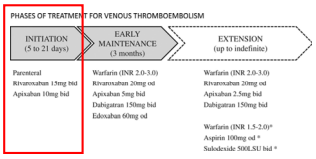
Case

- + 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?



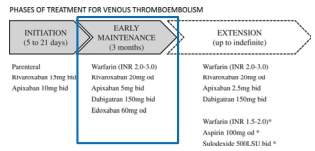
- LMWH or UFH until stable

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.

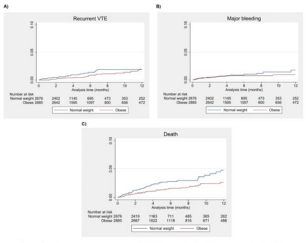


Fig. 2. Kaplan Meier curves: 2A. Recurrent VTE. 2B. Major bleeding. 2C. Death. Abbreviations: VTE: venous thromboembolism.

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

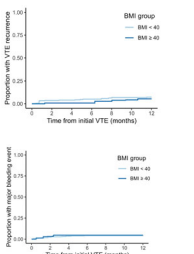


Table 2 Selected primary and secondary outcomes displayed by BMI group, including statistical results from the propensity score analysis

	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

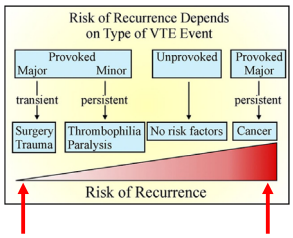
- At 6 months follow up -?discussions regarding AC
  - Can he/should he stop given the current situational event?
  - If he continues – what dose?

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.

16

VTE Recurrence



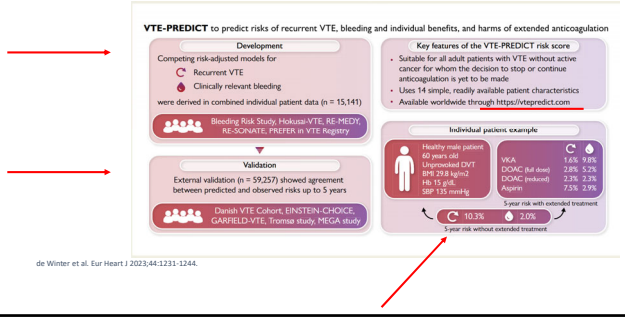
- Clinical features associated with increased risk for VTE and recurrence
  - Age
  - Gender
  - Some thrombophilia
  - Provoked events vs. idiopathic events
  - Biomarkers
  - Patient co-morbidities – IBD, CTD, immobility, obesity, smoking, cancer

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

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

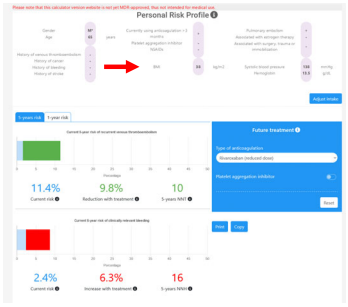
17

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

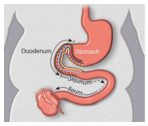
6). We suggest not to use DOAC for treatment or prevention of VTE in the acute setting after bariatric surgery (because of concerns of decreased absorption), and instead, to initiate such patients on parenteral anticoagulation in the early postsurgical phase. We suggest that switching to VKA or DOAC 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.

22

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.

24

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

25

SVM Society for Vascular Medicine

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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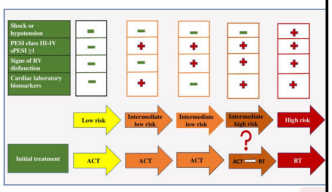
Intermediate-Risk PE

- 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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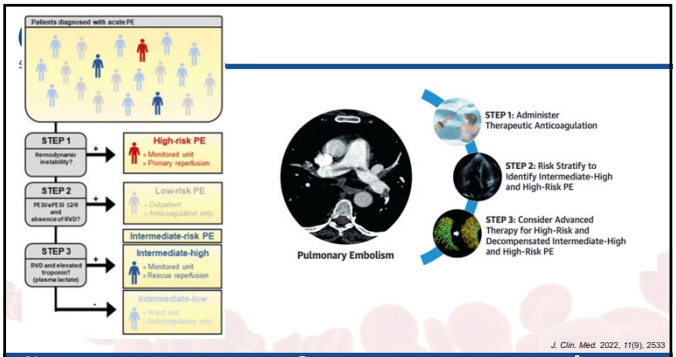

J. Clin. Med. 2022, 11(9), 2533

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.

@SVM_tweets vascularmed.org @VascularMed

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

5

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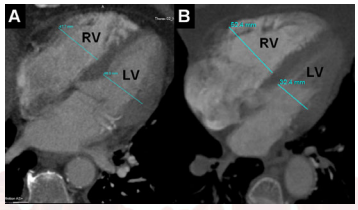
RV/LV ≥0.9 ratio is independent predictor of adverse outcomes



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

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6

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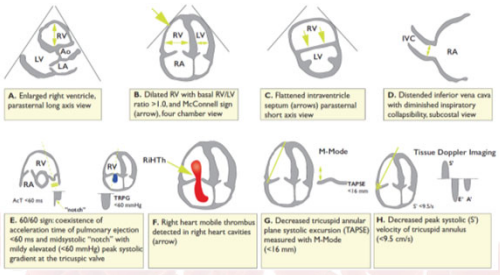
Echocardiographic Predictors of Risk in PE



7

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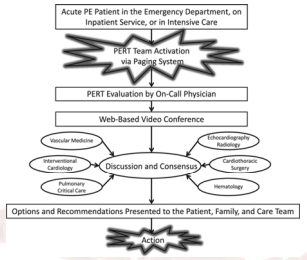

6.8 Recommendations for multidisciplinary pulmonary embolism teams

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

8

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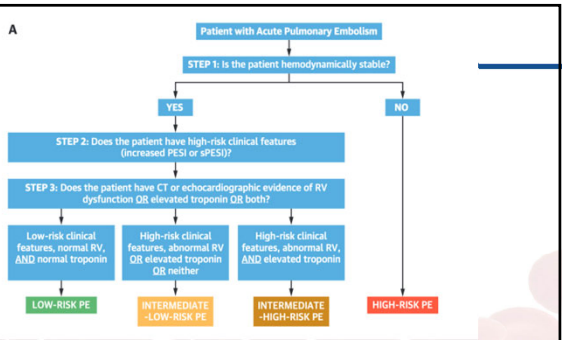
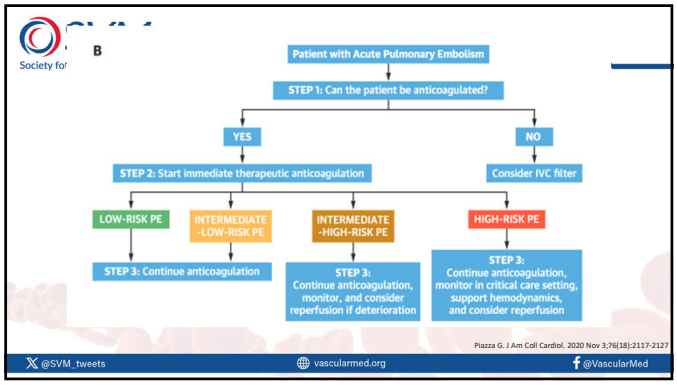


Piazza G. J Am Coll Cardiol. 2020 Nov 3;76(18):2117-2127

9


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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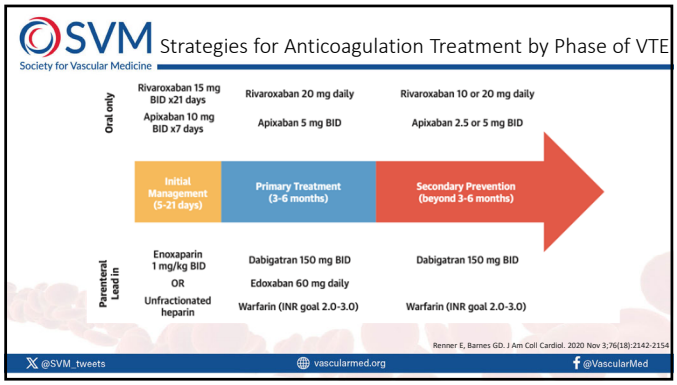
10


SVM
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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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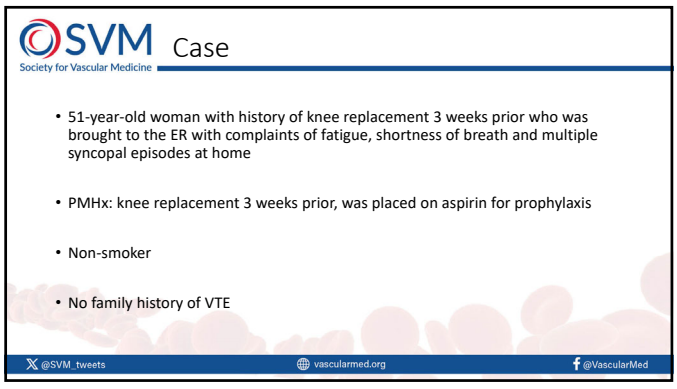
11


SVM
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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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12

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

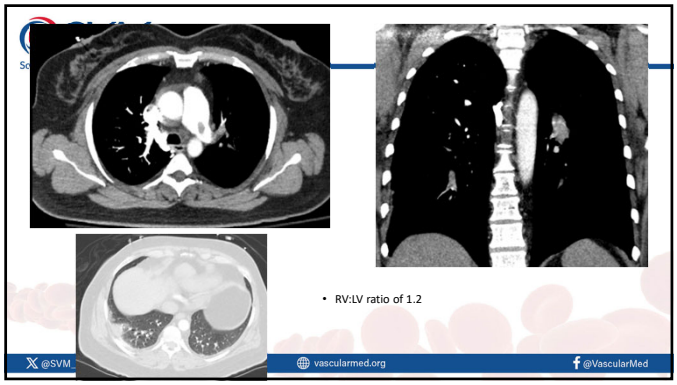
- *How would you risk stratify this patient?*
- *Which factors elevate her risk?*

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

15


• RV:LV ratio of 1.2
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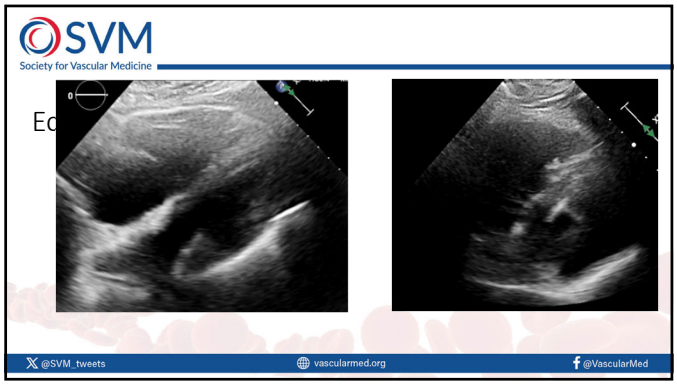
16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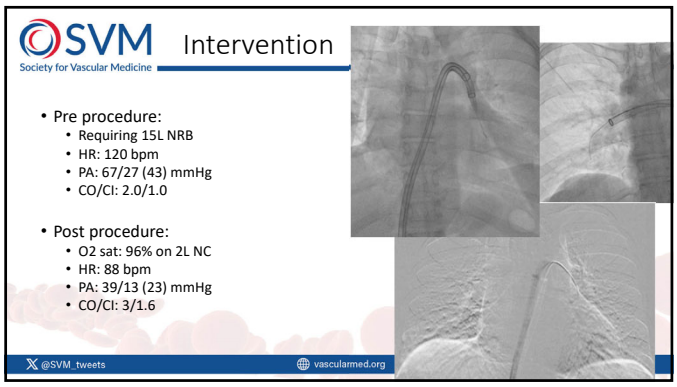
17


SVM
Society for Vascular Medicine
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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18

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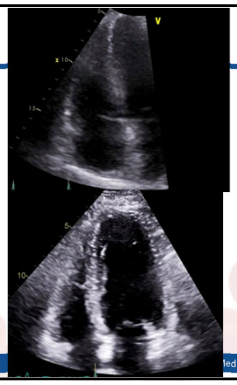
- POD 1 Echocardiogram
  - Improved RV size and function
  - On 2L NC
- POD 3 discharged home on Apixaban
  - Off oxygen
- 1 month follow up echo with normal RV size and function



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19

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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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20

Consultant Case Files: The Swollen Limb

Gaurav Parmar, MD, MPH, RPVI, FSVM, FACC
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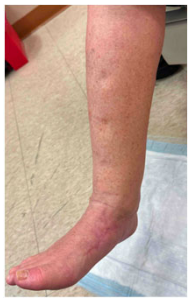
1

Disclosure

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

2

Referral for Refractory Right Leg Edema (for 2 years)



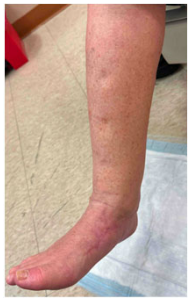
3

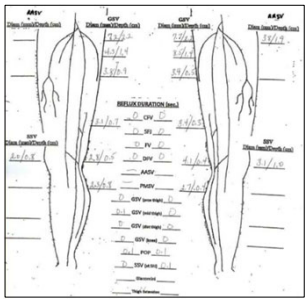
Five Cardinal Rules for the Mx of Leg Edema

1. Leg edema is mostly multifactorial
2. Let the Gravity do its job:
   i. Assumption: Dependent ankle edema is the default state
   ii. What mechanisms are at work to "overcome" the gravity?
3. Try to find (fix) the primary mechanism
4. Identify reversible from irreversible factors
5. Address as many factors as can be easily and practically addressed

4

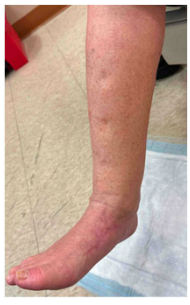
Referral for Refractory Right Leg Edema (for 2 years)

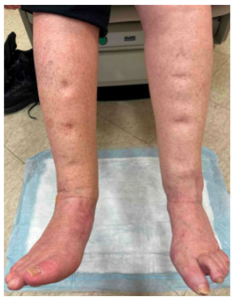




5

Referral for Right (?) Leg Swelling





6

History and Physical Examination

- Establish a correct diagnosis for the correct treatment approach

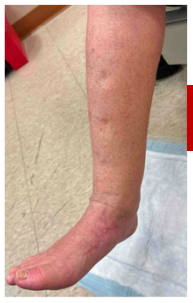
7

Correct Management requires Correct Diagnosis

Unilateral		Bilateral	
Recent[a]	Chronic[b]	Recent[a]	Chronic[b]
Unilateral DVT	Primary venous disease	Bilateral DVT	Chronic venous disease/ post-thrombotic syndrome
Ruptured Baker's cyst	Post-thrombotic syndrome	Acute heart failure	Pulmonary hypertension
Ruptured leg muscle	Iliac vein compression	Acute renal/liver failure	Heart/renal/liver failure
Compartment syndrome	Lymphedema	IVC thrombosis	Idiopathic edema
Intramuscular hematoma	Vascular malformation	IVC tumors	Chronic IVC occlusion, IVC aplasia/hypoplasia
Infection	Reflux sympathetic dystrophy	Drugs	Drugs (see Table 2)
Superficial vein thrombosis	Mass/tumor[c]	Bilateral infections	Lymphedema
Mass/tumor[c]	Venous advential cystic disease		Lipedema
Fracture	Infection		Pregnancy, premenstrual edema
Sprain/strain	Static foot disorders		Obesity
Insect/animal bites	Radiation		Malabsorption syndrome, hypoalbunemia
	Atrophy/hypertrophy		Spinal cord injury/immobility
	Overgrowth syndromes		Static foot disorders
			Thyroid disease
			Obstructive sleep apnea

8

Referral for Refractory Right Leg Edema (for 2 years)



- No Deep or Superficial Vein Reflux
- Echocardiogram Normal

DEPENDENT EDEMA

- CBC: Normal (no anemia/thrombocytopenia)
- CMP: Normal
  - Albumin: Normal
  - Electrolytes: Normal
  - Normal Renal Function
  - Normal Liver Function

9

Management

- Goal setting is extremely important
  - –Functional
  - –Realistic
  - –Feasible

10

10

Factors Contributing to the Limb Swelling

1. Increased Hydrostatic Pressure:	**Optimize BP Control**
2. Reduced Oncotic Pressure:	**Protein**
3. Reduced Osmotic Pressure: i. Electrolytes: Hyponatremia ii. Cells: Pancytopenia, Anemia, Thrombocytopenia iii. Osmoles: Hypoglycemia	**Nutrition / Salt / Glucose**
4. Medical Co-morbidities:	**HF / CKD / Cirrhosis-NASH**

11

11

Evidence for Leg Elevation

A systematic review and meta-analysis of randomized controlled trials, "Comparison of three interventions in the treatment of chronic venous insufficiency: Compression, Medication, and Exercise."
Leg elevation, in combination with compression therapy, is effective in reducing limb edema in patients with chronic venous insufficiency
(J Vasc Surg. 2016 Mar;63(3):760-770)

"Clinical Efficacy and Patient Satisfaction with Different Moisturizing Ointments in the Prevention of Radiation Dermatitis," a randomized clinical trial.
Leg elevation was effective in reducing lower limb edema in patients undergoing radiotherapy for breast cancer
(JAMA Dermatol. 2018 Aug 1;154(8):913-918)

12

Gaurav M, MD (You) on 12/28/2023 10:34 AM

Hello Dr Parmar,

I took your advice and have regularly walked in the pool since mid-September. In a truly overachiever fashion, I have gone almost every day for a half hour.

It's been a game-changer. I have very little pain. I also have decreased my leg size by what I think is a significant amount. I can wear boots I haven't worn in years.

Thank you; you really make a difference, and I feel lucky that we talked; you were honest and proposed creative solutions. I hope you have a great New Year.

13

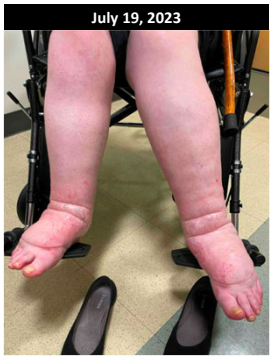
13

Ready?

Let's Solve Some Cases…

14

14



Chronic lower back pain

L3 chordoma s/p XRT

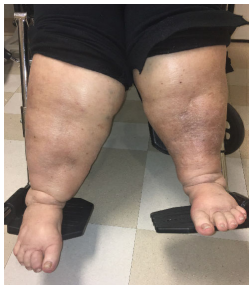
Resection of Chordoma on July 24, 2023

15

15

16

What is the Diagnosis?

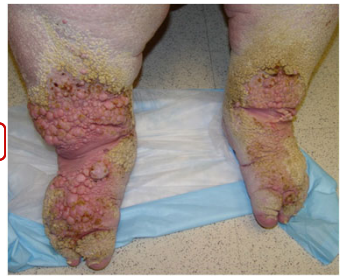


a) Chronic Venous Insufficiency
b) Lymphedema
c) Lipedema
d) Phlebolymphedema
e) Not enough information to make a diagnosis

17

Obvious? *or* Is It?

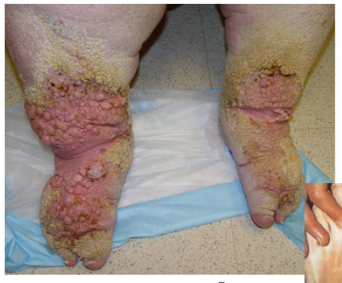
(a) Chronic Venous Insufficiency
(b) Lymphedema
(c) Phlebo-Lymphedema
(d) Lipedema



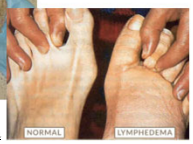
18

Lymphedema

Skin *Woody texture* due to
-Induration &
-Fibrosis
Pigskin
-Chronic lymphatic stasis
-Hyperkeratosis
-Lichenification
-Peau d'orange
-Papillomatosis
-Lipodermatosclerosis
-Elephantitis
Vesicles with
-Lymphorrhea or
-Chylorrhea



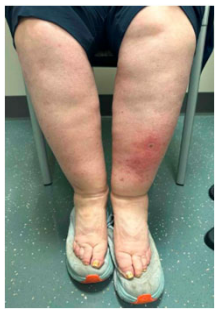
Dorsal hump
Foot edema

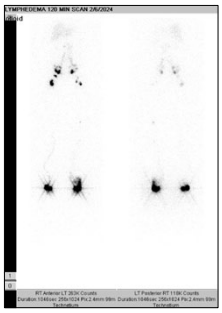


Square toes
Stemmer's sign

19

What is the Diagnosis?





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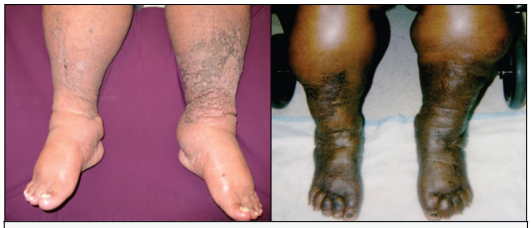
20

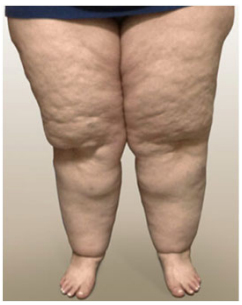
What is the Diagnosis?



Classic example of secondary phlebolymphedema in a morbidly obese patient. Note the marked bilateral calf, foot and toe swelling consistent with lymphedema, yet associated relative distal calf atrophy and hyperpigmentation consistent with chronic stasis lipodermatosclerosis. The distal calf papulonodular and verrucous appearance is consistent with elephantiasis.

21

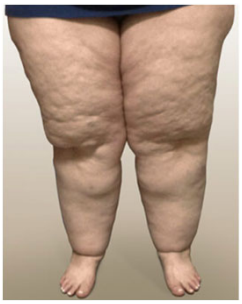
Obvious? *or* Is It?



a) Chronic Venous Insufficiency
b) Lymphedema
c) Lipedema
d) Phlebolymphedema
e) Obesity

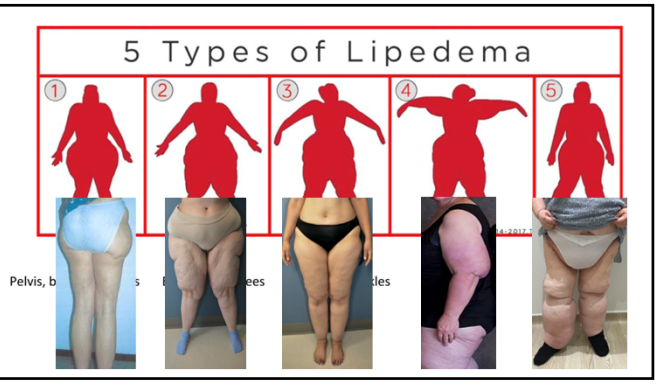
22

Lipedema



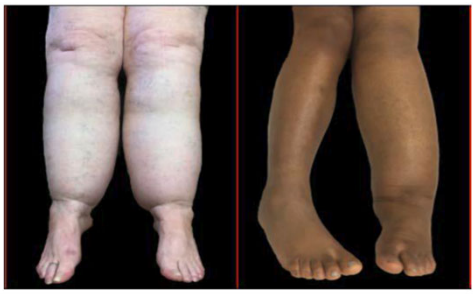
- **Symmetric**
- Arms/Legs (Proximal) w/o involving hands/feet
- "**Cuff**" sign
- Negative Stemmer's sign
- **Non-pitting**
- Increasing **Pain** over time
- **Tender** to Palpation
- **Easy Bruising**
- **Hypermobile joints**
- Skin **Soft** on touch
- Exclusively **Women**

23



24

Lipedema *vs.* Lymphedema

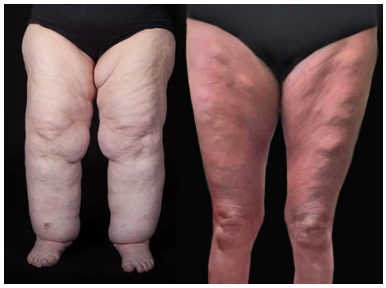


25

Lipedema *vs.* Obesity

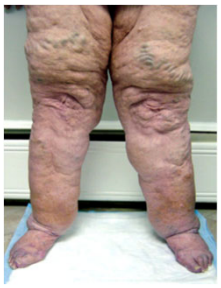
26

Lipedema vs Dercum's disease



27

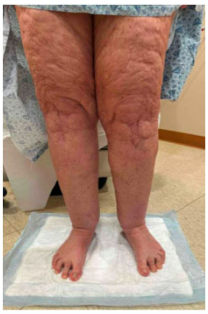
Can you get this one correct?

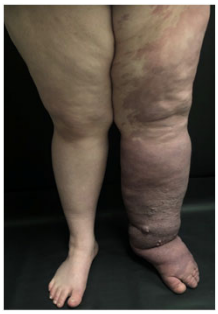


a) Chronic Venous Insufficiency
b) Lymphedema
c) Lipedema
d) Phlebolymphedema
e) Lipolymphedema
f) Phlebolymphedema with Lipedema

28

What is the Diagnosis?

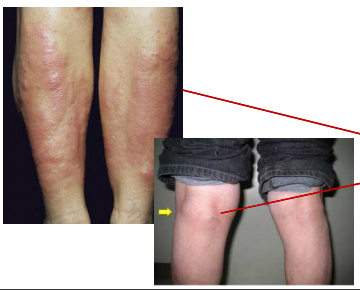




29

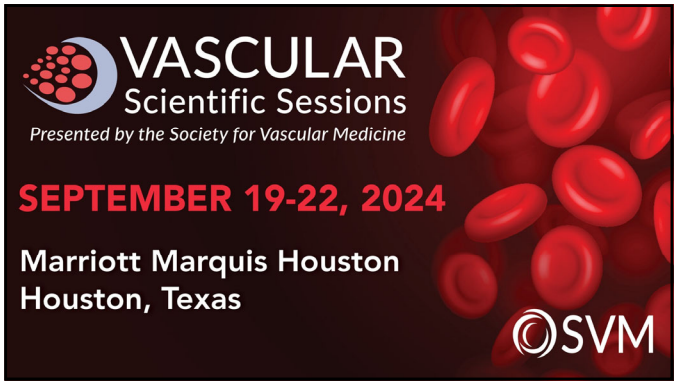
29

Causes and Contributors to Lower Extremity Swelling



1. Drug-induced peripheral edema
   - Nonsteroidal anti-inflammatory drugs
   - Antihypertensives
     - Calcium channel blockers
     - Beta blockers
     - Clonidine
     - Hydralazine
     - Minoxidil
     - Methyldopa
   - Hormones
     - Corticosteroids
     - Estrogens, progesterones, testosterone
   - Lyrica
   - Thioglitazones
   - Monoamine oxidase inhibitors
2. Myxedema (in severe hypothyroidism only)
3. Nephrotic syndrome
4. Congestive heart failure
5. Baker's cyst
6. Recurrent cellulitis
7. Trauma
8. Cirrhosis
9. Obesity
10. Protein losing enteropathy
11. Pulmonary hypertension
12. Calf muscle dysfunction

30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Presented by the Society for Vascular Medicine
SEPTEMBER 19-22, 2024
Marriott Marquis Houston
Houston, Texas
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31

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Consultant Case Files
-Lower Extremity Ulceration-

Eri Fukaya MD, PhD
Vascular Medicine, Division of Vascular Surgery
Stanford University School of Medicine

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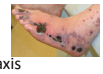
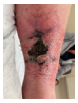
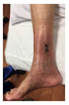
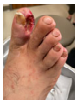
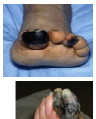
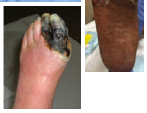
1

Wounds with Vascular Etiology

- Venous Leg ulcer (including lymphatic disease)
- Arterial ulcer (ischemic, thrombotic, embolic, vasospasm)
- Vasculitis
- Calcyphylaxis
- Mixed ulcer
- *Diabetic foot ulcer (high prevalence of PAD)*

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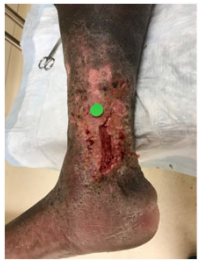
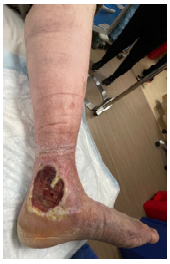
What We See In Clinical Practice

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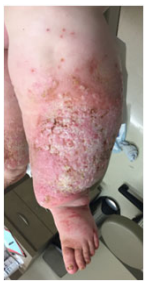
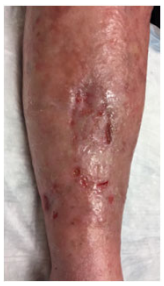
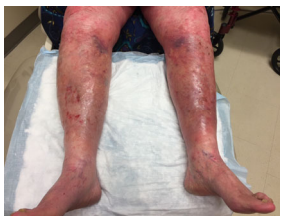
3

What We See In Clinical Practice

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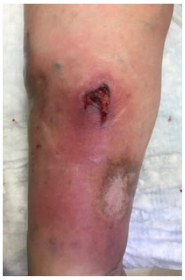
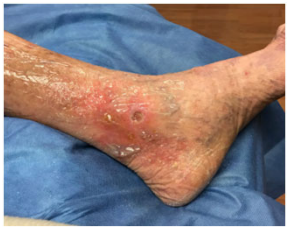
What We See In Clinical Practice

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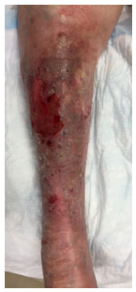
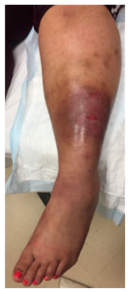
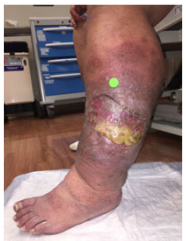
5

What We See In Clinical Practice



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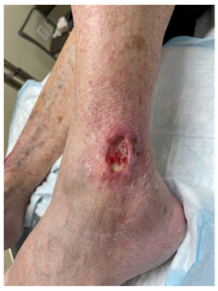
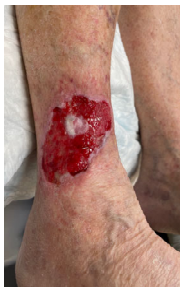
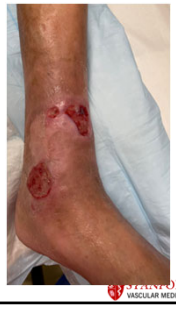
6

What We See In Clinical Practice

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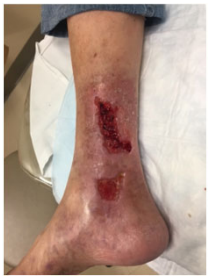
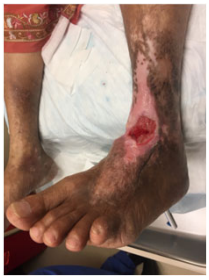
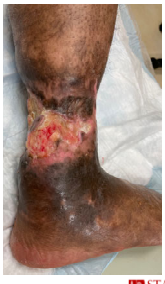
7

What We See In Clinical Practice

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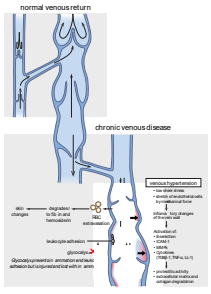
8

Pathophysiology of chronic venous insufficiency



↑ ambulatory venous pressure

↑ inflammation within the vein wall

Extravasation of inflammatory cells/molecules

MMP activation, extracellular matrix degradation

Varicose veins, skin changes, and VLU

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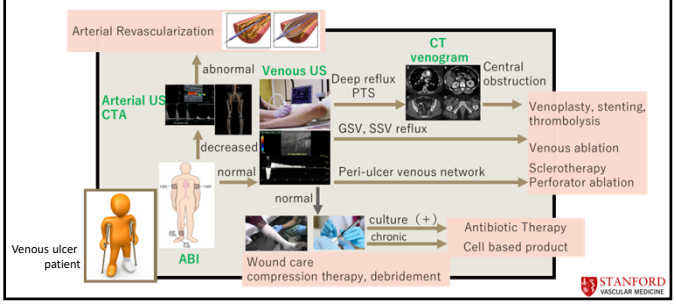
9

How to Approach the Venous Ulcer Patient



10

Stanford VLU Study Summary of Findings

- Patient characteristics:
  - <60: ↑ male, ↑ BMI, ↑ skin changes, ↑ diabetes
  - >60: equal gender composition
- Wound characteristics:
  - 50% recurrent, 55% multiple, 45% cellulitis
  - 40% due to trauma
- Care characteristics:
  - Compression compliance is low
- Ultrasound characteristics:
  - **Below knee GSV** reflux is most common
  - **Calf perforator reflux** is second most common

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11

ESCHAR (2004)

Comparison of surgery and compression with compression alone in chronic venous ulceration (ESCHAR study): randomised controlled trial

Jamie R Barwell, Colin E Davies, Jane Deacon, Kate Harvey, Julia Minor, Antonio Sassano, Maxine Taylor, Jenny Usher, Clare Walesby, Jonathan J Earnshaw, Brian P Heather, David C Mitchell, Mark R Whyman, Keith R Poskitt

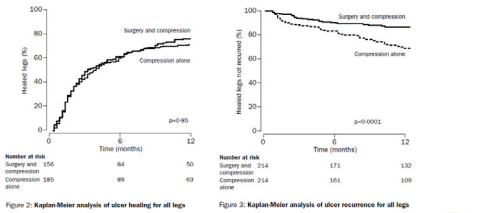

Figure 2: **Kaplan-Meier analysis of ulcer healing for all legs**

Figure 3: **Kaplan-Meier analysis of ulcer recurrence for all legs**

Lancet 2004

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12

EVRA (2018)

A Randomized Trial of Early Endovenous Ablation in Venous Ulceration

Manjit S. Gohel, M.D., Francine Heatley, B.Sc., Xinxue Liu, Ph.D., Andrew Bradbury, M.D., Richard Bulbulia, M.D., Nicky Cullum, Ph.D., David M. Epstein, Ph.D., Isaac Nyamekye, M.D., Keith R. Poskitt, M.D., Sophie Renton, M.S., Jane Warwick, Ph.D., and Alun H. Davies, D.Sc., for the EVRA Trial Investigators*

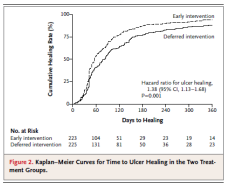

Figure 2. Kaplan–Meier Curves for Time to Ulcer Healing in the Two Treatment Groups.

Table 2. Timing and Type of Endovenous Intervention.

Variable	Early Intervention (N = 224)	Deferred Intervention* (N = 226)
	no. (%)	
Timing of endovenous treatment after randomization†		
Within 2 wk	203 (90.6)	1 (0.4)
Before ulcer healing	200 (89.3)	1 (0.4)
After ulcer healing	3 (1.3)	0
Between 2 and 4 wk	9 (4.0)	1 (0.4)
Before ulcer healing	9 (4.0)	1 (0.4)
After ulcer healing	0	0
Between 4 wk and 6 mo	6 (2.7)	103 (45.6)
Before ulcer healing	4 (1.8)	4 (1.8)
After ulcer healing	2 (0.9)	99 (43.8)
After 6 mo	0	66 (29.2)
Before ulcer healing	0	19 (8.4)
After ulcer healing	0	47 (20.8)
No treatment	6 (2.7)	55 (24.3)‡
Type of endovenous intervention		
Endothermal ablation only§	71 (31.7)	54 (23.9)
Foam sclerotherapy only¶	111 (49.6)	100 (44.2)
Mechanochemical ablation only	5 (2.2)	1 (0.4)
Endothermal ablation and foam sclerotherapy¶	27 (12.1)	16 (7.1)
Mechanochemical ablation and foam sclerotherapy¶	3 (1.3)	0
Abandoned treatment‖	1 (0.4)	0
No treatment	6 (2.7)	55 (24.3)

63% 51.3%

NEJM 2018

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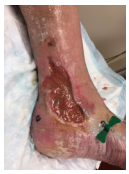
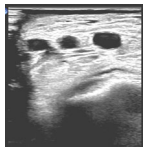
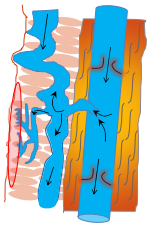
13

Peri-ulcer Venous Network (PUVN)





Ulcer



- Veins surrounding and/or under ulcer
- May be masked by swelling or lipodermatosclerosis
- Visualization may only be possible with ultrasound

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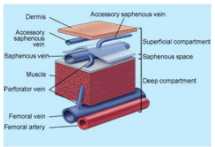
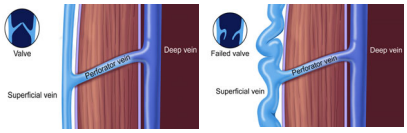
14

Importance of IPVs





- Stuart (JVS 2001) found that in patients with:
  - CEAP class 4 → 83% IPV
  - CEAP classes 5 & 6 → 90% IPV
- Most IPVs are associated with superficial reflux

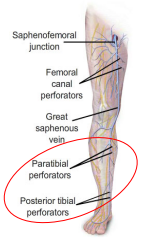
Stuart WP, et al. *J Vasc Surg.* 2001;34:774-8.

15

15

Medial Calf Posterior Tibial Perforator Veins

- Most pathologic perforators
- Connect GSV with the posterior tibial veins
- 2/3 with skin changes have IPV as well as superficial or deep reflux
- 63% of recurrent varicose veins are associated with IPV



Glovicski P, et al. J Vasc Surg. 1996;125:1-7
Myers KA, et al. J Vasc Surg. 1995;21:605-12
Rutherford RB, et al. Eur J Vasc Surg. 2001:21:458-460

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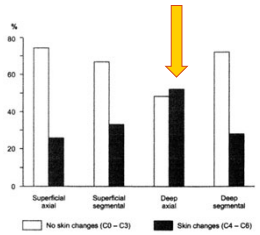
16

Incompetent Deep Veins



Danielsson et al J Vasc Surg. 2003 Dec;38(6):1336-41

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17

Prevalence of Skin Changes/Ulcer and Reflux Patterns (%)

Class	*No reflux*	*Superficial only*	*Deep only*	*Both*	*Superficial (total)*	*Deep (total)*
0 (n = 11)	55	36	9	0	36	9
1 (n = 69)	25	56	5	14	56	19
2 (n = 45)	27	44	7	22	66	29
3 (n = 30)	17	23	23	37	60	60

Class 0 asymptomatic
Class 1 mild to moderate (swelling, varicose veins)
Class 2 moderate (skin changes)
Class 3 severe (ulceration)

Welch et al J Vasc Surg. 1996 Nov;24(5):755-762

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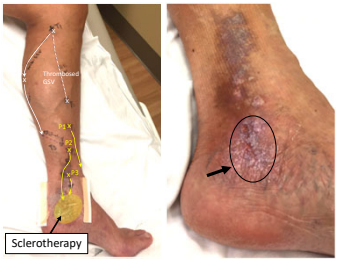
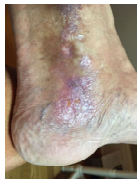
18

Case: 64M Recurrent skin breakdown at the ankle



CEAP 6
Recurrent venous ulcer in PTS
Proximal GSV reflux (minimal)
Axial deep reflux (CFV, FV, POPV)
Posterior tibial mid calf perforator reflux



Communicating tributary veins from calf perforators

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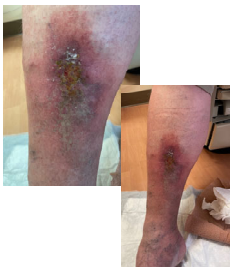
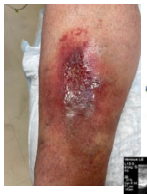
19

Case: 46M VLU with recurrent cellulitis



GSV ablation



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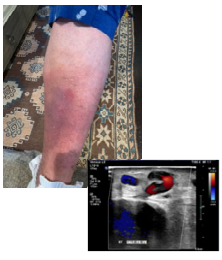
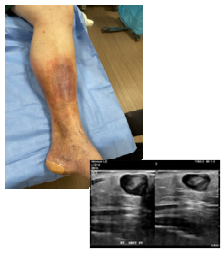
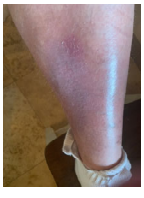
20

Case: 46M VLU with recurrent cellulitis







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21

Thank you!

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22

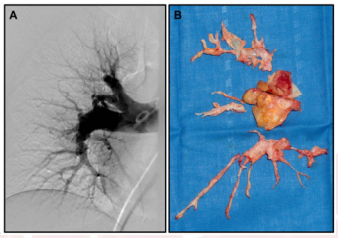
Post PE Impairment and CTEPH

Kamal Gupta, MD, FSVM
Delbert D. Neis, MD Professor of Cardiovascular Disease
Vice Chair (Academics)
Director, Interventional Cardiology Fellowship
Department of Cardiovascular Medicine
University of Kansas School of Medicine
Kansas City, KS

1

Chronic Thromboembolic Pulmonary HTN (CTEPH)

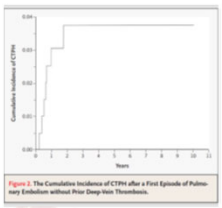
- Most well recognized, well studied and severest of all post PE syndromes
- Clinically manifests as
  - Dyspnea, Fatigue, Hypoxia
  - Right heart failure
  - Arrhythmias, Syncope
  - Eventually fatal



Int. J. Mol. Sci. **2019**, *20*(3), 784;

2

CTEPH: Incidence



N Engl J Med 2004;350:2257-64

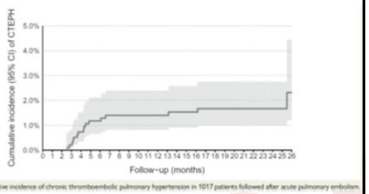


Figure 1 Cumulative incidence of chronic thromboembolic pulmonary hypertension in 1017 patients followed after acute pulmonary embolism.

European Heart Journal (2022) 43, 3387–3398

3

Spectrum of Lesions in CTEPH

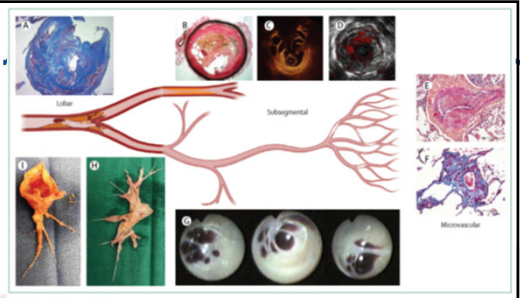


Figure 1: Types of lesion in CTEPH
(A) Histological section through an obstructed lobar artery. (B) Histological section through an obstructed subsegmental artery. (C) Optical coherence tomography of a subsegmental artery. (D) Intravascular ultrasound of a subsegmental artery. (E, F) Histological sections showing microvascular changes. (G) Angioscopy showing webs in subsegmental arteries. (H) Surgical specimen of right lower lobar obstruction. (I) Surgical specimen with lobar, segmental, and subsegmental obstructions. CTEPH=chronic thromboembolic pulmonary hypertension. Created with BioRender.com.

4

CTEPH: Hemodynamic Consequences

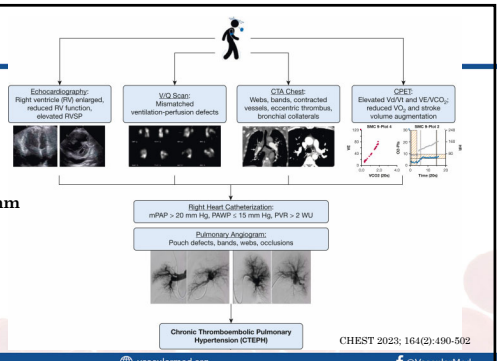
- Increased PVR
- Reduced PA compliance
- Hypoxia
- Increased PA pressure
- Increased RV afterload
- Eventual RV failure

Diagnosis of CTEPH

- **Non resolved Thrombi on Imaging**
- **Elevated RVSP (Mean PAP > 20 mmHg)**
- **Normal PCWP (< 15 mmHg)**
- **Elevated PVR (> 2 WU)**

5

CTEPH Diagnostic Algorithm



CHEST 2023; 164(2):490-502

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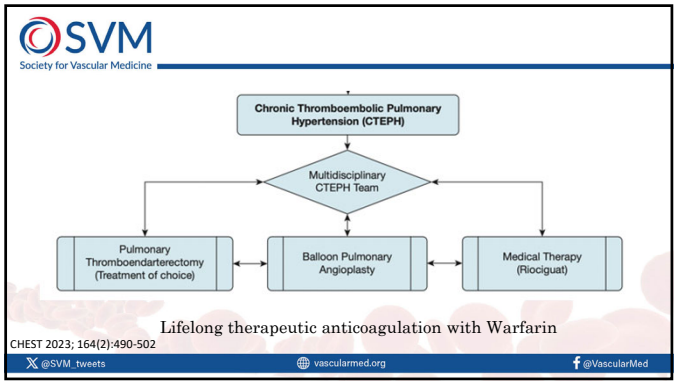
SVM
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Chronic Thromboembolic Pulmonary Hypertension (CTEPH)
Multidisciplinary CTEPH Team
Pulmonary Thromboendarterectomy (Treatment of choice)
Balloon Pulmonary Angioplasty
Medical Therapy (Riociguat)
Lifelong therapeutic anticoagulation with Warfarin
CHEST 2023; 164(2):490-502
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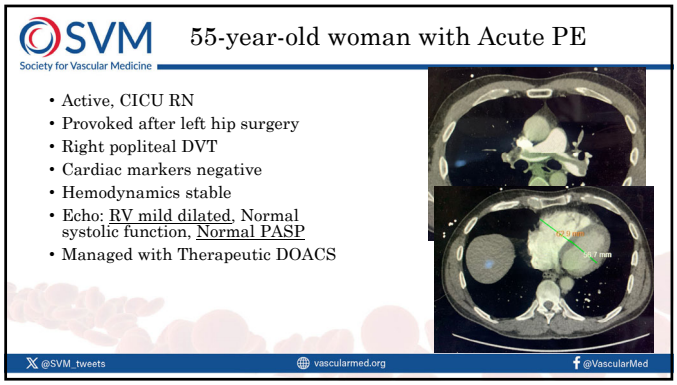
SVM
Society for Vascular Medicine
55-year-old woman with Acute PE
• Active, CICU RN
• Provoked after left hip surgery
• Right popliteal DVT
• Cardiac markers negative
• Hemodynamics stable
• Echo: RV mild dilated, Normal systolic function, Normal PASP
• Managed with Therapeutic DOACS
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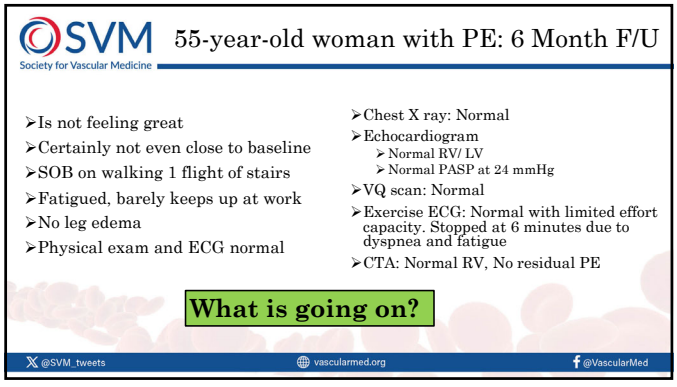
SVM
Society for Vascular Medicine
55-year-old woman with PE: 6 Month F/U
➢Is not feeling great
➢Certainly not even close to baseline
➢SOB on walking 1 flight of stairs
➢Fatigued, barely keeps up at work
➢No leg edema
➢Physical exam and ECG normal
➢Chest X ray: Normal
➢Echocardiogram
➢Normal RV/ LV
➢Normal PASP at 24 mmHg
➢VQ scan: Normal
➢Exercise ECG: Normal with limited effort capacity. Stopped at 6 minutes due to dyspnea and fatigue
➢CTA: Normal RV, No residual PE
What is going on?
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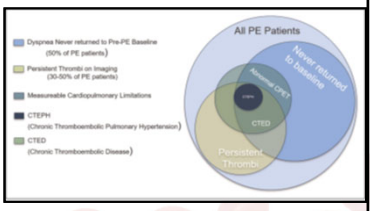
Beyond CTEPH

- 40-60% of post PE patients have dyspnea and effort intolerance
- A variable percentage had residual Thrombus

- 20-50% have abnormal VQ scans/ Residual Thrombus 3-6 months post PE
- <10% of these eventually have CTEPH (2-4 % incidence)
- Not all patients with residual thrombus have symptoms



Blood Rev 2014; 28:221–226.

10

Post PE Impairment Syndromes

Definition: New or progressive dyspnea, effort intolerance or impaired functional (or mental) capacity after ≥ 3 months of anticoagulation after PE

1. **Evidence of residual thrombus on imaging and exercise abnormal hemodynamics**
   - **CTEPH**: Resting mPAP > 20mmHg
   - **CTEPD:** Resting mPAP ≤ 20 mmHg
2. **Normal exercise hemodynamics with or without residual thrombus on imaging**
   - Functional Post PE limitation Syndrome

11

Chronic thromboembolic pulmonary disease (CTEPD)

- Same anatomic and mechanistic changes in the pulmonary vasculature as CTEPH but less severe and perhaps less progressive?
- A normal resting Echo does not exclude CTEPD

Diagnostic Criterion:

- Residual thrombus in pulmonary vasculature
- **Normal resting mPAP and normal PCWP**
- Effort intolerance related to abnormal hemodynamics
- Abnormal cardiopulmonary exercise test (CPET)

May have:

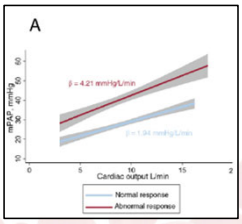
- Incomplete echocardiographic RV recovery
  - Dilatation
  - Systolic/ Diastolic dysfunction

12

CTEPD: Hemodynamics

Key feature is increased RV afterload with effort as determined by

- PA compliance
  - Loss PA compliance can occur early even with normal resting PVR and mPAP
  - Results in increased exercise PAP (> 30. mmHg)
  - Disproportionate rise in mPAP compared to rise in CO
    - High mPAP/ CO slope on RHC (> 3)
- Increased PVR (Static overlaod): mPAP-mRAP/ CO



Rev Esp Cardiol. 2024;77(2):158–166

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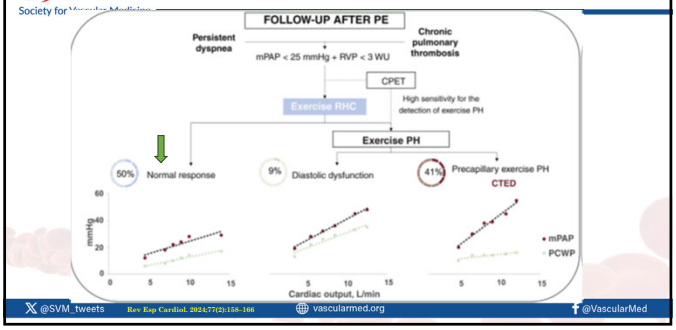

14

CTEPD: Cardiopulmonary exercise test (CPET)

- CPET studies the integrative response to exercise and helps assess the cause of effort intolerance
  - Cardiovascular
  - Pulmonary
  - Musculoskeletal
  - Hematopoietic
  - Neuropsychological

15

CTEPD: Cardiopulmonary exercise test (CPET)

- Max V02
- Anaerobic threshold
- Disturbances in gas exchange due to dead space ventilation etc.
- Low stroke volume reserve with exercise

- CPET findings in CTEPD
  - Max V02 < 80%
  - Inefficient gas exchange due to worsening dead space ventilation on exercise
  - Poor cardiac reserve due to RV dysfunction due to PA compliance issues
- CPET findings in Deconditioning
  - Max V02 < 80%
  - Normal gas exchange
  - Normal cardiac reserve

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Back to our case of 55-year-old RN, 6 months post PE

- Is not feeling great
- Certainly not even close to baseline
- SOB on walking 1 flight of stairs
- Fatigued, barely keeps up at work
- No leg edema
- Physical exam and ECG normal

- Chest X ray: Normal
- Echocardiogram
  - Normal RV/ LV
  - Normal PASP at 24 mmHg
- VQ scan: Normal
- Exercise ECG: Normal with limited effort capacity. Stopped at 6 minutes due to dyspnea and fatigue
- CTA: Normal RV, No residual PE

How would you investigate?

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Back to our case of 55-year-old RN, 6 months post PE

We need to assess for:

- Reduced V02 Max
- Inefficient pulmonary gas exchange
  - Dead space ventilation
- Abnormal cardiac reserve due to altered PA compliance/ RV dysfunction on exercise
  - Increased PAP
  - Increased PA/ CO slope

CPET

- Reduced V02 Max 60%
- No evidence of dead space ventilation
- Normal exercise Right heart cath

Normal hemodynamics without residual thrombus on imaging: **Post PE functional limitation**

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Management of Post PE Impairment Syndromes

CTED

- Not much data
- No defined role of vasodilators or Pulmonary endarterectomy*
- Perhaps cardiopulmonary rehab?
- Referral to a specialized center and a multispecialty team

Functional Post PE Impairment

- Assess for secondary causes
- Psychological counselling
- Rehabilitation programs

* Small single arms studies of PEA have shown improved hemodynamics and excellent 5-year survival

Eur Resp J 2014;44:1635-1645, J Heart Lung Transplant 2019;38(suppl):S130

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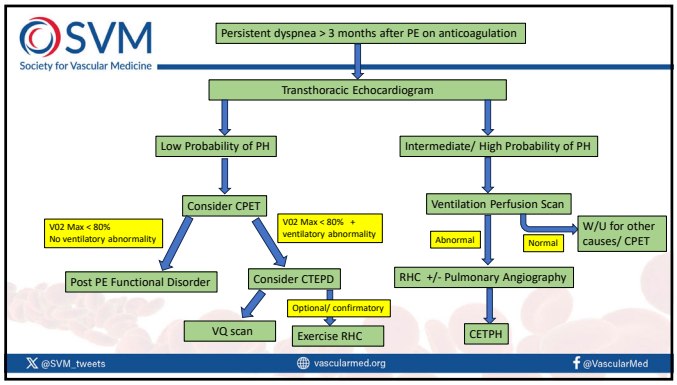

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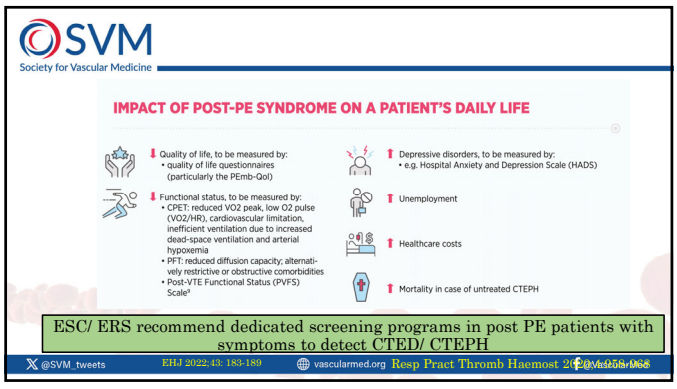

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"That's all Folks!"
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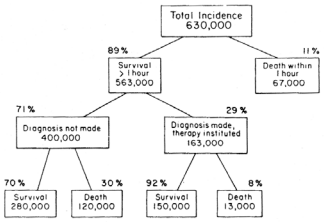
Chronic Pulmonary Arterial Disease: When to suspect, options for treatment

Vivian Bishay, MD
Associate Professor, Vascular and Interventional Radiology
Icahn School of Medicine at Mount Sinai

1

PE Mortality



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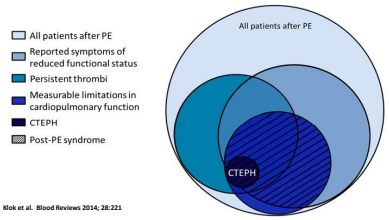
Disclosures

- No relevant disclosures

3

Post PE Syndrome

Spectrum of disease from Acute to Chronic



Klok et al. Blood Reviews 2014; 28:221

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Post-PE Syndrome

- RV Dysfunction: 18.1%
- Functional Impairment: 11.3% NYHA III-IV
- 6-MWT: 415m (5th percentile)
- SF-36: PCS 44.8 (40th Percentile)

Sista AK, Vasc Med, 2017

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Post-PE syndrome and CTEPH

- Post- PE syndrome: a phenomenon of permanent functional limitations after PE occurring in 46.5% of patients
  - Persistent deconditioning, anxiety, and/or ventilator or circulatory impairment as a result of acute PE
- Chronic thromboembolic pulmonary hypertension is a type of post-PE syndrome
  - At least 1 persistent lobar or segmental, unmatched perfusion defect on ventilation/perfusion (V/Q) imaging despite ≥ 3 months of therapeutic anticoagulation
  - Evidence of pulmonary hypertension on right heart catheterization (RHC): mPAP >20mmHg, PCWP <15mmHg, and PVR >3WU

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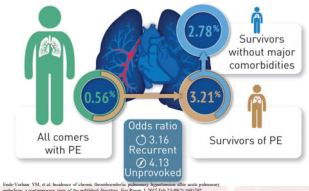
CTEPH

- The prevalence of CTEPH after PE ranges between 0.1% and 9.1%
  - Meta-analysis of 16 studies



Ende-Verhaar YM, et al. Incidence of chronic thromboembolic pulmonary hypertension after acute pulmonary embolism: a contemporary view of the published literature. Eur Respir J. 2017 Feb 23;49(2):1601792.

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CTEPH

- 3-5% post acute PE
  - Prospective study of 223 with PE documented
  - 1% (6m), 3.1% (12m), 3.8% (24m)
- Rarely are cases identified after 2 years
- 2500 US/yr

Tapson et al Proc Am Thor Soc 2006, Bonderman et al Eur Respir J 2009, Pepke-Zaba et al Circulation 2011, Meignan Arch Intern Med 2000, Pundgo et al NEJM 2004

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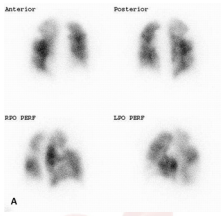
CTEPH

- Resting mPAP > 20mmHg
  - Mismatched perf defects on V/Q
    - Sensitivity of V/Q scintigraphy for CTEPH is 96-97% vs 51% for CTPA
    - V/Q scintigraphy also has a negative predictive value approaching 100%
  - PH on echo
  - >3m of therapeutic AC



N Engl J Med 2004; 350:2257-2264
Proc Am Thorac Soc. 2006 Sep;3(7):564-7.

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Risk Factors

Related to DVT/PE

- Multiple episodes of PE
- Larger perfusion defects
- Degree of elevation of PA pressures at PE dx
  - RVSP > 50 mmHg → 3 – 5 x greater increase in persistently elevated pressures (ref 17,18)
  - mPAP > 30 mmHg (ref 19)
- Fibrinogen variants resistant to lysis
- Presence of APL-Ab / LAC
- Increased levels of factor VII
- H/o malignancy

Unrelated to DVT/PE

- Younger age
- Thyroid replacement
- Ventriculo-atrial shunt
- Infected pacemaker
- H/o splenectomy
- IBD
- Chronic osteomyelitis
- Infected tunneled catheters
- HLA polymorphisms
- Non O blood groups

Ribeiro et al Circ 1999, Thomas et al Thorax 2012, Riedel et al Chest 1982

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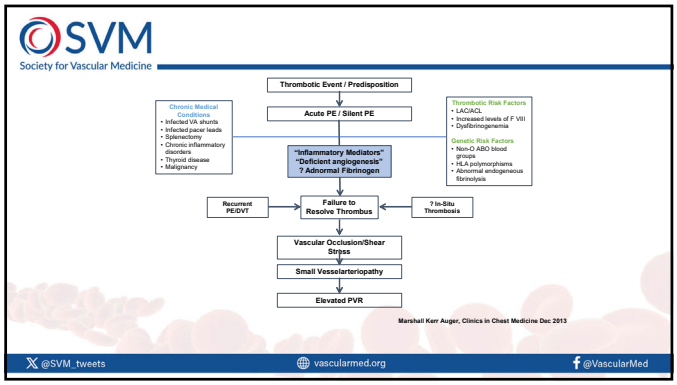

Marshall Kerr Auger, Clinics in Chest Medicine Dec 2013

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Goals of post- PE follow-up

- Monitor clinical course after PE diagnosis
- Ensure adequate choice, duration and dose of anticoagulation
- Address risk factors for recurrence
- Ensure appropriate management of IVC filters
- Monitor for complications: bleeding and recurrent VTE
- Monitor for development of the post-PE syndrome, including but not limited to chronic thromboembolic pulmonary hypertension (CTEPH)

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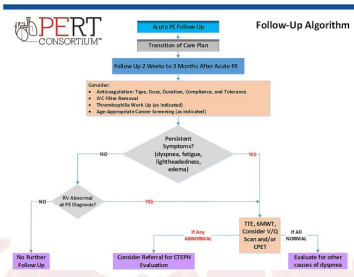
Clinical practice patterns after PE

- Large practice variation and low level of evidence
- 2019 PERT Consortium Consensus Practice and 2019 ESC Guidelines for PE have published guidelines on post-PE follow-up
  - No clear guidelines on the diagnosis, treatment or prevention of the post-PE syndrome exist

13

Clinical practice patterns after PE



14

Post-PE Syndrome

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- Functional Impairment: 11.3% NYHA III-IV
- 6-MWT: 415m (5th percentile)
- SF-36: PCS 44.8 (40th Percentile)

Sista AK, Vasc Med, 2017

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CTEPH

	Odds ratio	95% CI
Age ≥ 60 years	2.9	1.2–7.2
Known diabetes mellitus	Infinitely low*	
Severe renal insufficiency (eGFR < 30 mL min^{-1})	Infinitely low*	
Immobility, recent long travel, trauma, or surgery	Infinitely low*	
Pregnancy/peripartum period	Infinitely low*	
Hormone (replacement) therapy	Infinitely low*	
Unprovoked PE	20	2.7 to > 100
Onset of symptoms > 14 days before diagnosis	7.9	3.3–19
Hemodynamically unstable at presentation	Infinitely high**	
Any right ventricular dysfunction at presentation	4.1	1.4–12
Known hypothyroidism	4.3	1.4–13
Ventriculo-atrial shunt	Infinitely low*	
Thrombolysis or embolectomy	Infinitely low*	

Klok FA, Dzikowska-Diduch O, Kostrubiec M, Vliegen HW, Pruszczyk P, Hasenfuß G, Huisman MV, Konstantinides S, Lankeit M. Derivation of a clinical prediction score for chronic thromboembolic pulmonary hypertension after acute pulmonary embolism. J Thromb Haemost. 2016 Jan;14(1):121-8. doi: 10.1111/jth.13175. Epub 2015 Dec 29. PMID: 26509468.

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Barriers to diagnosis of CTEPH

- Early diagnosis of CTEPH remains a challenge
  - Mean diagnostic delay of 14 months demonstrated in the European CTEPH registry
    - Median time from last acute PE to CTEPH dx was 12.5 months
    - At diagnosis, the majority of patients were NYHA functional class III or IV
    - Patients with a longer delay had higher pulmonary pressures at diagnosis
    - Longer delay was associated with a higher risk of mortality
    - Recurrent VTE and obesity associated with longer diagnostic delay
  - Factors leading to delay:
    - Non- specific clinical presentation
    - Validated, cost-effect screening tools unavailable
    - Diagnostic misclassification as acute PE

Pepke-Zaba J, et al. Chronic thromboembolic pulmonary hypertension (CTEPH): results from an international prospective registry. Circulation. 2011 Nov 1;124(18):1973-81.
Klok FA, et al. Determinants of diagnostic delay in chronic thromboembolic pulmonary hypertension: results from the European CTEPH Registry. Eur Respir J. 2018 Dec 6;52(6):1801687.

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Barriers to diagnosis of CTEPH

- Healthcare system barriers
  - Only 61% of patients symptomatic with post-PE syndrome are referred for further testing for CTEPH evaluation
  - Before CTEPH is diagnosed, patients consulted a median of 4 different physicians for a median of 13 consultations
  - Abnormal test results not recognized by providers, therefore not triggering further workup
  - Cumbersome diagnostic algorithm involving multiple healthcare providers

Tapson VF, et al. Monitoring for Pulmonary Hypertension Following Pulmonary Embolism: The INFORM Study. Am J Med. 2016 Sep;129(9):978-985.e2.
Ende-Verhaar YM, et al. Healthcare utilization in chronic thromboembolic pulmonary hypertension after acute pulmonary embolism. J Thromb Haemost. 2018 Nov;16(11):2168-2174.

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Post-PE Clinic

- 1st visit: 2-8 weeks after hospital discharge
  - If RV dysfunction present on TTE during acute PE, repeat TTE done 6-8 weeks after discharge to ensure RV recovery
  - Anticoagulation check: duration, compliance, tolerance and refill supply
  - IVC filter removal
  - Age appropriate cancer screening +/- thrombophilia w/u
- 2nd visit: 3-6 months after hospital discharge
  - If persistent respiratory symptoms: repeat TTE and/or V/Q scan, 6MWD, +/- CPET
  - Anticoagulation: confirm duration assessment
    - If pt had a DVT with episode of acute PE, eval for residual or chronic DVT to help determine duration of anticoagulation

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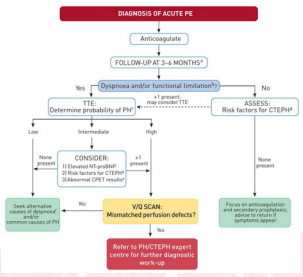
Clinical practice patterns after PE



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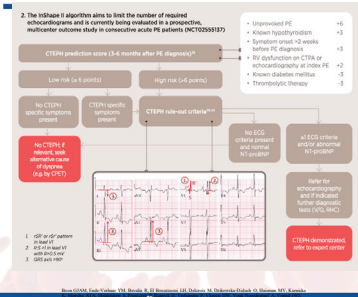
Clinical practice patterns after PE



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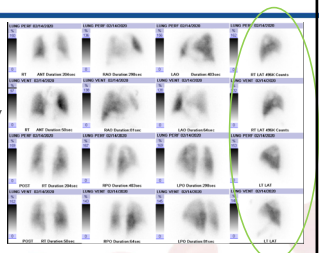
Post-PE Clinic

- CTEPH evaluation pathway
  - Abnormal TTE with or without persistent pulmonary symptoms → V/Q scan (8 views, including lateral view)→ if abnormal, proceed with RHC + pulmonary angiogram→ discussion at multidisciplinary CTEPH meeting (Pulmonary, IR, CT surgery teams)



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Diagnosis of CTEPH

Suspect
Echocardiogram
VQ Scan

Confirm
Right Heart Catheterization
Pulmonary Angiogram
(or CTPA, MRA)

Assess Risk
Hemodynamics
Comorbidities
Surgeon/CTEPH Team Experience

Kim NH, Delcroix M, Jenkins DP. *et al.* Chronic Thromboembolic Pulmonary Hypertension. *J Amer Coll Card,* 2013; 62(25)(Suppl. D):D92-D99

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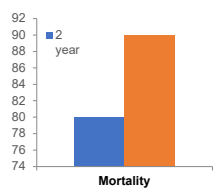
Mortality after dx of CTEPH



Reidel et al Chest 1982, Corsico et al AJRCCM 2008, Lewczuk et al Chest 2001

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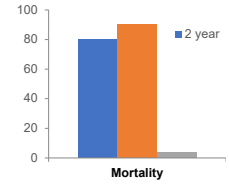
Mortality after dx of CTEPH: PEA



PEA = pulmonary thrombendarterectomy

Reidel et al Chest 1982, Corsico et al AJRCCM 2008, Lewczuk et al Chest 2001

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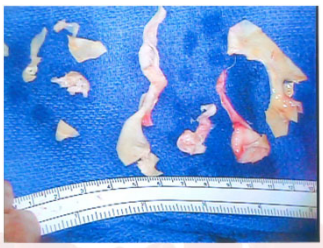
Pulmonary thromboendarterectomy



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PEA

- Survival:
  - 5yrs 82%, 10yrs 75%
- Peri-op mortality 2.2 – 5.2%
- >30% pts inoperable
- Residual PH between 5 and 35%
- Access issues

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BPA: indications

- Unsuitable for PEA
- Residual or recurrent PH
- Pts who decline PEA and consent to BPA after understanding risks and benefits of both
- ? Renal dysfunction
  - eGFR 47 to 51 post BPA

28

Lesion selection

- Segmental & subsegmental
- Distal Reconstruction
- Tapered (vs flush segmental occlusions)
- Upper vs Lower
- Tech success
  - <50% pouching defects
  - 90-100% ring-like stenoses, webs, and abrupt vascular narrowings
    - Kawakami classification

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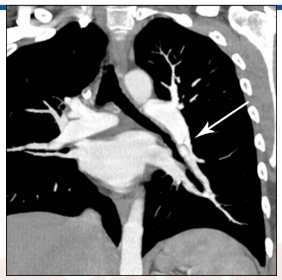

30

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Pulm Angiography

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31

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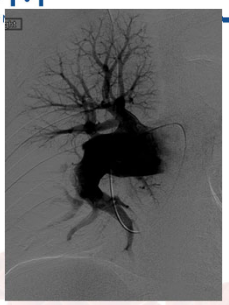

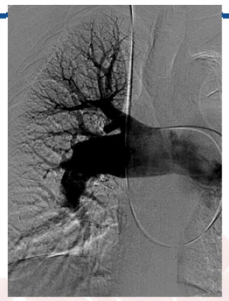

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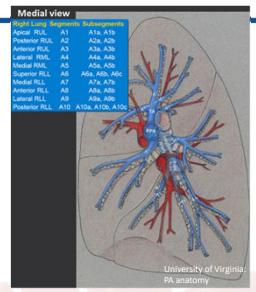
AP view

Right Lung	Segments	Subsegments
Apical RUL	A1	A1a, A1b
Posterior RUL	A2	A2a, A2b
Anterior RUL	A3	A3a, A3b
Lateral RML	A4	A4a, A4b
Medial RML	A5	A5a, A5b
Superior RLL	A6	A6a, A6b, A6c
Medial RLL	A7	A7a, A7b
Anterior RLL	A8	A8a, A8b
Lateral RLL	A9	A9a, A9b
Posterior RLL	A10	A10a, A10b, A10c



Medial view

Right Lung	Segments	Subsegments
Apical RUL	A1	A1a, A1b
Posterior RUL	A2	A2a, A2b
Anterior RUL	A3	A3a, A3b
Lateral RML	A4	A4a, A4b
Medial RML	A5	A5a, A5b
Superior RLL	A6	A6a, A6b, A6c
Medial RLL	A7	A7a, A7b
Anterior RLL	A8	A8a, A8b
Lateral RLL	A9	A9a, A9b
Posterior RLL	A10	A10a, A10b, A10c

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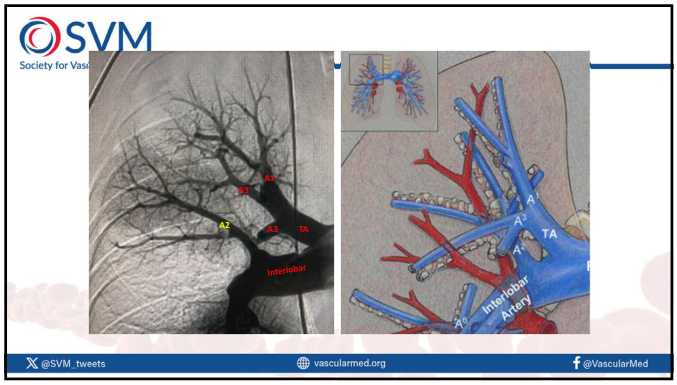
33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A1
A3
A2
A3
TA
Interlobar
A1
A3
TA
A2
Interlobar Artery
A2
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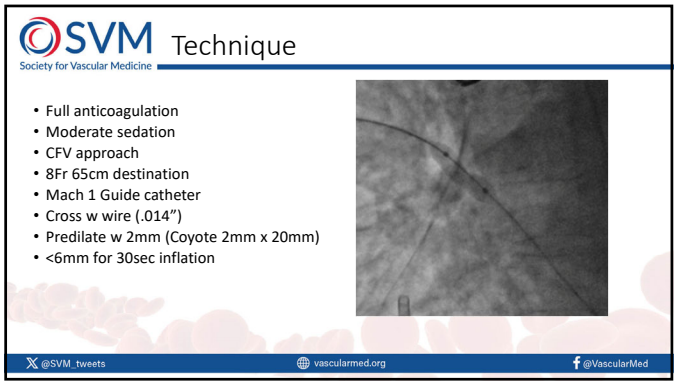
34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Technique
• Full anticoagulation
• Moderate sedation
• CFV approach
• 8Fr 65cm destination
• Mach 1 Guide catheter
• Cross w wire (.014")
• Predilate w 2mm (Coyote 2mm x 20mm)
• <6mm for 30sec inflation
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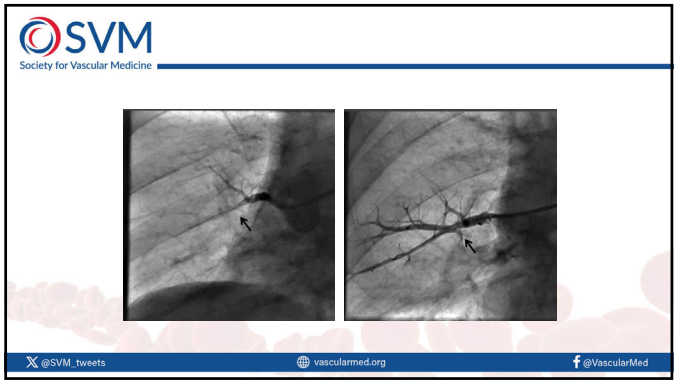
35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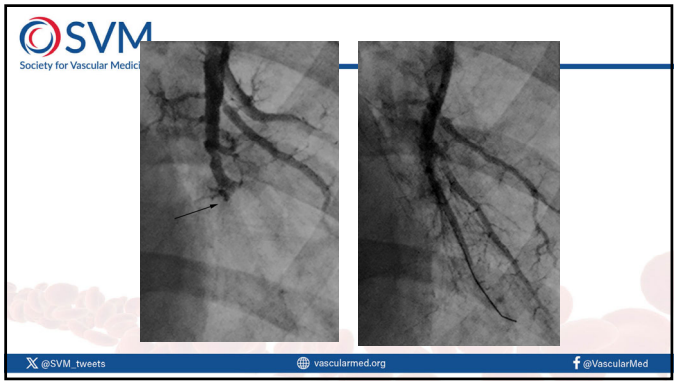
36



37

Staged Approach

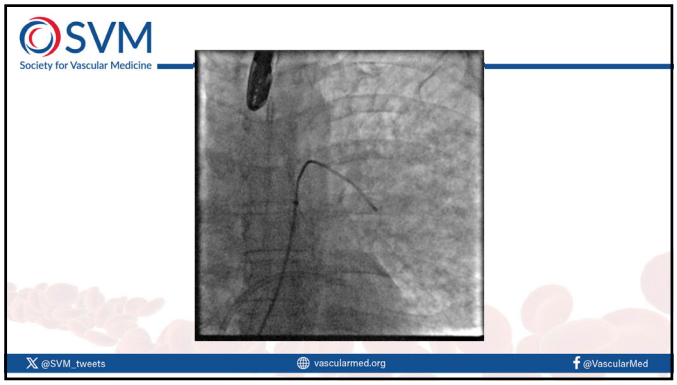
- 6-8 sessions per pts, 6 wks apart
  - Single Lobe
  - 60mins fluoro, 250cc contrast
  - mPAP
    - >50: 1-2 lesions
    - 40-50: 3-5 lesions
    - <40: 5-8 lesions

38

Complications

- 5-10%
  - Reperfusion pulmonary edema
    - Cough, hemoptysis, hypoxia
  - Vascular Injury
    - German experience 226 sessions; 1.8% mortality
    - Kawakami: 1.6% ring stenosis, 43% tortuous lesions

39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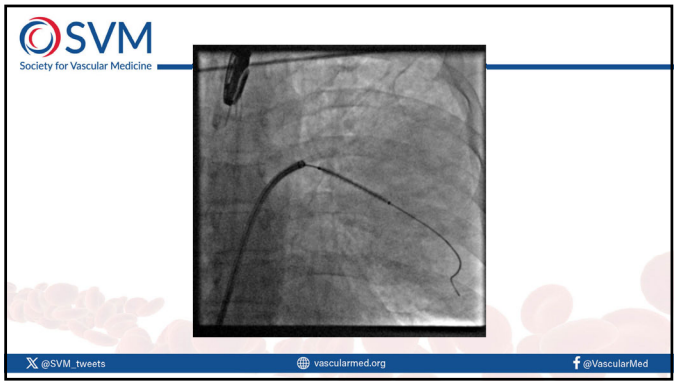
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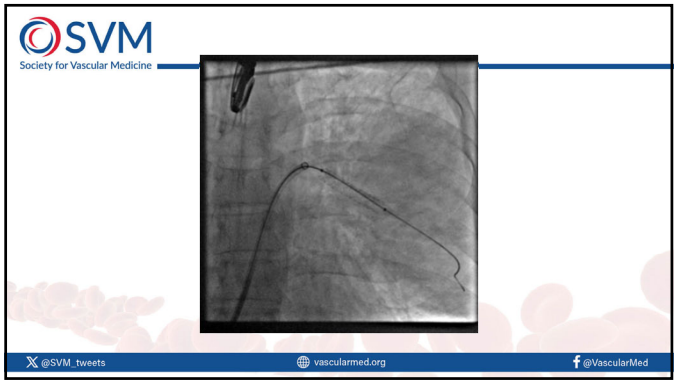
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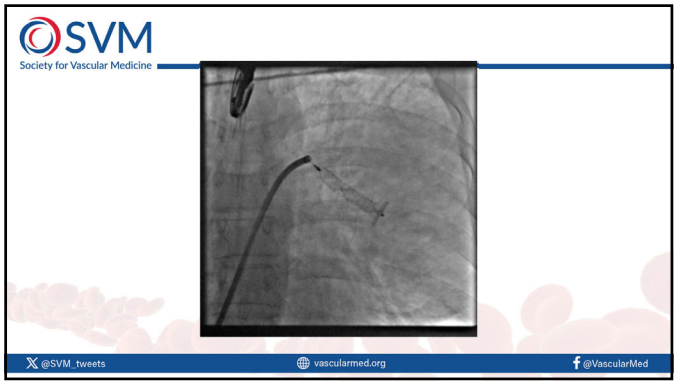
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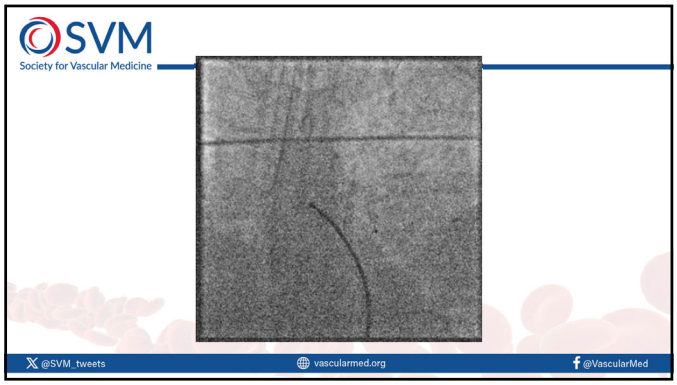
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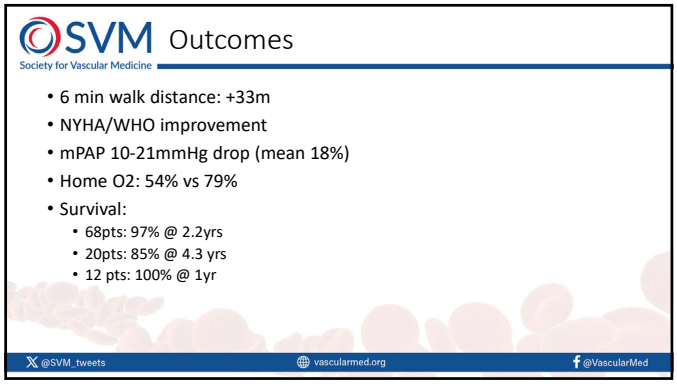
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Outcomes
• 6 min walk distance: +33m
• NYHA/WHO improvement
• mPAP 10-21mmHg drop (mean 18%)
• Home O2: 54% vs 79%
• Survival:
• 68pts: 97% @ 2.2yrs
• 20pts: 85% @ 4.3 yrs
• 12 pts: 100% @ 1yr
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45

Summary

- PE not just an acute disease
- Post PE syndrome common
- CTEPH morbid and high associated mortality
- BPA
  - Challenging technically
  - Complications expected
  - Pt and lesion selection vital

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46