Venenerkrankungen -IM Angiologie-

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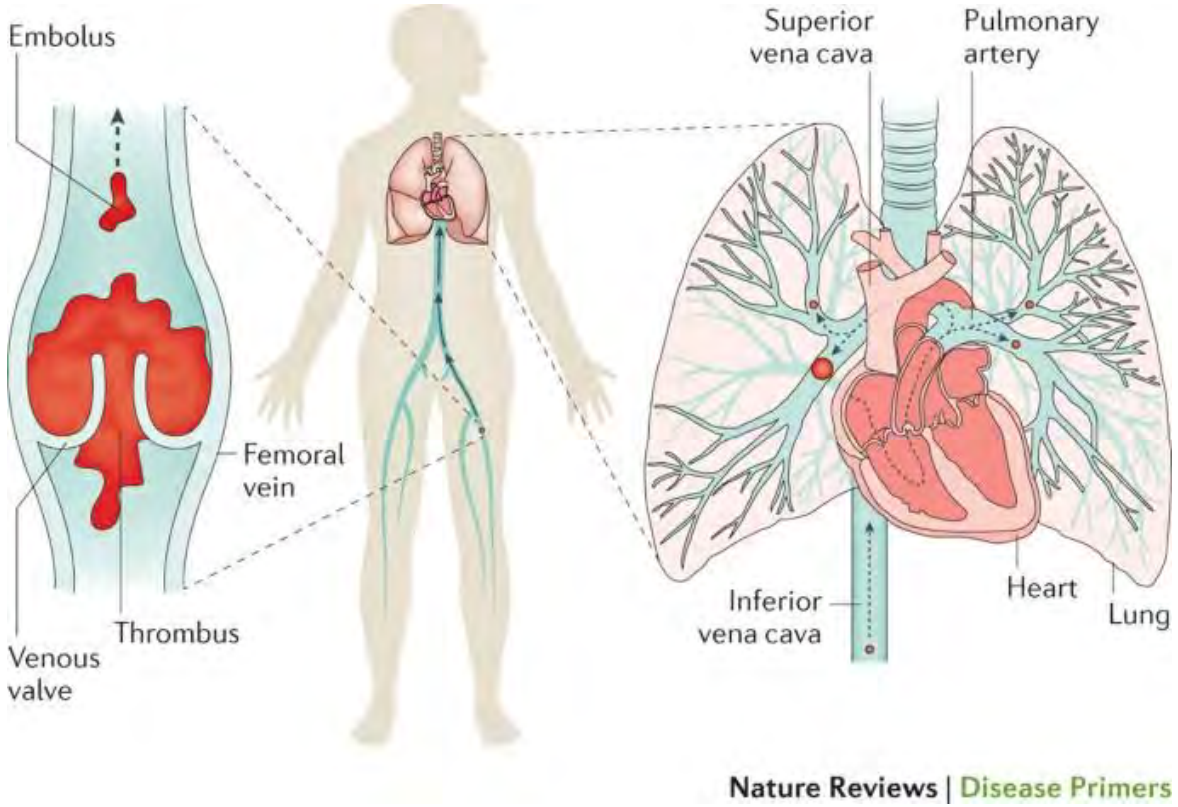
Venenerkrankungen

1. Acute venous thromboembolism (VTE)
   - deep vein thrombosis (DVT)
   - pulmonary embolism (PE)

2. Chronic venous insufficiency (CVI) and post-thrombotic syndrome (PTS)

Venous Thromboembolism (VTE)

Deep vein thrombosis (DVT) and pulmonary embolism (PE)



Symptomatic PE (+/- DVT)
30% of VTE

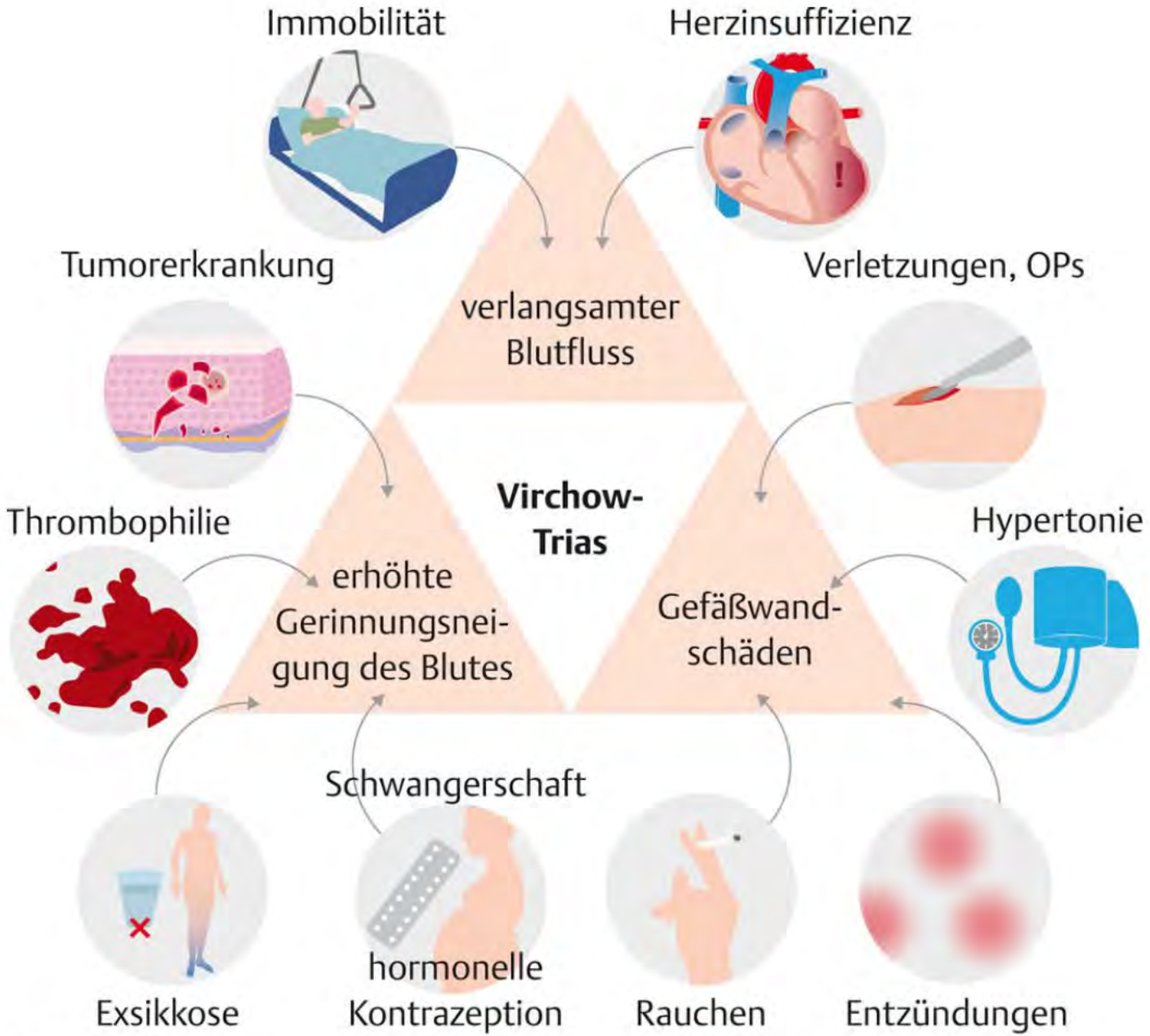
No identifiable risk factors	**40%**
Cancer	**20%**
Hospital-associated	**40%**

VTE risk linearly increases with age

Third most frequent cardiovascular disease
Incidence rate 2/1.000 pop-year (increasing trend)

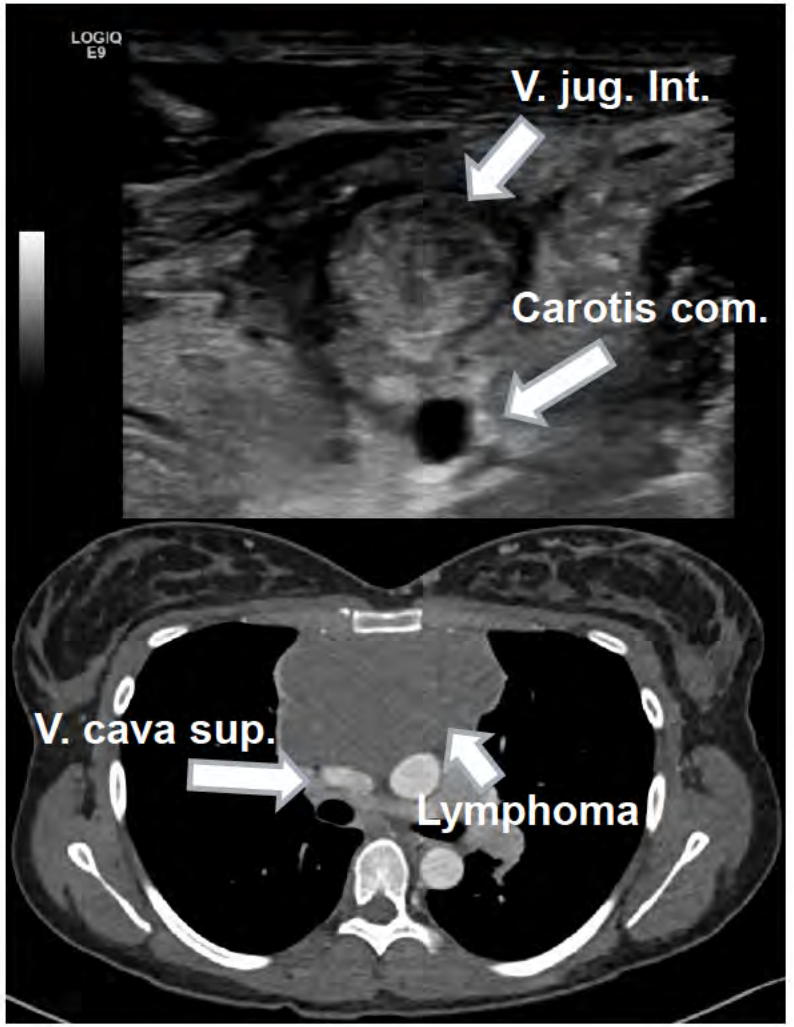
Huisman M, Barco S et al.. Nat Rev Dis Primers 2019

Östrogen + Tumorkompression der Vena Cava



W, 29

- pregnant SSW 10
- flu (one week)
- acute thrombosis V. jug., V. brachiocephalica, V. subclavia
- compression due to lymphoma



Frauen, die Östrogen (z.B. Kontrazeptiva) einnehmen, haben eine 10 mal höhere Warscheinlichkeit eine Venenthrombose zu entwickeln

M (31) with **thorax pain, dyspnoea, syncopal episodes, and left leg pain**

Personal history / comorbidities:
- on methadone (prior drug abuse)
- depression

Transported to the ER with 4L O2

Signs and symptoms of deep vein thrombosis (usually unilateral)

- Swelling
- Pain
- Redness
- New collateral veins
- A feeling of warmth
- Cramping/soreness
- (Signs/symptoms of PE)

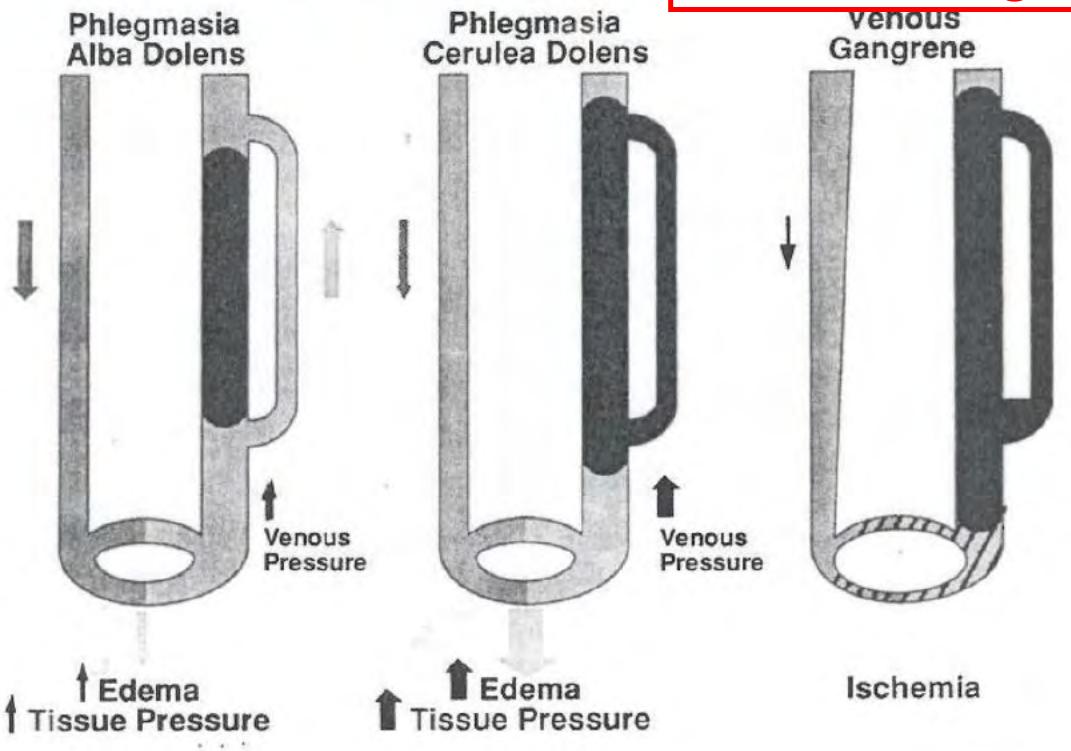
→ Very **aspecific**

Krankheit

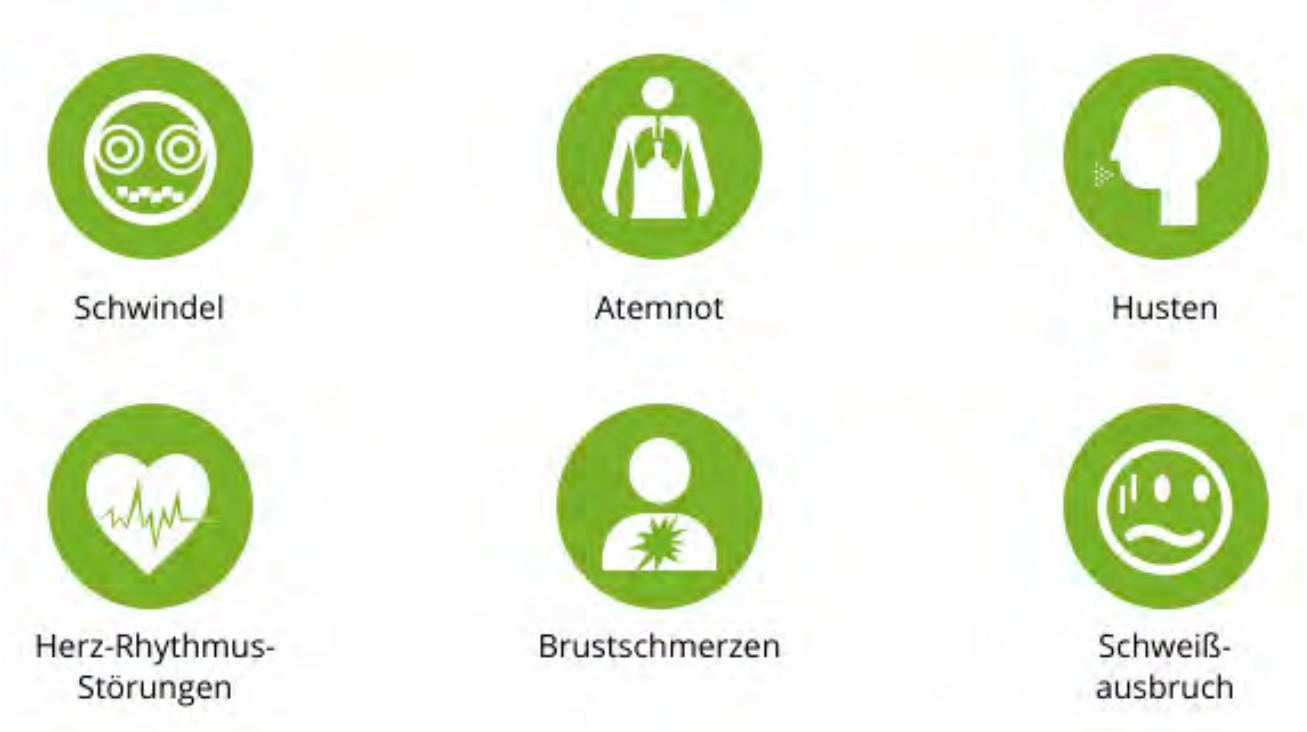
Phlegmasia caerulea dolens

Kein Durchfluss möglich

Wichtig



Signs and symptoms of pulmonary embolism



- Tachypnea (>20/min) or need for O2
- Syncope
- DVT (>50%)
- **Hemodynamic decompensation / shock / CPR**
- Even more aspecific signs/symptoms than DVT!

Blood pressure 100/60 mmHg

Heart frequency 140 beats/min

SaO2 92% with 6L/min

Lactates 1.5 mmol/L

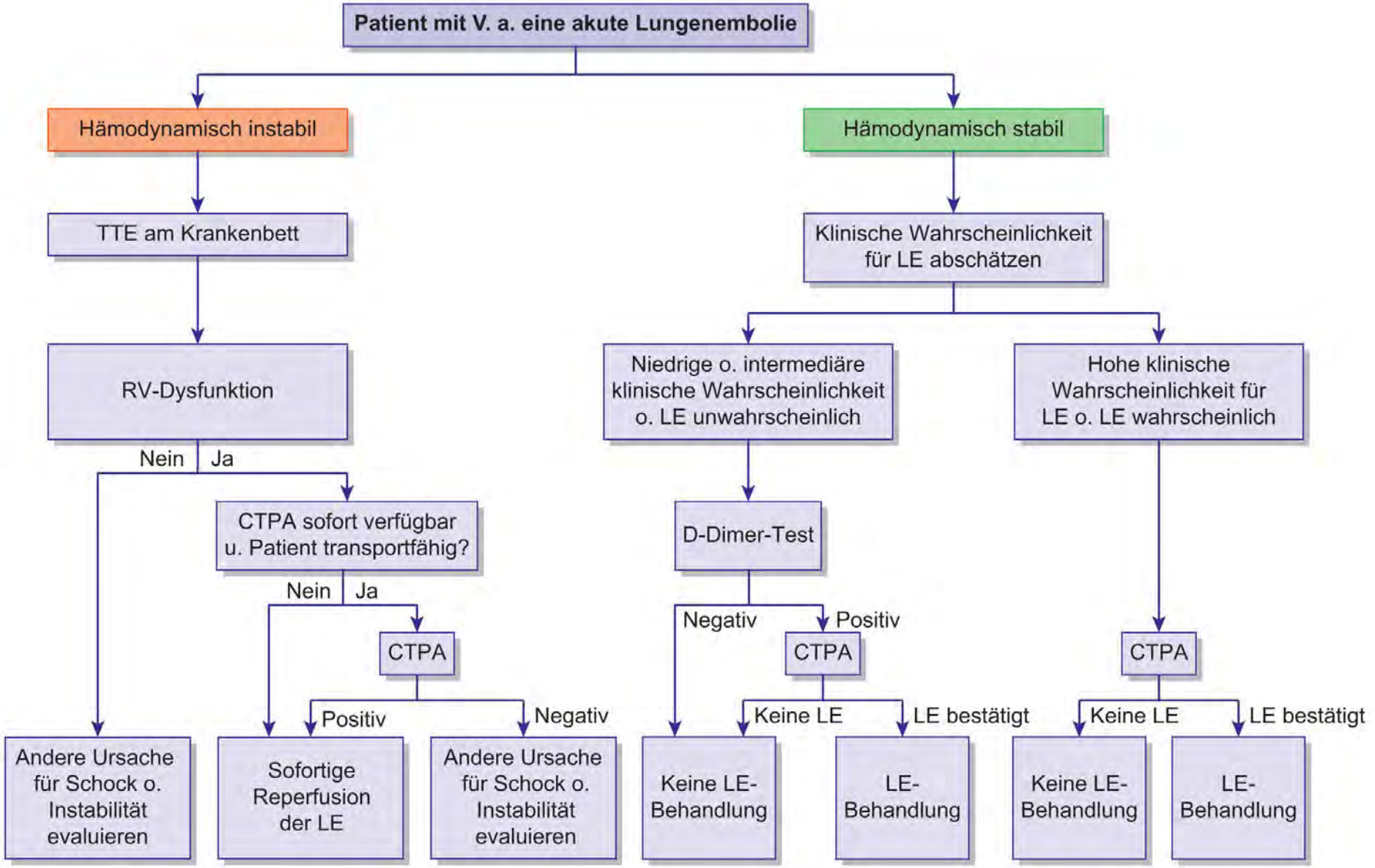
Entzündung				
CRP (C-reakt.Prot.)	< 5	mg/l	98 *	85 *
Herz und Muskel				
CK, total	< 190	U/l	79	142
Myoglobin	28 - 72	µg/l	27 *	
Troponin T, High Sensitive	< 14	ng/l	92 *	134 *
NT-proBNP (Roche)	< 85.8	ng/l	1599 *	
Schilddrüse				

What to do?

Bei Verdacht

- Give heparin/LMWH
- D-dimer Wenn Vortestwahrscheinlichkeit hoch
- Coronary angiography
- CT-angiography
- Lower-extremity sonography
- Pulmonary embolism response team
- Echocardiography Nicht unbedingt nötig

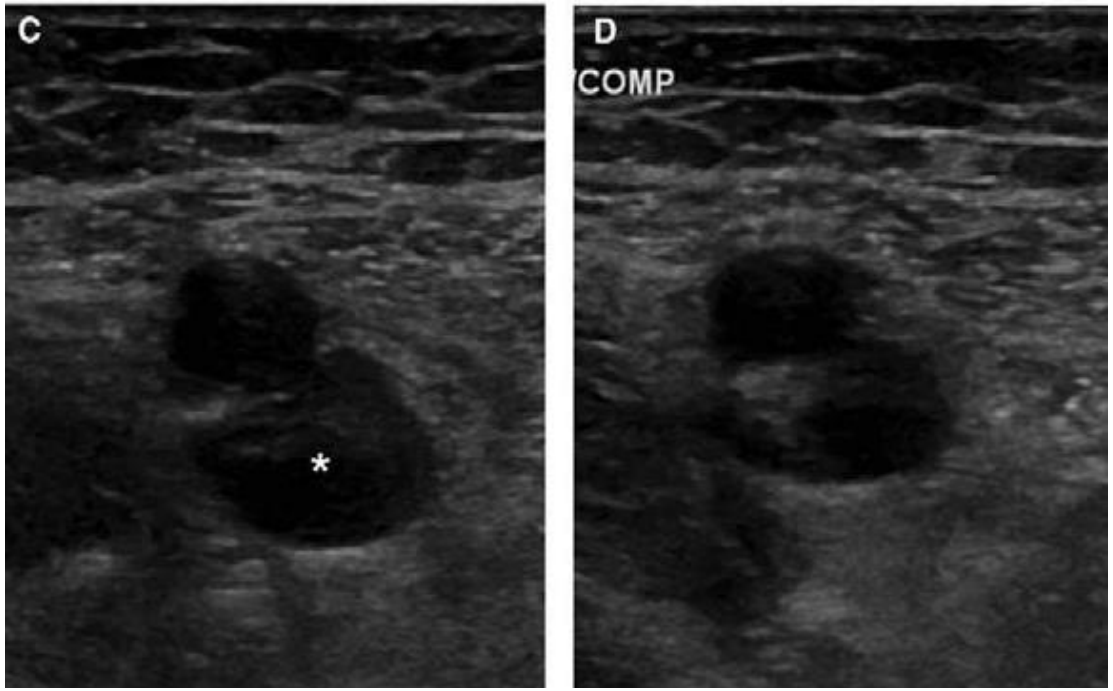
Diagnosis of acute PE



Ven. Duplexsonographie

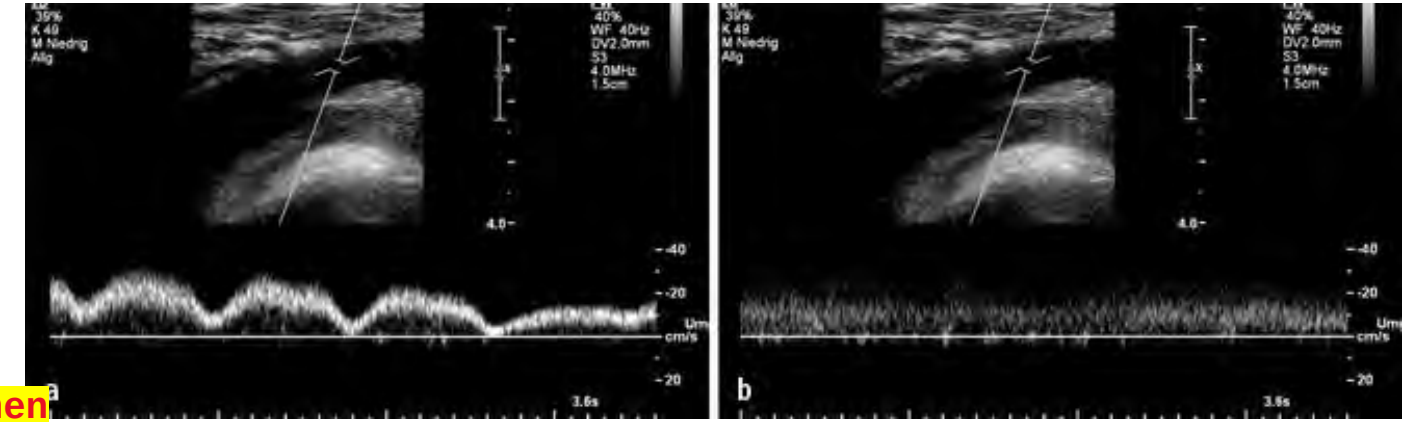
1) Kompression

Bei Schwangerschaft auch nicht kompressibel



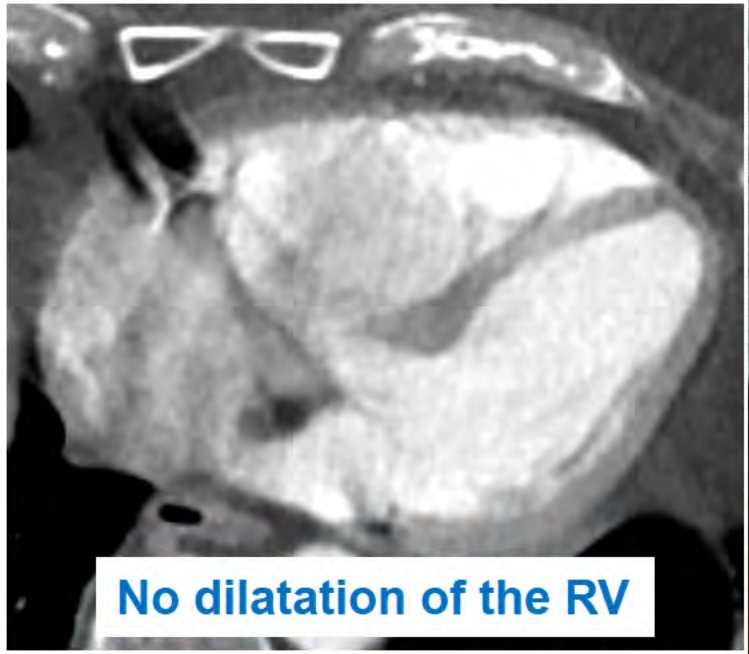
2) Flusssignal

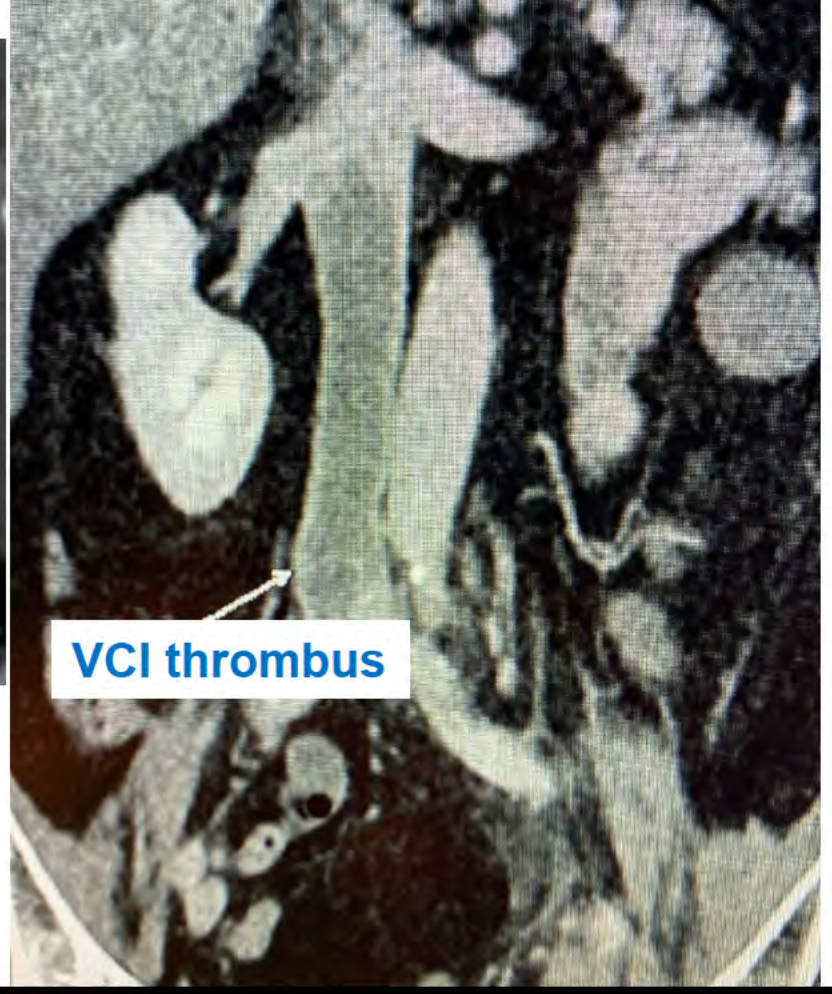
Bandförmig --> Fliesst über kollateralvenen

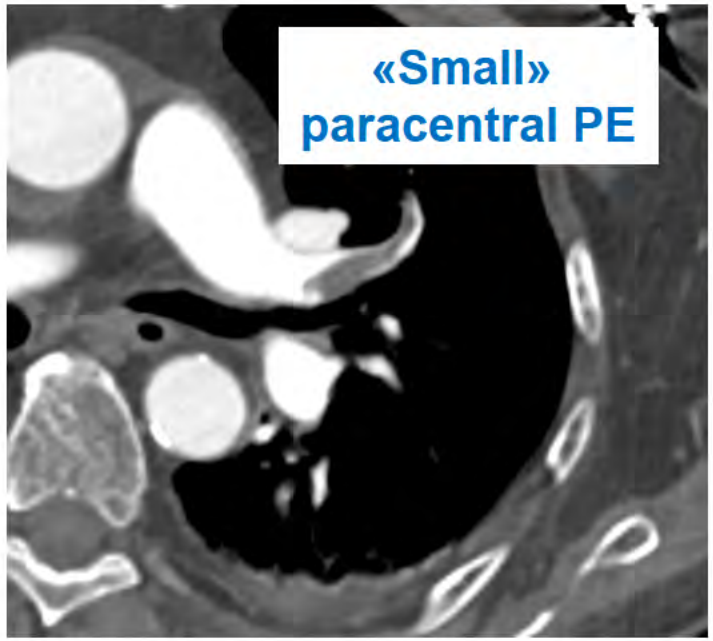


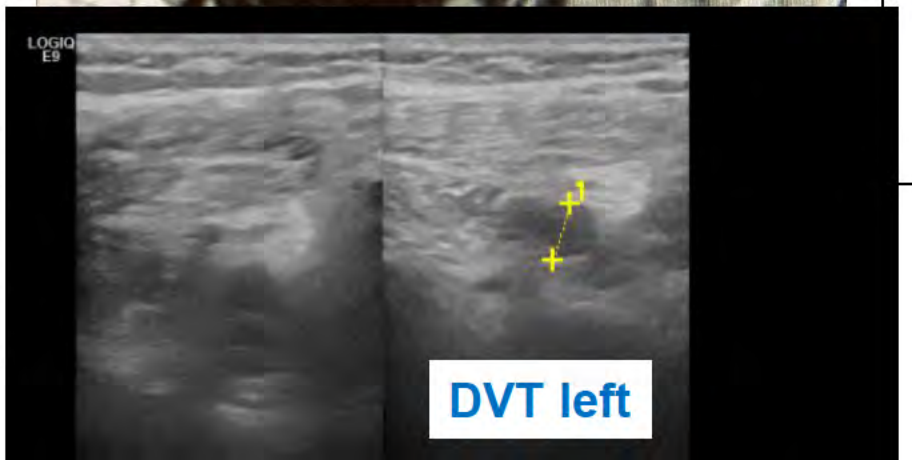
Normal

Pathologic









What to do?

- Heparin/LMWH
- DOACs
- Systemic lysis
- Endovascular thrombectomy
- Cava filter
- Surgical thrombus removal

Acute VTE

Early discharge

Choice of the anticoagulant agent

ICU Monitoring or Reperfusion

Duration of anticoagulant treatment

Comprehensive evaluation (e.g occult cancer, thrombophilia)

Post-PE impairment
Postthrombotic syndrome
CTEPH

First 24 hours **First week** **First 3-6 months**

LOW RISK	INTERMEDIATE RISK	HIGH RISK
HOME TREATMENT 		CLOSE MONITORING / I.C.U. 

HOSPITALIZATION

2019 ISTH Capsules, *Res Pract Thromb Haemost*, 2019

OK for almost all patients with *isolated* deep vein thrombosis (without PE)

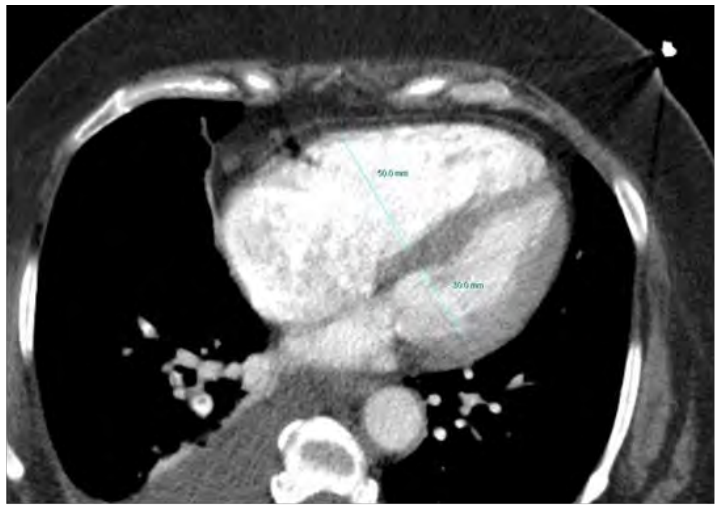
If PE is present:

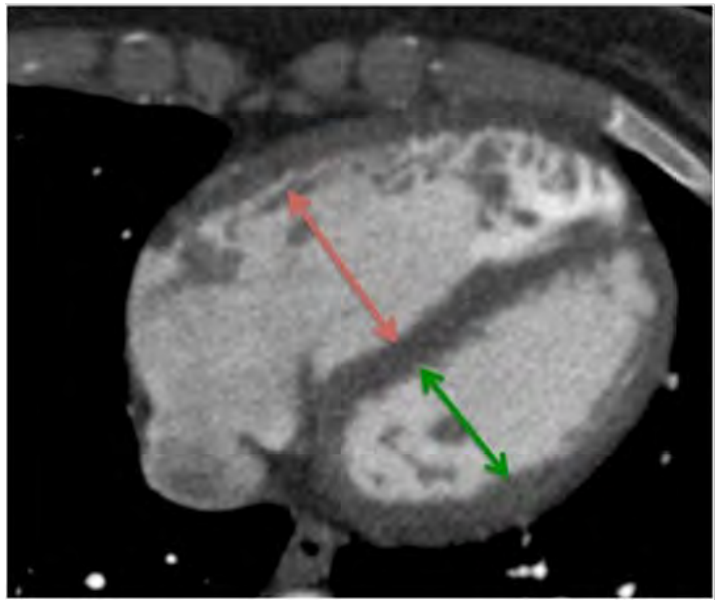
- low clinical risk (scores) plus
- no right ventricular dysfunction (CT or echo)

Early discharge after PE: absent Hestia criteria or sPESI = 0

	Simplified PESI	Hestia criteria
Age	Age > 80 years	-
PE-related	Heart rate > 110 bpm	Haemodynamically unstable (clinical judgement, heart rate, systolic BP), thrombolysis needed
	Systolic BP < 100 mmHg	
	SaO_2 < 90 %	SaO_2 < 90 %
Comorbidities	Cardiopulmonary diseases	-
	Cancer	
	Implicit?	Severe medical conditions (requiring hospitalization), high bleeding risk, prior HIT
		Organ dysfunction
Pregnancy		Pregnancy
Feasibility		Lack of social, familiar, or medical support
RV dysfunction	Implicit?	Implicit? → severe medical conditions

Hestia studies from the Leiden group (Huisman, Klok)
sPESI validations from the Madrid group (Jimenez)



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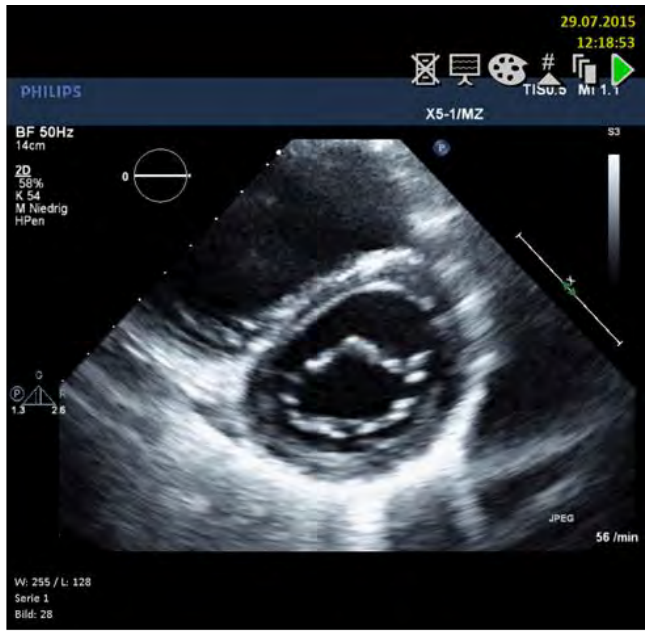
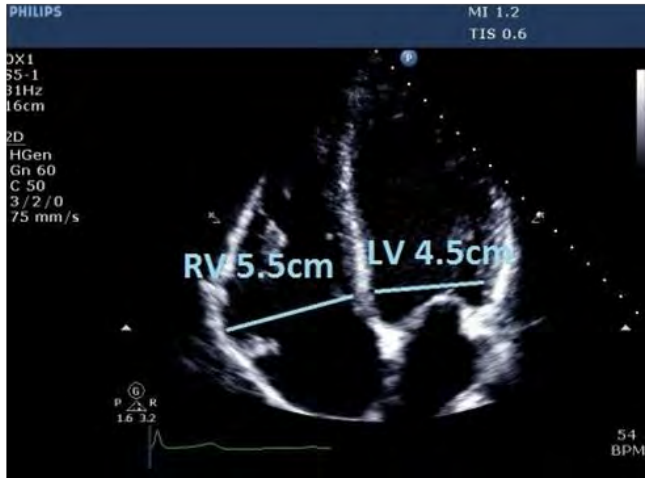

29.07.2015
12:18:53
PHILIPS
X5-1/MZ
BF 50Hz
14cm
2D
58%
K 54
M Niedrig
HPen
JPEG
56 /min
W: 255 / L: 128
Serie 1
Bild: 28


PHILIPS
MI 1.2
TIS 0.6
RV 5.5cm
LV 4.5cm

Wie definiert man die hämodynamische Instabilität?

- Persistierende arterielle Hypotonie mit systolischem Blutdruck <90 mmHg,

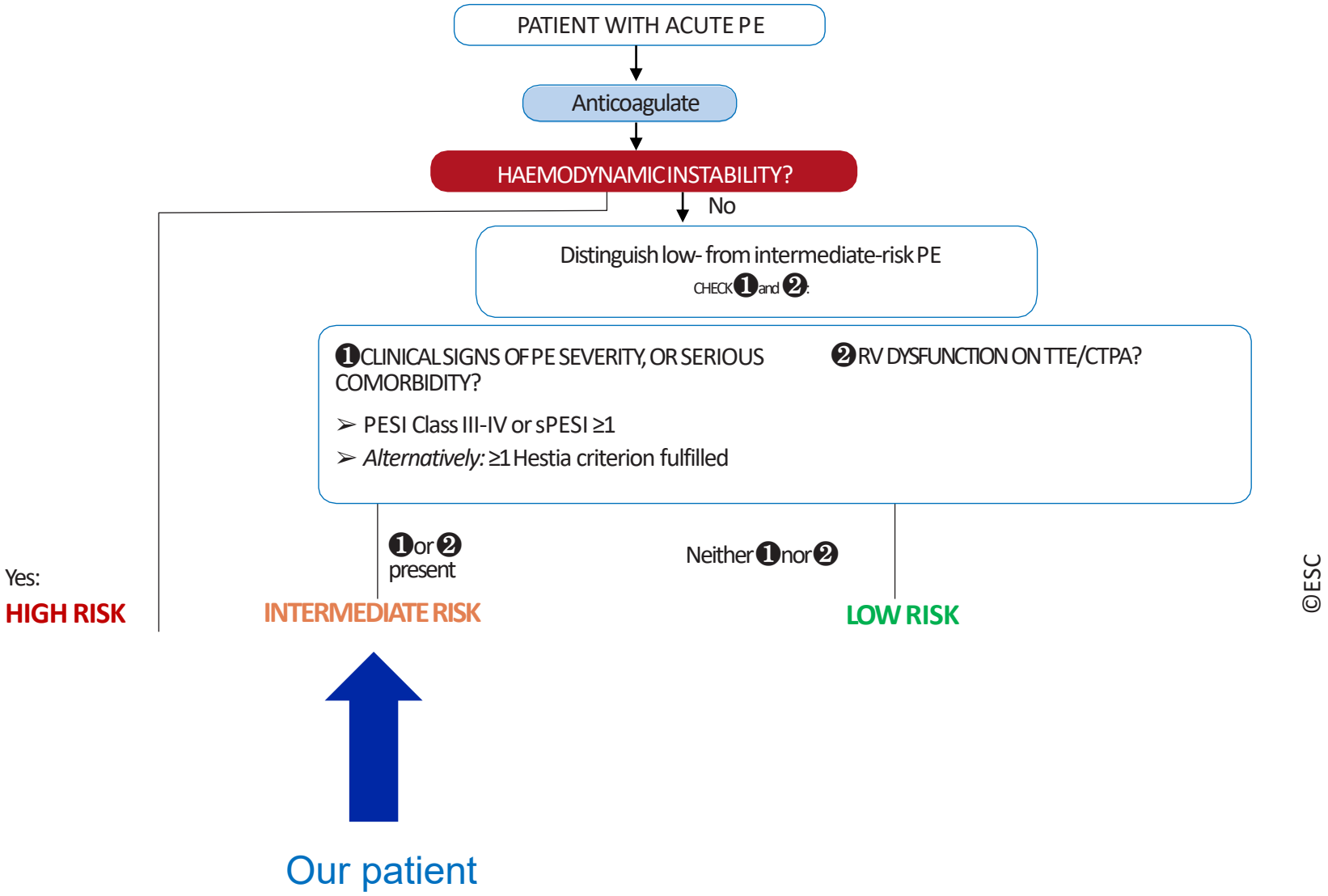
oder

- Abfall des systolischen Blutdrucks um > 40 mmHg über mehr als 15 Min.,

oder

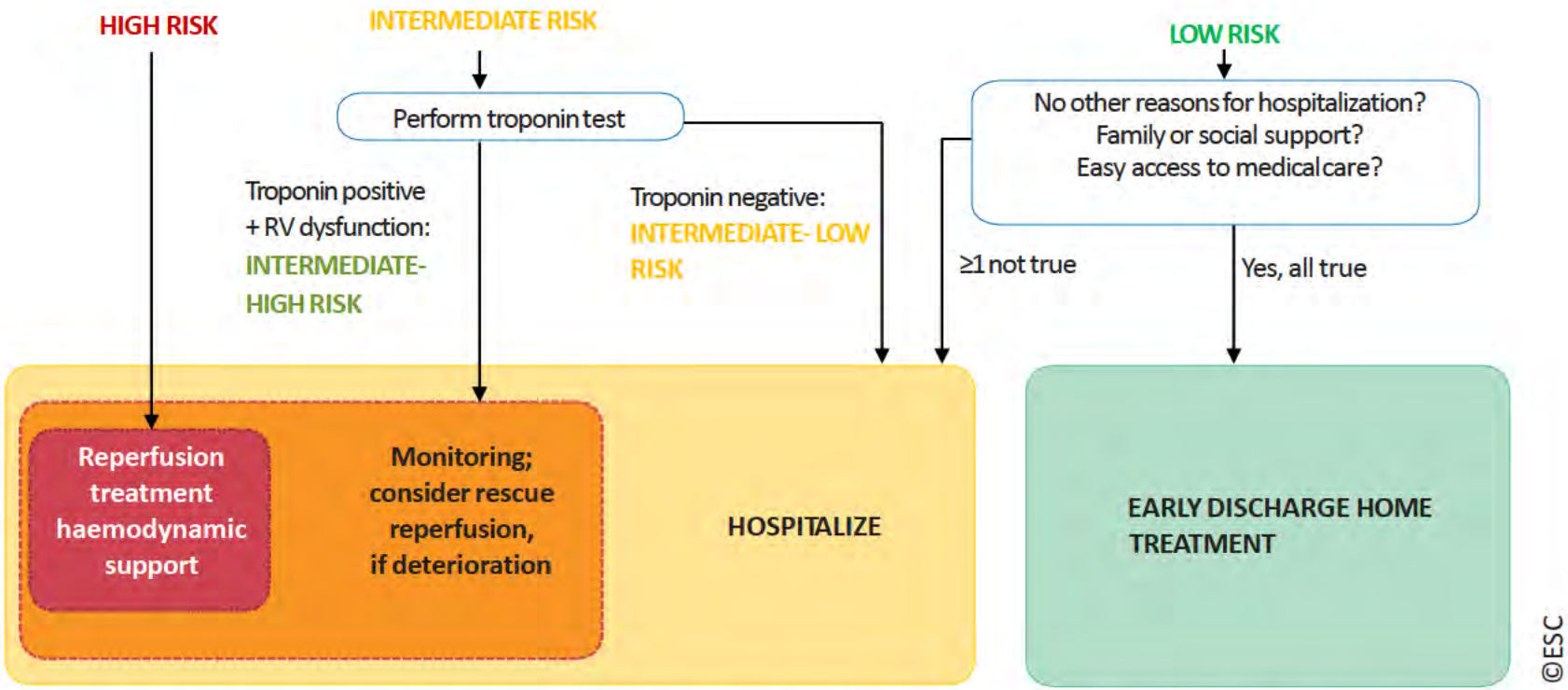
- CPR

Risk-adjusted management strategy for acute PE (1)



Our patient

Risk-adjusted management strategy for acute PE (2)



CTPA = computed tomography pulmonary angiography; PESI = Pulmonary Embolism Severity Index; RV = right ventricular; TTE = transthoracic echocardiography.

Anticoagulation in acute PE

LOW RISK	INTERMEDIATE RISK	HIGH RISK
INITIAL ANTICOAGULATION WITH ORAL AGENTS (DOACs) 		PARENTERAL ANTICOAGULATION 
PRIMARY REPERFUSION NOT RECOMMENDED		PRIMARY REPERFUSION

2019 ISTH Capsules, *Res Pract Thromb Haemost*, 2019

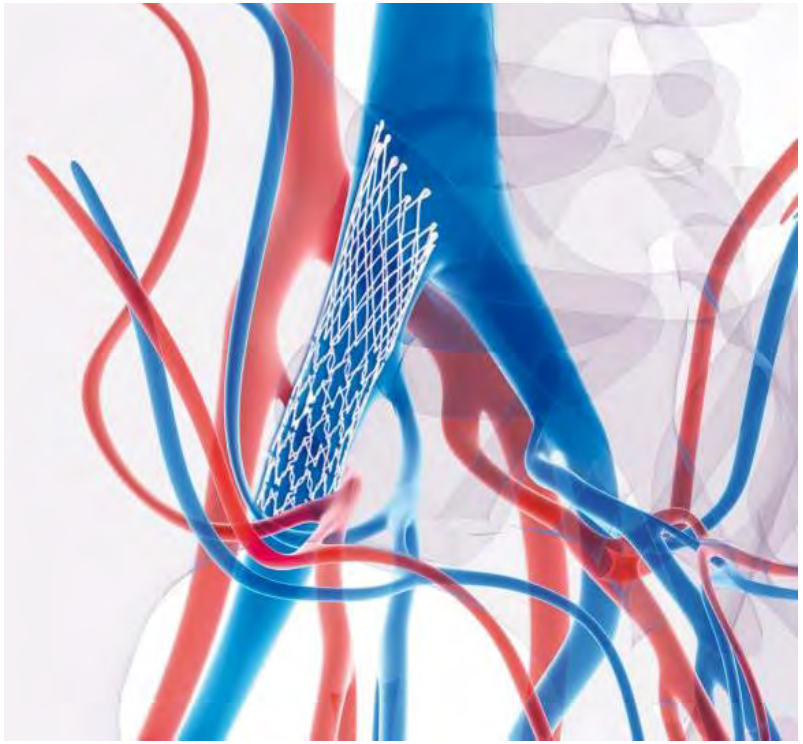
Principles of initial management of acute DVT

- Fixed-dose **direct oral anticoagulants** in most patients (≥3 months)
- **LMWH/UFH** in patients with gastric cancer or (reduced dose) if thrombocytopenia <50000 G/L or if surgery planned
- **Leg compression** (stockings class II)
- **VKA** only if antiphospholipid syndrome known / highly suspected or if other reasons for VKA

Genetic thrombophilia test (almost) never needed

Guidances and guidelines for iliofemoral DVT

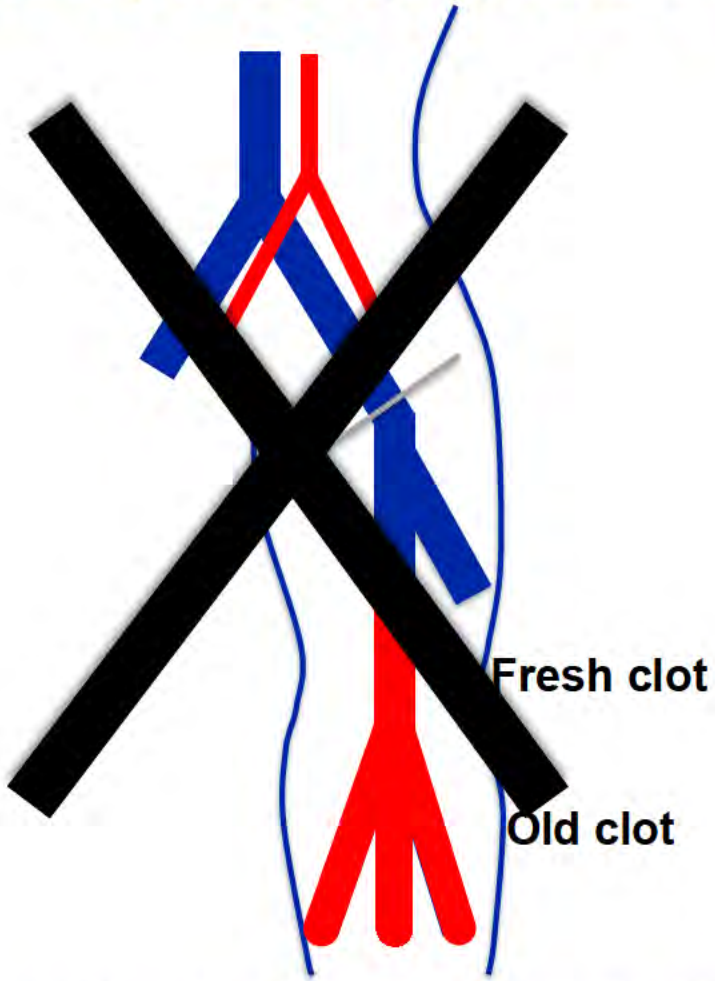
- Thrombus removal for patients with phlegmasia and in selected patients with iliofemoral deep vein thrombosis
- Systemic thrombolysis *not* recommended
- Self expanding metallic stents at the time of clot removal in the case of compression



InterEPID guideline

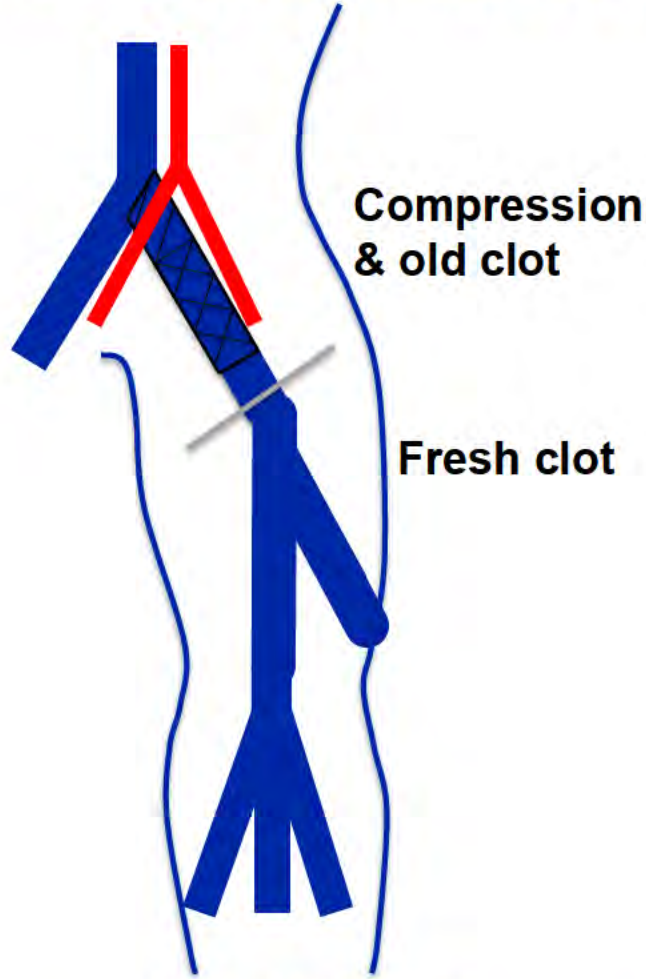
ESVS guidelines

Ascending femoropopliteal DVT



Inflow unlikely to be improved by catheter therapies

Descending iliofemoral DVT



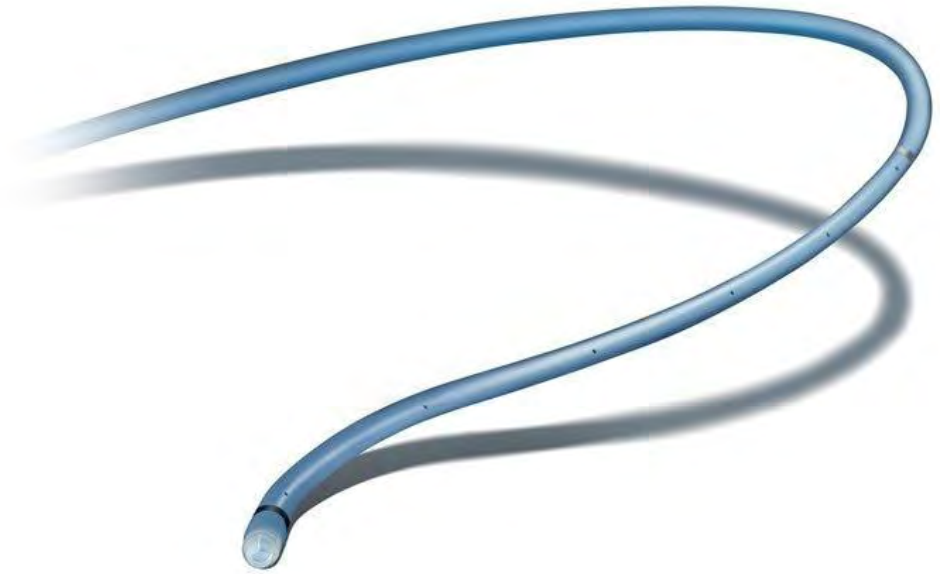
Inflow improved
by catheter therapies & stent

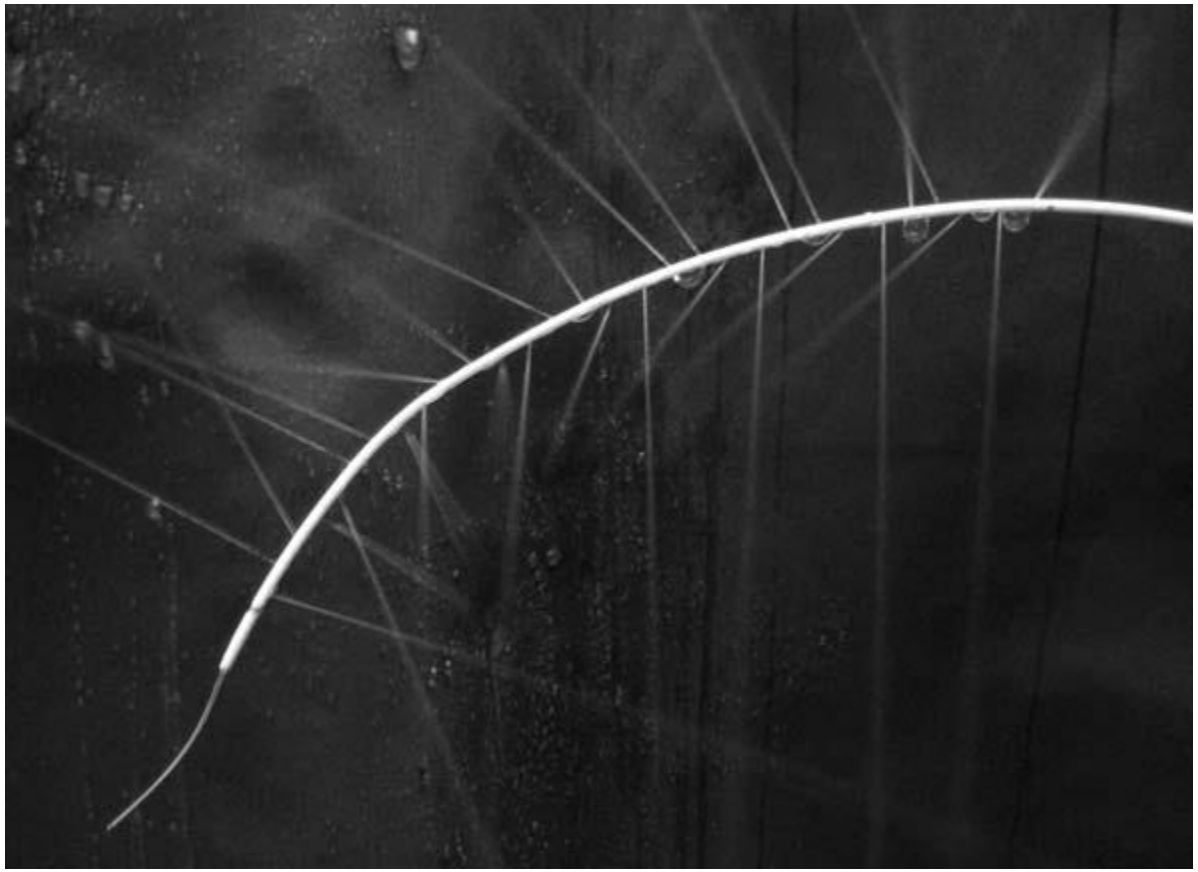
Our patient

PE	DVT	Cava thrombosis
«intermediate-low» risk sligthly elevated troponin no right ventricular dilatation	Ascending DVT Common iliac vein (May-Thurner point) not thrombosed Symptomatic but no phlegmasia	High risk of embolization Cava filter risky (dilated VCI and need for suprarenal placement)
No reperfusion needed **Anticoagulation alone**	No reperfusion strictly needed **Anticoagulation alone**	**Anticoagulation plus either endovascular thrombectomy or local lysis**

Standard catheter-directed thrombolysis

- 5F catheters *without* ultrasounds
- Multiside hole infusion catheter



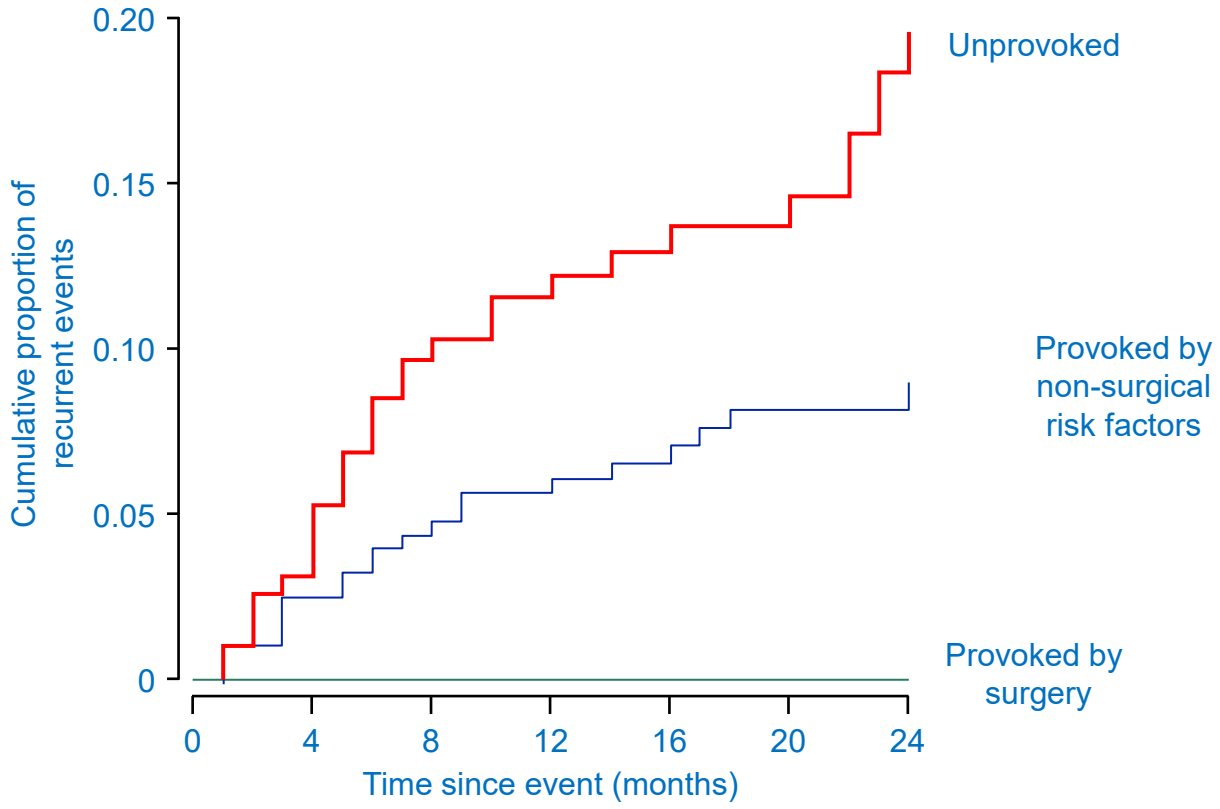


Isolated distal DVT (without cancer)	**Reversible major transient risk** factors for VTE	No identifiable risk factors	**Active cancer** or cancer treatment	**Recurrent VTE or persisting risk factor** (i.e. autoimmune disease, transplantation, CTEPH, VTE familiar history + thrombophilia)
3-month AC	**3-month AC**	**Long-term AC**	**Long-term AC (until cancer cured)**	**Long-term AC**
		After 6 months, reduced-dose AC		**After 6 months, reduced-dose AC**
		Risk scores/D-dimer → **stop** AC in some patients		

Impact of Clinical Risk Factors on VTE Recurrence

Cumulative proportions of recurrent thrombosis after cessation of anticoagulant therapy*

(N=558)



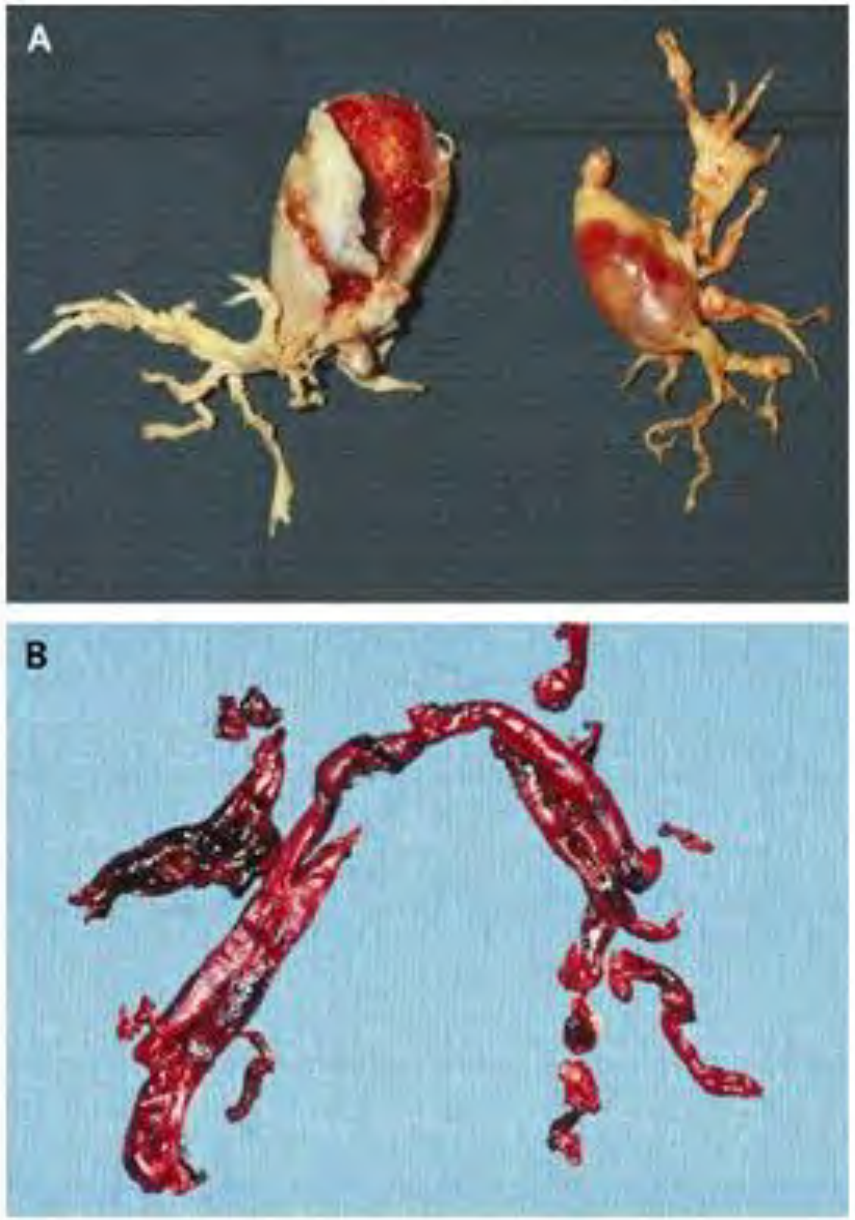
*Patients with malignant disease and antiphospholipid syndrome were excluded from the study

Baglin T *et al*, *Lancet* 2003;362:523–526

- Anticoagulation effectively resolves VTE, but stopping treatment increases the cumulative risk of VTE recurrence
- The cumulative incidence of recurrent VTE is approximately 10% in the first year if anticoagulation is stopped

CHRONIC PE
= CTEPH (1-4%)

ACUTE PE



N Engl J Med 2004;350:2236-2238

CENTRAL ILLUSTRATION: Sequence of Events

The Right Ventricle and Its Load in Pulmonary Hypertension

Pulmonary vessel narrowing leads to increased vascular load on right ventricle (RV)

RV adapts by increasing muscle contractility and wall thickness ("coupling")

To maintain cardiac output, RV dilates and heart rate increases

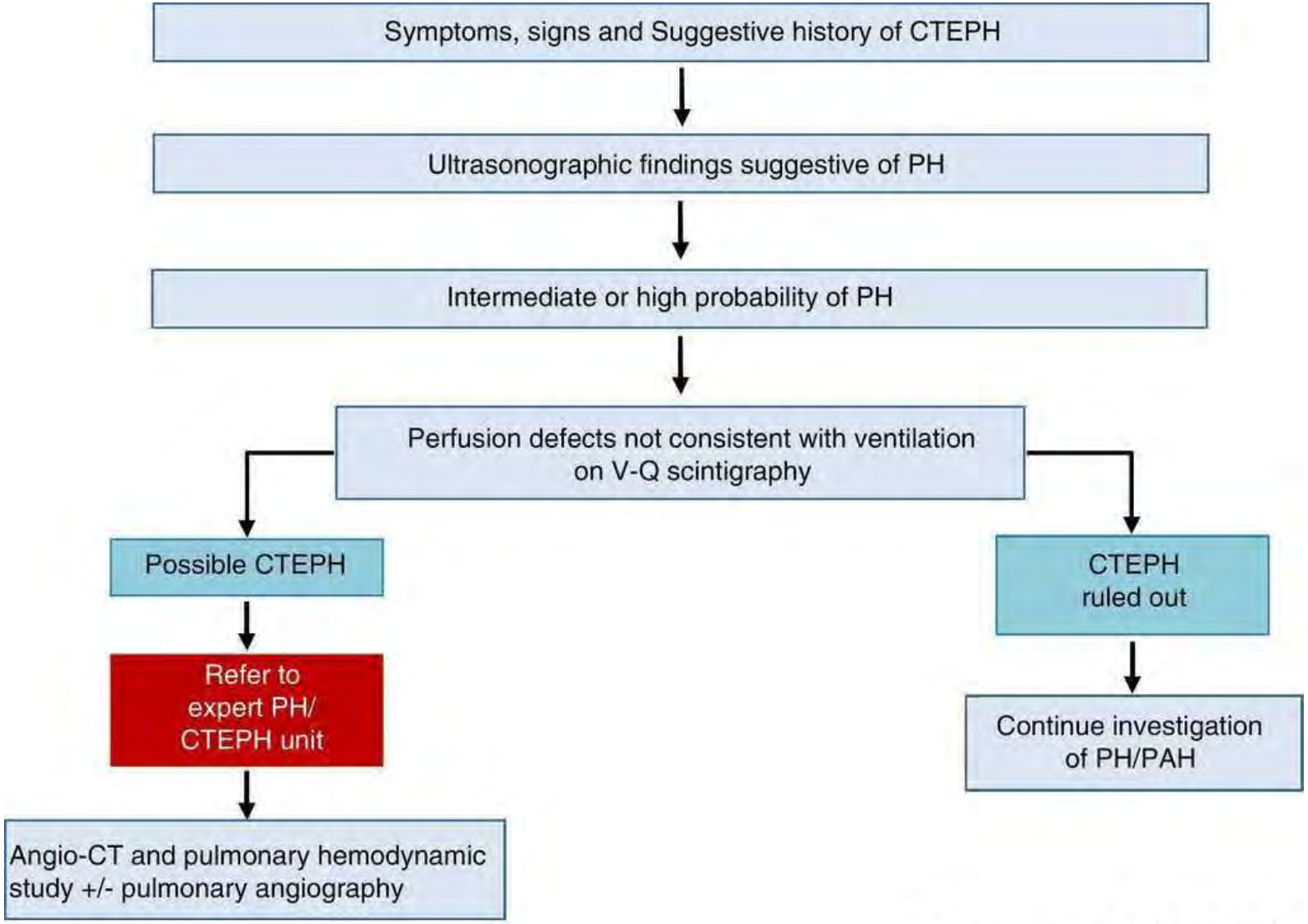
Increase in wall stress and oxygen consumption per gram follow

Leftward septal bowing results

Final stage: Uncoupling occurs with high metabolic demand and reduced output

Vonk Noordegraaf, A. et al. J Am Coll Cardiol. 2017;69(2):236-43.

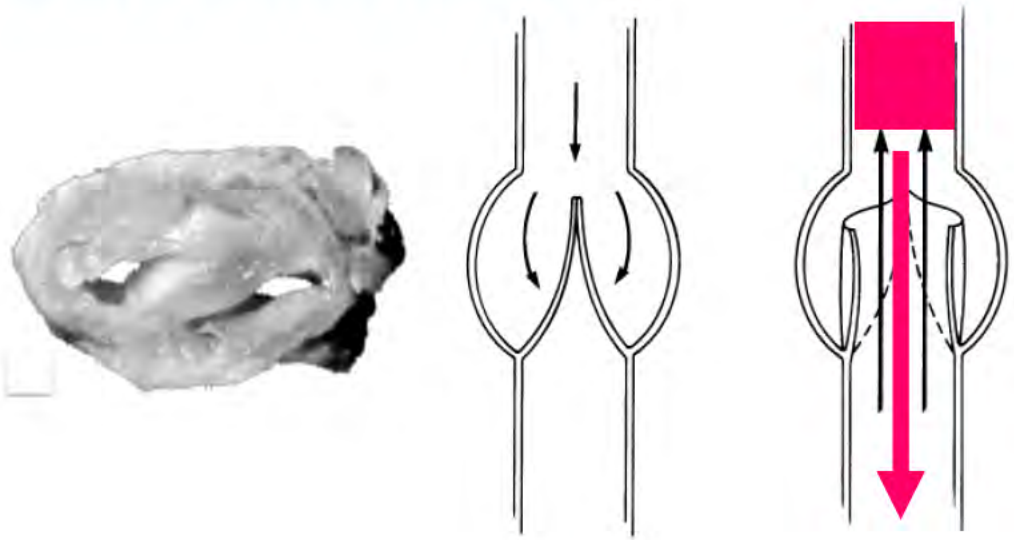
Follow-up: CTEPH screening at 3-6 months



Arch Bronconeumol. 2018;54:205–15

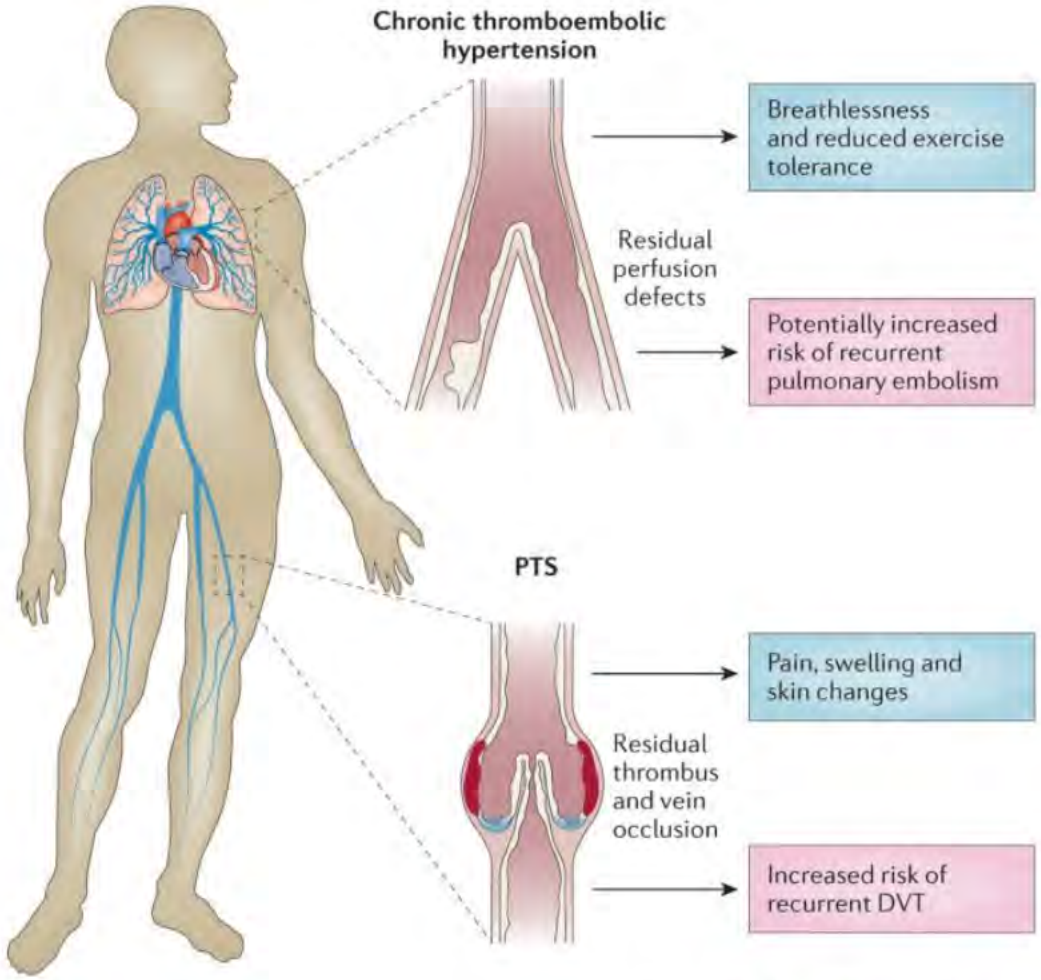
Definition des Postthrombotischen Syndroms (PTS)

Sekundäre chronisch venöse Insuffizienz (CVI) bedingt durch einen Zustand nach tiefer Beinvenenthrombose



Hauptmechanismen: Reflux, Obstruktion

Beim PTS: oft Reflux und Obstruktion in Kombination



Klassifikation des Postthrombotischen Syndroms: Villalta Score

Symptoms	Signs
Pain	Pretibial oedema
Heaviness	Induration of the skin,
Cramps	Hyperpigmentation
Pruritus	New venous ectasia
Paraesthesia	Redness
	Pain during calf compression
	Leg ulceration

For each item a score of 0 (=no or minimal) to 3 (severe) is assigned. A total score 5–14 is a mild-to-moderate PTS, a score of ≥15 or a leg ulcer is always severe PTS.

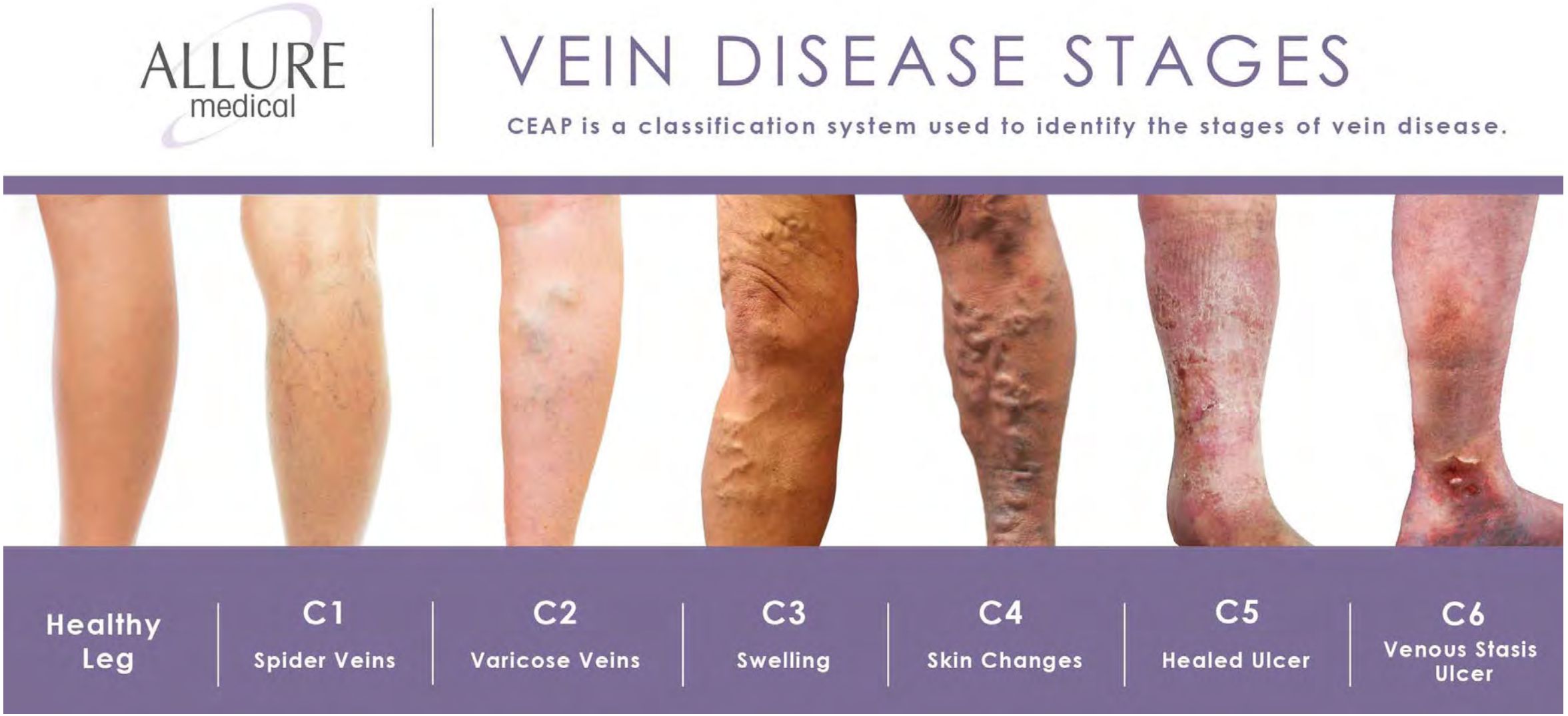
Prandoni et al. , Ann Int Med 1996

PTS Häufigkeit nach TVT

- Cohort study mit 387 Patienten mit symptomatischer TVT
  - Follow up 2y, mit Villalta Scale nach 1/4/8/12/24M
  - Resultate:
    - Whd ganzem Studienintervall→fast 50% mit PTS!
      - ca. 30% mild
      - ca. 10% moderate
      - 3% severe
  - PTS ist der Hauptdeterminant der Lebensqualität (QOL) 2 Jahre nach TVT
  - Therapie: Antikoagulation, Kompressionstherapie, Revaskularisation der (Becken)venen bei gutem In-flow

[1]Kahn et al, Ann Intern Med. 2008 [2]Kahn et al, J Thromb Haemost. 2008

Chronic vein insufficiency (CVI)
which includes post-thrombotic syndrome (PTS)



Typen von Ulzerationen

Abb. 1 ▶ Ulcus cruris venosum (postthrombotisch) seit über 40 Jahren

Abb. 2 ▶ Ulcus cruris mixtum: postthrombotisches Syndrom, periphere arterielle Verschlusskrankheit, sekundäres Lymphödem

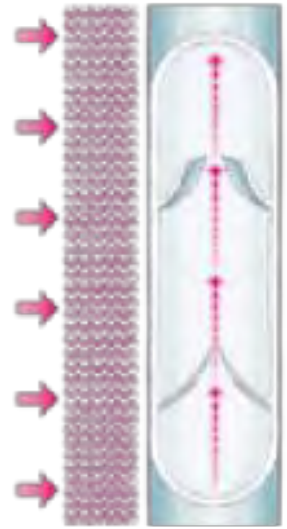
Abb. 3 ▶ Prätibiales Ulcus cruris arteriosum, ABI 0,4

Ulkus venosum	57-80%
Ulkus cruris mixtum	4-30%
Ulkus arteriosum	3-20 %
Ulkus bei Vasculitis	2-13 %
Sonstige Ursachen	5-10 %

Herrmanns: Gefässchirurgie 2010: 15: 273-87

Kompressionstherapie

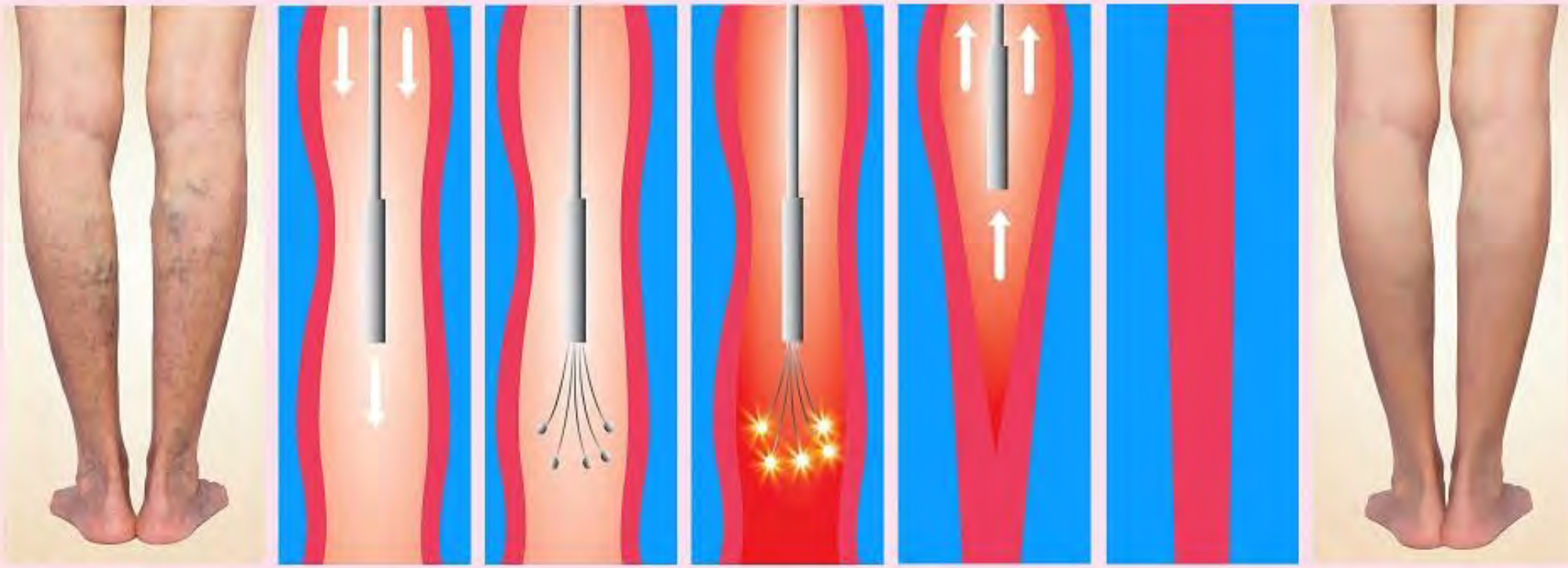
Krankhaft veränderte Vene mit defekten Venenklappen



Krankhaft veränderte Vene mit medizinischem Kompressionsstrumpf

Bei venösen Ulcerationen Kompression = primärer Therapie-Ansatz

VARICOSE VEINS TREATMENT
WITH RADIOFREQUENCY ABLATION or OBLITERATION



BEFORE

Catheter inserted into the vein

Electrodes are placed in the vein

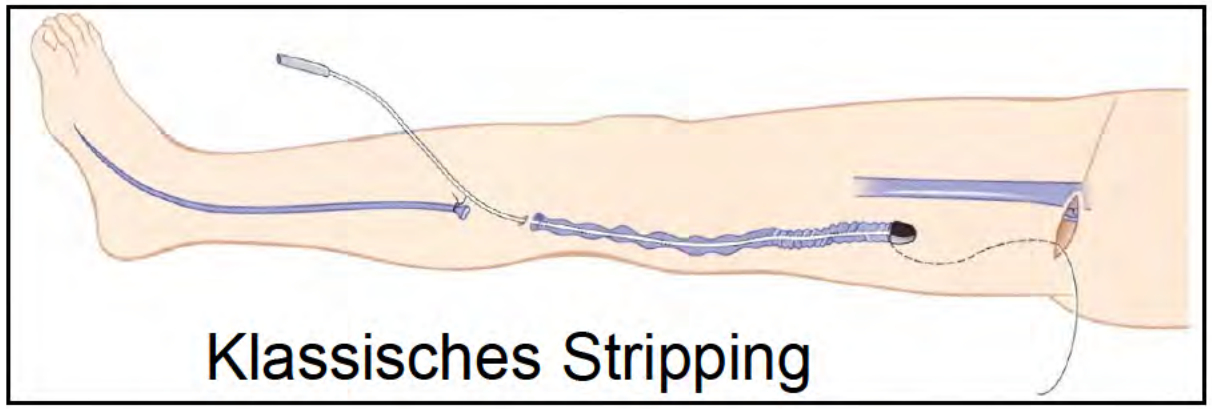
A radiofrequency wave is sent

Catheter withdrawn, closing vein

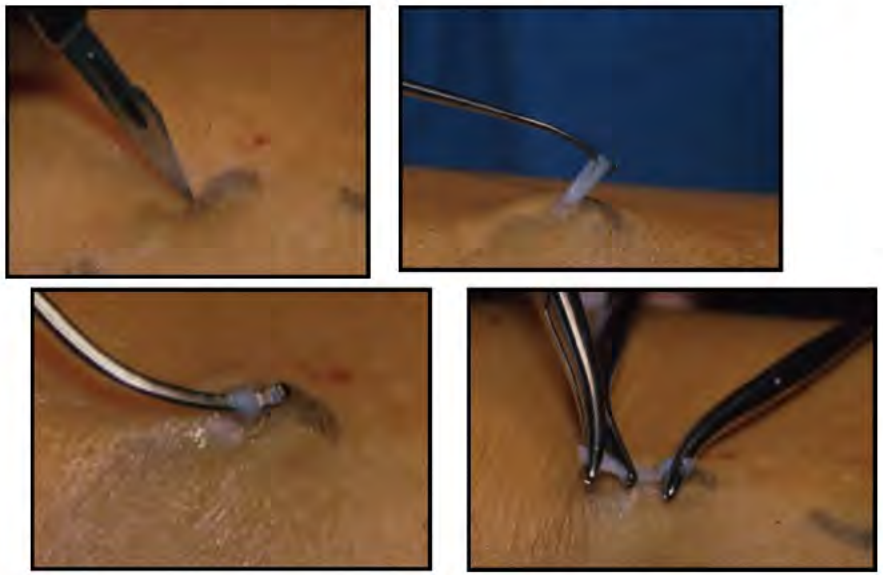
Closed vein following treatment

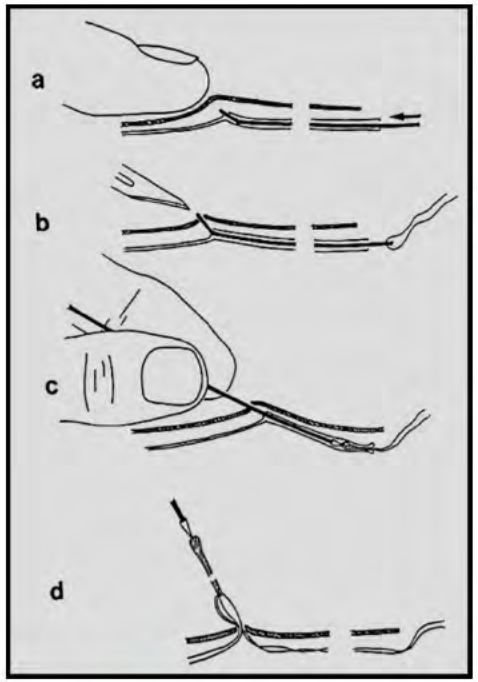
AFTER

Stripping Methoden



Mini-Phlebektomie





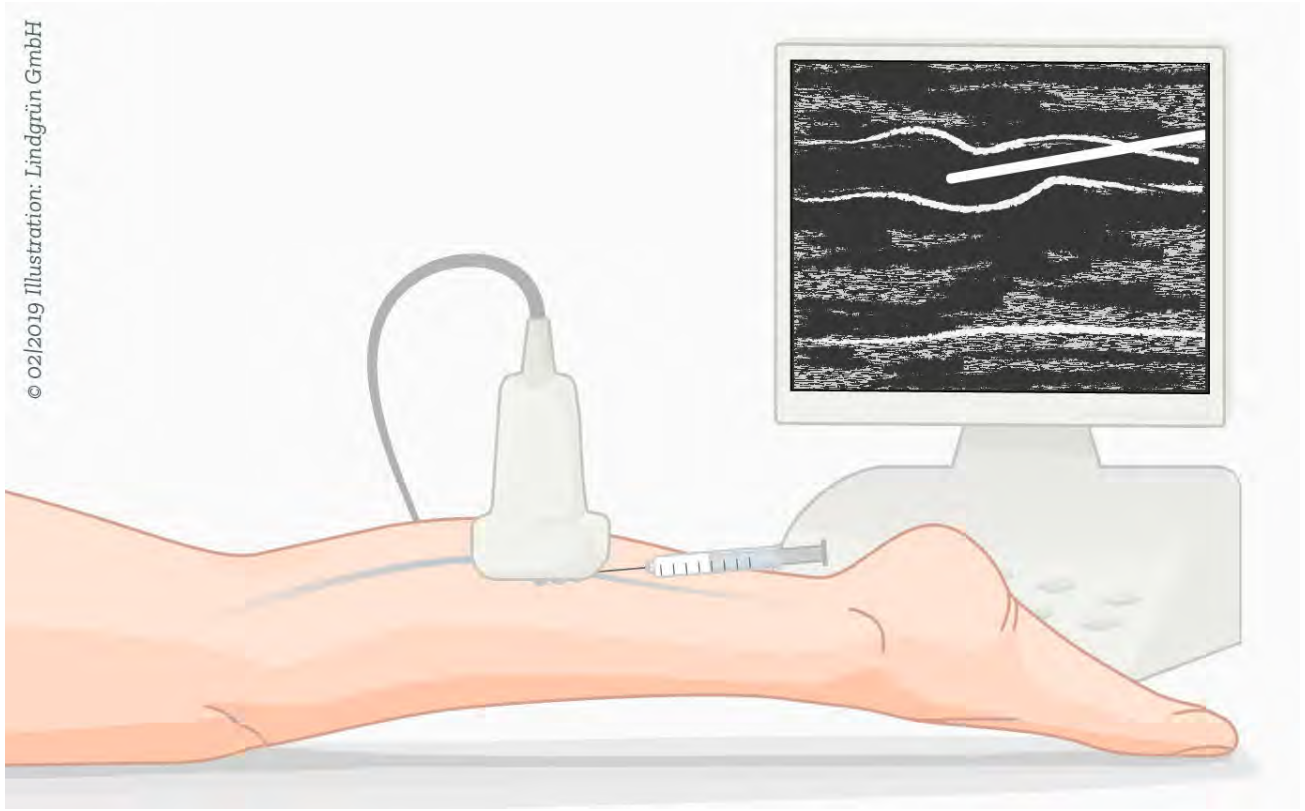
Perforation-

Invagination

-Stripping

Hach W: VenenChirurgie 2005

Schaumtherapie



USZ Universitäts Spital Zürich

Thanks for your attention

Back up slides für Selbststudium

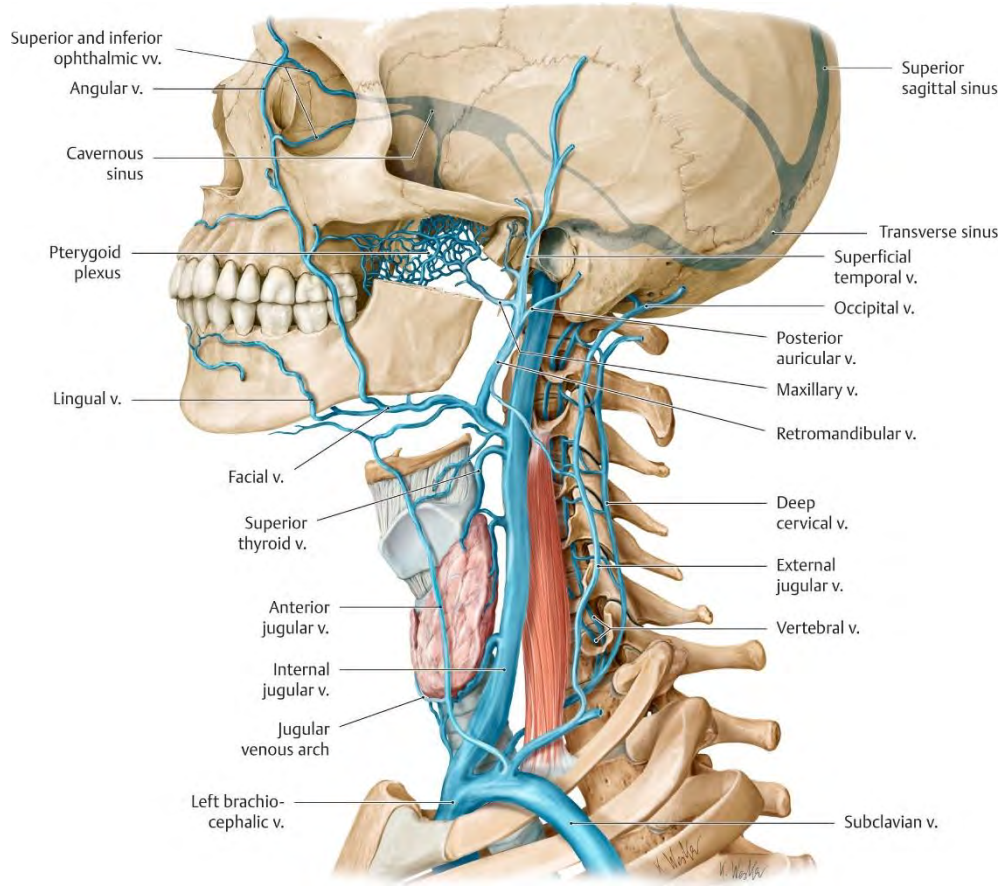
VTE Prophylaxis modalities

- **Mechanical**
  - Graduated Compression Stockings
  - Intermittent Pneumatic Compression
  - Inferior Vena Cava Filters

- **Pharmacologic**
  - Heparins/ LMWH
  - Fondaparinux
  - Vitamin K Antagonists/ NOACs

- **Combines** Mechanical - Pharmacologic

The example of Virchow´s triad in jugular vein thrombosis



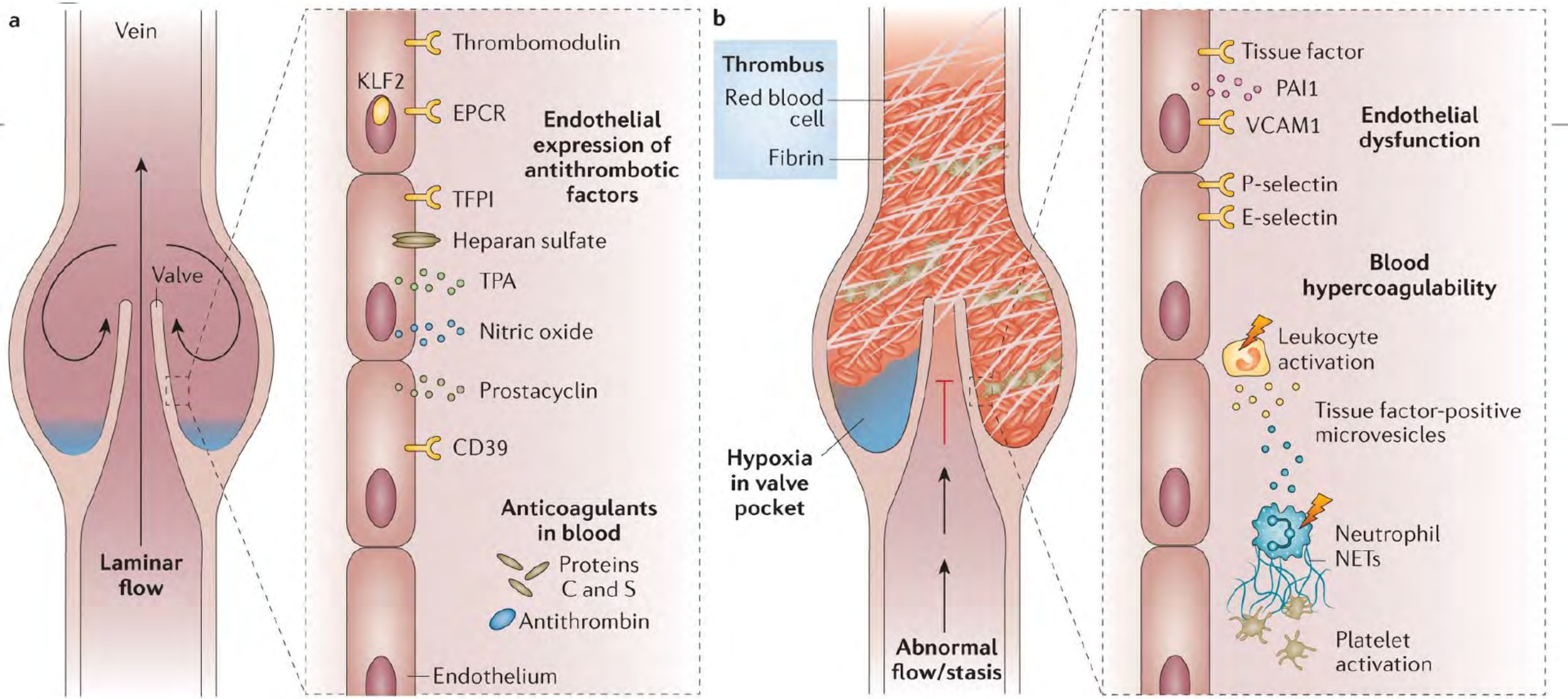
Sigmoid/cavernous/petrosal sinus → *Jugular*

- otitis, mastoiditis, sinusitis
- head injury
- other causes of CVT (cancer, pregnancy, oral contraception, JAK2+ myeloproliferative diseases)

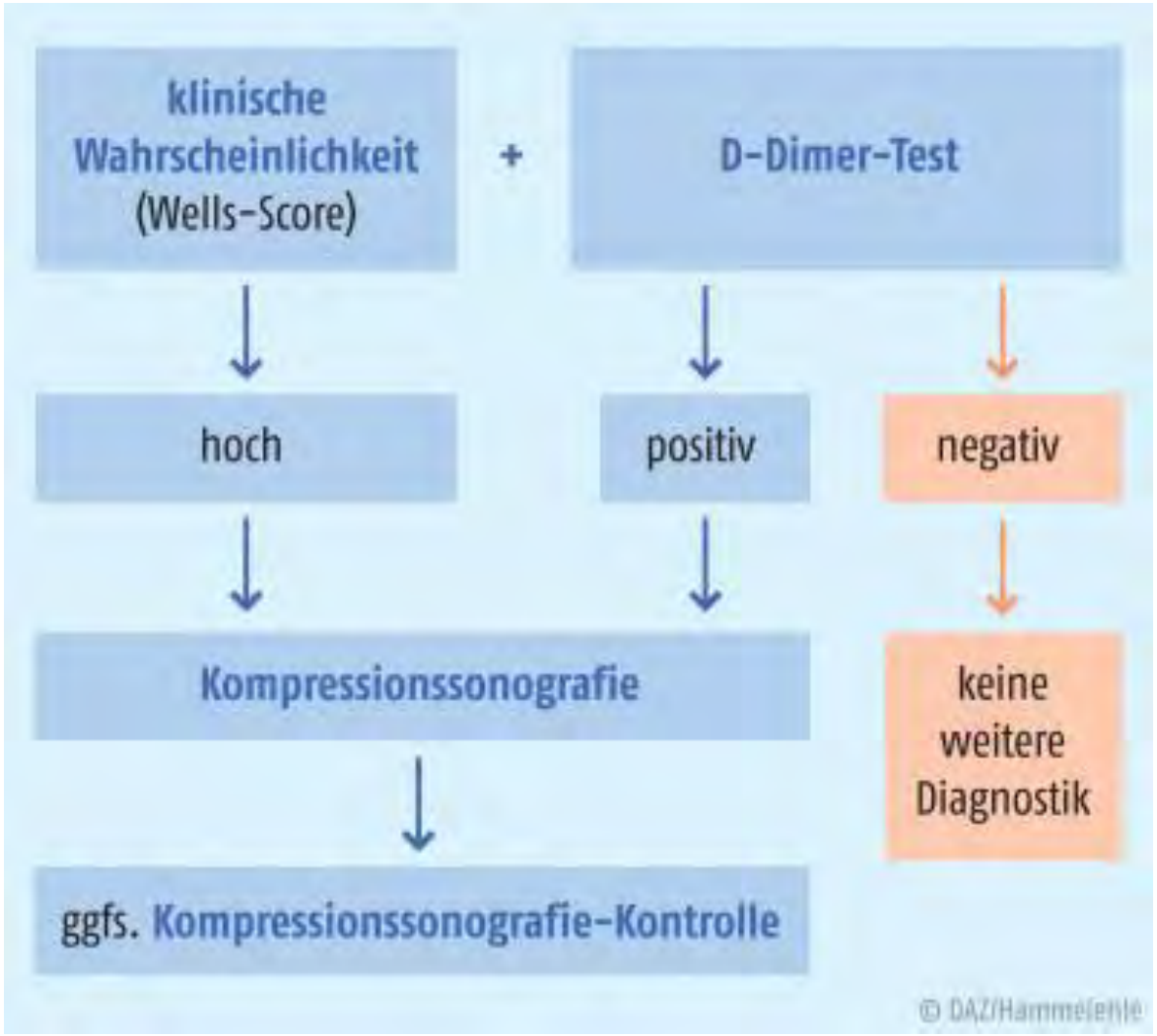
PE ← *Upper extremity/Jugular* → Cerebral

- **catheter-related**: chemo, TPN, pacemaker lead
- thoracic outlet syndrome
- neck/mediastinal lymphadenonopathy
- ovarian hyperstimulation syndrome
- cancer
- local surgery or mass
- Lemierre syndrome due to Fusobacterium spp
- antiphospholipid syndrome

Journal of Internal Medicine, 2020; doi: 10.1111/joim.13114


a
Vein
Valve
Laminar flow
Thrombomodulin
KLF2
EPCR
Endothelial expression of antithrombotic factors
TFPI
Heparan sulfate
TPA
Nitric oxide
Prostacyclin
CD39
Anticoagulants in blood
Proteins C and S
Antithrombin
Endothelium
b
Thrombus
Red blood cell
Fibrin
Hypoxia in valve pocket
Abnormal flow/stasis
Tissue factor
PAI1
VCAM1
Endothelial dysfunction
P-selectin
E-selectin
Blood hypercoagulability
Leukocyte activation
Tissue factor-positive microvesicles
Neutrophil NETs
Platelet activation

Diagnosis of acute DVT



Pretest Probability
TVT: Wells-Score

klinische Charakteristik	Score
aktive Krebserkrankung	1,0
Lähmung oder kürzlich Immobilisation der Beine	1,0
Bettruhe (>3 Tage) grosse Chirurgie (<12 Wochen)	1,0
Schmerz / Verhärtung entlang der tiefen Venen	1,0
Schwellung ganzes Bein	1,0
Unterschenkelschwellung >3 cm gegenüber Gegenseite	1,0
eindrückbares Ödem am symptomatischen Bein	1,0
Kollateralvenen	1,0
früher dokumentierte TVT	1,0
alternative Diagnose mindestens ebenso wahrscheinlich wie TVT	-2,0
TVT-Wahrscheinlichkeit	**Score**
hoch	≥2,0
nicht hoch	<2,0

* modifiziert nach Wells 2003
Quelle: Hach-Wunderle V. Diagnostik und Therapie der venösen Thrombose. Hamostaseologie 2005;25:356–366

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

Predisposing factors for VTE (1)

Strong risk factors (OR >10)
Fracture of lower limb
Previous VTE
Spinal cord injury
Hospitalization for heart failure or atrial fibrillation/flutter (within previous 3 months)
Hip or knee replacement
Major trauma
Myocardial infarction (within previous 3 months)

VTE = venous thromboembolism.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

Predisposing factors for VTE (2)

Moderate risk factors (OR 2–9)
Arthroscopic knee surgery
Autoimmune diseases
Blood transfusion
Central venous lines
Intravenous catheters and leads
Chemotherapy
Congestive heart failure or respiratory failure
Erythropoiesis-stimulating agents
Hormone replacement therapy (depends on formulation)

VTE = venous thromboembolism.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

Predisposing factors for VTE (3)

Moderate risk factors (cont'd)
In vitro fertilization
Oral contraceptive therapy
Postpartum period
Infection (specifically pneumonia, urinary tract infection, and HIV)
Inflammatory bowel disease
Cancer (highest risk in metastatic disease)
Paralytic stroke
Superficial vein thrombosis
Thrombophilia

VTE = venous thromboembolism.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

Predisposing factors for VTE (4)

Weak risk factors (OR <2)
Bed rest >3 days
Diabetes mellitus
Arterial hypertension
Immobility due to sitting (e.g. prolonged car or air travel)
Increasing age
Laparoscopic surgery (e.g. cholecystectomy)
Obesity
Pregnancy
Varicose veins

VTE = venous thromboembolism.

PE Differential Diagnosis

- Myocardial Infarction
- Aortic Dissection
- Pneumonia/Pleuritis
- Pneumothorax
- Pericarditis
- Congestive Heart Failure
- Musculosceletal Syndromes
- Anxiety/ Hyperventilation

Treatment of RV failure in acute high-risk PE (3)

Mechanical circulatory support		
Veno-arterial ECMO/ extracorporeal life support	Rapid short-term support combined with oxygenator	Complications with use over longer periods (>5–10 days), including bleeding and infections; no clinical benefit unless combined with surgical embolectomy; requires an experienced team

ECMO = extracorporeal membrane oxygenation; RV = right ventricular.

Recommendations for the regimen and duration of anticoagulation after PE in patients without cancer (3)

Recommendations	Class	Level
Patients in whom extension of anticoagulation beyond 3 months should be considered		
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE and no identifiable risk factor.	IIa	A
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a persistent risk factor other than the antiphospholipid antibody syndrome.	IIa	C
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a minor transient or reversible risk factor.	IIa	C

Recommendations for the regimen and duration of anticoagulation after PE in patients without cancer (2)

Recommendations	Class	Level
Patients in whom extension of anticoagulation beyond 3 months is recommended		
Oral anticoagulant treatment of indefinite duration is recommended for patients presenting with recurrent VTE (that is, with at least one previous episode of PE or DVT) not related to a major transient or reversible risk factor.	I	B
Oral anticoagulant treatment with a VKA for an indefinite period is recommended for patients with the antiphospholipid antibody syndrome.	I	B

DVT = deep vein thrombosis; VKA = vitamin K antagonist.

CEAP – Klassifikation Chronisch venöse Insuffizienz

C Clinical Classification

0 keine Zeichen

1 Teleangiektasien/retikuläre Venen

2 Stamm/ Astvaricosis

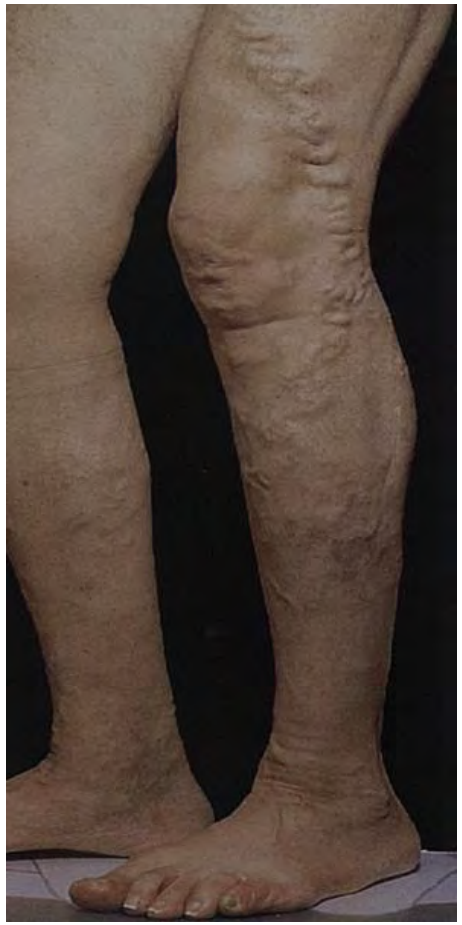
3 Oedem

4 Hautveränderungen

5 geheiltes Ulkus

6 florides Ulkus

CEAP – Klassifikation Chronisch venöse Insuffizienz



E Etiology Classification

Ec kongenital

Ep primär

Es sekundär

A Anatomic Classification

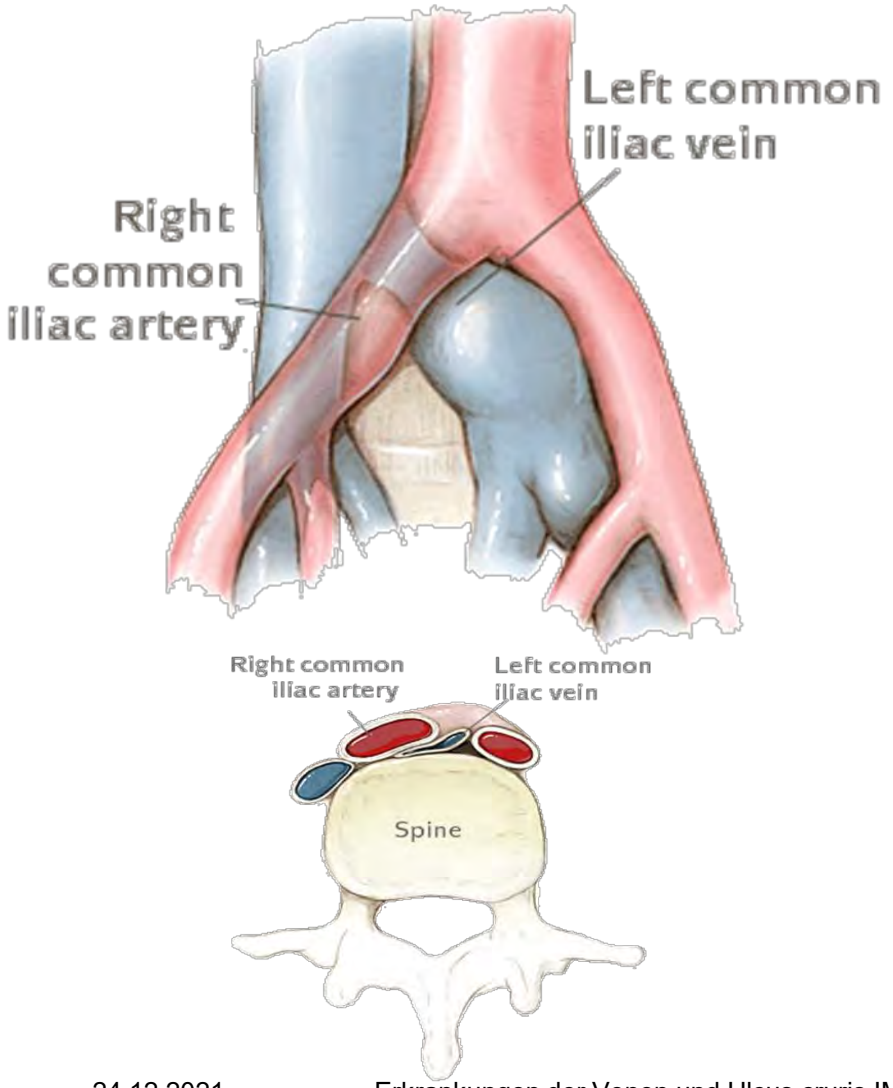
+ Segmente (1-18)

A_S	oberflächliche Venen
A_D	tiefe Venen
A_P	Perforans- Venen

May-Thurner-Syndrom

- Inzidenz der May-Thurner-Anatomie: 22%
- Häufig asymptomatisch
- Erhöhte Inzidenz für linksseitige DVT bei Vorliegen der anatomischen Variante
- Entwicklung einer DVT abhängig von weiteren Faktoren
- Frauen im Alter zwischen 20 und 50 J. am häufigsten betroffen: Lendenlordose verstärkt sich in Pubertät und Schwangerschaft

May-Thurner Syndrom – (Iliac Vein Compression Syndrome)



- Beobachtung von Virchow 1851
- 1956 May and Thurner: Beschreibung einer Stenosierung der linken Vena iliaca communis unter der rechten Arteria iliaca communis
- Repitetitive Kompression der Vene: Fibrose, Synechiaen, Sporn
- **Stenose/Okklusion der Vene**

Behandlungsoptionen bei Postthrombotischen Syndrom

- Antikoagulation
- Kompression
- Endovaskuläre Stentrekonstruktion
- Varizenbehandlung (Kompression, Schaum, Laser, RF, Varizenchriurgie)