

Tiefe Beinvenenthrombose, Postthrombotisches Syndrom

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Tiefe Beinvenenthrombose (TVT)

- Jährliche Inzidenz VTE 1-3 Fälle pro 1000 Personen
- Inzidenz / Risiko steigen mit zunehmendem Lebensalter an
- Aszendierende > transfasziale > deszendierende TVT
- Lungenembolie in 10% als Frühkomplikation
- Postthrombotisches Syndrom in 20-50% als Spätfolge

Rabinovich A et al. J Thromb Haemost 2017;15:230-41

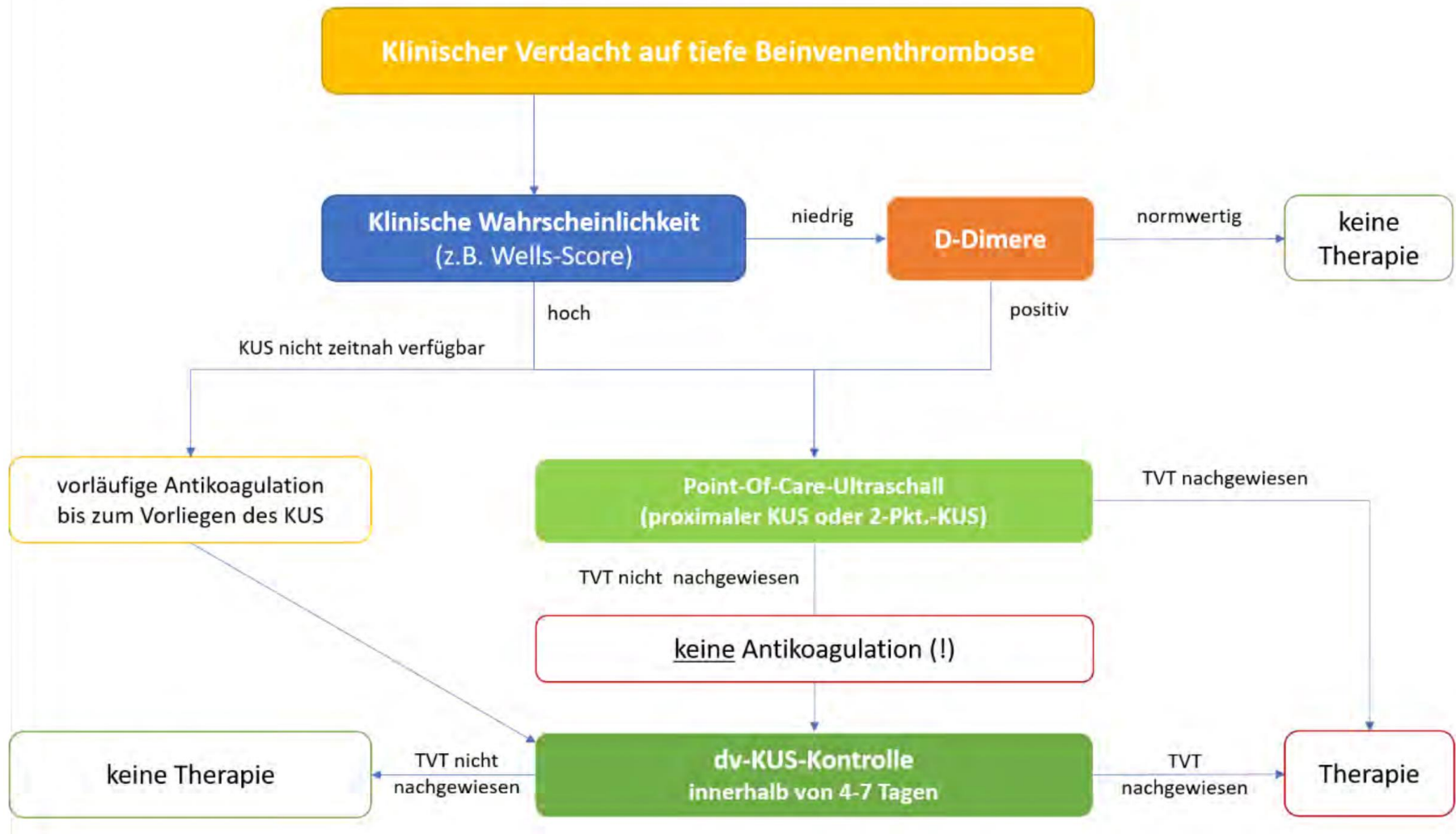
S2-Leitlinie: Diagnostik und Therapie der Venenthrombose und der Lungenembolie 2015

Fallbeispiel 1

40-jähriger Mann mit schmerzhafter Schwellung des rechten Beines seit 2 Tagen, hat plötzlich begonnen. Keine Vorerkrankungen, bisher immer gesund.



Diagnose-Algorithmus



S2k-Leitlinie DGA 2023

Wells Score

Klinische Charakteristik	Score
Aktive Tumorerkrankung	1
Lähmung oder rezente Immobilisation der Beine	1
Bettruhe >3 Tage oder gr. Chir. Eingriff innerhalb 12 Wochen	1
Schmerz entlang der tiefen Venen	1
Schwellung des gesamten Beines	1
Beinumfangdifferenz > 3 cm (10 cm dist. Tub. tib.)	1
Eindrückbares Ödem	1
Kollateralvenen	1
Frühere TVT	1
Alternative wahrscheinliche Diagnose	-2

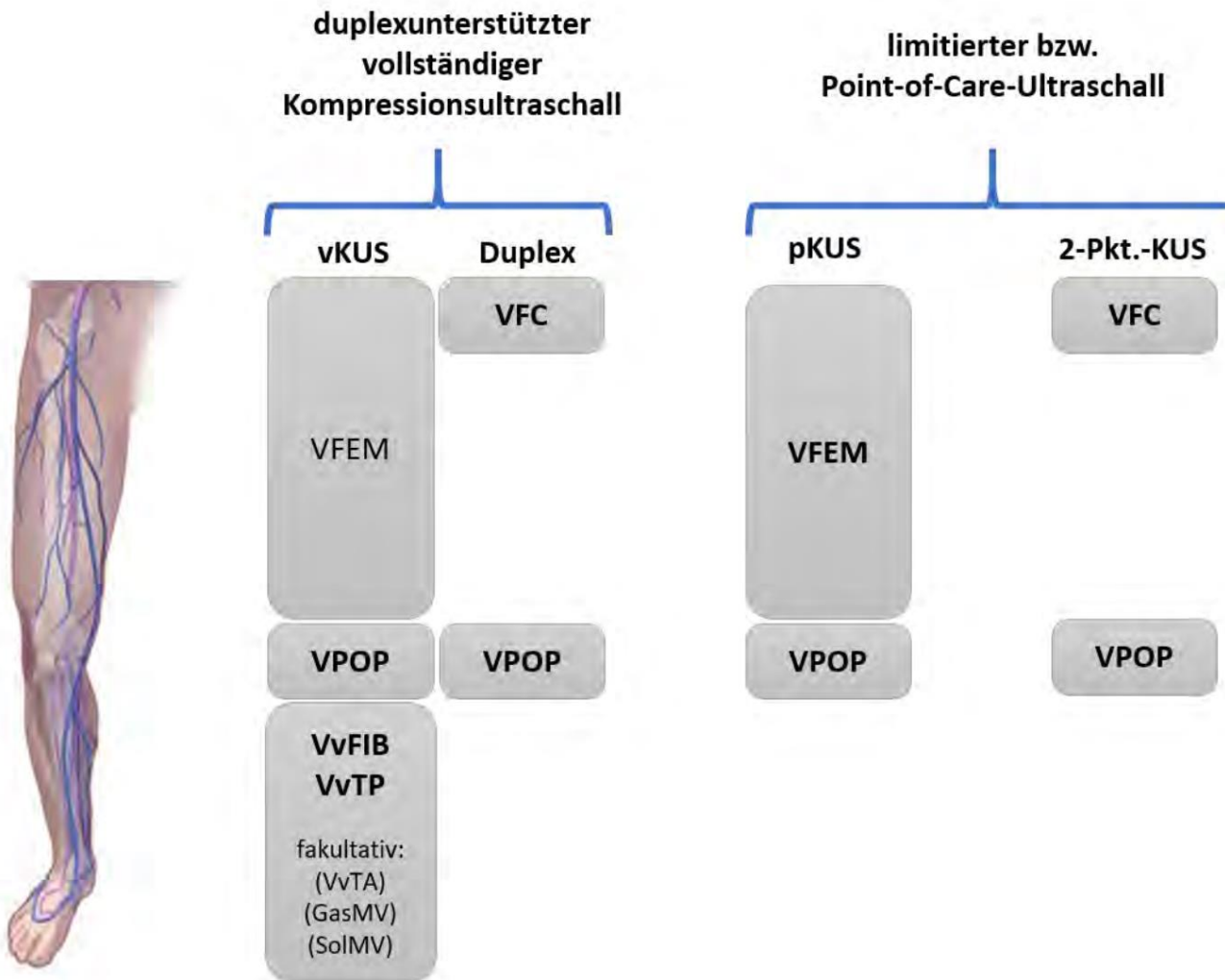
Score ≥ 3 : hohe Wahrscheinlichkeit

Score 1-2: mittlere Wahrscheinlichkeit

Score <1: niedrige Wahrscheinlichkeit

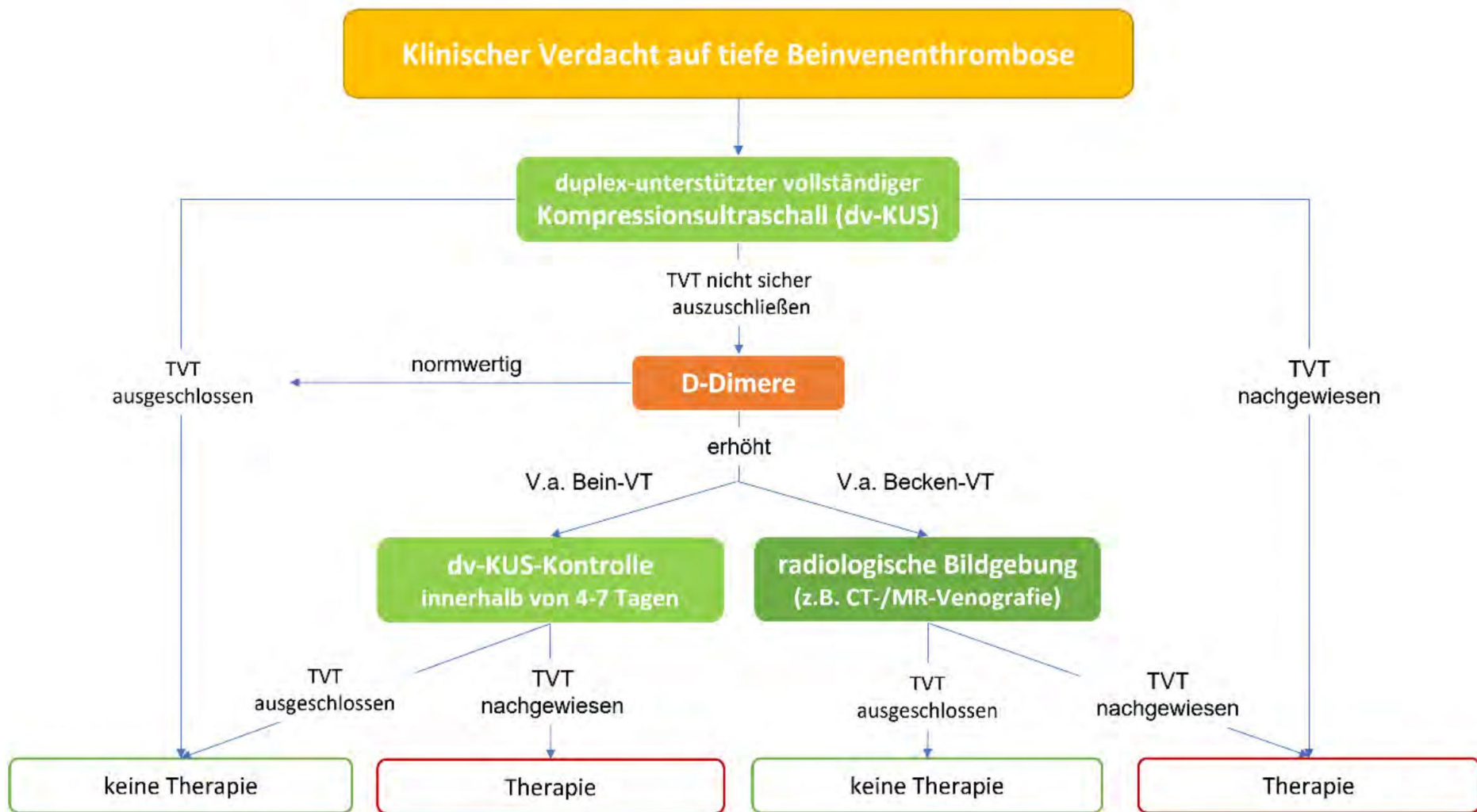
Wells PS et al. Lancet 1995;345:1326-30

POCUS - TVT

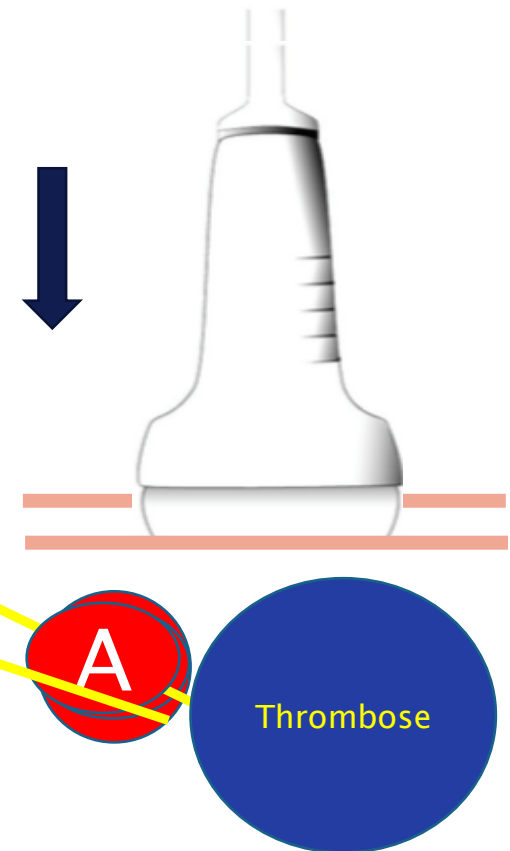
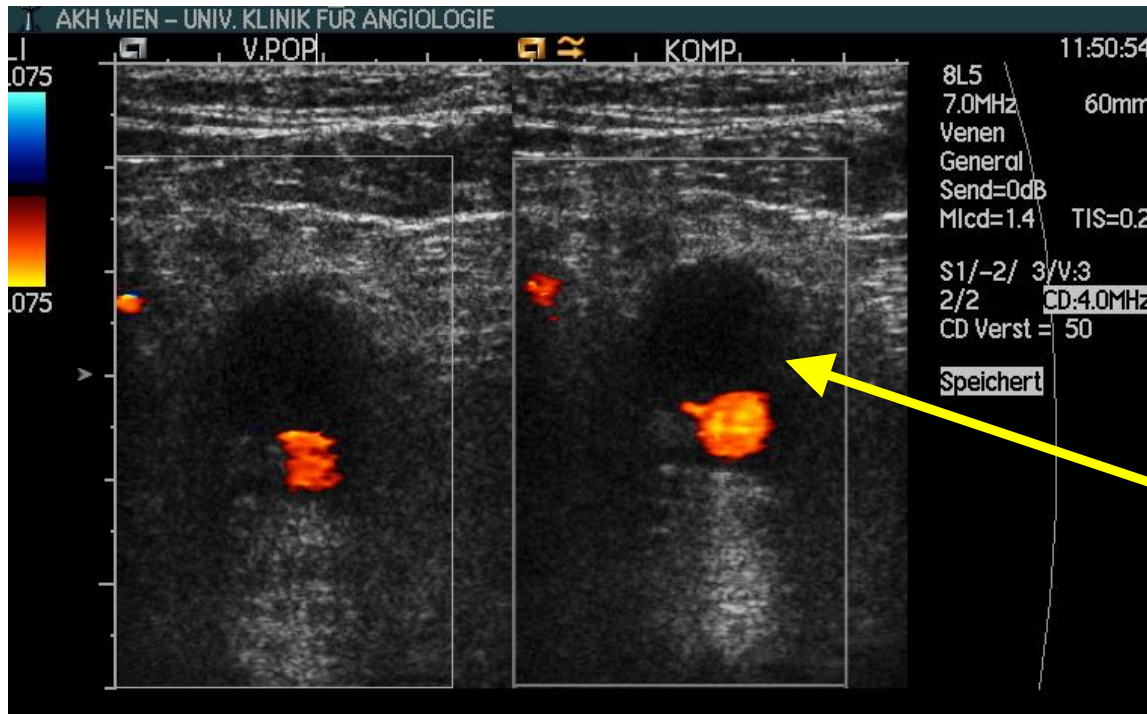


S2k-Leitlinie DGA 2023

Diagnosealgorithmus - TVT

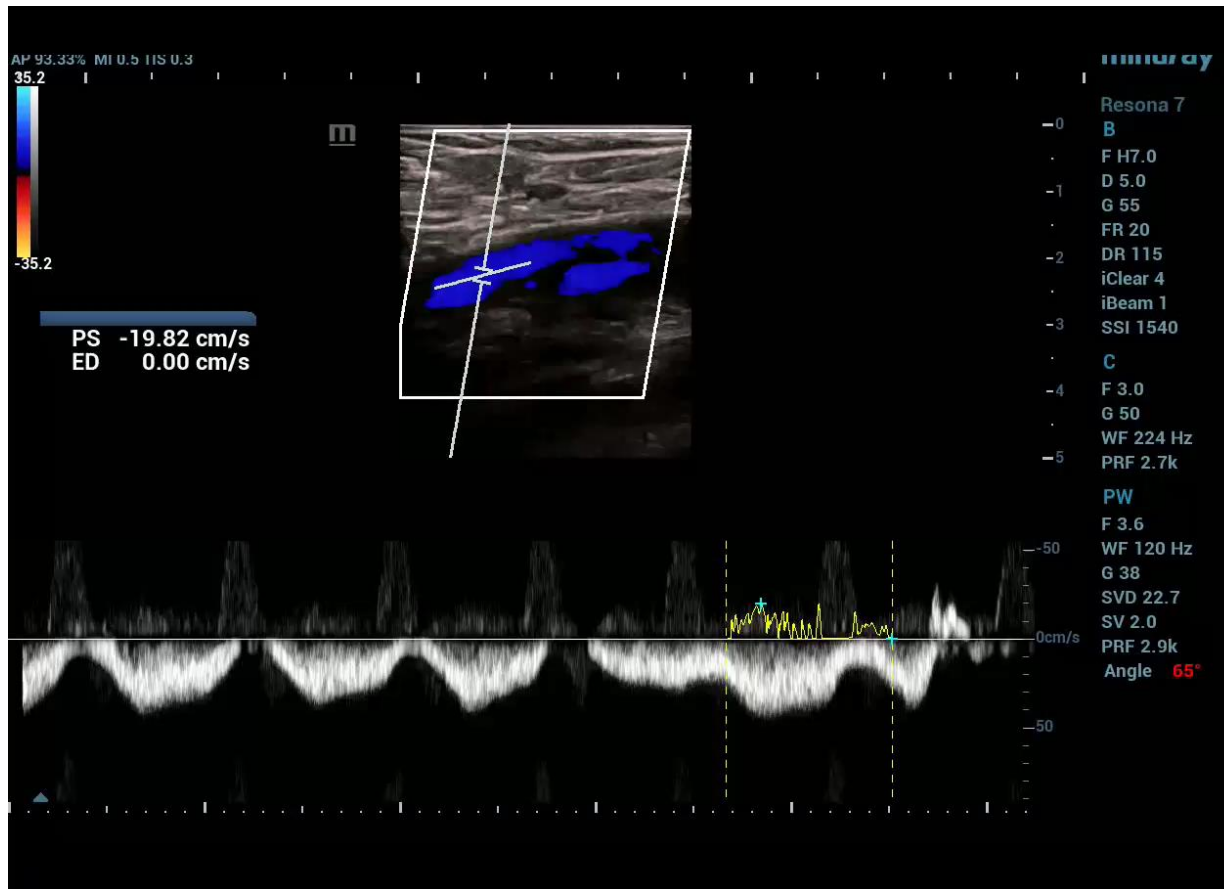


Kompressionsultraschall



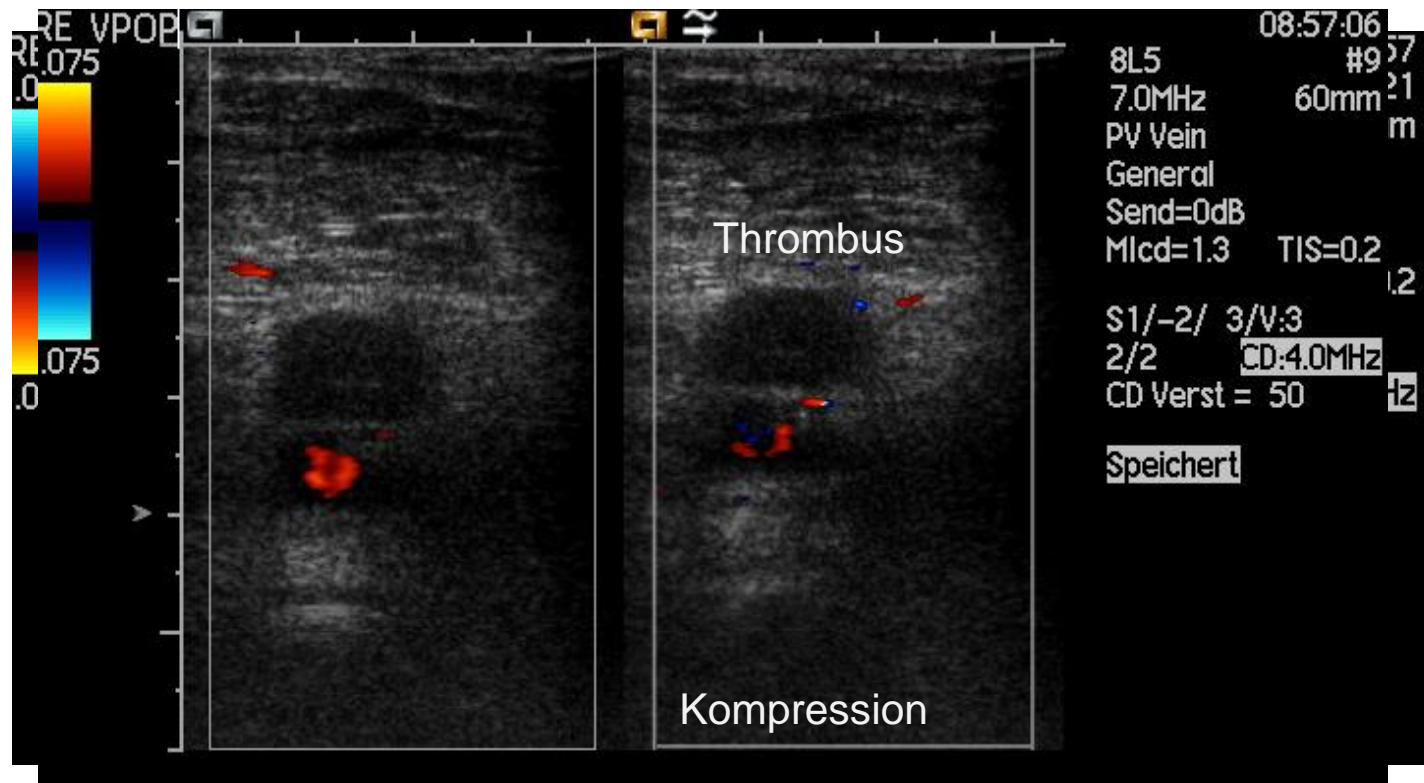
Duplexdiagnostik Beckenvenen

Atmungsabhängige Modulation



Fallbeispiel 1

40-jähriger Mann mit schmerzhafter Schwellung des rechten Beines seit 2 Tagen, hat plötzlich begonnen. Keine Vorerkrankungen, bisher immer gesund.



Antikoagulation: DOAKs

Dabigatran (direkter oraler Thrombininhibitor):

Mindestens 5 Tage:

LMWH (körpergewichtsadaptiert):

- Enoxaparin 1 mg/kg KG 2x tgl
- Dalteparin 100 E/kg KG 2x tgl
- (Dalteparin 200 E/kg KG 1x tgl)

Fondaparinux (körpergewichtsadaptiert):

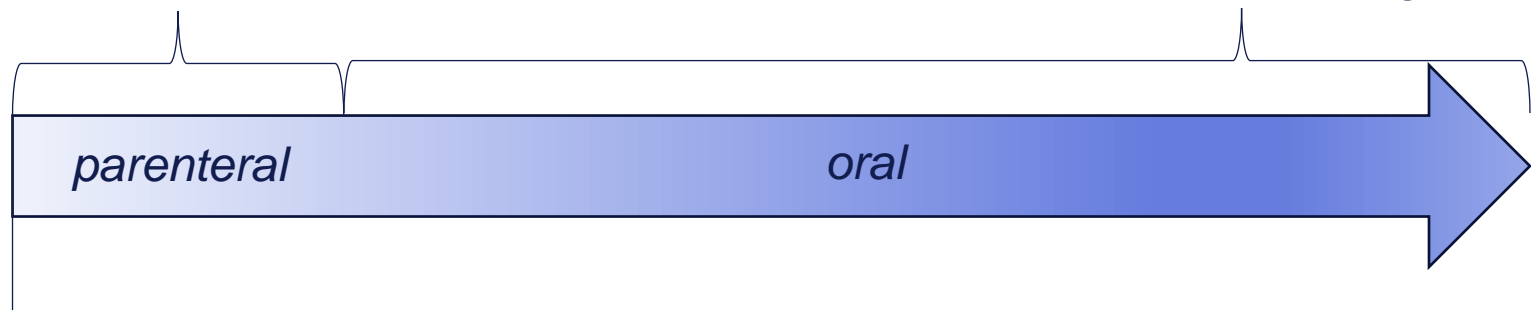
- KG < 50 kg: 5 mg 1x tgl
- KG 50-100 kg : 7.5 mg 1xtgl
- KG > 100 kg: 10 mg 1xtgl

Dabigatran:

150 mg 2x tgl

KI bei - GFR < 30 ml/min

- Schwangerschaft



Diagnose

Schulman S et al. N Engl J Med 2009

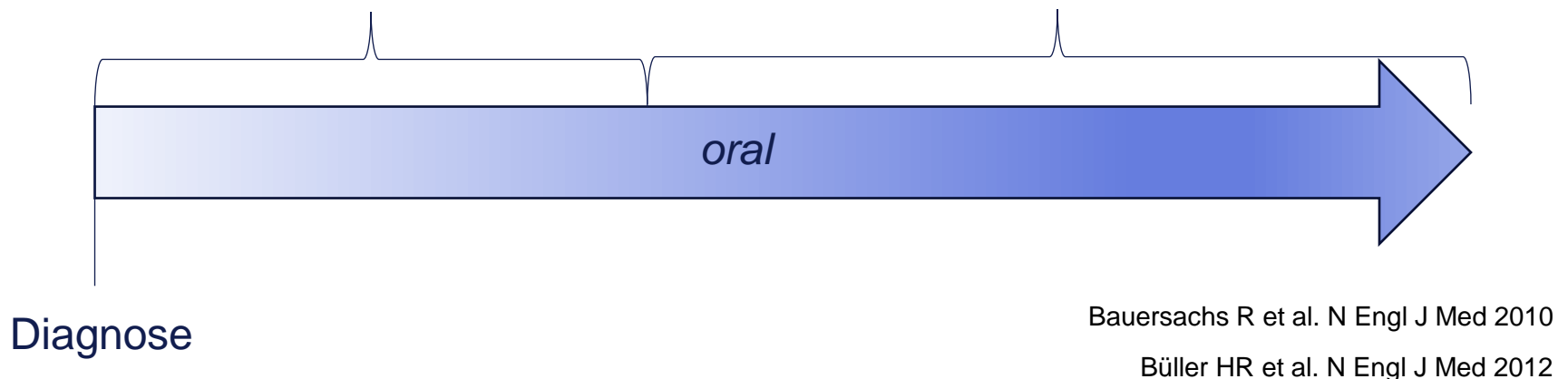
Schulman S et al. Circulation 2014

Antikoagulation: DOAKs

Rivaroxaban (direkter Faktor Xa Inhibitor):

3 Wochen:
Rivaroxaban:
15 mg 2x tgl

Rivaroxaban:
20 mg 1x tgl
KI bei - GFR < 15 (-30) ml/min
- Schwangerschaft



Antikoagulation: DOAKs

Apixaban (direkter Faktor Xa Inhibitor):

1 Woche:

Apixaban:

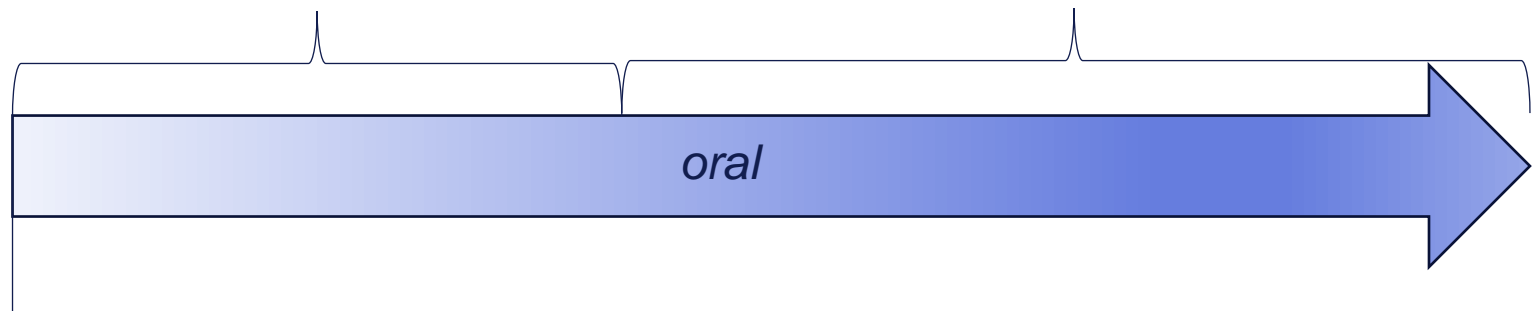
10 mg 2x tgl (2x 2 Tabl á 5 mg)

Apixaban:

5 mg 2x tgl

KI bei - GFR < 15 ml/min

- Schwangerschaft



Diagnose

Agnelli G et al. N Engl J Med 2013

Antikoagulation: DOAKs

Edoxaban (direkter Faktor Xa Inhibitor):

Mindestens 5 Tage:

LMWH (körpergewichtsadaptiert):

- Enoxaparin 1 mg/kg KG 2x tgl
- Dalteparin 100 E/kg KG 2x tgl
- (Dalteparin 200 E/kg KG 1x tgl)

Fondaparinux (körpergewichtsadaptiert):

- KG < 50 kg: 5 mg 1x tgl
- KG 50-100 kg : 7.5 mg 1xtgl
- KG > 100 kg: 10 mg 1xtgl

Edoxaban:

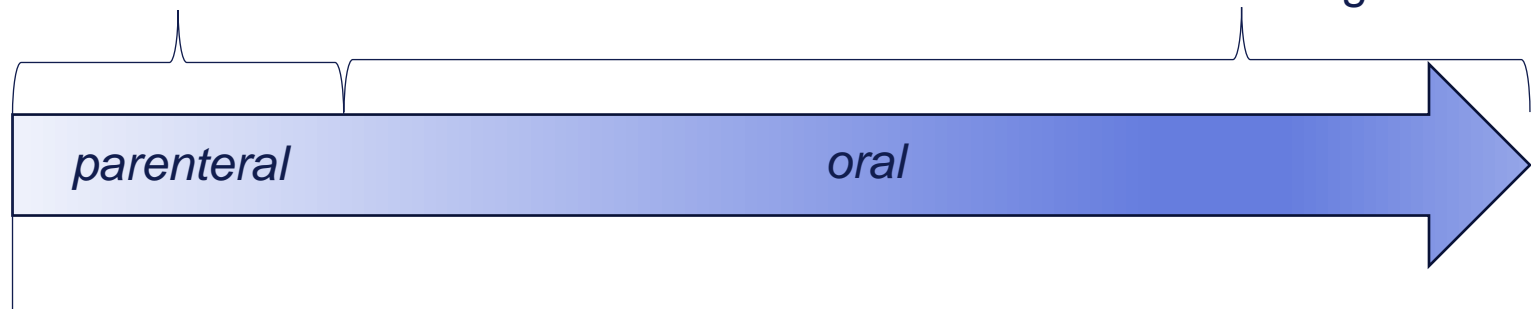
60 mg 1x tgl

30 mg 1x tgl bei:

- GFR < 50 ml/min
- KG < 60 kg: 30 mg

KI bei - GFR < 15 ml/min

- Schwangerschaft



Diagnose

Büller HR et al. N Engl J Med 2013

Antikoagulation: Vitamin K Antagonisten

Mindestens 5 Tage:

LMWH (körpergewichtsadaptiert):

- Enoxaparin 1 mg/kg KG 2x tgl
- Dalteparin 100 E/kg KG 2x tgl
- (Dalteparin 200 E/kg KG 1x tgl)

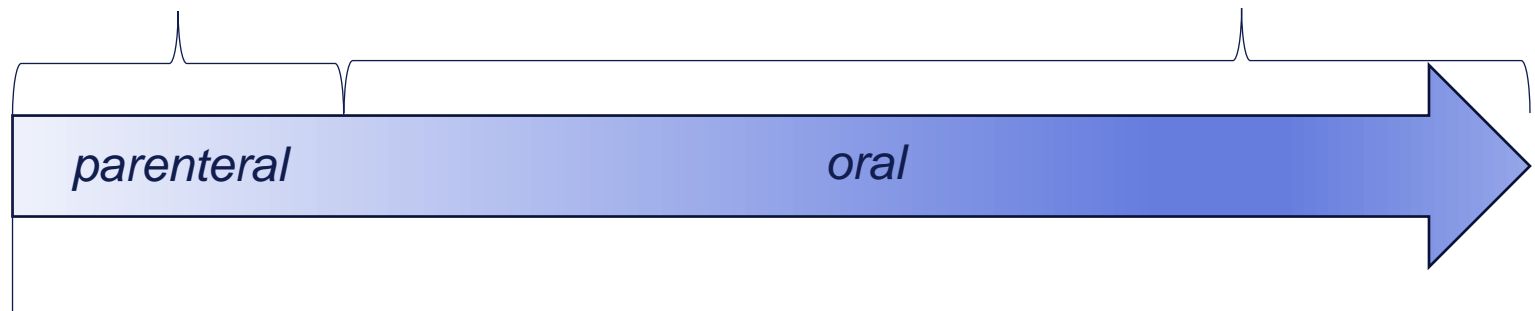
Fondaparinux (körpergewichtsadaptiert):

- KG < 50 kg: 5 mg 1x tgl
- KG 50-100 kg : 7.5 mg 1xtgl
- KG > 100 kg: 10 mg 1xtgl

VKA:

INR-Ziel 2-3

24h Überlappend im Ther-bereich
KI bei Schwangerschaft



Diagnose

Phasen der Antikoagulation nach VTE

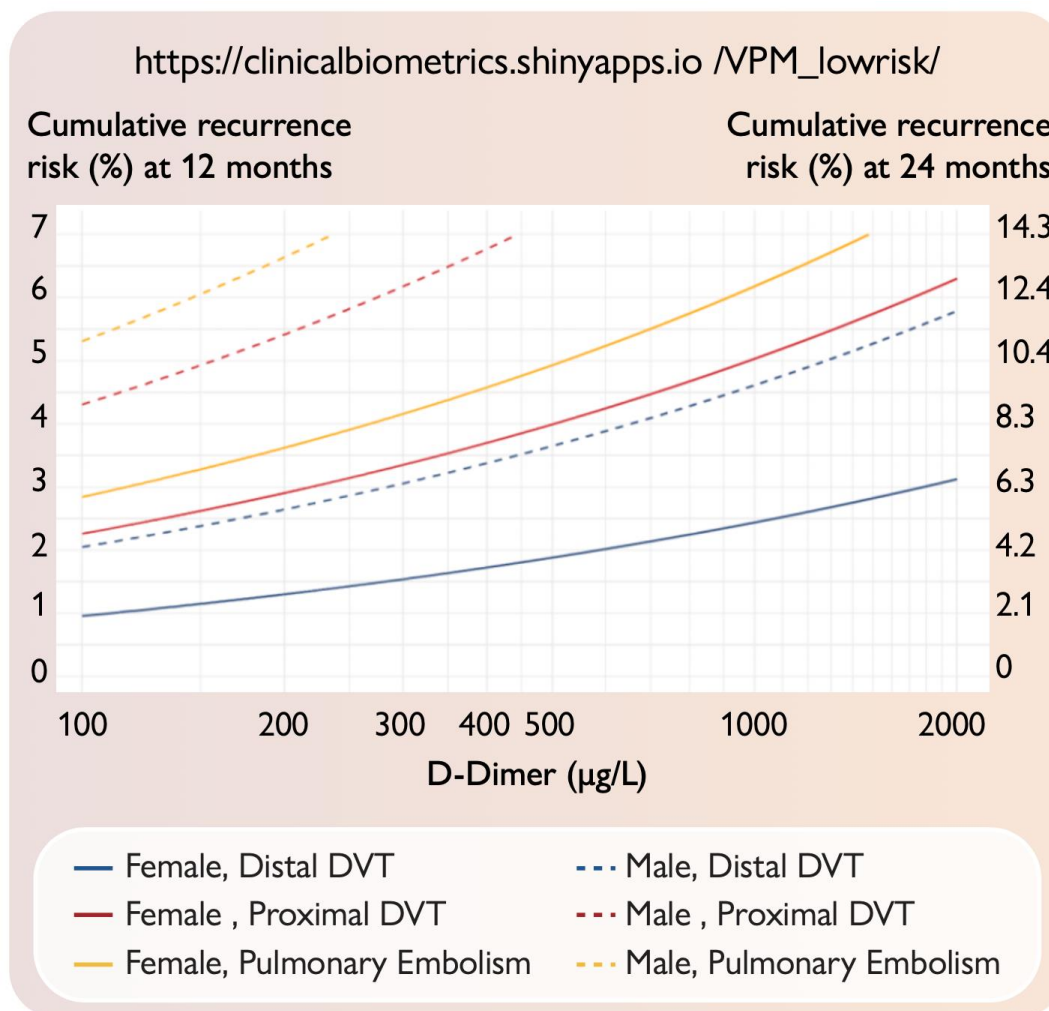
Therapiephase

Phase der Rezidivprophylaxe



S2k-Leitlinie DGA 2023

Dauer der Antikoagulation nach VTE



Kyrla PA et al. Eur Heart J 2024;45:45-53

Dauer der Antikoagulation nach VTE

Kriterium	für fortgesetzte Therapie	gegen fortgesetzte Therapie
Risikofaktor	fortbestehend	passager
Genese	unklar	getriggert
Rezidiv	ja	nein
Blutungsrisiko	gering	hoch
Bisherige Antikoagulationsqualität	gut	schlecht
D-Dimere (nach Therapieende)	erhöht	normal
Residualthrombus	vorhanden	fehlend
Geschlecht	Mann	Frau
Thrombus-Ausdehnung	langstreckig	kurzstreckig
Thrombus-Lokalisation	proximal	distal
Schwere Thrombophilie	ja*	nein**
Patientenpräferenz	dafür	dagegen

* z.B. Antiphospholipid-Syndrom,

** z.B. Heterozygote Faktor V- oder heterozygote Prothrombinmutation

S2-Leitlinie: Diagnostik und Therapie der Venenthrombose und der Lungenembolie 2015

Fallbeispiel 1

40-jähriger Mann mit schmerzhafter Schwellung des rechten Beines seit 2 Tagen, hat plötzlich begonnen. Keine Vorerkrankungen, bisher immer gesund.



Kompressionstherapie?

Kompressionstherapie

Brandjes DP et al. Lancet 1997 (open lable RCT 194 Pts)



Prandoni P et al. Ann Intern Med 2004 (open lable RCT 180 Pts)



SOX trial: Kahn SR et al. Lancet 2014 ("blinded" RCT, 803 Pts)



OCTAVIA study: Mol GC et al. BMJ 2016 (RCT, 518 Pts)



Berntsen CF et al. Am J Med 2016 (Meta-Analysis)



Subbiah R et al. Lancet Haematol 2016 (Meta-Analysis)



ACCP: In patients with acute DVT of the leg, we suggest against using compression stockings routinely to prevent PTS (Grade 2B).

This recommendation focuses on prevention of PTS, not on treatment of symptoms.

Stevens SM et al. Chest 2021

Postthrombotisches Syndrom



20-50% nach akuter Beckenbeinvenenthrombose (klinisch schwerwiegend: 10%)

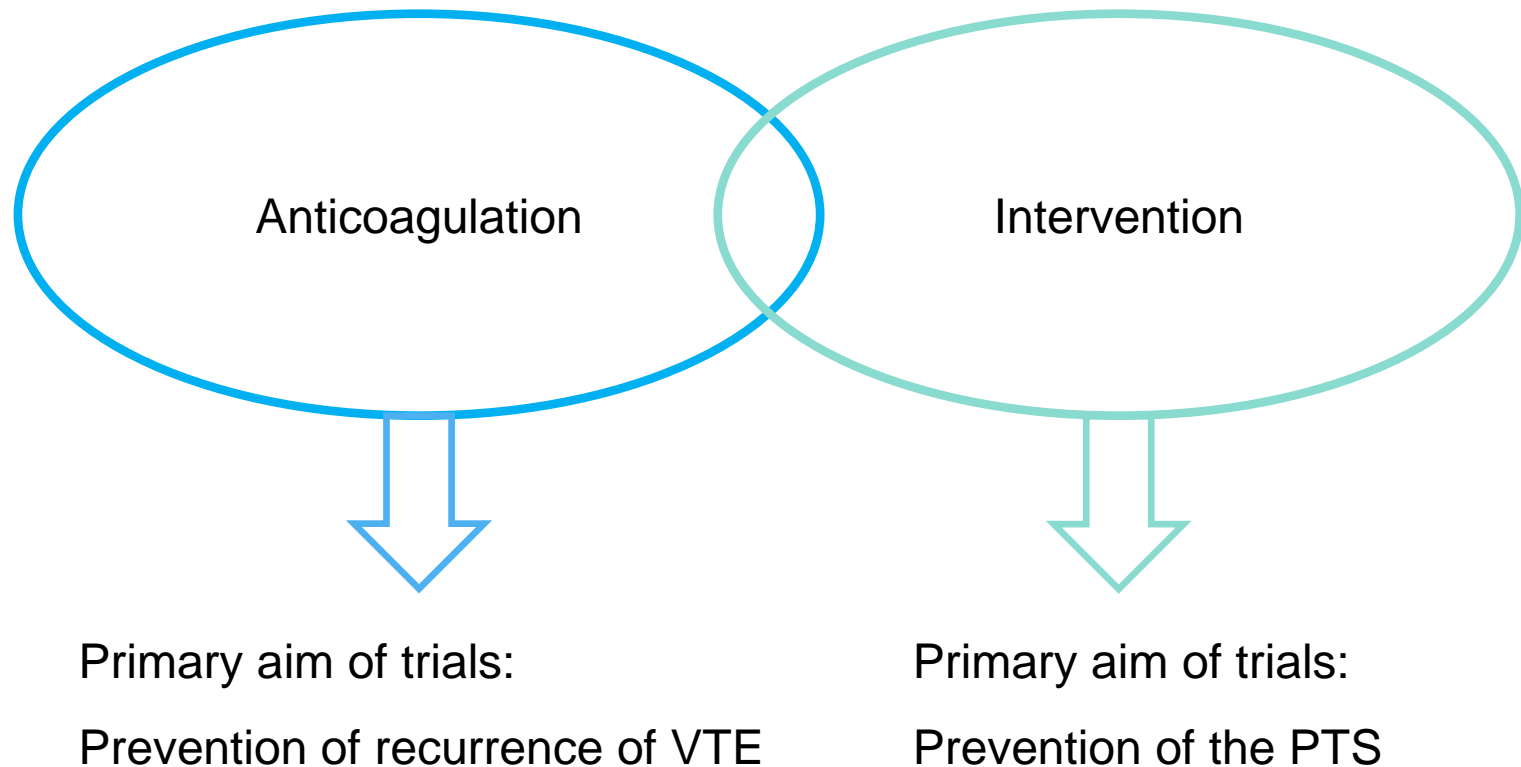
Risikofaktoren

At DVT diagnosis	During follow-up after DVT	NO risk factor	Controversial / further research needed
Proximal DVT	Recurrent ipsilateral DVT	Unprovoked vs. Secondary DVT	Type of anticoagulant used (LMWH, DOAC, Vitamin K antagonist)
Older age	Inadequate INR control during first 3 months after DVT		
History of ipsilateral DVT	Pre-existing primary venous insufficiency	Inherited thrombophilia	Sonographic and biochemical properties of the initial or residual clot
		Total duration of anticoagulation	Biomarkers of inflammation (CRP, IL-6, IL-8, IL-10, ICAM-1, MMPs)
			D-Dimer
			F VIII

Open vein hypothesis

Rabinovich A et al. J Thromb Haemost 2017

Different treatment goals



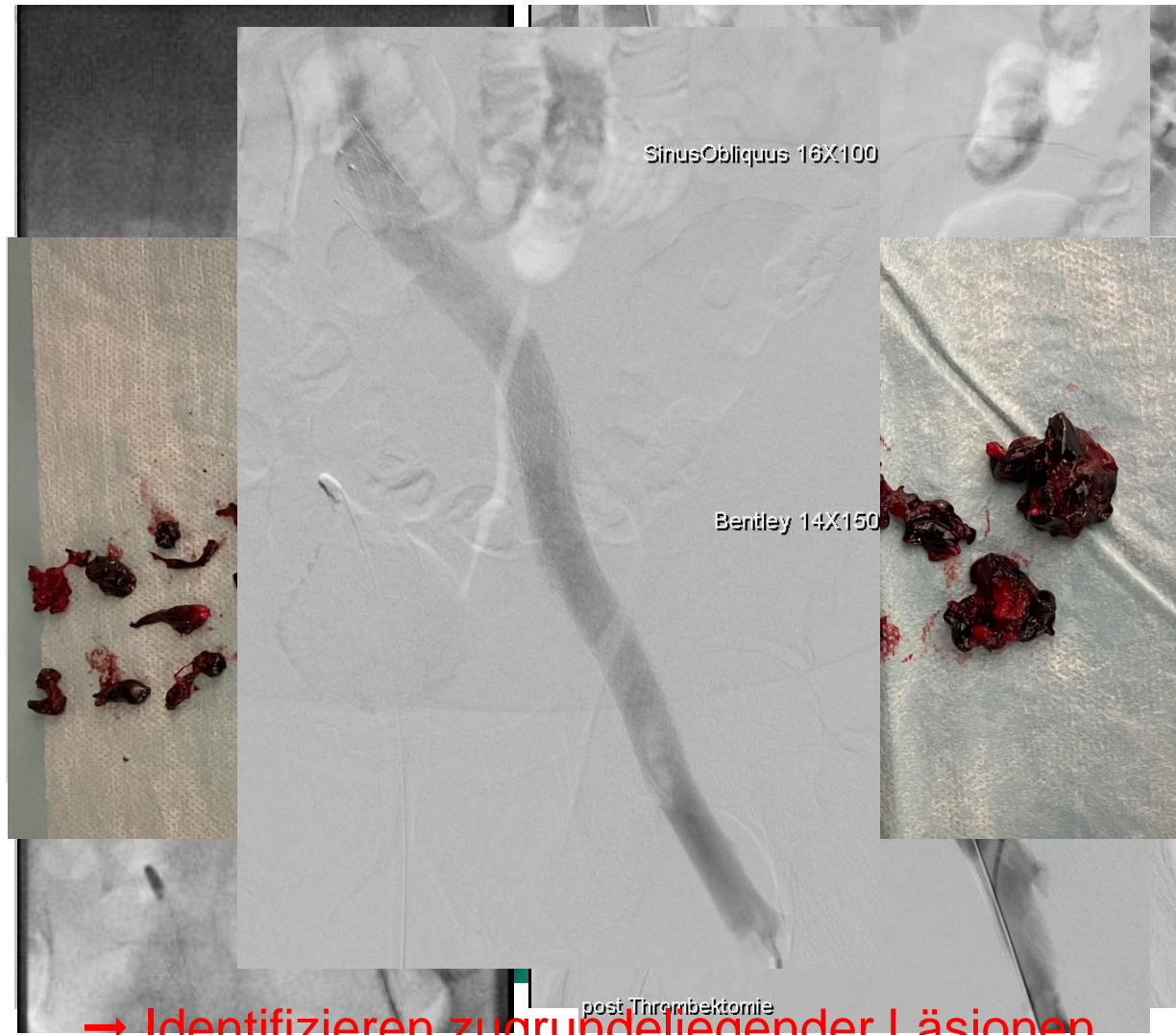
Fallbeispiel 2

64-jähriger Patient mit akuter iliofemoraler Thrombose links

Schwellung und Schmerzen des linken Beines seit 1 Woche

FK: Diabetes mellitus Typ II, keine VTE bisher

Fallbeispiel 2



Society recommendations #1

CHEST
OFFICIAL PUBLICATION OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

Volume 157-11 • January 2020

CONTENTS

18 Cardiothoracic Catheterization-Induced Lung
Artery Thrombosis in Patients With Acute
Coronary Syndrome: A Systematic Review
and Meta-Analysis
Lopez E, A. Al-Lawati, M. Al-Murayri, et al.

25 Meeting the Challenge of Identifying New
Thrombotic Risk Factors in the Genomic
Era
Chen Y, K. W. Chan, S. D. Durrant, et al.

34 CHEST IMPRESSIONS
Incidence and Mortality of Acute
Respiratory Distress Syndrome in Patients
With COVID-19
Khan MM, Brown JR, K. Al-Lawati, et al.

42 Study Visit in the Democratic Republic
of the Congo: A Review of the Literature
and Recommendations for Clinical
Trials
Liu H, H. Al-Lawati, K. W. Chan, et al.

47 CORP
Sustained COVID-19 by Using Visual
and Quantitative CT Imaging Features
Jing Y, J. Li, J. Li, et al.

51 CRITICAL CARE
Burden of Substance Abuse-Related
Admissions to the Medical ICU
Dodd M, H. Al-Lawati, K. W. Chan, et al.

57 Plasma Viscosity of DVT Levels Are
Associated With Risk of Thrombotic
Events
Huang J, J. Li, J. Li, et al.

65 DEEPER LUNG DRAINAGE
Right Ventricular to Left Ventricular Ratio of
CT Pulmonary Angiogram Predicts Mortality
in Ischemic Lung Disease
Huang J, J. Li, J. Li, et al.

EDUCATION AND CLINICAL PRACTICE

88 Accuracy of Serial Lung Ultrasound
Measurements for the Diagnosis of Acute
Heart Failure in the ED: A Multicenter
Prospective Study
Khan MM, Brown JR, K. Al-Lawati, et al.

91 The Neurokinin-1 Receptor Antagonist
Dequalinium Is a Novel Anticough Therapy
for Chronic Refractory Cough: Results From
a Phase 2 Pilot Study (DEQUALIN-2)
Jain S, K. W. Chan, S. D. Durrant, et al.

95 PULMONARY AND CARDIOVASCULAR
Impact of the New Pulmonary Hypertension
Definition on Heart Transplant Outcomes:
Expanding the Hemodynamic Risk Profile
Jain S, K. W. Chan, S. D. Durrant, et al.

98 Retrospective Validation of the BODEm 2.0
Risk Score With the Australian and New
Zealand Pulmonary Hypertension
Registry Cohort
Jain S, K. W. Chan, S. D. Durrant, et al.

103 BLEEP
Upper Airway Stimulation vs Positive
Airway Pressure Support on CPAP and
Spontaneous Ventilation in OSA
Huang J, J. Li, J. Li, et al.

106 Sleep Pharmacotherapy for Chronic Sleep
Disorders in Pregnancy and Lactation
Huang J, J. Li, J. Li, et al.

109 PEDIATRIC ONCOLOGY
A Randomized Trial of Nebulized
Liposomal Lipidation Spray in Thoracic
Carcinoma for Topical Sensitization During
Surgical Resection
Huang J, J. Li, J. Li, et al.

112 Quality of Evidence: A Report of
Surveys for Early Stage Non-small Cell Lung
Cancer in the United States
Huang J, J. Li, J. Li, et al.

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ELSEVIER

Thrombolytic and mechanical interventions in acute DVT

PICO Question:

Should thrombolytic, mechanical, or pharmaco-mechanical interventions vs. anticoagulant therapy alone be given to patients with acute deep vein thrombosis?

Guidance Statement:

6. In patients with acute DVT of the leg we suggest anticoagulant therapy alone over interventional (thrombolytic, mechanical, or pharmaco-mechanical) therapy (weak recommendation, moderate-certainty evidence).

Stevens SM et al. Chest 2021

Society recommendations #2

Second consensus document on diagnosis and management of acute deep vein thrombosis: updated document elaborated by the ESC Working Group on aorta and peripheral vascular diseases and the ESC Working Group on pulmonary circulation and right ventricular function

Lucia Mazzolai^{1*}, Walter Ageno², Adriano Alatri¹, Rupert Bauersachs^{3,4},
Cecilia Becattini⁵, Marianne Brodmann⁶, Joseph Emmerich⁷,
Stavros Konstantinides^{4,8}, Guy Meyer⁹, Saskia Middeldorp⁹, Manuel Monreal¹⁰,
Marc Righini¹¹, and Viktor Aboyans¹²

¹Division of Angiology, Heart and Vessel Department, Lucerne University Hospital, Charité de Non-Possibile 16, CH-1011 Lucerne, Switzerland; ²Department of Medicine and Surgery, University of Padova, Via Nave 2, 35100 Verona, Italy; ³Department of Vascular Medicine, Wittenbergstrasse 63, 4420 Dortmund, Germany; ⁴Department of Vascular Medicine, Center for Thrombosis and Hemostasis, University Medical Center Mainz, Langenbeckstr. 1, 55131 Mainz, Germany; ⁵Department of Internal and Cardiovascular Medicine—Stroke Unit, University of Bologna, P.zza Maggiore 15, 40138 Bologna, Italy; ⁶Department of Internal Medicine, Division of Angiology, Medical University Graz, Austria; ⁷Department of Vascular Medicine, Groupe Hospitalier Pitié-Salpêtrière and University of Paris, Paris, France; ⁸Department of Cardiology, Democritus University of Thrace, Alexandroupoli, Greece; ⁹Department of Vascular Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam, Cardiovascular Sciences, Amsterdam, The Netherlands; ¹⁰Department of Internal Medicine, Hospital General de Tarragona, Tarragona, Spain; ¹¹Division of Angiology and Hemostasis, Department of Internal Medicine, Geneva University Hospital, Geneva, Switzerland; and ¹²Department of Cardiology, Dapkin University Hospital and Ischemic 109, Tropical Neuroepidemiology, School of Medicine, 2 Avenue Pasteur 67081 Strasbourg, France

Received 19 October 2020; revised 22 February 2021; accepted 1 May 2021; accepted 7 May 2021

This consensus document is proposed to clinicians to provide the whole spectrum of deep vein thrombosis management as an update to the 2017 consensus document. New data guiding clinicians in indicating extended anticoagulation, management of patients with cancer, and prevention and management of postthrombotic syndrome are presented. More data on benefit and safety of non-vitamin K antagonists oral anticoagulants are highlighted, along with the arrival of new antidotes for severe bleeding management.

Keywords Consensus • Deep vein thrombosis • Ultrasound • Anticoagulation • Diagnosis • Pulmonary embolism • Cancer • Postthrombotic syndrome • Gastrointestinal thrombosis • Pregnancy • Risk • Compression

* Corresponding author. Tel: +41 31 3407048; e-mail: lucia.mazzolai@kch.ch

† deceased

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In light of these results, there is no clear benefit of systematic acute proximal DVT reperfusion. Hence, CDT should not be performed routinely. It can be reserved for very severe cases, such as phlegmasia cerulea dolens

Society recommendations #3

CLINICAL PRACTICE GUIDELINE DOCUMENT

European Society for Vascular Surgery (ESVS) 2021 Clinical Practice Guidelines on the Management of Venous Thrombosis^{1,2}

Stavros K. Kakkos ^{1,2,3}, Manjit Gohel ^{4,5}, Niels Baekgaard ⁶, Rupert Bauemachs ⁷, Sergi Bellmunt-Montoya ⁸, Stephen A. Black ⁹, Arina J. ten Cate-Hoek ¹⁰, Ismail Balamy ¹¹, Florian K. Enzmann ¹², George Garoulakis ¹³, Anders Gottsäter ¹⁴, Beverly J. Hunt ¹⁵, Armando Manóvilha ¹⁶, Andrew N. Nicolaides ¹⁷, Per Morten Sandset ¹⁸, Gerard Stansby ¹⁹

ESVS Guidelines Committee ¹, Gert J. de Borst, Frederico Bastos Gonçalves, Nabil Chahfá, Robert Hinchliffe, Philippe Kolh, Igor Koncar, Jes S. Lindholt, Rikita Tulum, Christopher P. Taine, Frank Vermeulen, Anders Warhainen

Document reviewers ², Marianne G. De Maesseneer, Anthony J. Comerota, Peter Glavicić, Marike J.H.A. Krulj, Manuel Monreal, Paolo Prandoni, Melina Vega de Cienfuegos

DEDICATION

These guidelines are dedicated to the memory of Dr Olav Kjaer of McMaster University in Hamilton, Ontario, Canada. Dr Kjaer extensively reviewed the first and second versions of the manuscript and he was always very punctual. In the first review round he submitted a review of 16 pages with many detailed and helpful comments. Unaware of his illness, we invited him to review the final version of the guidelines on June 2, 2020, but sadly he passed away one day later, on June 3, 2020. We will always remember Dr Kjaer for his many contributions to the field of Thrombosis and Antithrombotic Treatment, including these guidelines.



Olav Kjaer,
1957–2020

(picture reproduced with permission from White J & Bates SM. Obituary for Dr. Olav Kjaer. *J Thromb Haemost*. 2020;18:2783–2784).

In selected patients with symptomatic iliofemoral deep vein thrombosis, early thrombus removal strategies should be considered.

¹ For a full list of the authors' affiliations, please refer to Appendix.

² Working Committee: Giovanni E. Rabbini (Chair, France, Geneva), Manjit Gohel (co-chair, Cambridge and London, UK), Niels Baekgaard (Copenhagen, Denmark), Rupert Bauemachs (Darmstadt, Germany), Sergi Bellmunt-Montoya (Barcelona, Spain), Stephen A. Black (London, UK), Arina J. ten Cate-Hoek (Maastricht, The Netherlands), Ismail Balamy (Paris, France), and Florian K. Enzmann (Gießen, Austria), George Garoulakis (Athens, Greece), Anders Gottsäter (Malmö, Sweden), Beverly J. Hunt (London, UK), Armando Manóvilha (Porto, Portugal), Andrew N. Nicolaides (London, UK and Nicosia, Cyprus), Per M. Sandset (Oslo, Norway), and Gerard Stansby (Sheffield, UK).

³ ESVS Guidelines Committee: Gert J. de Borst (Utrecht, The Netherlands), Frederico Bastos Gonçalves (Lisbon, Portugal), Nabil Chahfá (Copenhagen, Denmark), Robert Hinchliffe (Leeds, UK), Philippe Kolh (Lyon, France), Igor Koncar (Zagreb, Serbia), Jes S. Lindholt (Copenhagen, Denmark), Rikita Tulum (Tallinn, Estonia), Christopher P. Taine (Paris, France), Frank Vermeulen (Ghent, Belgium), and Anders Warhainen (Helsinki, Finland).

⁴ Document reviewers: Marianne G. De Maesseneer (Rotterdam, The Netherlands), Anthony J. Comerota (Alexandria, VA, USA), Peter Glavicić (Stockholm, MN, USA), Marike J.H.A. Krulj (Groningen, The Netherlands), Manuel Monreal (Barcelona and Madrid, Spain), Paolo Prandoni (Bologna, Italy), Melina Vega de Cienfuegos (Cádiz and Barcelona, Spain).

⁵ These authors contributed equally.

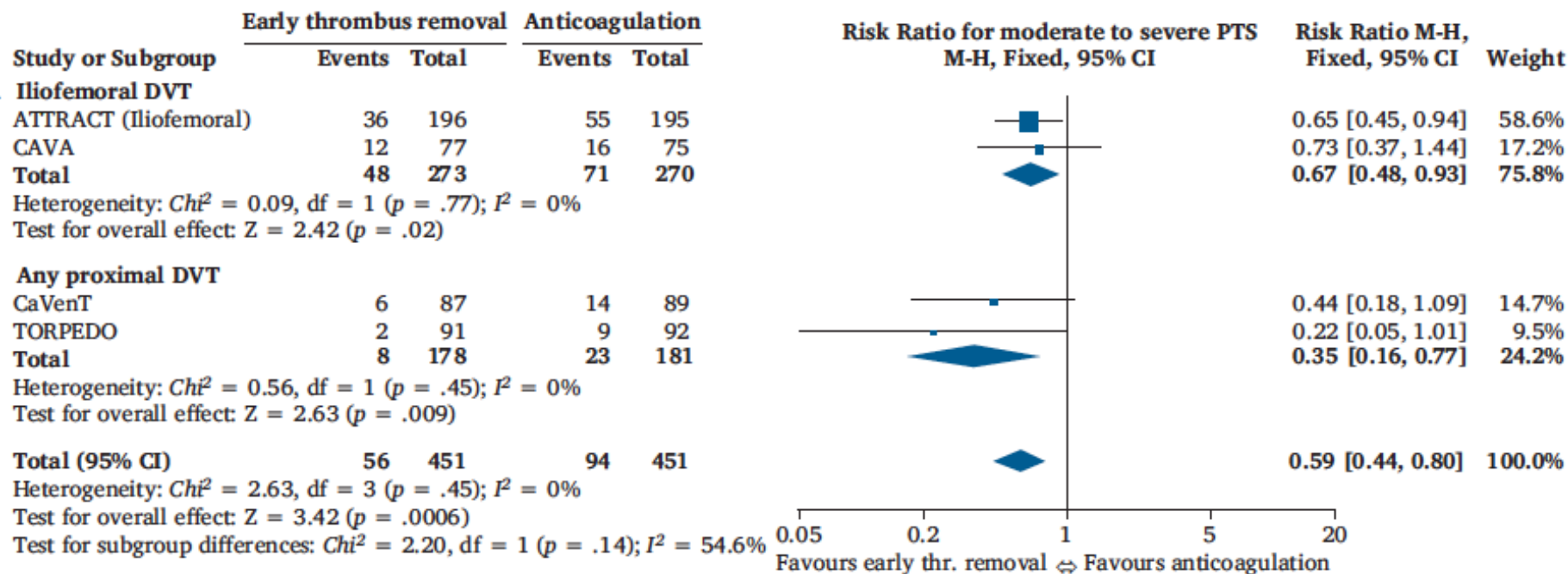
⁶ Corresponding author.

Email address: kakkos@vsnl.com (Stavros K. Kakkos).
1179-5548/© 2020 Published by Elsevier B.V. on behalf of European Society for Vascular Surgery.
<https://doi.org/10.1016/j.jvs.2020.09.023>

Ergebnisse der RCT

Interventional treatment vs. conservative treatment

Effect on „*moderate to severe*“ postthrombotic syndrome (PTS)



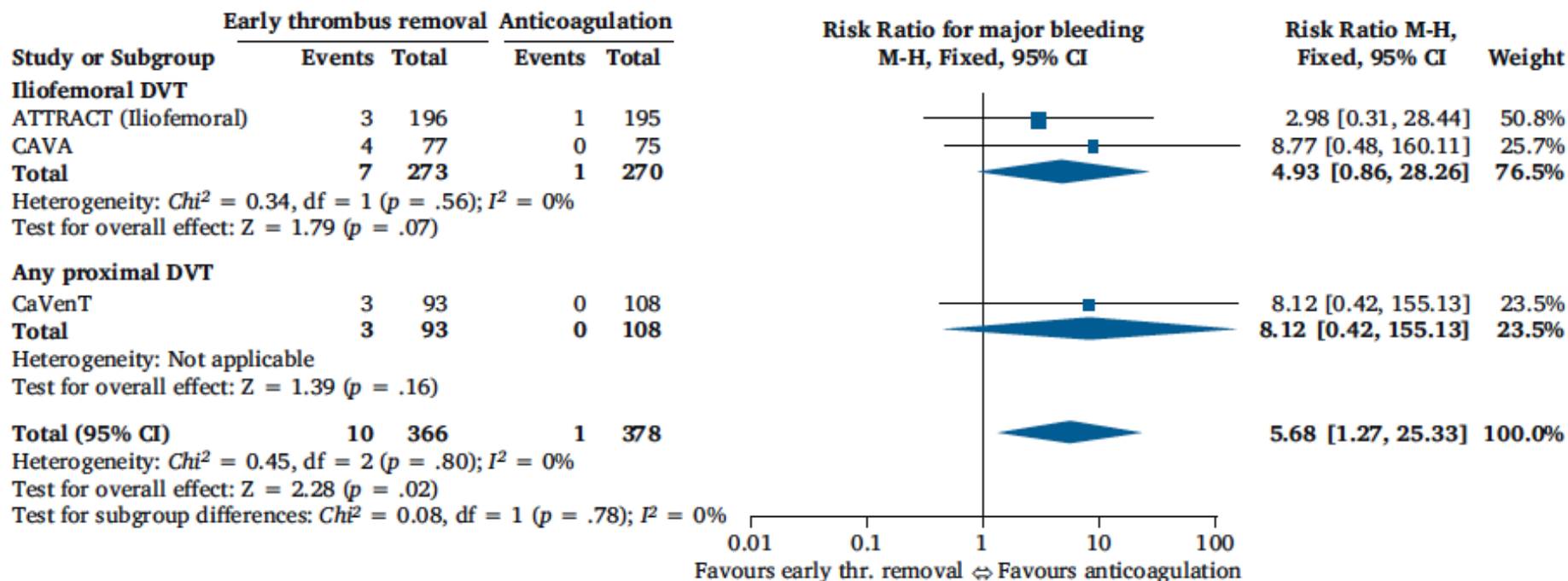
„Moderate to severe PTS“: Villalta score ≥ 10

Kakkos SK et al. Eur J Vasc Endovasc Surg 2021

Ergebnisse der RCT

Interventional treatment vs. conservative treatment

Effect on *major bleeding*



„Moderate to severe PTS“: Villalta score ≥ 10

Kakkos SK et al. Eur J Vasc Endovasc Surg 2021

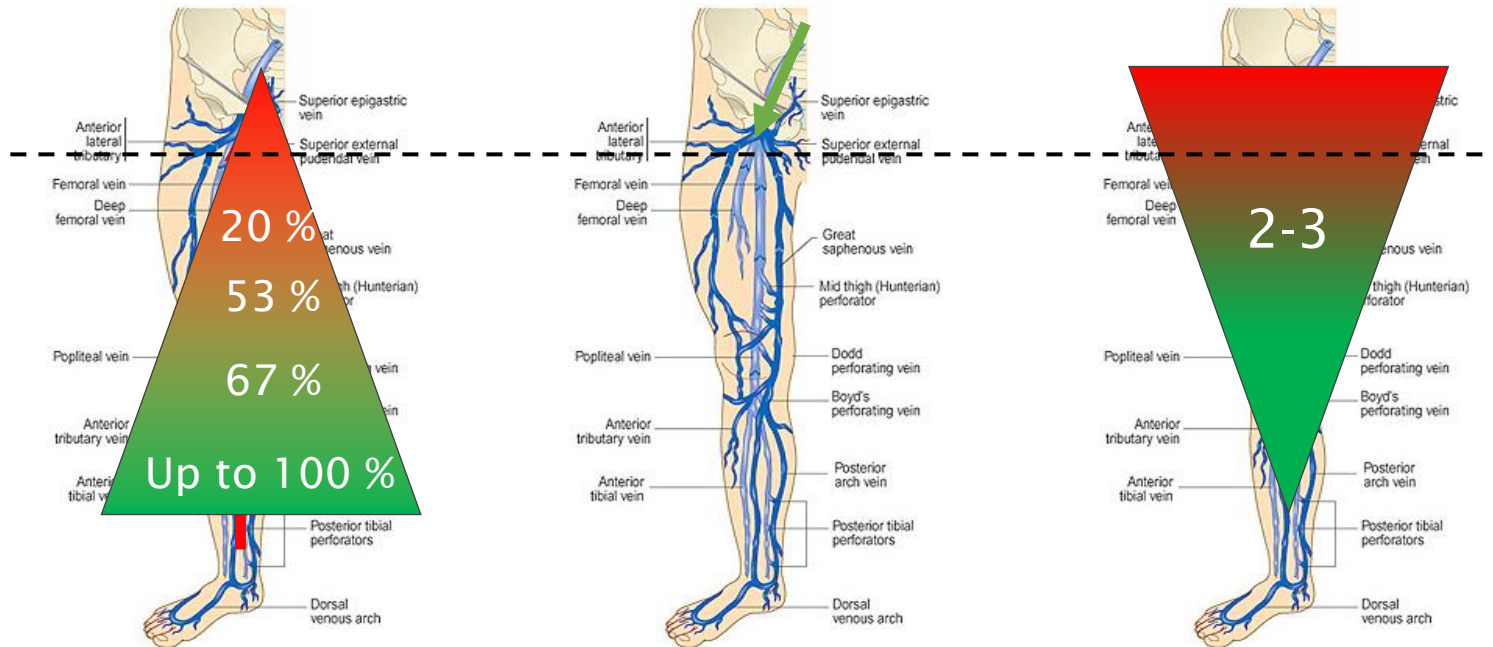
Es ist komplizierter...

- Unterschiedliche TVT-Entitäten (Iliofemoral versus femoropopliteal TVT)

Unterschiedliche Thrombose-Entitäten

Thrombus resolution after 6 months Ascending DVT Descending DVT

PTS risk (OR)



Vasa 2016, Supplement 90. DOI 10.1024/0301-1526/a000485

antyradar.info

Überlegungen

- Unterschiedliche TVT-Entitäten (Iliofemoral versus femoropopliteal TVT)
- Zugrundeliegende Läsionen diagnostizieren (CT, IVUS)
- Einsatz venöser Stents
- Duplex-Kontrollen und klinische Nachkontrollen
- Diagnose und scoring des postthrombotischen Syndroms

Villalta Scale

Villalta scale **range 0 - 33**

Symptoms	Clinical signs
Pain	Pretibial oedema
Cramps	Skin induration
Heaviness	Hyperpigmentation
Paresthesia	Redness
Itching	Venous ectasia
	Pain on calf compression

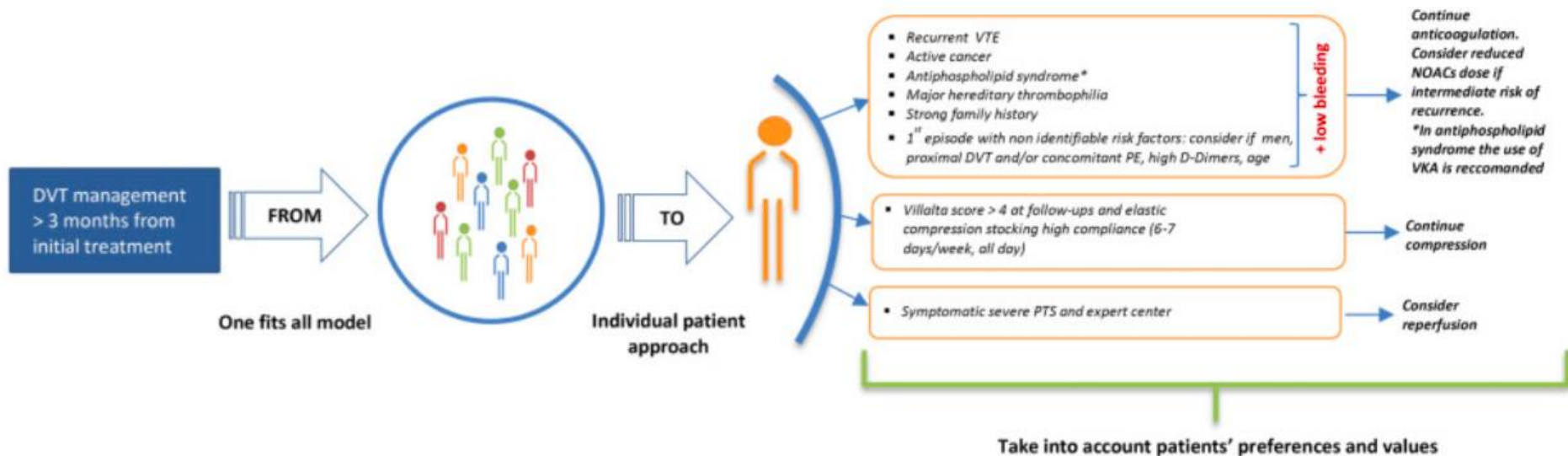
Venöse Claudication?

**Binärer Endpunktauswertung in
Interventionsstudien?**

Utne KK et al. Thromb Haemost 2016

Indikationsstellung bei akuter TVT

- Deszendierende Beckenvenenthrombose
- Anamnesedauer < 14 Tage
- Niedriges Blutungsrisiko



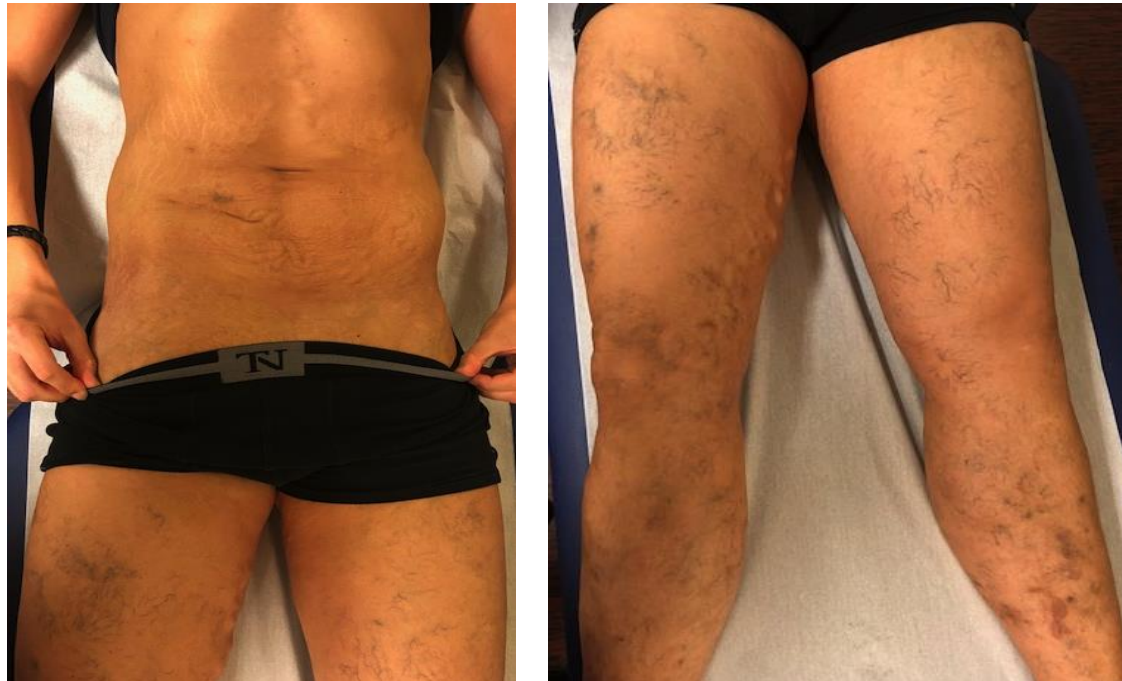
Mazzolai L et al. Eur J Prev Cardiol 2021

Fallbeispiel 3

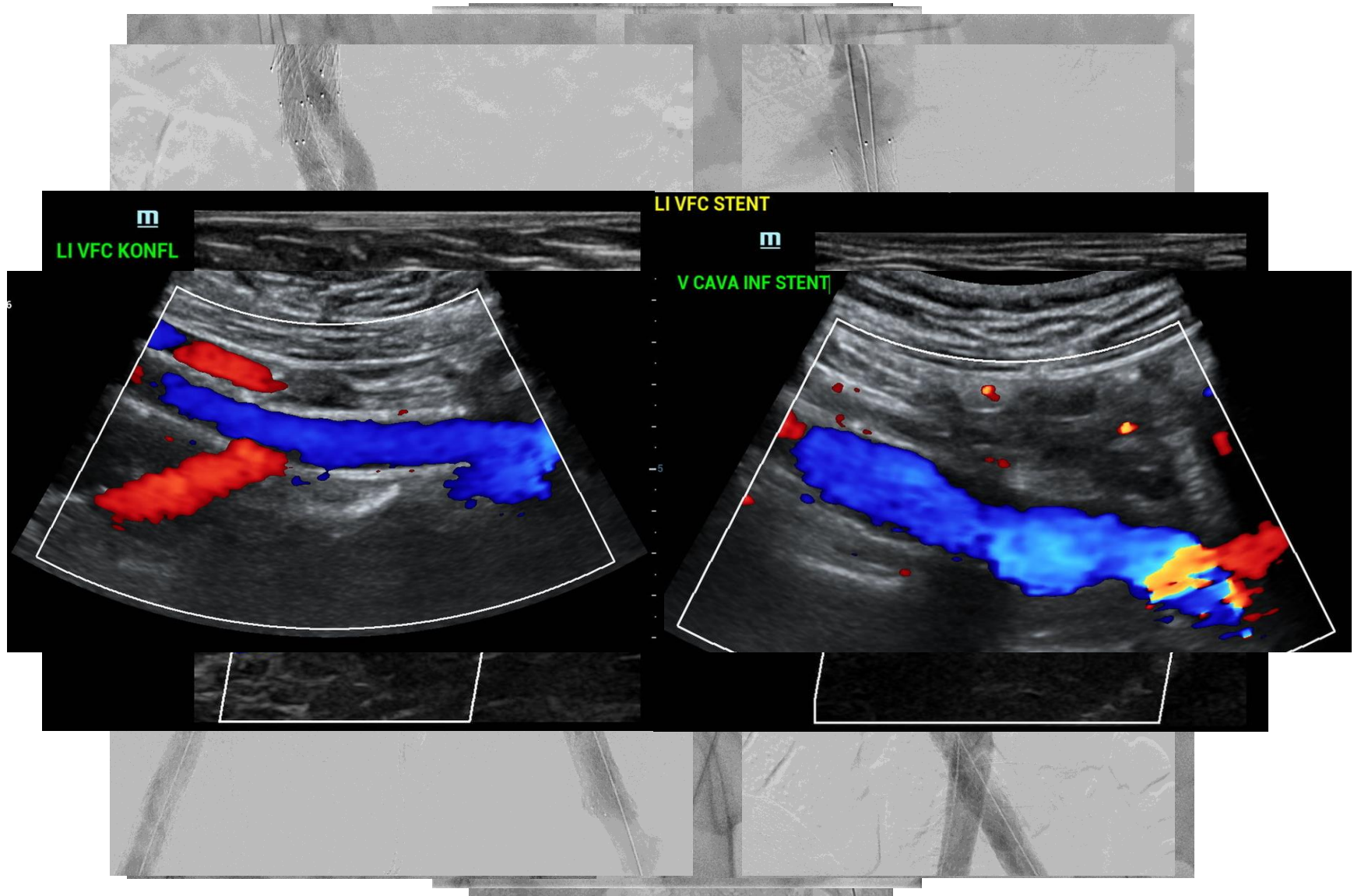
37-jähriger Patient mit seit 5 Jahren bestehenden chronischen Schmerzen,
Druckgefühl und Schwellungsneigung beider Beine.
Venöse Claudicatio in beiden Beinen nach 70 Metern.

FK: Thrombose der Beckenvenen rechts und der V. cava inferior vor 5 Jahren

Med.: laufende Antikoagulation seitdem (initial Marcoumar, zuletzt Rivaroxaban)



Fallbeispiel 3



Empfehlungen

ESVS recommendation 2021:

For patients with active or healed venous leg ulceration and iliac vein outflow obstruction, venous stenting should be considered. [Class IIa, LOE B]

De Maeseneer MG et al. EJVES 2022

ESVS recommendation 2015:

In patients with **clinically relevant chronic ilio-caval or ilio-femoral obstruction** or in patients with **symptomatic non-thrombotic iliac vein lesions**, percutaneous transluminal angioplasty and **stent placement using large self expanding stents** should be considered. [Class IIa, LOE B]

Wittens C et al. Eur J Vasc Endovasc Surg 2015

Konservative Behandlung des postthrombotischen Syndroms

- Kompressionstherapie

Kompressionsstrümpfe (Kompressionsklasse II – III, ev. IV)

Pneumatische Kompressionssysteme

Mechanische Kompressionssysteme

- Medikamentöse Therapie

mikronisierte gereinigte Flavonoidfraktion, Oxerutin, rotes Weinlaub, Rosskastanien,...: Symptomreduktion ?

mikronisierte gereinigte Flavonoidfraktion: adjuvant bei venösen Ulzera ?

- Physikalische Therapie

Wadenmuskelpumpentraining (2 kleine RCTs: 31 Pts., 95 Pts.)

Wittens C et al. Eur J Vasc Endovasc Surg 2015;49(6):678-737

Rabinovich A et al. J Thromb Haemost 2017;15:230-41

Zusammenfassung

- Bei Verdacht auf TVT: Ultraschall
- Alternativ: Wells-Score und je nach Vortestwahrscheinlichkeit POCUS
- Intervention: junge Patient:innen mit iliofemoraler TVT-Lokalisation
- 3 Monate Antikoagulation bei VTE mit transientem Risikofaktor
- Langfristige Antikoagulation bei persistierendem Risikofaktor

Tiefe Beinvenenthrombose, Postthrombotisches Syndrom

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