

## Venous Thromboembolism in the Context of Chronic Venous Disease

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## Chronic Venous Disease

### Spectrum of Diseases

- morphological/functional venous abnormalities of long duration manifested by symptoms and/or signs indicating the need for investigation/care
- 50-85% prevalence



Source: F.C. Brunacci, D.K. Anderson, T.A. Baker, D.L. Dunn, L.S. Kim, J.J. Miller, B. Nishimura, B. Potts. *Essentials of Vascular Surgery*, 1st Edition. © McGraw-Hill Education. All rights reserved.

### Chronic Venous Insufficiency

- CEAP: C3-C6 Disease
- 9.4% in Men; 6.6% in Women

Ruckley CV et al, *J Vasc Surg* 36:520-525, 2002

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## Chronic Venous Disease

### CEAP Etiology Classifications

**Congenital**

- Disorder present at birth
- Does not have to present early

**Primary**

- Vein and valve abnormalities
- Venous reflux essential

**Secondary**

- Acquired condition due to identifiable cause
- Trauma, obesity, superficial phlebitis, hormonal effects, DVT

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## Venous Thromboembolism (VTE)

### Annual Incidence

0.75-2.7/1000 persons

Raskob GE, et al, *Arterioscler Thromb Vasc Biol* 34:2363-2371, 2014

### What is the risk of VTE among patients with CVD?

**Depends on the etiology**

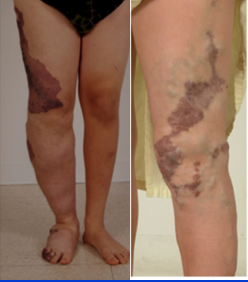
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## Types of Congenital CVD

**Klippel-Trenaunay Syndrome (KTS)**  
capillary, venous, arterial malformations

**Parkes-Weber Syndrome (PWS)**  
capillary, venous, arterial, lymphatic malformations

**KILT Syndrome**  
Kidney, inferior vena cava abnormalities, leg thrombosis



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### Risk of VTE Congenital CVD

**KTS**  
 Few higher level studies  
 8-22% incidence of VTE  
 > 100 fold increased risk of DVT/PE with pregnancy  
 Risk independent of pregnancy status  
Oduber CE et al. Neth J Med 71:246-252, 2013; Horbach SE et al. BJOG 134:1780-1788, 2017; Marvin EK et al. J Am Acad Dermatol 81:1277-1282, 2019

**PWS**  
 Data primarily limited to case reports involving DVTs

**KILT**  
 Characterized by thromboses (typically deep system)

Children  
**If no risk factors...evaluate for congenital abnormalities/syndromes**  
**Appears to be increased risk of VTE**

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### VTE in Congenital CVD

**Limited data regarding treatment or prophylaxis**  
 Long-term LMWH or VKA have been reported

Few studies evaluate direct oral anticoagulants or aspirin  
 Diversity Trial – Dabigatran (Brandao LR, et al. Blood 135:491-504, 2020)  
 Einstein-Jr – Rivaroxaban (Male C, et al. Lancet Haematol 7:e18-e27, 2020)

Should utilize prospective registry databases

Requires patient-tailored approach

Risk/benefit monitoring by specialist

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### Non-congenital CVD

Primary versus secondary often not well delineated

VTE risk in primary CVD - Few studies  
 DVT patients were 4.7x more likely to have primary valvular reflux and estimated 2/3 of DVT patients had primary CVD  
(Shaydakov M, Comerota A, Lurie F. J Vasc Surg Venous Lymphat Disord 4:161-166, 2016)

5% occurrence of VTE in a retrospective observational study of 641 patients (C0-C6) and recurrence in more advanced disease (C4-C6)  
(Musil D, Kaletova M, Herman J. Phlebology 32:135-140, 2017)

**More studies needed**

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### Varicose Veins

Can be primary or secondary

Increased risk of VTE  
 HR 5.3 in a retrospective cohort study >400,000 pts  
(Chang SL et al. JAMA 319:807-817, 2018)

Risk decreases with age  
 OR 4.2 (age 45) versus OR 1.9 (age 60), 0.9 (age 75)  
 Unclear why (Heit JA et al. Arch Intern Med 160:809-815, 2000)

Increases risk of other high-risk groups  
 Cancer (Konigsbrugge O et al. J Thromb Haemost 11:1993-2000, 2013)  
 Surgical patients (Prandoni P. Arch Intern Med 162:1966-1971, 2002)

VVs may not predict VTE recurrence (Heit JA et al. Arch Intern Med 160:761-768, 2000)

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### Varicose Veins

Thromboprophylaxis in appropriate setting

- Medical/Surgical Hospitalization
- Studies need to assess which pts need prolonged thromboprophylaxis

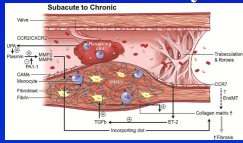
Variable VTE risk w/ treating varicosities

- More severe disease associated with higher risk
- High-risk patients should receive thromboprophylaxis
- Our group uses the 2005 Caprini RAM All patients receive SQ heparin 5000 IU
- Pts w/ score of  $\geq 8$  receive SQ Lovenox (40mg) x 7 days

Similar VTE rates between higher/lower scores  
 1.4% DVT, 0.3% Proximal, 1.1% Distal (of 1738 pts)  
(Braet DJ et al. J Vasc Surg Venous Lymphat Disord 11:928-937, 2023)

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### Post-thrombotic Syndrome



Unclear risk of recurrent DVT

One study found 2.6-fold increased risk at 48 months (Stain M et al. J Thromb Haemost 3:2671-2676, 2005)

Another study of 846 pts over 33 months found no increased HR (Prandoni P et al. Thromb Res 141:91-92, 2016)

Indefinite anticoagulation not warranted

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### Post-thrombotic Syndrome

Residual vein thrombosis (RVT) may be helpful

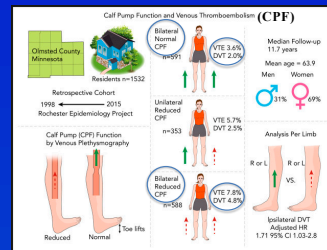
- Presence at 3 months: ↑ recurrence (HR 2.03)  
*(Prandoni P et al. Semin Thromb Haemost 41:133-140, 2015)*
- ↑ risk after full anticoagulation for 24 months and then VKA withdrawal  
10.4% incidence in those with RVT  
1.4% incidence in those without RVT  
*(Siragusa S et al. Am J Hematol 86:914-917, 2011)*

#### Limitations with standardization

- Technician dependent
- Patient dependent

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### Post-thrombotic Syndrome



**Optimal Cutoff EF 23.1%**

*Houghton DE et al. Vasc Med 28:57-58, 2023*

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### Main Points

- Guidelines currently do not consider CVD, its severity, or its manifestations in standardize scoring systems
- More studies needed  
VTE and treatment/prevention in the setting of CVD
- Delineate between primary vs. secondary etiologies
- Also continue to assess RVT

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Thank You

*Samuel and Jean Frankel Cardiovascular Center  
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