Experimental insights into acute DVT and PTS

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Deep Vein Thrombosis

- Incidence: 250,000 – 900,000 pts per year in US
  - 100,000 – 300,000 related deaths per year
- Treatment: Anticoagulation (bleeding risk)
- Late: Post-thrombotic syndrome

Deep Vein Thrombosis

- Nets are extruded DNA complexed with histones; primarily from PMNs
- Defense mechanism
- Pathological ‘side effect’ may be thrombosis

Acute DVT

Plasma DNA is Elevated in Patients with Deep Vein Thrombosis

J.A. Diaz, MD1, T.A. Rochs, PhD1, T.O. Jackson2, J.A. Kramer-Hoving, MD3, B. Lilesle4, P.K. Henke, MD1, O.D. Myers Jr, DVM, MPH1, C.D. Wagner, MD3, T.W. Wakefield, MD3, and for the Michigan Research Venous Group

- Prospective biomarker study
- Duplex confirmed
- DVT = 47; Control = 28; NI = 19

Circulating DNA

DVT (+) vs Control: P < .01
DVT (+) vs DVT (-): P < .01
DVT (-) vs Control: NS

Neutrophil histone modification by peptidylarginine deiminase 4 is critical for deep vein thrombosis in mice

Kanghong Ma, et al. PNAS May 21, 2013 vol. 110 no. 21
Mainstays of therapy to prevent PTS

- Rapid and therapeutic anticoagulation
- Leg elevation
- Compression
- ? Invasive techniques to clear thrombus?

Overview of PTS

Models of VT

Diagram of stasis (A) and stenosis (B) VT models. (C) Thrombus size decreases over time; N = 8-12; * = P < .05. D: II and E: examples of 4 and 8d VT. T = thrombus.
**Statins!**

A Randomized Trial of Rosuvastatin in the Prevention of Venous Thromboembolism


**Statin therapy reduces thrombus burden in stasis-induced murine VT.**


**Early venous thrombus resolution is accelerated in atorvastatin-treated animals.**


**IL-6 and PTS**

- IL-6 is both a biomarker for incident PTS as well as associated with experimental vein wall injury
- Human trials are on going and anti-IL6R Ab is used for RA


Potential Translation

- Non anticoagulant DNAse may be useful for selected non occlusive DVT
- Flow derived VT is different than stasis VT
  - Implications for therapy, prognosis?
- Statins for PTS prevention?
  - Timing and dosage
  - Human trail underway
- Anti-IL-6 receptor or soluble agonist (sgp130) to inhibit fibrosis, promote re-endothelialization