Experimental insights into acute DVT and PTS

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NO DISCLOSURES

Deep Vein Thrombosis

- Incidence: 250,000 – 900,000 pts per year in US
  - 100,000 – 300,000 related deaths per year
    - AHA statistics; Circulation 2009, 2015
- Treatment: Anticoagulation (bleeding risk)
- Late: Post-thrombotic syndrome

Mainstays of therapy to prevent PTS

- Rapid and therapeutic anticoagulation
- Leg elevation
- Compression – Little effect
- ? Invasive techniques to clear thrombus
  - CaVenT and ATTRACT not a game changer

What is new?

- Mast cells – who knew?
- Recurrent VT is different than primary VT
- IL-6 – late effects
Models of experimental VT

Diaz JA, et al. ATVB 2012;32:556

- Stenosis model
- Kit\textsuperscript{Wsh} = mast cell depleted mice
- No VT at 24 hr

Recurrence DVT is a major risk factor for PTS in humans

Mast Cells Granular Contents Are Crucial for Deep Vein Thrombosis in Mice

VT at 6 hrs

1= WT control
2= WT + 40/80
3= WT + histamine
4= Kit\textsuperscript{Wsh} + saline
5= Kit\textsuperscript{Wsh} + histamine

Agents applied to IVC for 10 min

Pre-Clinical Model to Study Recurrent Venous Thrombosis in the Inferior Vena Cava

Vein Wall Weight to Length

Pre-Clinical Model to Study Recurrent Venous Thrombosis in the Inferior Vena Cava
IL-6 and PTS

- IL-6 works via a classical signaling route (direct receptor binding) and a circulating receptor that acts ‘trans’ that is proinflammatory/fibrotic
- Human anti-IL6R Ab is used for RA

Inflammation markers and their trajectories after deep vein thrombosis in relation to risk of post-thrombotic syndrome

- N = 803 from SOX trial
- Prospective acquired blood for markers

Early post-thrombotic venous inflammation is characterized by greater IL-6 pathway upregulation in occlusive thrombi and in the

Pre-Clinical Model to Study Recurrent Venous Thrombosis in the Inferior Vena Cava

A

Collagen qRT-PCR

Collagen Iα

Collagen III

B

Sirius Red Stain and Quantification

Sirius Red Stain for Collagen

Potential Translation

• Anti-histamine for VT prevention?
  – More study, other models
• Prevent recurrent DVT!
  – Primed vein wall for fibrosis
  – DOACs can do better?
• Anti-IL6R or anti-gp130 to prevent PTS -- work in progress this year

Thank you