Post-Thrombotic Syndrome
Prevention and Management

Dr. Ashwini Bennett
Disclosures

• No disclosures relevant to this presentation
Outline

• Importance of VTE and PTS
• Aetiology of PTS
• PTS risk factors
• PTS clinical assessment
• PTS prevention
• PTS management
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- Importance of VTE and PTS
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- PTS prevention
- PTS management
Why is this topic relevant to you?

• VTE is very common

• VTE can cause PTS

• Severe PTS may result in venous leg ulcers
VTE is very common

- Australia 2008 \(^1\)
  14,716 cases
  $1.72 billion

- Annual incidence VTE Perth, WA \(^2\)
  0.57 per 1000 residents (95% CI 0.47 to 0.67)

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2: Access Economics 2008 report
VTE is very common

Comparison of deaths by selected causes, 2003


Access Economics 2008 report
VTE can cause PTS

- PTS occurs in~ 1/3 symptomatic DVT
  Can be up to 50%, especially proximal DVT

- Severe PTS (± ulceration) occurs in 5 to 10% DVTs

Severe PTS is a cause of morbidity

- Ulcers
- Discomfort
- Decreased mobility
- Occupational issues
- Poorer QOL than chronic lung disease, diabetes, arthritis

Severe PTS ≈ QOL as CCF or cancer

PTS prevalence

• VTE cohort study
  Monash Health and Alfred Health
  N=235 (July 2011 to Feb 2014)
  PTS in 17.5% of patients
  - 68% mild
  - 23% moderate
  - 9% severe

Aoki et al. 2014. Abstract for European Haematology Association congress
Outline

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• **Aetiology of PTS**
• PTS risk factors
• PTS clinical assessment
• PTS prevention
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PTS risk factors

- More proximal DVT \(^1\)
- Incomplete resolution of signs/symptoms by 1 month post-DVT \(^2\)
- Recurrent ipsilateral DVT \(^3\)
- ↑ BMI \(^1\)
- Older \(^1\)
- Possible \(^4\)

Female, hormonal therapy, varicose veins, abdominal surgery

PTS risk factors

• Probably not at increased risk

Family history

Thrombophilic states
(e.g. antiphospholipid antibodies, factor V Leiden, prothrombin gene mutation, deficiency of protein C/S/ATIII)

Outline

• Importance of VTE and PTS
• Aetiology of PTS
• PTS risk factors
• **PTS clinical assessment**
• PTS prevention
• PTS management
Clinical assessment

• Diagnosis mainly clinical
  E.g. Oedema, pain, hyperpigmentation, pruritus, induration, lipodermatosclerosis

• Radiologic findings: Supportive but not diagnostic
  E.g. Valvular incompetence

• Can mimic DVT
  Defer diagnosis until 3-6 months after acute episode
  Remain vigilant for recurrent DVT
Clinical scoring systems

• Villalta: Most commonly used

• Ginsberg $^{1, 2}$
  Identifies a more severe subset of PTS

• (Other)
  E.g. Brandjes, Widmer, CEAP, Venous Clinical Severity Score

# Villalta Score

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Cramps</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Heaviness</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Pruritus</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>Signs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pretibial edema</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Indurated skin</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Erythema</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Venous ectasia</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Pain on calf compression</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Ve nous ulcer</td>
<td>Absent or present</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Mild PTS:** 5-9 points
- **Moderate PTS:** 10-14 points
- **Severe PTS:** ≥ 15 points or venous ulcer

VISUAL GUIDE FOR THE ASSESSMENT OF POST-THROMBOTIC SYNDROME

<table>
<thead>
<tr>
<th>No or Minimal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Edema</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No loss of body substance; swelling with pressure over ankle or shin</td>
<td>Minimal loss of skin and subcutaneous tissue; swelling with pressure over ankle or shin</td>
<td>Headache or swelling and loss of skin, subcutaneous tissue; swelling with pressure over ankle or shin</td>
<td>Severe swelling and loss of skin, subcutaneous tissue; swelling with pressure over ankle or shin</td>
</tr>
<tr>
<td><strong>Hyperpigmentation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>Pale, scattered brownish discoloration around site</td>
<td>Obvious brownish discoloration around ankle and lower leg</td>
<td>Pale, scattered brownish discoloration around ankle and lower leg</td>
</tr>
<tr>
<td><strong>Venous ulcers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No nodules or crusted wounds</td>
<td>A few fresh, subtle, pale, non-specific ulcers around the ankle or foot area</td>
<td>Ullers turn dark and prominent, multiple ulcers or ulcerative lesions around the ankle and foot area</td>
<td>Ullers turn dark and prominent, multiple ulcers or ulcerative lesions around the ankle and foot area</td>
</tr>
<tr>
<td><strong>Redness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal color of leg</td>
<td>Pale, reddish rash or lower leg</td>
<td>Reddish discoloration of lower leg</td>
<td>Reddish discoloration or purplish discoloration of ankle and lower leg</td>
</tr>
<tr>
<td><strong>Scleroderma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin of ankle and calf thickened and shiny, hard, and shiny, with swelling, tissue or bony structures</td>
<td>Skin of ankle and calf thickened and shiny, hard, and shiny, with swelling, tissue or bony structures</td>
<td>Skin of ankle and calf thickened and shiny, hard, and shiny, with swelling, tissue or bony structures</td>
<td>Skin of ankle and calf thickened and shiny, hard, and shiny, with swelling, tissue or bony structures</td>
</tr>
<tr>
<td><strong>Pain during calf compression</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>Present, patient rated it mild in intensity</td>
<td>Present, patient rated it moderate to severe in intensity</td>
<td>Present, patient rated it severe in intensity</td>
</tr>
</tbody>
</table>

**Note:** Nodules may be less apparent in patients with lower body skin.
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PTS prevention

• (Prevent initial DVT)
• Adequate treatment of initial DVT
  E.g. INR in therapeutic range

• Thrombolysis
CaVenT study: Ileofemoral DVT. PTS at 24 months:
CDT arm: 37/101 (41.1%)  p= 0.04
Control: 55/108 (55.6%)  ARR= 14.4%, NNT=7

ATTRACT study ongoing

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ECS: Entering the lions’ den

Daniel in the lion’s den: Rubens
Elastic compression stockings

- Graduated elastic compression stockings

Not TEDS

Class II: 20-30 mm Hg at ankle
Class III: 30-40 mm Hg at ankle
ECS in PTS

• Earlier studies suggested up to 50% reduction in PTS incidence with appropriate use of ECS

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>PTS in control arm</th>
<th>PTS in ECS arm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brandjes</td>
<td>1997</td>
<td>194</td>
<td>69 (70%)</td>
<td>30 (31%)</td>
</tr>
<tr>
<td>Prandoni</td>
<td>2004</td>
<td>180</td>
<td>44 (49.1%)</td>
<td>23 (24.5%)</td>
</tr>
</tbody>
</table>

• Other studies with different design have found no effect

E.g. Ginsberg Arch Intern Med 2001
SOX trial

• SOX Trial
Double-blind RCT, 2004-2010
First proximal DVT
2 year follow-up

Randomised to

30-40mm Hg graduated ECS
or
Placebo stocking (<5mmHg)

SOX trial

• Primary efficacy outcome
  PTS diagnosed using Ginsberg criteria at ≥ 6 months
  ECS arm: 44/409 (14.2%)  HR 1.13 (95%CI 0.73-1.76)
  Placebo arm: 37/394 (12.7%)  p=0.58

• Secondary efficacy outcome
  PTS diagnosed using Villalta criteria at ≥ 6 months
  ECS arm: 176/409 (52.6%)  HR 1.00 (95%CI 0.81-1.24)
  Placebo arm: 168/394 (52.3%)  p=0.96
SOX trial

• No major adverse events in either arm

• Minor adverse events equal in both groups
  E.g. Rash, itching
Strengths of SOX trial

- N = 806
- Double-blinded
- Prospective RCT
- Multi-centre
- 2 scoring systems
- 2 year follow-up
Limitations of SOX

Compliance

Scoring systems subjective

High rate loss to follow-up

Delay in starting stocking use?

Advice on how to apply stockings

Really blinded? (yes)

Correspondence to Lancet editor in response to publication of SOX trial results
ECS: A pragmatic approach

- Ipsilateral class II compression stocking all patients with proximal DVT
- Use during waking hours
- Remove before bed-time
- Ideally for 2 years
- Correctly fitted by orthotic supplier
- If not tolerated/too expensive/too inconvenient: Patient may consider ceasing
- 1 pair class II stockings $110 below knee, $150 thigh-high. Last for 6 months.
PTS management: Other options

• Early physical activity
  May ↓ PTS rate compared to bed rest

• Venous ulcer management
  Specialist management
PTS management: **Not routine**

- **Intermittent pneumatic compression**
  Portable venous return assist devices
  E.g. Venowave ®

- **Venoactive medications**
  Aescin (horse chestnut seed): May ↓ symptoms of CVI
  Hydroxyethylrutosides: May ↓ PTS symptoms

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2: Pittler. Cochrane review 2006
Take home messages

• PTS is common and under-appreciated

• Ongoing monitoring for PTS required

• Severe PTS can → Venous ulcers

• Villalta score

• Compression stockings may be useful