Is C2 Disease Progressive?

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I Have No Disclosures Relevant To This Presentation

The Epidemiology of CVD

- Cross sectional sample of 3072 subjects

Factors Associated with CVD Progression
Kostas T, J Vasc Surg 2010

- 5 yr follow up of 73 asymptomatic limbs after unilateral vein surgery
- 32% of limbs with increase in C class by ≥ 2
- Factors associated with clinical deterioration
  - Standing > 4 hrs (p ≤ 0.001)
  - BMI ≥ 30 (p ≤ 0.001)
  - Non-compliance with elastic stockings (p ≤ 0.001)

Factors Associated with CVD Progression
Initial Class | C1 | C2 | C3 | C4
---|---|---|---|---
C0 | 5  | 10 | 8  |    
C1 | 6  | 3  |    |    
C2 | 2  | 2  |    |    
C3 |    |    |    |    
C4 |    |    |    |    

The Progression of 1st CVD
The Bonn Vein Study II, Rabe E, in press

- 6.6 year follow-up of Bonn I participants
- 2% per year progression to CVI (C3 – C6)
- Risk factors for progression
  - Age
  - Arterial Hypertension
  - Obesity

Initial Class | C0-C1 | C2 | C3 | C4 | C5 | C6 | Any
---|---|---|---|---|---|---|---
C0-C1 (1269) | 161 (12.7) | 95 (7.6) | 22 (1.7) | 1 (0.1) | 3 (0.2) | 0 | 22.2%
C2 (91) non saph | 15 (16.5) | 2 (2.2) | 1 (1.1) | 0 | 0 | 9.9%
C2 (132) saphenous | 28 (21.2) | 14 (10.6) | 0 | 0 | 31.6%
C3 (204) | 9 (4.4) | 0 | 0 | 0 | 4.4%
C4 (133) | 1 (0.8) | 1 (0.8) | 6.1%
C5 (3) |    |    |    |    | 100%
C6 (1) |    |    |    |    | 100%

CVD Prevalence

- 0.0%
- 14.2%
- 11.6%
- 2.9%
- 0.7%

Risk factors for progression
- Age
- Arterial Hypertension
- Obesity

Factors Associated with Clinical Deterioration
- Standing > 4 hrs (p ≤ 0.001)
- BMI ≥ 30 (p ≤ 0.001)
- Non-compliance with elastic stockings (p ≤ 0.001)
Most patients with CVD do not progress to C4 – 6
Advanced CVD is a multifactorial disease
• Age
• Obesity
• Gender
• Hypertension
• Occupation
• HFE polymorphisms
• AT deficiency
Number needed to prevent 1 ulcer (NNT) is low and will likely remain unknown

Multiple postulated single nucleotide polymorphisms (SNPs)
• Iron metabolism
  - HFE (hemochromatosis protein)
  - Ferroportin gene (FPN)
• Wound healing (MMP12)
• Coagulation (Factor XIII, protective)
DNA array genotyping in 638 subjects
- 333 C3 – C6 patients
- 305 healthy controls

<table>
<thead>
<tr>
<th>Gene</th>
<th>SNP</th>
<th>VLU Risk</th>
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<tbody>
<tr>
<td>HFE</td>
<td>C282Y</td>
<td>6 – 7x</td>
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<tr>
<td>FPN</td>
<td>8G8G</td>
<td>5x</td>
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<tr>
<td>MMP12</td>
<td>82AA</td>
<td>2x</td>
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• Disease progression is a multifactorial process
  - Venous disease may be the promoting factor
  - Other deterministic factors
    - Environmental & demographic factors
    - Genetic factors
• Attributing progression to venous disease alone is overly simplistic
• The value of prophylactic intervention for unselected C2 – 3 disease is unlikely to be demonstrated
• Factors determining progression to C4 – 6 disease need to be better elucidated