Is Venography Alone Adequate to Evaluate the Deep Veins?

“We develop strategies to compensate for the shortcomings of venography and convince ourselves it’s adequate.”
– Peter Neglén, MD, Ph.D.

- Venogram poor diagnostic sensitivity
- 34% of pts. w/ chronic venous symptoms had iliac vein obstruction and normal venogram
- Collaterals, 43% of limbs that were stented


Study Objectives

Primary Objectives

1. Prospectively compare multiplanar venography vs. Intravascular Ultrasound (IVUS) for diagnosing treatable iliac/common femoral vein obstruction (ICFVO)
2.
3.

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Study Design

- Prospective, multi-center, single-arm
- 14 Sites: US (n = 11) and Europe (n = 3)
- 100 patients
  - CEAP 4-5, n=50; CEAP 6, n=50
- Follow-up visits: 1m and 6m

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Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N = 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (female:male)</td>
<td>43:56</td>
</tr>
<tr>
<td>Index leg (left:right)</td>
<td>63:37</td>
</tr>
<tr>
<td>Age (mean ± SD, range)</td>
<td>62 ± 12 (30 – 85)</td>
</tr>
<tr>
<td>Race (Caucasian)</td>
<td>86 %</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>33.6 ± 7.5</td>
</tr>
<tr>
<td>CEAP</td>
<td>N</td>
</tr>
<tr>
<td>0-3</td>
<td>0 (by protocol)</td>
</tr>
<tr>
<td>4a</td>
<td>33</td>
</tr>
<tr>
<td>4b</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
</tr>
</tbody>
</table>

Baseline Imaging:

Venogram and IVUS (Site-Reported)

<table>
<thead>
<tr>
<th>Venogram and IVUS Findings</th>
<th>Veins Segment*</th>
<th>Percent of Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Segments Assessed</td>
<td>300</td>
<td>100.0%</td>
</tr>
<tr>
<td>Lesion on IVUS but not Venogram</td>
<td>63</td>
<td>21.0%</td>
</tr>
<tr>
<td>Lesion on Venogram but not IVUS</td>
<td>5</td>
<td>1.7%</td>
</tr>
<tr>
<td>Lesion on both Venogram and IVUS</td>
<td>62</td>
<td>20.7%</td>
</tr>
<tr>
<td>No appreciable stenosis, Venogram or IVUS</td>
<td>170</td>
<td>56.7%</td>
</tr>
</tbody>
</table>

*Common Iliac, External Iliac, and Common Femoral veins

IVUS more sensitive for ICFVO Stenosis vs. Venogram

IVUS vs. Venogram:

Diameter (Core Laboratory)

- Diameter estimation by IVUS underestimated compared to IVUS.
- Venogram missed 26% of >50% diameter-reduction lesions.
- IVUS determined stenoses, in general, were 10.9% more severe (mean) than by Venogram (P < .001).

IVUS vs. Venogram:

Area (Core Laboratory)

- 17.7% of significant CSA lesions (defined by >50% area reduction) were missed with 3-view venograms.
Procedure Decision Making

Site Investigator:
- Venogram vs. IVUS -> Stent?
- 60/100 (60%) pts., Decision To Stent Changed due to IVUS
- n=50 pts., Stent Number, Increased (0->1 stent or 1->2 stents) due to IVUS
- Without IVUS, undertreat ICFVO!

6-month Follow-up Change in revised Venous Clinical Severity Score (rVCSS) after Stenting

<table>
<thead>
<tr>
<th>rVCSS</th>
<th>Baseline</th>
<th>30 days</th>
<th>P value</th>
<th>Baseline</th>
<th>6 months</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>score worsening (-)</td>
<td>14.4 ± 4.6</td>
<td>15 (6, 27)</td>
<td>&lt;0.001</td>
<td>14.4 ± 4.6</td>
<td>15 (6, 27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>score improvement (+)</td>
<td>10.9 ± 5.3</td>
<td>10 (1, 26)</td>
<td>&lt;0.001</td>
<td>10.9 ± 5.3</td>
<td>10 (1, 26)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- rVCSS scores are presented as both mean ± standard deviation and median (range).
- A lower score connotes improved health.

Demographics

rVCSS assessment at baseline, 30 days, and 6 months, stented population (n = 68)

Receiver Operating Curve (ROC)
Baseline Stenosis vs. rVCSS @ 6 mos

<table>
<thead>
<tr>
<th>Stenosis</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;52%</td>
<td>(p=0.29)</td>
<td></td>
</tr>
<tr>
<td>&gt;56%</td>
<td>(p=0.05)</td>
<td></td>
</tr>
<tr>
<td>&gt;54%</td>
<td>(p=0.04)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion:
IVUS vs. Multiplanar Venogram for ICFVO

- Primary Endpoint: (CEAP 4-6 pts.)
  - IVUS more sensitive for identifying significant ICFVO
  - IVUS more accurate for degree of stenosis
  - IVUS best guide for Stent Intervention
  - >50% baseline stenosis measured w/ IVUS, predicted clinical improvement (rVCSS>4) @ 6-months

Thank You!
Intravascular Ultrasound and vein stent placement

- >50% baseline stenosis measured w/ IVUS, predicted clinical improvement (rVCSS>4) @ 6-mos.
  - IVUS Diameter, \( P = .05 \)
  - IVUS Area, \( P = .04 \)
- >61% Baseline diameter stenosis Nonthrombotics best predicts clinical improvement

**Conclusion:** Post-Hoc Analysis

Non-thrombotic Subset (N=48)

- IVUS baseline diameter stenosis:
  - Significant and better predictor of future improvement in clinical symptoms (\( P = .03 \)) than area stenosis.
  - Higher threshold baseline stenosis for stenting (>61%, Youden Index 0.36).
- Post-intervention stenotic change:
  - All imaging significant predictors clinical improvement
    - MPV, \( P = .05 \)
    - IVUS-diameter and IVUS-area, \( P = .001 \)

When to Stent?

- What is iliac/common femoral vein threshold stenosis which when stented yields clinical improvement in CEAP 4-6 pts?
**Methods**

- Stenosis: Core lab over read of Venograms/IVUS
- Revised Venous Clinical Severity Score (rVCSS) >4 “Improved”
- ROC analysis assess diagnostic utility & predictive accuracy of venogram (diameter) & IVUS (diameter / area) baseline measurements of stenosis vs. rVCSS @ 6-mos.
- Youden Index calculated (maximize sensitivity & specificity of imaging modality determined stenosis for ideal threshold value at which Venogram or IVUS has highest likelihood to predict clinical improvement

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**Non-thrombotic Subset**

- Of the 68 stented subjects
- 48 classified non-thrombotic stenosis
- Non-thrombotic lesions
  - Eccentric ($P = .005$) (i.e. elliptical)
  - Stenotic ($P = .03$)
Study Objectives

Secondary Objectives

1. Prospectively compare multiplanar venography vs. Intravascular Ultrasound (IVUS) for diagnosing treatable iliac/common femoral vein obstruction (ICFVO)

2. Prospectively compare clinical decision making regarding treatment based on multiplanar venography vs. IVUS

3. Characterize the patient response to iliofemoral venous stenting [Venous Clinical Severity Score (VCSS) @ 6-month follow-up]

Demographics

- 68/100 limbs stented
- 37 males / 31 females
- Mean age 62 ± 12 years (Range, 30 – 85 years)
- 48 (71%) non-thrombotic
- 20 (29%) post-thrombotic
- CEAP Clinical Class
  - C6 n=36
  - C5 n=8
  - C4A n=22
  - C4B n=2

Recognize: Advanced Venous Dx.

Swelling / Pigment

Swelling / Dermatitis

Skin Pigment / Ulcer

Sample Case

Demographics

- 84 y/o male patient
- BMI = 25.8

History

Non-Contributory

Diagnostic Venography: AP Views

Physical Exam

Study Leg: Left

CEAP C6: 10 x 14 mm Ulcer, present for > 12mos

History

Non-Contributory

Multiplanar Venography

VIDIO Case

Demographics

84 y/o male patient
BMI = 25.8

History

Non-Contributory

Physical Exam

Study Leg: Left

CEAP C6: 10 x 14 mm Ulcer, present for > 12mos

History

Non-Contributory

3D RAO View

3D LAO View
Intravascular Ultrasound
VIDIO Case

Diagnosis:
Non-Thrombotic Iliac Vein Lesions (NIVL) x2

Common Iliac Vein
- 58% Cross-Sectional Area Reduction
- Tightest Stenosed Area of 72 mm²

External Iliac Vein
- 38% Cross-Sectional Area Reduction
- Tightest Stenosed Area of 88 mm²

Ulcer Size (N=50 at Baseline)

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Mean</th>
</tr>
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<tbody>
<tr>
<td>Baseline</td>
<td>30.7 cm²</td>
</tr>
<tr>
<td>1 month</td>
<td>22.6 cm²</td>
</tr>
<tr>
<td>6 months</td>
<td>24.9 cm²</td>
</tr>
<tr>
<td>Baseline vs. 1 month P &lt; .001</td>
<td></td>
</tr>
<tr>
<td>Baseline vs. 6 months P = .003</td>
<td></td>
</tr>
<tr>
<td>1 Month vs. 6 months P = .649</td>
<td></td>
</tr>
</tbody>
</table>

- Median size of the ulcers decreased from 30.7 cm² at baseline to 22.6 cm² at 1 mos.
- The decrease in ulcer size was statistically significant.
- 24% of ulcers healed at 1 mos.
- 50% were healed at 6 mos.

Ulcer Size: Stented vs. Non-stented Subjects

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Mean in Stented Subjects (N = 36)</th>
<th>Mean in Non-Stented Subjects (N=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects</td>
<td>34.6 cm²</td>
<td>20.5 cm²</td>
</tr>
<tr>
<td>Baseline</td>
<td>26.0 cm²</td>
<td>12.2 cm²</td>
</tr>
<tr>
<td>1 month</td>
<td>27.5 cm²</td>
<td>14.4 cm²</td>
</tr>
<tr>
<td>Baseline vs. 1 month P = .002 P = .021</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline vs. 6 months P = .002 P = .021</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Month vs. 6 months P = .855 P = .202</td>
<td></td>
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Wilcoxon Signed Rank Test

- Ulcer Size: Non Stented > Stented @ 6 mos.
- Compared to Baseline size
- Ulcer Recurring at 6 mos.?

VIDIO Investigators

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Institution</th>
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</thead>
<tbody>
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<td>University of Alabama; Birmingham, AL</td>
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Core Lab “Over Reads, Vgram & IVUS”: Syntactx
Sponsor: Philips/Volcano Corp.