Saphenous Vein Wall Thickness in Age and Venous Reflux-Associated Remodeling in Adults

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Vein wall thickness

Most studies have used an **ex-vivo histological evaluation**. **Limited in-vivo** studies to assess pathologic changes -post thrombotic vein wall remodeling -saphenous vein grafts after implantation

There are no studies comparing data from saphenous veins in patients with CVD to age and sex-matched controls.
Aim of study

To determine vein wall thickness in saphenous veins of patients with CVD and compare it to

1. Non refluxing saphenous segments

2. Younger normal individuals

3. Age- and sex-matched controls

The examination was performed in the **standing position**.

Pulse wave Doppler using a **3 to 9 MHz** linear array transducer.

Reflux in the superficial veins was defined as a retrograde flow lasting **>0.5s**.

In this study, **only patients with >2s reflux** were selected to assure that there was a clear pathology.

The distribution and extent of reflux was reported in detail and the vein **segments with and without reflux** were grouped separately.
Normal GSV in the lower thigh

Reflux in GSV from SFJ to upper calf

Patients with GSV reflux >2s were selected
Exclusion criteria

- Superficial or deep vein thrombosis
- Trauma
- Inflammatory conditions unrelated to venous disease
- Diabetes
- Unable to stand
- Morbid obesity
- Surgery in the lower extremities
- Focal dilations, varicosities and aneurysms
- Heavy calcification not allowing accurate measurements
SSV wall thickening – Post-thrombotic

1.2 mm
GSV lower calf wall calcification
Intra- and inter-observer variability

It was calculated by performing 3 separate measurements in the thigh and calf in 5 subjects from each group (n=15) for a total of 90 measurements.
Demographics of the patients and the control groups

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>No. Limbs</th>
<th>Sex</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>M</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Control Group 1</td>
<td>10</td>
<td>20</td>
<td>5</td>
<td>21 (2)</td>
</tr>
<tr>
<td>Control Group 2</td>
<td>10</td>
<td>20</td>
<td>5</td>
<td>64 (7)</td>
</tr>
<tr>
<td>Venous Reflux Patients</td>
<td>40</td>
<td>40</td>
<td>13</td>
<td>49 (8)</td>
</tr>
</tbody>
</table>

Group 1 Age vs. Group 2 Age,  \[p<0.0001\]
Group 1 Age vs. Patient Group Age,  \[p<0.0001\]
Group 2 Age vs. Patient Group Age,  \[p<0.0001\]
A 17MHz linear array transducer, was used with an axial resolution of 0.1mm, which is smaller than the venous wall to ensure valid measurements.

Measurements were done in the standing position where the veins are fully distended - and also eliminate variations.

The posterior wall was used for the measurements because the interface between the blood and the intima allows optimal measuring conditions. The thickest area of the venous wall was measured.
High definition real zoom magnification was used in order to optimize the measurements and reduce error. The ultrasound beam was set at 90 degrees to obtain the best imaging definition.

The ultrasound beam focus was placed in the posterior wall to optimize the lateral resolution.

The B-mode and Time Gain Compensation (TGC) were set to make the vein lumen dark.

Measurements were done at the blood wall interface to the outer wall of the vein.
Normal superficial vein wall in a young individual

- Peri-venous fat
- Lumen
- Wall thickness
Normal vein

0.28 mm
Real zoom

0.35 mm

Normal vein
Increased wall thickness in a competent GSV

F 60y, GSV had no reflux

0.5 mm
Intraobserver Variability – Bland-Altman plot

Difference between the 2 Readings vs. Mean of 2 Readings (mm)

- Controls: R1
- Controls: R2
- Patients: R1
- Patients: R2
Interobserver Variability – Bland-Altman plot

Difference between the 2 Readings

Mean of 2 Readings (mm)

Controls: T1
Controls: T2
Patients: T1
Patients: T2
<table>
<thead>
<tr>
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<th>Group 2</th>
<th>Patients: Segments Without Reflux</th>
<th>Patients: Segments With Reflux</th>
</tr>
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<tbody>
<tr>
<td><strong>No. Limbs Evaluated</strong></td>
<td>20</td>
<td>20</td>
<td>18</td>
<td>31</td>
</tr>
<tr>
<td><strong>Vein Wall Thickness: Thigh (mm)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>0.3 (0.03)</td>
<td>0.4 (0.05)</td>
<td>0.45 (0.07)</td>
<td>0.58 (0.1)</td>
</tr>
<tr>
<td>Range</td>
<td>0.27 - 0.34</td>
<td>0.34 - 0.47</td>
<td>0.3 - 0.55</td>
<td>0.38 - 1.3</td>
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<tr>
<td>95% CI</td>
<td>0.29-0.31</td>
<td>0.38-0.42</td>
<td>0.42-0.48</td>
<td>0.54-0.62</td>
</tr>
<tr>
<td><strong>Vein Wall Thickness: Calf (mm)</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean (SD)</td>
<td>0.31 (0.03)</td>
<td>0.39 (0.04)</td>
<td>0.47 (0.08)</td>
<td>0.59 (0.12)</td>
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<tr>
<td>Range</td>
<td>0.26 - 0.34</td>
<td>0.32 - 0.45</td>
<td>0.32 - 0.56</td>
<td>0.35 - 1.4</td>
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<td>0.30-0.32</td>
<td>0.37-0.41</td>
<td>0.43-0.51</td>
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P-values for the comparison of thigh vs. calf measurements within each group were all >0.29. P-values for the comparison of thigh vein wall thickness measurements between each group was <0.0001, except for Group 2 vs. Patients: Segments without Reflux which had a p-value of 0.012.
## Vein Wall Thickness: Thigh (mm)

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Vein Wall Thickness Measurements for Each Participant Group

Vein Wall Thickness (mm)

Group 1 Thigh n = 20
Group 1 Calf n = 20
Group 2 Thigh n = 20
Group 2 Calf n = 20
Pts: No Reflux Thigh n = 18
Pts: No Reflux Calf n = 23
Pts: Reflux Thigh n = 31
Pts: Reflux Calf n = 27
Vein Wall Thickness Measurements for Each Participant Group

- Group 1 Thigh: n = 20
- Group 1 Calf: n = 20
- Group 2 Thigh: n = 20
- Group 2 Calf: n = 20
- Pts: No Reflux Thigh: n = 18
- Pts: No Reflux Calf: n = 23
- Pts: Reflux Thigh: n = 31
- Pts: Reflux Calf: n = 27

The plot shows the vein wall thickness measurements with error bars for each group. The red circle highlights the data point for Pts: No Reflux Thigh, which seems to have the smallest vein wall thickness compared to other groups.
Human GSV from a patient that underwent CABG

Age-related qualitative and quantitative changes in venous intimal collagen

Russel modification of Movat Pentachrome stain
Organized structure of alternating smooth muscle cells interspersed by longitudinally arranged collagen bundles. Smooth muscle cells appear spindle shaped with a prominent nucleus.

Smooth muscle cells exhibit prominent vacuoles and are elliptical instead of spindle shaped. The smooth muscle cells are separated by diffusely deposited collagen bundles which impart a disorganized wall architecture.
GSV calf reflux – increased wall thickening in a nondilated vein
In patients with CVD both the refluxing and competent GSV segments had a thicker wall compared to both control groups.
“Normal venous segments” that are in continuity to varicose veins have the same biochemical properties of the vein wall as varicose veins.

This suggests that vein wall changes precede valvular changes.
Conclusions

Vein wall thickness significantly increases with age and in patients with venous reflux.

The increased vein wall thickness in non-diseased segments of patients with venous reflux compared with age- and sex-matched controls suggests that the venous wall is affected before the reflux is present.

This is demonstrated for the first time in-vivo in humans and is compatible with the venous wall theory for developing reflux.
Best wishes from New York!