Venous Incompetence: The Key to Understanding and Treating Venous Ulcers

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Disclosure

➢ NOTHING...
Venous Insufficiency Ulcer
Venous Insufficiency Ulcer

Also know as

- Venous Stasis Ulcer
- Ulcerative Venous Reflux Disease
Statistics / Clinical Frequency

➢ Affects 2-5 % of the population
➢ 24 Million have some form of Varicose Vein Disease or Venous Insufficiency
➢ 6 Million develop skin changes of Chronic Venous Insufficiency
➢ 1 Million to 500,000 affected with Venous Ulcers
➢ Account for 70-80% of all vascular ulcers treated and the majority of all chronic ulcers
Demographics / Age

➢ Not just a disease of the elderly
➢ Over 40% report their first ulcer by age 50
➢ 13% of patients with Chronic Venous Insufficiency had their first ulcer by age 30
Recurrence is Common

➢ Of the ulcers that heal, as many as 72% may recur at one year
➢ Improving clinical outcomes is important
➢ Costs of treatment are considerable
  • Cost of Venous disease $1.9 – 2.5 billion
  • Cost per case approximately $40,000
➢ Cost of Days lost of work
➢ Quality of life issues

Anatomy is Important

- Deep System
- Superficial System
Deep Venous System

- Anterior Tibial Vein
- Posterior Tibial Vein
- Peroneal Vein
- Popliteal Vein
- Femoral Vein
- Iliac Vein
Superficial Venous System

- Greater Saphenous
- Lesser Saphenous
- Branch Veins superficial
- Connected to the deep system by a series of perforator veins in the leg
- Joins the deep system at the foramen ovale in the groin
Venous Anatomy

- Superficial System is connected to the Deep System by a series of perforator veins in the leg
- Deep and Superficial join at the foramen ovale (groin)
Physiology / Venous Pressure

- In a healthy leg/vein
- Standing - approx 80 mmHg
- Supine - approx 10 mmHg
- Valves open with high pressure / close with low pressure
- Blood flow is uni-directional back to heart
Physiology / Calf Muscle Pump

- CMP augments the return of blood from the leg
- As the foot is dorsiflexed, the calf compresses the deep veins creating a pressure up to 250 mmHg
- Blood propelled cephalad towards the heart
When the foot is flexed, the pressure drops and flow from the superficial system through the perforators is augmented.

Valves close to prevent the back flow of blood.
Pathophysiology

- Damage to the valves leads to increased venous pressures.
- Without a competent valve, the blood becomes a column of water with high pressure at the bottom of the column.
- Superficial veins become varicose.
Pathophysiology

- As the calf muscle pump activates, the high pressure from the deep system is transmitted to the superficial system.
- Increased pressure in the superficial system leads to increasing dilation of the veins thinning the vessel walls.
Healthy Physiology
Pathophysiology

- Reversal of flow through the perforators
Pathophysiology

- Increasing pressure in the vessels leads to leakage of fluid and protein from the capillaries into the tissues.
- Hydrostatic pressure overcomes the osmotic tissue gradient in the dermal capillaries.
Causes of Venous Insufficiency: Valvular Damage

- Immobility / Prolonged Standing or Sitting
- Obesity
- Pregnancy
- Smoking
- Thrombophlebitis
- Deep Vein Thrombosis
  - Hip or knee replacement
  - Abdominal surgery
- Hyper coagulable states
  - Cancer

DVT and Valve Damage results in Chronic Venous Insufficiency
Venous Transudate

- Water
- Protein rich
- Red blood cells
  - Cause Hemosiderin deposition and staining
- Becomes **Exudative** with inflammation
- WBCs become activated and release proteolytic enzymes
  - MMPs, Elastases, Proteases
Clinical Assessment

➢ History important in diagnosis
  • DVT
  • Trauma
  • Joint replacement hip or knee
  • Standing long hours
  • Morbid obesity
  • Pregnancy
  • CHF
  • Immobility
272 patients with 401 lower extremity ulcers
- Mean age 60 yrs (range 14-90)
- Mean body mass index 28.9 (+/- 7.76)
- 167 patients overweight (BMI > 25 kg/m²)

Positive correlation between BMI and clinical severity of disease (p<.001)

Overweight patients were significantly more likely to have skin changes and ulceration (p<.001)

Overweight is a separate risk factor for skin change and ulceration in patients with chronic venous disease
Clinical Features
Common Signs & Symptoms

- Varicose or Spider Veins
- Swelling
- Ulcers or Open Sores
- Skin Changes Color/Texture/Rash

Talking to patients is critical – signs and symptoms are not just visual

- Heaviness
- Burning
- Aching
- Pain
- Fatigue
- Itching
- Cramping
- Restless leg
Clinical Features

Edema

- Usually insidious in onset
- Resolves with leg elevation
- Progressive over time below the knee
- Aching discomfort relieved with leg elevation as in bed rest
- Varicosities worsen as does edema
- Edema worsens and impacts oxygenation by increasing diffusion distance from capillaries and cells
Clinical Features

**Hyperpigmentation**
- Gaiter distribution
- Hemosiderin staining
  - extravasated blood with edema
- Blood cells lyse and release hemosiderin (iron containing pigment) and melanin
- Progressive hyperpigmentation with fibrosis and chronic inflammation
Clinical Features

Ulceration

- Trauma to legs that are compromised
- Fail orderly process of healing
- Medial malleolus most common
  - Lateral
  - Tibial
  - Calf
- Irregular borders with flat wound bed
- Wound bed friable congested
- Pain usually relieved with elevation
- Surrounding skin changes -- Lipodermatosclerosis
Lipodermatosclerosis
This is a condition that occurs where there is progressive replacement of skin and subQ tissue with Fibrous Tissue.

**ACUTE PHASE**
- Skin is Painful, Thickened, Red, Hot and Tender
- Most often misdiagnosed
  - Cellulitis
  - Thrombophlebitis

**CHRONIC PHASE**
- Skin is Thick, Hard, and Contracted
- Tissue is tight
- Ankle is narrower and described as “Inverted Champagne Bottle”
- Last step is the conversion scar tissue
# Differentiating Arterial vs Venous Ulcers

## Arterial Ulcer
- Location: Toes or foot
- Appearance: Irregular margin, cool cyanotic
- Foot temperature: Cold
- Pain: Usually severe
- Sensation: Variable, often decreased
- Arterial Pulses: Absent
- Veins: Collapsed

## Venous Ulcer
- Location: Malleolus or metatarsal
- Appearance: Typically sloped edges; may have exudate, irregular shape
- Foot temperature: Warm
- Pain: Mild
- Sensation: Present variable (pain, temperature)
- Arterial Pulses: Present variable (pain, temperature)
- Veins: Dilated, varicosities, edema

*70-90% of lower extremity ulcers are venous*.

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Noninvasive Assessment

- Duplex Ultrasonography
  - Venous
  - Arterial
Venous Doppler US

➢ R/O DVT or other clot
➢ US findings
  • No flow or abnormal flow
  • Vein incompressible
Venous Duplex US

- Confirm diagnosis VI
  - Reflux >500ms
  - Vein diameter >5mm
Arterial Duplex US

- Waveform Signals
  - Triphasic
  - Biphasic
  - Monophasic

- Velocities
  - Increase with stenosis
Ankle Brachial Index

➢ 0.9 – 1.1 normal perfusion
➢ 0.7 – 0.9 adequate perfusion
➢ 0.7 – 0.5 significant arterial occlusive disease
➢ > 1.2 Non Compressible

• ABI > .8  30 – 40 mmHg compression
• ABI 0.6 – 0.8  17-25 mmHg compression
• ABI ≤ 0.5 only with medical supervision

Ulcer Healing Stratification

Factors that Impact Healing

Positive Prognostic Factors
- DFU: <2 cm², <2 months, < Wag 2
- VLU: < 10 cm²
- <2 months
- Absence of PAD
- PU: Stage ≤ Stage III

Negative Prognostic Factors
- DFU: ≥2 cm², ≥2 months, ≥ Wag 2
- VLU: ≥ 10 cm²
- ≥2 months
- Absence of PAD
- PU: Stage ≥ Stage III

Assess Healing

Sufficient Decrease in 4 wks
- DFU: >50% Closure from baseline
- VLU: ≥ 30% closure from baseline
- PU: No data

Negative Prognostic Factors
- DFU: ≥2 cm², ≥2 months, ≥ Wag 2
- VLU: ≥ 10 cm²
- ≥2 months
- Absence of PAD
- PU: Stage ≥ Stage III
Ulcer Healing Stratification

Factors that Impact Healing

Positive Prognostic Factors
- VLU < 10 cm²
- < 12 months

Negative Prognostic Factors
- VLU > 10 cm²
- > 12 months

Initial Data Evaluation

Wound/Ulcer Evaluation

Assess Healing

Sufficient Decrease in 4 wks

Negative Prognostic Factors

4 Week Evaluation

VLU
- 30% Closure
- < 30% Closure
Predictive Healing Factors

Positive Prognostic Indicators

- Ulcer size < 10cm²
- Ulcer duration < 12 months
- Absence of PAD ABI >0.8

81% chance to heal at 24 weeks

Negative Prognostic Indicators

- Ulcer size ≥ 10cm²
- Ulcer duration ≥ 12 months
- Presence of PAD ABI <0.8

22% chance to heal at 24 weeks

Falanga V, Et al Rapid healing of venous ulcers and lack of clinical rejection with an allogeneic cultured human skin equivalent. Arch Dermatol 1998 134(3) 293-300
Treatment

Cochrane Review

➢ Dressing choice not shown to affect ulcer healing
➢ COMPRESSION is paramount!!!
Once healing occurs continued use of compression needed to augment the calf muscle pump

**Class of Compression**

- **Class**  
  - I  
  - II  
  - III  
  - IV  
- **Ankle Pressure**  
  - 20-30 mm Hg  
  - 30-40 mm Hg  
  - 40-50 mm Hg  
  - > 60 mm Hg
LaPlace’s Law

- Sub-bandage Pressure is DIRECTLY proportional to Bandage Tension
- It is INVERSELY proportional to the radius or curvature of the limb to which it is applied
- Must consider Two Important Factors:
  - The WIDTH of the Bandage
  - The Number of LAYERS applied
LaPlace’s Law

Sub-Bandage Pressure (mmHg) = \frac{(T \times N) \times 4630}{C \times W}

- \(T\) = Tension
- \(N\) = Number of Layers
- \(C\) = Circumference (cm)
- \(W\) = Width of Bandage (cm)
LaPlace’s Law (continued)

Sub-Bandage Pressure (mmHg) \[ \frac{(T \times N) \times 4630}{C \times W} \]

- **Numerator:** Tension and # of Layers
  - If you have an increase in these then you have an INCREASE in sub-bandage pressures

- **Denominator:** Circumference of Leg & Width Bandage
  - If you increase these then you DECREASE sub-bandage Pressures
Treatment / Compression

Sequential Compression Pumps

➢ Sequential and gradient cyclical compression
➢ Mechanical augmentation of edema control and return
➢ Improves healing of ulcer over no compression
Venous Leg Ulcers are Inflammatory Ulcers

- MMPs present in ulcers are Endopeptidases
  - Break down Extracellular Matrix
  - Inhibited by TIMPS
  - Tissue Inhibitors of Metalloproteinases
- Ulcers have a high level of MMP-8, MMP-9, MMP-12
Venous Leg Ulcers are Inflammatory Ulcers

Beidler SK et al demonstrated that compression reduces MMP expression in the VLU.
Clinical Protocols

➢ How often should patients be seen?
➢ Does Wound Center referral make a difference?
Art and Evidence of Healing Venous Stasis Ulcers

- Observed rate of healing 85.6%
  Benchmark 87%
- Evaluated the current treatment algorithm
- Weekly visits for dressing change and compression

Art and Evidence of Healing Venous Stasis Ulcers

- Examined their methodology for treating Venous Insufficiency Ulcers and their outcomes
- Single Layer vs Multi Layer Compression
- Length of Compression Therapy
- Frequency of Change

Wilcox, JR The Art and the Evidence of Healing Venous Stasis Ulcers. Monograph 2006 with permission
Clinical Practice Findings

- Compression Dressings don’t last seven (7) days
- Multi Layer compression works better
- Single Layer compression should not be used if less than 15° dorsiflexion
- Wound Dressings don’t last seven (7) days

Wilcox, JR The Art and the Evidence of Healing Venous Stasis Ulcers. Monograph 2006 with permission
Clinical Practice Findings

  - Looked at 250 Patients
  - Used multilayer wrap and Unna boot applied weekly over 6 months
  - Then compared to bi-weekly changes (twice a week) for 6 months

Wilcox, JR The Art and the Evidence of Healing Venous Stasis Ulcers. Monograph 2006 with permission
Clinical Practice Findings

➢ Weekly Compression Wraps
  • Profore Multi-Layer  87.5% healing
  • Unna Boot Single-Layer  89.0% healing
  • Switched to Bi-weekly (twice a week compression)  96.1% healing

Improved Healing Rate
8.6%
Visit Frequency  VLU Healing

➢ After adjustment for patient age, the geometric mean for time to heal

- Biweekly Visit Group was 22.15 days
- Weekly Visit Group was 77.09 days
  ✓ 95% CI: 21.78 to 26.79 and 70.63 to 84.33, respectively
  ✓ This difference was highly significant p < .000001
Visit Frequency  VLU Healing

Percent of Healed Wounds at 4 Weeks

- Weekly Visits: 71.698%
- Bi-weekly Visits: 1.960%

(N = 206)

Warriner RA, Wilcox JR  Influence of Wound Care Center Visit Frequency on Wound Healing Outcomes of Diabetic Foot and Venous Leg Ulcers WHS 2010  with permission
Clinical Considerations

- Twice weekly visits
  - Compression Wraps
  - Dressing Changes
- More frequent Debridement???
- 4 week Follow-up & Progress Review
- Monitor those tough to heal
- Advanced Modalities???
  - for those not meeting benchmark healing
Clinical Considerations

- 30 Day Review
- Healing ≥ 30%
- Predicts Healing

- 30 Day Review
- Healing < 30%
- Predicts Non Healing
Guidelines for the treatment of venous ulcers

Martin C. Robson, MD,1,2; Diane M. Cooper, PhD, RN,1,3; Rummana Aslam, MD;4 Lisa J. Gould, MD, PhD;5 Keith G. Harding, MBChB, MRCGP, FRCSEd;6 David J. Margolis, MD, MSCE, PhD7; Diane E. Ochs, RN8; Thomas E. Serena, MD;2 Robert J. Snyder, DPM5; David L. Steed, MD;9 David R. Thomas, MD10; Laurel Wiersma-Bryant, RN, BC, ANP12

1. Cochrane the panel
2. University of South Florida, Tampa, FL
3. Healthpoint Ltd., Fort Worth, TX
4. University of California, San Francisco, CA
5. University of Texas Medical Branch, Galveston, TX
6. University of Cardiff, Cardiff, Wales, UK
7. University of Pennsylvania, Philadelphia, PA
8. Private practice, Warrington, PA
9. University of Pittsburgh, Pittsburgh, PA
10. St. Louis University, St. Louis, MO, and
11. Washington University, St. Louis, MO

An advisory panel of academicians, private practice physicians, podiatrists, nurse clinicians, research nurses, industrial scientists, and an epidemiologist was chosen to develop guidelines for the treatment of venous ulcers of the lower extremity.

METHODS

Previous guidelines, meta-analysis, PubMed, MEDLINE, EMBASE. The Cochrane Database of Systematic Reviews, recent review articles of venous ulcer treatment, and the Medicare/CMS consensus of usual treatment of chronic wounds were all reviewed for evidence. Guidelines were formulated, the underlying principle(s) enumerated, and evidence references listed and coded. The code abbreviations for the evidence citations were as follows:

- STAT: Statistical analysis, meta-analysis, consensus statement by commissioned panel of experts
- RCT: Randomized clinical trial
- LIT REV: Literature review
- CLIN S: Clinical case series
- RETROS: Retrospective series review
- EXP: Experimental laboratory or animal study
- TECH: Technique or methodology description
- PATH S: Pathological series review

There were major differences between our approach to evidence citations and past approaches to evidence-based guidelines. Most past approaches relied only on publications regarding clinical human studies. Laboratory or animal studies were not cited. We used well-controlled animal studies that present proof of principle, especially when a clinical series corroborated the laboratory results. It was also clear that principles that have been validated for other chronic wound types are often applicable to venous ulcers. Therefore, evidence was sometimes cited that was not specific for venous ulcers. Because of these variations, a different system was used to grade the evidence weight supported by a given guideline. The level strength of evidence supporting a guideline is listed as Level I, Level II, or Level III. The guideline levels are:

- Level I: Meta-analysis of multiple RCTs or at least two RCTs support the intervention of the guideline. Another route would be multiple laboratory or animal experiments with at least two clinical series supporting the laboratory results.
- Level II: Less than Level I, but at least one RCT and at least two significant clinical series or expert opinion papers with literature reviews supporting the intervention. Experimental evidence that is quite convincing, but not yet supported by adequate human experience is included.
- Level III: Suggestive data of proof of principle, but lacking sufficient data such as meta-analysis, RCT, or multiple clinical series.
- NB: The suggestion in the guideline can be positive or negative at the proposed level (e.g., meta-analysis and two RCTs stating intervention is not of use in treating venous ulcers).

RESULTS

Guidelines have been formulated in eight categories for the treatment of venous ulcers of the lower extremities. The categories are:

- Diagnosis
- Compression
- Infection Control
- Wound Bed Preparation
- Dressings
- Surgery
- Adjuvant Agents (Topical, Device, Systemic)
- Long-Term Maintenance

Each of the separate guidelines underwent a Delphi consensus among the panel members to be critically evaluated. There was a consensus of at least ten panel members on each individual guideline. The majority of the able guidelines had unanimous concurrence. The draft guidelines were presented at an open conference on October 3, 2005. Following the conference and audience discussion, a period of one month was allowed for written comments and submission of additional evidence literature. The draft guidelines were then modified, taking into consideration

Clinical Guidelines

Guidelines have been formulated in eight categories for the treatment of venous ulcers of the lower extremities. The categories are:

- Diagnosis
- Compression
- Infection Control
- Wound Bed Preparation
- Dressings
- Surgery
- Adjuvant Agents (Topical, Device, Systemic)
- Long-Term Maintenance
Classification of CVI

C1: Telangiectasia or Reticular Veins
C2: Varicose Veins
C3: Edema
C4a: Pigmentation or Eczema
C4b: Lipodermatosclerosis or Atrophie Blanche
C5: Healed Venous Ulcer
C6: Active Venous Ulcer
CVI Classification CEAP
Clinical-Etiology-Anatomy-Pathophysiology

- Clinical Presentation 1-6
- Etiology: Primary, Secondary or Congenital
- Anatomic Distribution: Veins are divided into 18 anatomic segment
  - Superficial
  - Perforator
  - Deep
- Pathophysiology:
  - Obstruction
  - Reflux
  - Both
CEAP Classification

- Class 0 No Signs of Venous Disease
- Class 1 Telangiectasias or Reticular Veins
- Class 2 Varicose Veins
- Class 3 Edema
- Class 4 Skin Changes
- Class 5 Healed Ulceration
- Class 6 Active Ulceration
C.E.A.P Example
C(2), E(p), A(s), P(r)

➢ C = Class 2 = Varicose Veins

➢ E = Primary ( p)

➢ A = Superficial ( s)

➢ P = Reflux ( r)
May Thurner Syndrome

➢ Right Iliac Artery compresses the Left Iliac Vein
➢ Increases the risk of DVT in left extremity
➢ Leads to venous hypertension and reflux
MTS Stenting

64% Ulcers remained Healed at 4 years
Treatment

➢ Conservative
  - Compression

➢ Ablation
  - Thermal vs Nonthermal

➢ Surgical
  - Stripping
  - Sub Endofascial Ligation of Perforators (SEPS)
Treatment Options for Venous Insufficiency

- Thermal Tumescent
  - EVLT™ System
  - ClosureFast™ Catheter
- Non-Thermal, Non-Tumescent
  - ClariVein™ Catheter
  - Varithena™ Foam
- Non-Thermal Non-Tumescent Non-Sclerosant
  - VenaSeal™ System
- Surgical Stripping
<table>
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<tr>
<th></th>
<th>RF Ablation (n=125)</th>
<th>Endovenous Laser Ablation (n=125)</th>
<th>Vein Stripping (n=125)</th>
<th>Ultrasound-Guided Foam Sclerotherapy (n=125)</th>
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<tbody>
<tr>
<td>Efficacy at 1 year (reflux-free rate)</td>
<td>95.2%</td>
<td>94.2%</td>
<td>95.2%</td>
<td>83.7%*</td>
</tr>
<tr>
<td>Post Intervention Pain Scores* <strong>(1 – 10)</strong></td>
<td>1.21**</td>
<td>2.58</td>
<td>2.25</td>
<td>1.60**</td>
</tr>
<tr>
<td>Time to return to normal activities (days)</td>
<td>1**</td>
<td>2</td>
<td>4</td>
<td>1**</td>
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<tr>
<td>Time to resume work (days)</td>
<td>2.9**</td>
<td>3.6</td>
<td>4.3</td>
<td>2.9**</td>
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<tr>
<td>Indirect cost (€) Lost work</td>
<td>560</td>
<td>840</td>
<td>1120</td>
<td>560</td>
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<tr>
<td>Total costs (€)</td>
<td>1996</td>
<td>2200</td>
<td>2199</td>
<td>1554</td>
</tr>
</tbody>
</table>

*p < 0.001 UFGS compared to other groups  
**p < 0.001 compared to EVLA and stripping  
***In the 10-day period post-procedure.

Rasmussen et al. Randomized clinical trial comparing endovenous laser ablation, radiofrequency ablation, foam sclerotherapy and surgical stripping for great saphenous varicose veins. BJS 2011;98:1079-1087.
Laser vs Radiofrequency

Laser Ablation
- Continuous pullback
- Energy source is on throughout treatment
- Varied energy
  - 810nm and 1470nm allow for varied energy levels
  - Energy delivery varies by manual pullback speed of the physician
- Small area treated at any given time

Radiofrequency Ablation
- Segmental ablation
- No energy delivered during catheter pullback
- Consistent energy
  - Radiofrequency
  - Energy delivered does not vary by pullback speed
- Vein segment treated at one time
Cyanoacrylate Ablation
AZH Venous Cases
Venous hypertension results from valve insufficiency.
Edema, varicosities, lipodermatosclerosis.
Trauma leads to ulceration.
Difficult to heal.

Clinical Pearls
- Venous Duplex interrogation
- Consider central obstruction
- Compression essential to healing
  - Twice weekly changes improves healing
- Ablation enhances wound healing efforts

Summary