Beyond Compression Therapy: Team Approach to Venous Disease
Medical Management of Venous Insufficiency and Ulceration
Friday, September 8 11:00-11:15

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Disclosures

Medical/Scientific Boards:

• Hollister
• Acelity
• New Science
• Medline

Speaker’s Bureau:

• Hollister
Objectives

- Review an Organized Clinical Approach to the patient with a chronic venous ulceration
- Identify Key Parameters that help assess patient progress
- Conceptualize recent science with a model to understand Chronic Wound Pathophysiology
• 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
Organized Approach to Wound Care

1. Is there adequate perfusion and/or oxygenation?
2. Is non-viable tissue present?
3. Are signs/symptoms of infection and/or inflammation present?
4. Is edema present?
5. Is the wound microenvironment conducive to healing?
6. Is tissue growth optimized?
7. Is offloading or pressure relief appropriate?
8. Are host factors optimized?
Venous Doppler

- Confirm diagnosis
- R/O DVT or other clot
- Compression?
- Treat with anticoagulants
Evaluation and Treatment

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

Predicting Healing or Non-Healing

Factors that Impact Healing

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

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

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

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

VLU > 30% in first 4 weeks

Sheehan P. Early change in wound area as a predictor of healing in diabetic foot ulcers: Knowing “when to say when.” Plastic Reconstr Surg 2006; Suppl:1855-1859.


**Positive Prognostic Indicators**
- Ulcer size < 10cm²
- Ulcer duration < 12 Months
- Absence of PAD ABI >0.8

**Negative Prognostic Indicators**
- Ulcer size ≥ 10cm²
- Ulcer duration ≥ 12 months
- Presence of PAD ABI <0.8

81% chance to heal at 24 weeks

22% chance to heal at 24 weeks
Venous Leg Ulcer

- Margolis et al (2004) A wound/ulcer < 10 cm² in size and of < 12 months' duration has an 81% chance of healing by 24 weeks.
- A wound/ulcer ≥ 10 cm² in size and of ≥12 month’s duration has only a 22% chance of healing by 24 weeks.

Influence of Visit Frequency on VLU Healing

**VSU Average Days to Healing**
(i-heal® data, n=78 patients)

- **Weekly Visits**: 21 days
- **Bi-weekly Visits**: 90 days

P<0.001
Influence of Visit Frequency on VLU Healing

VSU Average Number of Visits

<table>
<thead>
<tr>
<th></th>
<th>Weekly Visits</th>
<th>Bi-weekly Visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>4</td>
<td>6</td>
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</tbody>
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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
After adjustment for patient age, the geometric mean for time to heal for the weekly visit group was 22.15 days versus 77.09 days for the biweekly group (95% CI: 21.78 to 26.79 and 70.63 to 84.33, respectively). This difference was highly significant $p < .000001$. 

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.
Why is it so hard to do the right thing in wound care?

Caroline E. Fife, MD; Marissa J. Carter, PhD, MA; David Walker, CHT

1. Department of Medicine, Division of Cardiology, The University of Texas Health Science Center, Houston, Texas,
2. Strategic Solutions Inc., Cody, Wyoming, and
3. Idelicure Inc., The Woodlands, Texas

• 17% VLU patients received adequate compression
• Lack of familiarity with Clinical practice Guidelines
• FAILURE TO PAY ATTENTION TO QUALITY MEASURES

expensive therapies over more economical ones. In the case of venous leg ulcers (VLUs), only 17% of patients received adequate compression. Provision of adequate compression among VLU patients has been similarly hindered by inadequate reimbursement policy. Lack of familiarity with clinical practice guidelines increases the cognitive effort for clinicians. Improving the economic model to favor the provision of effective basic care, creating easier-to-use products, and making clinical practice guidelines available at the point of service may make it easier to “do the right thing(s)” in wound care.
Venous Leg Ulcers are Inflammatory

- MMPs present in ulcers are endopeptidases
- Break down EC Matrix
- Inhibited by Tissue Inhibitors of Metalloproteinases (TIMPs)
- Ulcers have a high level of MMP-8, MMP-9, MMP-12
- Compression reduces the level of MMPs in the wound environment

Beidler SK et al demonstrated that compression reduces MMP expression in the VLU wound
Elevated MMP-1 in Venous Ulcers

Beidler, et al

% wound closure at 4 wks vs MMP1 level after 4 weeks of compression (pg/ug)

Good Healers
Intermediate Healers
Poor Healers
Change in MMP Level Precedes Wound Change

#1 - Wound Converted to Healing After MMP Decrease

~96% Open @ Day 36 = 1
Serial MMP levels assay may help to assess effectiveness of intervention / treatment.

MMP Degrades Collagen

pro-collagenase (inactive)
pro-MMP1
pro-MMP8
pro-MMP13

collagenase (active)
MMP1
MMP8
MMP13

gelatinase
MMP2
MMP9

stromelysin (MMP3)

collagen fibril
cleaved collagen fibril
collagen peptides

In vitro data


Collagen ExtraCellular Matrix
Broad-Spectrum MMP Reduction In Vitro Study
Periodic Reassessment

- At an interval, check your progress?
- Are you healing?
- Do you have the correct diagnosis?
- Have you fully evaluated the patient and their condition?
- Are there other complicating factors? Didn’t evaluate a marginal ABI?
- Has the patient’s condition changed? (Infection?) etc.
Elevated protease activity and non-healing wounds

- 28% of chronic wounds have elevated protease activity (EPA) as defined by their test (Threshold)
- Positive EPA Indicator Chronic Wounds have 90% probability that they won’t heal
- A wound does not need to have high levels of all proteases to be non-healing.
- Individual proteases seem to be able to compensate for one another in providing a highly proteolytic wound environment.

Multiple proteases contribute to Non Healing

- Individual protease is not causative of the excessive protease activity (EPA)
- A wound does not need to have high levels of all proteases to be non-healing.
- Individual proteases seem to be able to compensate for one another in providing a highly proteolytic wound environment.
- This highlights the need to measure multiple proteases in order to determine if proteolytic activity is causing a problem in the wound and preventing it from healing

Serena, Cullen, et al, Protease Activity Levels Associated with Healing Status of Chronic Wounds 2011
Proteolytic Wound Environment
More Than One MMP
Retrospective case review of 14 patients with total of 23 venous leg ulcers

Wounds were treated with CECM Collagen Dressing and compression

Results of the case review
  - 95.7% wounds closed at 12 weeks with use of CECM Collagen and compression
  - 97.9% average surface reduction at 12 weeks
  - No need for the 8 week conservative timeframe to use an advanced wound matrix dressings. Now, the wound can get a head start using CECM Collagen
  - Reduced the number of outliers ulcers that extend past 12 week healing time

VLU Wounds closed faster with CECM Collagen dressing

Effect of treatments on wound closure propensity

- CECM Collagen dressing
- Cellulose collagen

$p < 0.01$
Collagen Extra Cellular Matrix

- To reduce excess MMP activity, collagen dressings act as a sacrificial substrate\(^1\)

- Intact, native extracellular matrix promotes tissue granulation\(^2\) and epithelialization for final wound closure\(^3\)

- Extracellular Matrix regulates cellular function and next phenotype expression.
Venous Ulcer Combining Protease Management and Biofilm Management Strategy

- 68 yo female with a painful VLU present for 9 months
- Size 3.5 cm x 4.1 cm = 14.35 sq cm
- Large Size Negative risk factor for healing at 12 weeks
- Rate of healing by Secondary Intent 0.6 – 0.7 mm per day

www.medetec.co.uk/book%20abstracts/wound-healing-mechanisms.pdf accessed 2/28/2017
Venous Ulcer Healing by Secondary Intention With Collagen

January 21 to February 25
35 days