Prevention and Treatment of Circulatory Disorders of the Lower Extremity

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Overview

Lower Extremity Swelling
- Evaluation
- Treatment of Common Causes
Lower Extremity Ulcers
- Evaluation
- Treatment and/or Referral

Sx = Lower Extremity Swelling

- Primary Care visits (source: NAMCS)… principal reason for visit
  - 1997: 1.2 million visits
  - 2007: 2.5 million visits

Common Causes of Bilateral Lower Extremity Swelling

- Venous insufficiency
- Pulmonary hypertension
- Heart failure
- Idiopathic edema
- Lymphedema
- Drugs
- Premenstrual edema
- Pregnancy
- Obesity
### Uncommon Causes...

**Acute (< 72 hrs)**
- Bilateral DVT
- Acute worsening of systemic disease

**Chronic**
- Renal disease
- Liver disease
- Secondary lymphedema
- Pelvic tumor or lymphoma
- Dependent edema
- Diuretic-induced edema
- Preeclampsia
- Lipidemia
- Anemia

### Evaluation of LExt Swelling -- Red Flags

- Acute onset
- Age > 45 years
- Clinical suspicion of systemic cause (heart, liver, kidney)
- Hx or suspicion of pelvic malignancy or malignancy Rx (surgery, radiation)
- Symptoms of sleep apnea
- Medications

Ely JW et al. JABFM 2006;19:148-60

### Algorithm for Leg Edema

1. **Leg edema w/o apparent cause**
   - **Hx and PEx**
   - **Bilateral edema**
   - **Red Flags?**
     - **Yes** Systemic evaluation
     - **No**
       - Most common causes
         - **Yes** Treat for CVI
         - **No** Treat for idiopathic edema

Ely JW et al. JABFM 2006;19:148-60

### Systemic Evaluation — Red Flags

- Acute onset: -d-dimer +/- doppler US
- Age > 45 years: -echo
- Clinical suspicion:
  - Heart: -ECG, echo, CXR, BNP
  - Liver: -LFTs, albumin
  - Kidney: -urinalysis + micro; lipids
  - Suspicion malignancy: -abd/pelvic CT
  - Suspicion sleep apnea: -sleep study; echo
  - Lymphedema: -abd/pelvic CT
**Idiopathic edema**
- Menstruating women, but not confined to premenstrual period
- Fluid retention in upright position
  - Often > 2 lbs; also involves face/hands
- Treatment
  - Spironolactone, 50-100 mg daily, early AM
  - Intermittent recumbency, avoid heat, minimize salt, avoid excessive fluid intake
  - Compression stockings do NOT help

**Pathophysiology of CVI -epidemiology**
- Prevalence ≈ 2% general population
  - (Circulation 1973;58:839)
- Risk Factors
  - advanced age
  - female
  - prior deep venous thrombosis
  - post-phlebitic syndrome
  - (J Gen Intern Med 2000;15:425)
  - prior leg trauma or surgery

**Pathophysiology of CVI -anatomy**

**Determinants of Venous Return**
- muscle contraction
- one-way valves
- respiratory function

**Venous Pressure**
- Normal: 20-30 torr
- CVI: 60-90 torr

**Evaluation of Lower Leg Swelling -Diagnostic Testing for CVI**

**Chemistry**
- renal panel, urinalysis

**Imaging**
- Color duplex u/s-- preferred
  - 84% sensitive; 88% specific (c/w direct pressure measurements) (J Vasc Surg 1986; 4:237)
- Doppler US--for measuring ABPI
  - >0.9 = normal—less reliable in diabetics, elderly
  - 20% of venous ulcer pts with PAD (BMJ 1987; 294:929)
CVI Treatment --reduce swelling

- Leg Elevation
- Compression Therapy
- Drug Therapy
  - diuretics-- AVOID unless confirmed volume overload is exacerbating edema
  - horse-chestnut seed extract (Venostat®)
  - hydroxyethylrutosides (Venorutin®)

CVI Treatment: reduce swelling

- Horse-chestnut seed extract
  - Active ingredient: escin
  - Mechanism: inhibit leukocyte activation
  - Effectiveness: 8 placebo-controlled RCTs; 5 comparative RCTs (1083 pts) (Arch Dermatol 1998;134:1356)
    - decrease leg volume/size and symptoms
    - probably equivalent to compression and rutosides
  - Adverse effects: GI, dizziness, nausea, headache, pruritis (0.9 - 3.0%)
  - Dose: 50 - 75 mg bid (escin content) for 4-8 wk

Graduated compression stockings

- How much pressure?... (based on ankle pressure)
  - Class I: 20-30 mm Hg; Class II: 30-40 mm Hg
  - Class III: 40-50 mm Hg; Class IV: > 60 mm Hg

- Considerations in selecting type
  - consider patient age/dexterity...
  - custom stocking for severe or complicated
  - may need liner or extra padding to hold wound dressing

- Caveats
  - patient instructions important
  - remove at night to prevent ischemia
  - replace every 6 months

Prevention of CVI

- Treatment of post-phlebitic syndrome √
  - affects 20-30% of DVT patients, usually within first 2 years
  - daily use of elastic compression stockings reduce syndrome by 50% (Lancet 1997;349:759)

- Treatment of varicose veins √
  - only when deep veins intact

- Treatment of persons who stand all day ?
### Case History (1)
- 75 yo woman c/o 2 mo ulceration. Despite some discomfort, feels otherwise well.
- PMHx: CHF; varicose veins; denies tobacco
- PEx:
  - neurologic exam nl; no cellulitis
  - 2+ edema; pedal pulses?

### Differential Diagnosis
- chronic venous insufficiency (80%)
- peripheral arterial disease
- neuropathic (diabetic)
- pressure ulcer
- pyoderma gangrenosum
- vasculitis
- infection (fungal; mycobacterial)
- cancer (squamous; basal)

### Pathophysiology of CVI
- progressive changes (micro)
  - Venous Hypertension
  - Abnormal Capillaries ➔ Abnormal Lymphatics
  - Fibrin deposition ➔ RBC aggregation ➔ WBC activation ➔ Edema
    - Local hypoxia ➔ Inflammation
  - Venous Ulcer Formation

- progressive changes (macro)
  - varicose veins ➔ dependent edema ➔ dermatitis ➔ lipodermatosclerosis ➔ fibrosis ➔ ulceration
**Evaluation of Leg Ulcers**

The patient reports occasional leg pain and swelling, especially at the end of the day. She notes that her mother had varicose veins.

**Q:** What clinical characteristics suggest that leg ulcers are due to venous disease?

**Lower Leg Ulcers**

-Clinical Characteristics

- Inquire about...
  - **size**
    - large favors venous
  - **borders**
    - irregular favors venous
  - **depth**
    - shallow favors venous
  - **location**
    - if foot or above mid-calf… probably not venous
  - **pain**
    - intense pain favors PAD or infection

**Lower Extremity Ulcers**
Evaluation of Leg Swelling & Ulcer

- Physical examination
  - **Skin**
    - varicose veins; hyperpigmentation; dermatitis
    - atrophie blanche; lipodermatosclerosis
  - **Assess Peripheral Arterial Disease**
    - pulses; capillary refill time; hair loss; toe nail abnormalities
  - ? **Osteomyelitis**
    - visible or palpable bone
    - bone scan +/- bone biopsy
  - ? **Infection or Malignancy**
    - especially for ulcers > 3 mo… biopsy & culture

Peripheral Arterial Disease

- PAD is major marker for heart disease
- 1/20 Americans over 50 has PAD
- Affects 8-12 million people in the US
- 5 x increase of cardiovascular ischemic event
- 2-3 x increase in total mortality compared to those without PAD

PAD Risk Factors

<table>
<thead>
<tr>
<th>Category</th>
<th>Diagnosis</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>ABI &lt; 0.9</td>
<td>4-6 million</td>
</tr>
<tr>
<td>Claudication</td>
<td>Muscle pain, ache, cramps, fatigue</td>
<td>2-4 million</td>
</tr>
<tr>
<td>Critical Limb</td>
<td>Pain at rest, ulceration, gangrene</td>
<td>400,000-1 million</td>
</tr>
<tr>
<td>Ischemia</td>
<td></td>
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The Scope of the Problem

Ankle-Brachial Index (ABI)

Normal ≥ 1.0  
Mild 0.75 to 0.99  
Moderate 0.5 to 0.74  
Severe < 0.5

Case History (3)

An ABI=1.0.  
You diagnose a chronic venous ulcer based on clinical grounds.

Q: How will you treat the patient?

Venous Ulcer Treatment - overview

- Up to 50% will have chronic ulcer > 1 yr
- High cost and resource intensive care

- Goals
  - reduce venous hypertension
  - improve oxygen delivery
  - maintain healthy granulation tissue

Venous Ulcer Treatment - compression

- Mechanical compression therapy:  
  Priority
  - ulcer healing rates; superior to wound care alone
  - factors: ambulatory status, ankle size, leg contour
    - acute phase: non-elastic compression
    - maintenance phase: elastic compression
Venous Ulcer Treatment
- reduce swelling; Unna’s Boot

- Non-elastic compression using zinc-impregnated bandages
- High pressure with ambulation, low pressure at rest (safer for CVI + PAD)
- ~ weekly application
- primary indication for venous ulcer treatment

Venous Ulcer Treatment
- wound dressing & debridement

- Avoid topical antibiotics and antiseptics
- Good data do not exist for debridement
- Types: autolytic, chemical, mechanical, surgical, biologic
  - probably no marginal gain over simple non-adherent dressing
  - key is to maintain a moist wound env’t

Venous Ulcer Treatment
- systemic therapies

- Growth factors (epidermal growth factor; platelet-derived growth factor)
  - promising; still under investigation
- Pentoxifylline
  - 800 mg tid… improves ulcer healing rates
- Stanozolol
  - androgenic steroid with fibrinolytic properties
  - improves lipodermatosclerosis; no effect on ulcers

Case History (5)
You prescribe multi-layer compression therapy, and leg elevation for 30” tid. She returns 1 month later with ulcer unchanged. Patient is getting frustrated.

Q: Is there anything else to try? Is a referral indicated?
Which ulcers will be refractory?

- Wound size > 5 cm² = 1 point
- Wound duration > 6 mo = 1 point

6-month heal rate

- score=0 93-95%
- score=2 17-37%

area-under-ROC=0.87 (Am J Med 2000:109:15)

Surgical Treatment of CVI
- Ablation of Saphenous Veins

*meta-analysis 64 studies involving 12,320 legs

3-yr success rate

- Stripping 78%
- Radiofrequency Ablation 84%
- Endovenous Laser Ablation 94% (p=0.01)
- Foam Sclerotherapy 77%


Radiofrequency ablation

- Catheter inserted in refluxing vein
- Catheter Positioned, Electrodes deployed
- RF Energy heats and contracts vein wall
- Catheter slowly withdrawn, closing vein
- Denuded vein is physically narrowed

Edinburgh Vein Study (J Clin Epi 2003;56:171-9)

- affects 25% to 50% of adults
- risk factors
  - increased height
  - women: increased BMI; <50% time sitting on job; HRT use; Family History
  - men: decreased BMI; lower educational level; Family History
- Risk Factors from other studies
  - age, multiple pregnancies, caucasian race

Varicose Veins: Epidemiology

Varicose Veins: Epidemiology

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Varicose Veins - Disease of Women?

Lee et al, J Clin Epi 2003;56:171

Varicose Vein Treatment Options

Goals: 1) control reflux; 2) cosmesis

- Ligation + Stripping
- Ligation + Sclerotherapy
- Endovenous Ablation
  - radiofrequency
  - laser
- Powered Phlebectomy

References