Evaluation of the Swollen Leg

- M. Joshua Berkowitz, MD, FACC, FSCAI, FSVM, Diplomate American Board of Venous and Lymphatic Medicine
- Director TCC Vein Center

“The Legs that walk in the Door”
Disclosures

- Chairman of BDMC Dept Cardiology
- Director of BDMC Cath Lab, Cardiac Diagnostics.
Evaluation of the Swollen Leg

- Common reason for referral
- Presumptive Dx is CHF
- Most common etiology is not CHF

An opportunity to make a brilliant diagnosis
Objectives

- Review basic physiology of edema
- Review Ddx of various etiologies of both unilateral and bilateral leg swelling
- Describe the best first line Conservative management modalities and second line Invasive treatment modalities.
Edema

- **Palpable** swelling produced by expansion of the interstitial fluid volume.
  - Capillary hydraulic pressure—filtration
    - CHF, venous obstruction, Venous Insufficiency
  - Decreased plasma oncotic pressure
    - Low albumin, protein loss, burns
  - Capillary permeability or interstitial oncotic pressure
    - Lymphedema, vascular injury, allergic reaction, burns
  - Lymphatic dysfunction — lymphatic uptake/flow

Increased capillary hydraulic Pressure

- **Most common cause of edema**
  - CHF
  - Venous HTN / obstruction
    - Local vs. systemic (DVT vs. pulmonary edema, cirrhosis)
  - Increased plasma volume
    - Renal disease
    - Pregnancy / premenstrual edema
    - Medications
Decreased Plasma Oncotic pressure

- Protein Loss
  - Nephrotic syndrome, Protein losing enteropathy

- Reduced protein synthesis
  - Liver disease
  - Malnutrition
Increased capillary permeability

- Burns /trauma
- Allergic reactions
- Inflammation
- Infection
- Medications
Lymphatic dysfunction

- Lymphedema
  - Primary vs. Secondary

- Lymph node enlargement / dissection

- Malignancy
Evaluation of the Swollen Leg

“Which leg is it?”

FIFTH ANNUAL SYMPOSIUM
Evaluation of the Swollen Leg

- Medical and Surgical history/systemic disease
  - Heart, kidneys, liver, lymph nodes
- Distribution
  - unilateral, bilateral
- Timing
  - Acute, intermittent, persistent, chronic
  - Improvement overnight?
- Type
  - Pitting, non-pitting, painful?
- Skin – texture, color
  - Ulcers, trophic, staining, telangectasias, varicosities
Evaluation of the Swollen Leg

Investigational Testing
- BMP, BNP, TSH
- UA
- ECG
- CXR
- Echocardiogram
- Duplex US
- Venous Mapping duplex
- MRV/CT/lymphoscintigraphy
Bilateral Leg Swelling

CVI
Medications
Idiopathic edema
Heart Failure/CM
Pulmonary HTN
Pregnancy
Protein losing enteropathy
Na overload – drug induced

Lymphedema
CKD
Cirrhosis
Lipedema
Obesity / OSA
Pretibial Myxedema

Medications associated with Edema “Big Four”

- Mechanism of renal Na retention / arteriolar vasodilation
  - Ca channel blockers – Diltiazem, amlodipine
  - Thiazolidinediones (glitazones) – Rosiglitazone, Pioglitazone
  - NSAIDS/ glucocorticoids
  - Gabapentin/pregabalin
Unilateral Leg Swelling

- Acute DVT / Post thrombotic syndrome
- Cellulitis
- Chronic Venous Insufficiency
- Lymphedema
Unilateral Leg Swelling – Other Causes

- Popliteal aneurysm
- Dependency
- Hemihypertrophy
- Hemangioma
- Arterial–venous malformation
- Hematoma
- Tumor
- Baker’s cyst
- Reperfusion edema
- Abcess/osteomyelitis
- Charcot arthropathy
- Trauma/compartment syndrome
- Gastrocnemius rupture

Case #1

- 79 yo woman former teacher
- hx of CVA, afib, htn
- chronic b/l leg fatigue, edema L>R
- Legs of equal temperature
- Normal pedal pulses
Chronic Venous Insufficiency

- Most common cause of chronic leg swelling and ulcers in population – 20% of working population.
- Unilateral or bilateral
Approximately 25 million Americans suffer from venous reflux disease.

72% of women and 42% of men will experience varicose veins by time they are in their 60’s.

Risk factors:
- Family history, pregnancy, obesity, standing profession, smoking, prior DVT, leg trauma.
2x more common than CAD
4–5x more common than Peripheral arterial disease
As “Baby boom” generation ages, incidence is expected to dramatically rise.
Abnormal Venous Function

- Disruption of one way valve system
  - Post thrombosis with valve injury, fibrosis.
  - Familial, genetically transmitted smooth muscle, collagen degradation in valve tissue leading to vein wall dilation.
- Dilation to accommodate increased volume (capacitance)
  - Pregnancy
  - Proximal venous obstruction
  - CHF
- Prolonged inactivity of calf muscle pump
- Hormonally mediated (estrogen/progesterone)
  - Smooth muscle relaxation, vein valve separation, abd pressure

Chronic Venous Hypertension (Insufficiency / Reflux)

Ambulatory venous hypertension

Coleridge Smith, Vasc Med 1997
Pressure → Skin changes

Payne et al, EJVES 1996
Venous Insufficiency is an Inflammatory Disease

High venous pressure, Increased osmotic pressure, capillary leak, Vascular extravasation

Poor skin nutrition/oxygenation, Inflammatory enzymes released

Edema, Dermal fibrosis, subc fat necrosis, LDS

Tissue hypoxia, capillary thrombosis, Ulceration
Venous Claudication

- Heaviness
- Fatigue
- Burning
- Swelling
- Tenderness along vein
- Restless legs
- *Edema*

- Ache
- Throbbing
- Leg cramps
- Itching, pruritis
- Night cramps
- Paresthesias

Increased during the day with prolonged standing

FIFTH ANNUAL SYMPOSIUM
Tissue Damage of Venous Insufficiency

- Edema
- Hyperpigmentation–hemosiderin
- Stasis dermatitis
- Lipodermatosclerosis
  - Fibrosing panniculitis, advanced hyperpigmentation, induration.
- Ulceration
- Cellulitis
- Cutaneous infarction
- Varicose deformities
GSV Reflux
Medical Management of CVI

- **Weight loss** – obesity increases venous htn
- **Exercise** – reduces pain sx’s and ulcer recurrence
- **Leg elevation** – reduces ambulatory venous pressures, reduces edema.
- **Compression**
- **Avoidance of high heels**

All have been shown to improve O$_2$ delivery to skin and reduce inflammation.
Graduated compression counteracts venous htn
- Accelerates venous return, improves deep venous flow
- Reduces lumen diameter of superficial and deep veins – less reflux
- More effective calf muscle pump
- Treats sx’s but not curative
- Anti-embolism stockings “TEDS” indicated for prevention of thromboembolism in non ambulatory patients. Range 8–18mmHg.
Compression

- Available 3 strengths
  - 20 - 30 mm – mild aching, edema, varicose veins
  - 30-40mm – Pain, edema, varicose veins, post ulcer
  - 40/50, 50/60 – Recurrent ulceration, lymphedema
- Need at least 3–6 months
- Need to be replaced q 6 months
- Effective, *but*...
  - Stockings are hot/uncomfortable
  - Many do not have strength, mobility
  - Availability, price if not covered
  - Compliance is POOR
- Graduated Compression
  Indicated for prevention and management of venous disorders in ambulating patients and wheel-chair bound patients

FIFTH ANNUAL SYMPOSIUM
Treatment Strategy for CVI

- Compression
- Wound Care
- Ablation of Axial superficial venous reflux.
  - Eliminate Superficial reflux – severe > 1 sec
  - Eliminate selected perforator reflux
    - Open or healed ulcer, may improve saphenous closure
- Long term weight loss, exercise plan
- Consider HCSE, Pentoxifylline as indicated.
Horse Chestnut Seed Extract & CVI

- Active component of HCSE is Escin which prevents leucocte activation, alters ionic movement resulting in increased venous tone and decreased filtration.
- Review of 13 studies, 1083 pts (8 placebo controlled) treating pts 100mg Escin 12 wks.
- Significant reduction in lower leg volume, leg pain, leg itching, and fatigue compared with placebo.
- Typical dose 300mg bid.
Case #2

- 62 yo M htn, dm
- Flew from London 3 days ago
- Edema, pain, warmth.
- Equal pulses
Acute Deep Venous Thrombosis

Risk Factors
- Age
- Immobilization
- Pregnancy/postpartum
- Major Surgery
- Cancer
- Previous hx DVT/HCS
- Stroke
- Major trauma
Deep Vein thrombosis

- Occurs in 250,000 annually in US
- Major cause of morbidity and mortality
- Acute pain, edema, warmth
- Complications associated with DVT
  - PE
  - Recurrent thrombosis
  - Post–thrombotic Syndrome
  - Phlegmacia Cerulea Dolens

Circulation 2004; 110 I-27-34.
Lancet 1997; 349: 759.
Phelgmacia Cerulea Dolens

- Total/near total thrombotic occlusion deep and superficial systems compromising arterial inflow with resultant tissue ischemia.
- Early thrombus removal is the key
Goals of DVT Therapy

- Improve symptoms
- Prevent PE
- Minimize risk of recurrent DVT
- Prevent Post-thrombotic syndrome (PTS)
  - Venous reflux due to valvular incompetence and venous htn due to chronic thrombotic obstruction.
  - Develops in 20–50% of pts with DVT
  - Occurs more frequently with extensive proximal/multilevel DVT
  - Worse without compression stockings

# Treatment for DVT

<table>
<thead>
<tr>
<th>Modality</th>
<th>Appropriate Patients</th>
<th>Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulants</td>
<td>All</td>
<td>Begin Immediately</td>
</tr>
<tr>
<td>Pharmocologic thrombolysis</td>
<td>Acute Iliofemoral DVT</td>
<td>Early is best, but can be effective up to months after acute event</td>
</tr>
<tr>
<td>Percutaneous mechanical thrombectomy</td>
<td>Acute Iliofemoral DVT</td>
<td>Early is best</td>
</tr>
<tr>
<td>Venous angioplasty and stenting</td>
<td>Chronic Iliac vein stenosis (MTS)</td>
<td>Early treatment after restoration of venous patency</td>
</tr>
<tr>
<td>Open surgical thrombectomy</td>
<td>Acute Iliofemoral DVT in pts with contraindication to thrombolysis or failed lysis</td>
<td>Early</td>
</tr>
</tbody>
</table>
2.9. In patients with acute proximal DVT of the leg, we suggest anticoagulant therapy alone over catheter–directed thrombolysis (CDT) (Grade 2c)

Remarks: Patients who are most likely to benefit from CDT (see text), who attach a high value to prevention of postthrombotic syndrome (PTS), and a lower value to the initial complexity, cost, and risk of bleeding with CDT, are likely to choose CDT over anticoagulation alone.
### Novel Anti-Coagulants

<table>
<thead>
<tr>
<th></th>
<th>Rivaroxaban*</th>
<th>Apixaban</th>
<th>Dabigatran</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target</strong></td>
<td>Xa</td>
<td>Xa</td>
<td>IIa</td>
<td>Xa</td>
</tr>
<tr>
<td><strong>Time to peak (hours)</strong></td>
<td>2-3</td>
<td>2-3</td>
<td>1.5-3</td>
<td>1-3</td>
</tr>
<tr>
<td><strong>Half-life (hours)</strong></td>
<td>4-9 up to 12 hrs &gt; 75 yr</td>
<td>10-14</td>
<td>14-17</td>
<td>8-10</td>
</tr>
<tr>
<td><strong>Renal excretion (%)</strong></td>
<td>66% 33% biliary</td>
<td>25% 75% biliary</td>
<td>80%</td>
<td>35%</td>
</tr>
<tr>
<td><strong>Antidote</strong></td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td><strong>Dosing For DVT</strong></td>
<td>Prophylaxis - 10 mg daily</td>
<td>Prophylaxis – 2.5 mg BID</td>
<td>Prophylaxis – 150 mg or 220 mg/d Treatment - 150 mg BID</td>
<td>Treatment – 60 mg daily</td>
</tr>
<tr>
<td></td>
<td>Treatment - 15 mg BID x 21 days then 20 mg daily</td>
<td>Extended treatment 2.5 or 5 mg BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Approval in US</strong></td>
<td>Prophylaxis THR, TKR Treatment of VTE</td>
<td>Prophylaxis THR, TKR, Treatment of VTE</td>
<td>No FDA indication for VTE</td>
<td>No FDA indication</td>
</tr>
</tbody>
</table>
"IT IS A PROMISING NEW DRUG WITH FEW SIDE EFFECTS... AND I'M SORRY YOU FIND THEIR T.V. ADS OFFENSIVE."
Case #4 – Swollen Leg

- 49 yo F
- Smoker, hypothyroid
- ED with 5 days left leg, thigh pain, swelling.
May Thurner Syndrome

Venous Scarring / Thrombosis
May Thurner Syndrome

- **Clinical presentation**
  - DVT/PE, Left Leg swelling, LLE Varicosities
  - More common in young female
    - 18–49% of patients 20–45 yrs with LLE DVT have MTS
- **CT Venogram, MRV, Venogram with IVUS**
- **Management**
  - Anticoagulation and compression.
  - Thrombolysis
  - Endovascular stenting to relieve obstruction
May Thurner – Iliac Compression
Case #4

- 60 yo M hx CAD/ anterior wall MI with LAD stent 6 yrs ago.
- 4 wks progressive doe, 3 pillow orthopnea
- + JVD on exam.
Capillary Pressure

- JVD, sob, PND/orthopnea
  - RV/LV failure
  - COPD, pulm HTN
  - Tamponade, constriction, restriction

- Normal JVD
  - Obesity, venous obstruction / insufficiency
  - Drug induced

FIFTH ANNUAL SYMPOSIUM
Case #5 – Swollen Leg

- 52 yo morbidly obese man with remote hx MVA, left leg trauma.

- 60 yo obese female history of b/l swelling since early adulthood, multiple hospitalizations for edema, cellulitis.
Lymphatic system collects and drains interstitial fluid that escapes capillary circulation.

Excessive fluid/protein accumulates in interstitial spaces when:
- Lymphatic absence/obstruction/functional impairment
- Chronic Inflammation
- Cellular proliferation
  - Fibrosis, hyperkeratosis, papillomatosis, hyperpigmentation

Unilateral or Bilateral

Usually non-tender, non-pitting

Lymphedema

- **Primary** – 10% of cases
  - Multiple Genetic causes
  - Congenital – <2 yrs
  - Praecox – 2–35 yrs
  - Tarda – > 35 yrs

- **Secondary** – 90%
  - obesity
  - Infectious
  - Malignancy
    - Radiation
    - Lymphatic, ovarian, prost
  - Iatrogenic
    - Node biopsy, resection
    - Vein harvest
  - Traumatic
  - CVI – *phlebolymphedema*
    - 20–30% pts have associated lymphatic dysfunction

---

FIFTH ANNUAL SYMPOSIUM
Lymphedema – Mgmt

- w/o treatment
  - Worsening edema, ulcers
  - Recurrent infections, potentially life threatening
  - Severe Disability
- Compression Tx – 30–40mm Hg
- Leg elevation
- Skin Hygiene
- PT, manual lymphatic massage, drainage
- Pneumatic compression

Swollen Leg – Lipedema

- Bilateral subcutaneous fat deposition
- Extends from buttocks to ankles
- Feet are spared “ankle cut off sign”
- Almost exclusively female
- Insidious onset starting in puberty
- Painful
- Often mistaken for lymphedema
  - Compression Tx makes it more painful.
  - Minimal Improvement with elevation
- Tx – weight loss, diet modification, avoidance of certain foods, can consider liposuction.
Not all Edema is same
Myxedema

- Waxy type of edema – mucin deposits in skin
- Non-pitting
- Decreased Thyroid activity
- Tx is to restore Thyroid function
31 year old obese diabetic man with left foot, ankle, and lower leg pain and swelling for approximately 1 year
• Treated for lymphedema with mechanical pumping and compression stockings

Charcot arthropathy
When is Compression NOT Indicated

- Severe PAD, CLI – always check ABI’s
- Lipedema
- Acute Charcot foot

Do NOT Compress!
What is this?

- 76 yo F referred for edema, ? CHF
- Non healing traumatic wounds

“Dishwasher Syndrome”
Conclusions

- Elicit thorough history, PE,
  - Remember to review medications
  - Calcium channel blockers, Thiazolidinediones, Gabapentin/pregabalin, NSAIDS

- Bilateral leg swelling
  - In the absence of causative medications or systemic Disease
  - CVI (older patients)–most common cause of edema. Look for associated skin findings.
  - Differentiate between CVI, lymphedema, and lipedema.
Conclusions

- Unilateral leg swelling
  - Acute DVT
  - CVI – unrecognized and disabling disease
  - Lymphedema
- Compression therapy should be first line Tx
  - May not be indicated
- Venous duplex/Mapping, CTV, MRV can be extremely useful diagnostic modalities
- Treatment (ablation) can have major impact on QOL
Thank You