Limb Salvage

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Dimensions in Cardiac Care November 4, 2014
Department of Vascular Surgery
Cleveland Clinic Foundation
WHAT DISEASE ARE WE TALKING ABOUT?

- PVD (PAD) Spectrum of diseases

Claudication - Rest Pain - Tissue Loss (Ulceration) - Gangrene

CRITICAL LIMB ISCHEMIA (CLI)
DISCLOSURES

• This is a vascular surgery talk.....there will be pictures
HOW BIG IS THIS PROBLEM?
SCOPE OF THE PROBLEM

• $14 Billion global industry
• US $2 Billion market
  • 10% AG between 2010 and 2017
• 20% of Americans >65 by 2020
• We will see:
  • More chronic disease states
  • More venous ulceration
  • More CLI, MI, Stroke
AMPUTATION IN US

• CDC 2008: 24 million Americans have diabetes
  • 7% of the population

• More will get diabetes
  • 1:3 people born in the U.S. in 2000 will develop diabetes in their lifetime = 625,000 new cases of diabetes/year!

• 15-25% diabetics will develop foot ulcers
  • 85% of amps preceded by diabetic ulcer

• 15-20% limbs with ulcer → amputation

OBESITY AND DIABETES
“THE PERFECT STORM”

Age-adjusted Percentage of U.S. Adults Who Were Obese or Who Had Diagnosed Diabetes

Obesity (BMI ≥ 30 kg/m²)

1994

2000

2009

Diabetes

1994

2000

2009

PREMISE: Diabetes and wound complications will continue to increase
National change in the total number of lower extremity revascularization procedures = not rising as fast.

Anderson et al. Cleveland Clinic
NATURAL HISTORY OF PAD

PAD initial presentation

Asymptomatic PAD 20-50%

Progressive Functional Impairment

Claudication 10-35%

Atypical Leg Pain 40-50%

Critical Limb Ischemia (1-2%)

1 Year Outcomes

Alive with 2 Limbs 50%

Amputation 25%

CV mortality 25%

Hirsch et al. Circulation
• Diagnosis of diabetes once every 17 seconds?

• Every 20 seconds somewhere in the world a lower extremity is amputated in a diabetic

• EVERY 20 SECONDS!!
"Houston, we have a problem." Jim Lovell
ECONOMICS OF LIMB SALVAGE

• Limb salvage with vein is 44% cheaper than amputation (AK & BK)
• Limb salvage with prosthetic is 26% cheaper than amputation
• Primary above knee amputation is up to 3 times more expensive than limb salvage
DOC, IT JUST STARTED WITH A LITTLE BLISTER...
RISK FACTORS FOR ULCERATION

- Bad….
- Nerves – sensory neuropathy - 60%
- Mobility: foot deformity, pressure
- Shoes
- History: previous amputation, ulcer
- Diabetes: uncontrolled, long duration
- Kidneys
- Eyes: delayed dx/prevention
Trauma

Neuropathy

Ulcere

Infection

Ischemia

The Diabetic Foot Triad
PAD PHYSICAL EXAM FINDINGS

- Diminished pulses
- Thickening of nail beds
- Hair loss
- Atrophy of sweat & apocrine glands
  - Dry scaly feet
- Dependent rubor
- Ulceration –tips of toes
- Gangrene
LEG ULCERS - DDX

- **Neurotrophic (Diabetic)**
  - Occurs on weight bearing surfaces
  - Callous around edges
  - Punched out base
- **Venous ulcer**
  - Hemosiderin deposition
  - Irregular edges
  - Lipodermatosclerosis
  - “Gaitor distribution”
- **Mixed Ulcers**
TESTING

- PVR:
  - Segmental limb pressures & waveforms
    - Toe pressures for DM
      - (Calcium can prevent compression of leg vessels)
  - ABI
    - Ankle Brachial Index:
      - Ratio
      - <0.4=CLI
PROGNOSTIC?

Mills et al, J Vasc Surg 2013
GETTING A ROADMAP

- Duplex
- CTA
  - Increasing preference
  - Limit - renal function
- MRA
CLASSIFYING WOUNDS?

- Identify high risk?
- Help to compare?
  - Between providers
  - Research
- Guide treatment?
- Predict outcome?
## Rutherford Fontaine Classification

<table>
<thead>
<tr>
<th>Fontaine</th>
<th>Rutherford</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage</strong></td>
<td><strong>Clinical</strong></td>
</tr>
<tr>
<td>I</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>IIa</td>
<td>Mild claudication</td>
</tr>
<tr>
<td>IIb</td>
<td>Moderate to severe claudication</td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Ischemic rest pain</td>
</tr>
<tr>
<td>IV</td>
<td>Ulceration or gangrene</td>
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</tbody>
</table>
OLD CLASSIFICATION SYSTEMS ARE NOT SUFFICIENTLY PROGNOSTIC

- Don’t take into account extent and depth of Wound
- Don’t quantify the level of perfusion or flow Ischemia
- Don’t describe presence or extent of Infection

• New Classification System

• WIFI (Wound Ischemia Foot Infection)
The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: Risk stratification based on Wound, Ischemia, and foot Infection (WIFI)

Joseph L. Mills, Sr, MD, a Michael S. Conte, MD, b David G. Armstrong, DPM, MD, PhD, a Frank B. Pomposelli, MD, c Andres Schanzer, MD, d Anton N. Sidawy, MD, MPH, e and George Andros, MD, f on behalf of the Society for Vascular Surgery Lower Extremity Guidelines Committee, Tucson, Ariz; San Francisco and Van Nuys, Calif; Brighton and Worcester, Mass; and Washington, D.C.
<table>
<thead>
<tr>
<th>Grade</th>
<th>Ulcer</th>
<th>Gangrene</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No ulcer</td>
<td>No gangrene</td>
</tr>
<tr>
<td>Clinical description: ischemic rest pain (requires typical symptoms + ischemia grade 3); no wound.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Small, shallow ulcer(s) on distal leg or foot; no exposed bone, unless limited to distal phalanx.</td>
<td>No gangrene</td>
</tr>
<tr>
<td>Clinical description: minor tissue loss. Salvageable with simple digital amputation (1 or 2 digits) or skin coverage.</td>
<td></td>
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</tr>
<tr>
<td>2</td>
<td>Deeper ulcer with exposed bone, joint or tendon, generally not involving the heel, shallow heel ulcer, without calcaneal involvement.</td>
<td>Gangrenous changes limited to digits</td>
</tr>
<tr>
<td>Clinical description: major tissue loss salvageable with multiple (≥3) digital amputations or standard TMA ± skin coverage.</td>
<td></td>
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</tr>
<tr>
<td>3</td>
<td>Extensive, deep ulcer involving forefoot and/or midfoot; deep, full thickness heel ulcer ± calcaneal involvement.</td>
<td>Extensive gangrene involving forefoot and/or midfoot; full thickness heel necrosis ± calcaneal involvement.</td>
</tr>
</tbody>
</table>

SVS grades 0 (none), 1 (mild), 2 (moderate), and 3 (severe).

<table>
<thead>
<tr>
<th>Grade</th>
<th>ABI</th>
<th>Ankle systolic pressure</th>
<th>TP, TiPO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>≤0.80</td>
<td>&gt;100 mm Hg</td>
<td>≥60 mm Hg</td>
</tr>
<tr>
<td>1</td>
<td>0.6-0.79</td>
<td>70-100 mm Hg</td>
<td>40-59 mm Hg</td>
</tr>
<tr>
<td>2</td>
<td>0.4-0.59</td>
<td>50-70 mm Hg</td>
<td>30-39 mm Hg</td>
</tr>
<tr>
<td>3</td>
<td>≤0.39</td>
<td>&lt;50 mm Hg</td>
<td>&lt;30 mm Hg</td>
</tr>
<tr>
<td>Clinical manifestation of infection</td>
<td>SVS</td>
<td>IDSA/PEDIS infection severity</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------------------------------------------------------</td>
<td>-----</td>
<td>------------------------------</td>
<td></td>
</tr>
<tr>
<td>No symptoms or signs of infection</td>
<td>0</td>
<td>Uninfected</td>
<td></td>
</tr>
<tr>
<td>Infection present, as defined by the presence of at least 2 of the following items:</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>• Local swelling or induration</td>
<td></td>
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<tr>
<td>• Erythema &gt;0.5 to ≤2 cm around the ulcer</td>
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<tr>
<td>• Local tenderness or pain</td>
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<td></td>
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<tr>
<td>• Local warmth</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>• Purulent discharge (thick, opaque to white, or sanguineous secretion)</td>
<td>1</td>
<td>Mild</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical manifestation of infection</th>
<th>SVS</th>
<th>IDSA/PEDIS infection severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local infection (as described above) with erythema &gt;2 cm, or involving</td>
<td>2</td>
<td>Moderate</td>
</tr>
<tr>
<td>structures deeper than skin and subcutaneous tissues (eg, abscess,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>osteomyelitis, septic arthritis, fasciitis), and</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No systemic inflammatory response signs (as described below)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local infection (as described above) with the signs of SIRS, as manifested by two or more of the following:</td>
<td>3</td>
<td>Severe*</td>
</tr>
<tr>
<td>• Temperature &gt;38° or &lt;36°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Heart rate &gt;90 beats/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Respiratory rate &gt;20 breaths/min or PaCO₂ &lt; 32 mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• White blood cell count &gt;12,000 or &lt;4000 cu/mm or 10% immature</td>
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<td></td>
</tr>
</tbody>
</table>
DIABETIC LIMB SALVAGE COLLABORATION
“TOE AND FLOW”

- Communication
- Consultation
- Cotreatment
  - Treatment guidelines c/w evidence based best practices
- Sum of our experiences
  - Interprofessional education
  - Patient education
- Vascular
- Podiatry
- Plastics
- Endocrine
- Nursing
- Wound care
- Physical therapy
HOW DO WE SAVE THE FOOT?

• Blood Flow!!!
• Need pulsatile flow to heal
  • 3x more blood flow to heal than to “maintain”
CHANGE IN PARADIAGM

START
INFLOW

? —

FINISH
OUTFLOW
FACTORS AFFECTING TREATMENT OPTIONS

- Quality
  - Good size
- Quantity
  - Enough length
  - One vs two pieces
- Location
  - Arm vs Leg
  - Small saphenous
- Non-vein options
  - Synthetic
  - Cadaveric
FACTORS AFFECTING TREATMENT OPTIONS

- Patient Longevity
  - Old vs young
  - Surgical comorbidities/risk

- Extent of Ischemic Injury
  - Rest Pain vs ulcer vs Gangrene
  - Long vs short blockage
### PREFERENCES

<table>
<thead>
<tr>
<th>Endovascular</th>
<th>Open</th>
</tr>
</thead>
<tbody>
<tr>
<td>• High surgical risk</td>
<td>• Low surgical risk</td>
</tr>
<tr>
<td>• Older</td>
<td>• Younger</td>
</tr>
<tr>
<td>• Short lesion</td>
<td>• Long occlusion</td>
</tr>
<tr>
<td>• Rest pain, shallow ulcer</td>
<td>• Gangrene, foot sepsis</td>
</tr>
<tr>
<td>• Poor vein options</td>
<td>• Good vein options</td>
</tr>
</tbody>
</table>
THERAPEUTIC INDECISION
THERAPEUTIC GOALS

- Limit treatment morbidity
- Amputation free survival
  - Ulcer healing
  - Pain relief
  - Functional return
- Most efficient route to healing
  - Cost/healing event, i.e. resource utilization
THERAPEUTIC CHALLENGES FOR ENDO

• Relatively worse durability in infrainguinal territory
• Increased costs for repeat interventions
• Burning “bridges” for future surgery
• Limited, poor quality data to compare Endo vs Bypass
• Minimizing lapses in open technical skills
IS THE BENEFIT REALLY WORTH THE RISK?
DIABETIC ENDOVASCULAR LIMB SALVAGE:

How Extensive is the problem?
Small wound + Unhealthy Patient + Bad vein

Endo Surgery
CLI

- Subintimally dissect it
- Excise
- Laser
- Freeze
- Angioplasty
- Stent
- Sand
- Drill
MULTIPLE ADDITIONAL OPTIONS

- Balloon Angioplasty
  - POBA, Subintimal, Cryoplasty, Cutting Balloons, Scoring Balloons, Drug Coated Balloons
- Stents
  - Nitinol Self Expanding, PTFE covered, Biodegradable stents
- Atherectomy
  - Directional, Orbital, Rotational, Laser
OUTCOMES

• Technical Success HIGH 80+%  
• Longterm?
  • In thigh (SFA) better with stenting compared to balloons alone
  
• Overall similar despite type of intervention  
  • ~75-80% @1yrs  
  • ~60% @ 3yrs
BALLOON: PRIMARY PATENCY

Lazarus et al, 2006 Eur J Endovasc
More than one Outflow vessel last longer
Shorter lesions last longer

Primary patency vs. length of angioplasty

Follow up (months) | 0 | 1 | 3 | 6 | 12
Limbs at risk
< 30 cm | 26 | 25 | 23 | 19 | 6
> 30 cm | 25 | 20 | 18 | 10 | 3

Lazarus et al, 2006  Eur J Endovasc
OTHER FACTORS

Worse Factors
• Diabetes
• Renal failure
• Diffuse disease
  • (multilevel)
• Progression of disease
• Advanced disease at presentation
• Embolization from treatment
  • Loss of outflow

Maintaining a healed wound
• More frequent interventions
• Treat more outflow vessels

J Vasc Surg. 2007 Nov;46(5):946-958; discussion 958
PROBLEM:
RESTENOSIS AND IN STENT STENOSIS
DRUG ELUTING STENTS AND BALLOONS

- Not same as coronary
- Years of research still ongoing
- Zilver PTX Randomized Trial
  - Paclitaxel coated stents in SFA
  - Last longer than bare metal stents 82% vs 63%
- Balloons similar results in SFA
- Tibial results still pending
Large wound + Healthy Patient + Good vein

Bypass Surgery
PREVENT III STUDY

- Best recent control data for CLI patients undergoing vein bypass grafting
- Ef2 decoy study control population
- 2.7% perioperative mortality
- 5.2% graft occlusion rate
- 16% mortality rate at 1 year
- 80% secondary patency rate at 1 year
- 88% limb salvage rate at 1 year

BYPASS FOR CLI

- Risk is considerable:
  - Immediate post operative mortality
  - Major limb amputation
  - Recent meta-analysis 31 studies
    - Bypass mortality as high as 11.6%

BYPASS SURGERY

- CRI predictor of poorer long term outcome for bypasses
- Wound healing problems in 10-35% of saphenous vein harvest sites
  - Risk factors:
    - Obese
    - DM
    - ESRD patient
  - Significant functional recovery time
ENDO VS OPEN
BASIL TRIAL-LEVEL 1 DATA

- Randomized trial intervention vs bypass for CLI
- Poor life expectancy with CLI
- Intervention shorter length of stay
- Equivalent 6 month amputation free survival
- Did not impact future surgical options

- Endo treatment of choice for pts with limited <2 year life expectancy
- Surgery better if >2 year survival

Lancet 2005;366:1925-1934
COMPARISON OF WOUND HEALING WITH BYPASS VS. ENDOVASCULAR INTERVENTION

LENGTH OF LESION MAIN FACTOR?

ANGIOSOMES
ARE THEY BETTER?
Intraoperative Fluorescence Vascular Angiography: During Tibial Bypass

Diana Perry, B.S., Manish Bharara, Ph.D., David G. Armstrong, D.P.M., M.D., Ph.D., and Joseph Mills, M.D.
<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>Direct</th>
<th>Indirect</th>
<th>N=; F/up @12m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attinger/Neville, 2009</td>
<td>Bypass</td>
<td>91%</td>
<td>82%</td>
<td>N=52</td>
</tr>
<tr>
<td>Varela, 2010</td>
<td>Bypass &amp; PTA</td>
<td>92%</td>
<td>71%</td>
<td>N=76</td>
</tr>
<tr>
<td>Alexandrescu, 2011</td>
<td>PTA</td>
<td>85%</td>
<td>76%</td>
<td>N=208</td>
</tr>
<tr>
<td>Iida, 2012</td>
<td>PTA</td>
<td>71% AFS</td>
<td>50% AFS</td>
<td>N=369</td>
</tr>
<tr>
<td>Azuma, 2012</td>
<td>Bypass</td>
<td>49%</td>
<td>49%</td>
<td>N=276</td>
</tr>
<tr>
<td>Soderstrom, 2013</td>
<td>PTA</td>
<td>72%</td>
<td>46%</td>
<td>N=250</td>
</tr>
</tbody>
</table>

“Direct”: flow to ulcer in the proper angiosome
“Indirect”: flow to ulcer via “choke vessels”-collaterals
CLI WOUND CARE PRINCIPLES

• Avoid moisture between toes
• Lambs wool
• Lanolin cream to dry skin on foot
• Until revascularized –
  • Minimize debridement
  • Avoid pressure
• Keep foot warm / Rooke boots
• Edema control
• Protect contralateral foot
ONCE REVASCULARIZED

- Debride Dead Tissue
  - Surgical
  - Enzymatic
- Control Bioburden
  - Appropriate ABX for infection
- Control Moisture and Edema
HYDROCOLLOIDS

- Superior in treating pressure ulcers
- Moisture to promote healing in most wounds is key
- No data in arterial lesions
ENZYMATIC DEBRIDEMENT

• Papain-urea based
• Collagenases
• Can be helpful to slowly remove eschar and fibrinous debris
• May damage adjacent healthy tissue
NEGATIVE PRESSURE WOUND THERAPY

• Wound must be free of necrotic debris
• Homemade devices as efficacious as brand names
  • Removes moisture
  • Promotes granulation
  • Can help control lymph leakage
• Promotes adherence of STSG
• Continuous vs Intermittent
SILVER DRESSINGS

- Shown to be antimicrobial
- MRSA can develop resistance gene
- No clear evidence to support its efficacy
CREAMS AND POTIONS

• Randomized study for wet to dry with Gauze vs hydrocolloid gels for surgical wounds
• Found gauze more effective and cheaper

CONCLUSION

• Team based approach to the complex vascular patient using a tailored approach which factors in:
  • Patient
  • Wound Severity
  • Infection
  • Perfusion Deficit
OUR FOCUS

- Longstanding focus on limb preservation, function
- However greatest risk is MI, Stroke
- “PAD is a surrogate marker for CAD disease”
- Equal focus on CV risk modification
IMPROVING OUTCOMES

• Risk factor reduction
  • Statins LDL<70
  • Ace/ARB
  • HgB A1c < 7.0
  • Stop Smoking!
• Exercise
• Earlier identification of disease
• More aggressive treatment of disease
• What endovascular technique better?