Current Status of Lower Extremity Bypass

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Overview

- 42% reduction in peripheral bypass
- 300% increase in endoluminal procedures
- Patients for bypass likely to be older, sicker, long-segment occlusions.

J Vasc Surg 2009;50:54-60

Complex Decision

Patient
- Comorbidity
- Longevity
- Ambulatory status

Anatomic
- Inflow
- Target
- Conduit

Procedural
- Anesthesia
- Harvesting
- Tunneling
- Reversed vs In situ
- Intraop Evaluation
- Medical

Outcome

2013 Peripheral Bypass

1. What are the preoperative predictors of success?
2. What are current benchmark outcomes w/autologous vein?
3. What patency can I expect with newer prosthetic grafts?
4. What are the optimal pharmacologic agents to augment patency?
5. What about intraoperative assessment?
6. Surveillance?

Patient Selection

- 77 year old diabetic male smoker
- Bilateral saphenous harvest for CABG
- Lesser saphenous small, upper cephalic vein by US
- Palpable femoral pulse, nl NIVA at high thigh
- Angio with normal inflow, long segment SFA and popliteal occlusion, single vessel peroneal runoff.
- Referring doctor looking for foot salvage.
Indications, Outcomes and Expectations

Indications and Expectations

- Critical Limb Ischemia
  - Ischemic rest pain requiring narcotics for > 2 weeks
  - Ankle pressure < 50 mmHg or toe pressure < 30 mmHg
  - Tissue loss
  - Goals: amputation-free survival, independence.
  - Mortality: 20% at 6 months, 50% within 5 years of Dx
- A validated tool to determine limb loss or death after bypass would be quite valuable.

Prevent III Risk Score for CLI

- Predict amputation free survival in patients undergoing open infrainguinal bypass.
- Developed retrospectively from a cohort of patients undergoing autogenous bypass in the PREVENT III trial.
- Externally validated in 3286 pts at 94 American centers.
- Accurate and generalizable for systemic (not graft) events.
- Application: Reliable prediction of patients who have a > 50% chance of death or amputation within 1 year of bypass surgery.

Prevent III Risk Score for CLI

<table>
<thead>
<tr>
<th>Scoring</th>
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<tbody>
<tr>
<td>Dialysis = 4 points</td>
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<tr>
<td>Tissue Loss = 3 points</td>
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<tr>
<td>Age ≥ 75 = 2 points</td>
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<tr>
<td>Hct ≤ 30% = 2 points</td>
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<tr>
<td>CAD = 2 points</td>
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</table>

Amputation free survival at 5-year

- Low risk < 3
- Medium risk 4-7
- High risk > 8

Our patient

- 77 year old diabetic male smoker s/p CABG
- PREVENT III Risk Score = 7
  - Tissue loss = 3 points
  - Age ≥ 75 = 3 points
  - CAD = 2 points
  - Not on dialysis, Hct = 39%
- Amputation-free survival = 73% at one year following bypass

Autologous Conduit
**PREVENT III**

- Project Ex Vivo Graft Engineering via Transfection
- Prospective, randomized, double-blinded, placebo-controlled multicenter North American trial
- Edifoligide would reduce the incidence of vein graft failure
- Negative study
- Largest trial to date of peripheral bypass
- 1404 patients undergoing bypass in 83 centers

*J Vasc Surg 2007;46:1180-90*

**Autologous saphenous vein caliber**

**PREVENT-III Trial**

- 1404 vein bypass grafts for CLI at 83 centers in NA
- Early graft failure (30 days)
  - Graft diameter < 3 mm = 14%  
  - Graft diameter 3-3.5 mm = 10%  
  - Graft diameter ≥ 3.5 mm = 7%
- Strongest predictor of loss of primary patency at one year (OR = 2.35) is vein diameter < 3 mm.
- If single segment GSV > 3.5 mm:
  - 72% primary and 87% secondary patency at one-year.

*J Vasc Surg 2007;46:1180-90*

**Vein quality and harvesting**

- Compliance, sclerosis, calcification, varicosities
- Harvesting
  - Warm ischemia, mechanical injury, endothelial disruption
  - Endoscopic/Minimally invasive-performance may be suboptimal (JVS 44 2006, NEJM 361 2009, Circ 2011, JVS 2012)
- Storage solution
  - Heparinized blood vs. crystalloid
    - If crystalloid consider Plasmalyte (neutral pH, NS/LR is acidic)
  - Chilled or warm
  - Vasodilators (papaverine)
  - No evidence or consensus

**Graft configuration**

- Reversed, non-reversed or in situ?
  - No biochemical, morphologic or hemodynamic data to support.
  - No difference when compared in RCTs
- Does it matter where the inflow is? Shorter or longer grafts?
  - PREVENT III—shorter grafts have better patency even when controlling for location of proximal and distal attachment points, graft diameter and vein type.
- Tunnel the graft anatomic or subcutaneously?
  - No evidence to suggest benefit.
- Proximal or distal anastomosis first?
- Arterial control: loops, tourniquet, intraluminal or clamp?

**Preferences for vein bypass**

- Surgeon does the vein mapping preop and in OR
- Two team approach
- Reverse the vein (usually)
- Heparinized Plasma-Lyte blood bath
- Tunnel subcutaneously (except for the AK popliteal)
- Tourniquet control for anything distal to the BK popliteal
- Distal anastomosis first: "parachute" the heel and three interrupted, mattressed sutures at the toe.
- Aggressive surveillance and reintervention

**Risk factors for vein graft failure**

- Indication:
  - Patients with CLI do worse
- Age:
  - Younger patients have higher risk of failure
- Race:
  - African-American race is predictive of early vein graft failure, lower secondary patency and increased amputation rates.
- Gender:
  - Female gender-1-year occlusion rate of 23% compared to 14% for male gender (despite controlling for vessel size)
- Tobacco use increases risk of graft failure by 3.1 fold
- Hyperlipidemia

*J Vasc Surg 2008;47:556-63*
Risk factors NOT associated with graft failure

- Renal failure
  - Make up 20% of all patients undergoing bypass
  - Increased risk of amputation and all-cause mortality
  - 30% of pts initiating dialysis survive 5 years.
  - 10 year study of 456 pts with stage V renal failure
    - 5 yr 1st and 2nd patency rates were 70 and 65% (not different from Stage I patients) (Owens J Vasc Surg 2007)
- Diabetes
  - Independent risk factor for amputation
  - No association with graft failure in either VA NSQIP or PREVENT III

Intraoperative Evaluation

- Examination
- Doppler assessment
- Completion angiogram
- Intraoperative duplex examination

Surveillance

- Background
  - As many as 1/3 of LE vein bypasses develop a stenosis.
  - Identify the failing bypass and intervene.
  - Primary-assisted patencies exceed secondary patency.
- Goal: Improve limb salvage
- Studies from the 90’s suggest a 20% improvement in primary assisted patency with intensive surveillance.
- Controversial:
  - Long-term patency is no better than with clinical assessment alone.

Vein Graft Surveillance Trial (Circulation 2005;112:2586-2591)
- European, multicenter, prospective, randomized, controlled.
- 554 patients-clinical or duplex follow-up program at 6 weeks, then 3, 6, 9, 12, and 18 months.
- At 18 months, patency, amputation rate and quality of life similar.
- TASC II Recommendation
  - Interview for new symptoms
  - Limb examination, pulse check and ABI
  - Postop, every 6 months for two years
- No recommendation in 2010 AHA/SIR/SVS performance measures for PAD (Circulation 2010;122:2583-2588)
Surveillance in High Risk Conduits

- PREVENT III
  - 30% of vein bypasses underwent revision within 1 year
  - No benefit of completion angiography
- Recommend surveillance in high risk bypass
  - < 3 mm
  - Non-single segment
  - Non greater saphenous conduit
  - Length > 50 cm
  - Intraoperative revision

Surveillance Recommendation

- Individualize
- Risk of stenosis decreases with time
  - Vein bypasses for CLI develop stenoses 5-10%/ yr.
- High risk bypass
  - Duplex surveillance q 1, 3, 6, 12, 18, 24 mos, annually.
- Ambulatory patient with normal ABI after bypass.
  - Duplex surveillance at 1, 3, 6 months (and annually).

Prosthetic Conduit

Prosthetic conduit

- Saphenous vein may be missing in as many as 40% of patients needing revascularization.
- Perfect prosthetic conduit
  - Nonthrombogenic
  - Compliance similar to native vessels
  - Suturability
  - Tensile strength
  - Host incorporation
  - Resistant to infection
- Nonbiologic options: Dacron, ePTFE, polyurethane

Prosthetic Graft Material Modifications

- Structural
  - Reinforcement
  - Cuffs
  - Laminates
- Endoluminal
Prosthetic Graft Modifications

<table>
<thead>
<tr>
<th>Graft Materials and Coatings</th>
<th>Protein Modifications</th>
<th>Endothelial Cell Seeding</th>
<th>NO Modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon</td>
<td>Heparin</td>
<td>1 Stage</td>
<td>Dazaxenodiolates</td>
</tr>
<tr>
<td>Silver</td>
<td>Thrombinodulin</td>
<td>2 Stage</td>
<td>S-nitrosolthiol</td>
</tr>
<tr>
<td>Silicone</td>
<td>Hirudin</td>
<td></td>
<td></td>
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<tr>
<td>Phospholipids</td>
<td>PA</td>
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<tr>
<td>Elastin</td>
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<td>FGF</td>
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<tr>
<td>Peptides</td>
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<td></td>
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<tr>
<td>Rapamycin</td>
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<tr>
<td>Paclitaxel</td>
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Circulation 2008;117:1873-188

Surgical Modification of Prosthetic Grafts

- Standard anastomosis
- Linton patch
- Taylor patch
- Miller cuff
- Vein boot
- AV fistula

Circulation 2008;117:1873-188

Too many choices

Pre-Cuffed PTFE vs. Vein Cuff

- Multicenter, prospective, randomized (industry sponsored)
- 91 infragenicular bypasses in 89 patients at 15 NA centers
  - 47 carbon lined, 6-7 mm, externally supported precuffed
  - 44 vein cuff of surgeons choice
  - 80% on warfarin, mean f/u 14 months
- No diff in primary patency at 1 and 2 years (49 and 44 %)
- No difference in secondary patency
- No difference in limb salvage


Pre-Cuffed PTFE vs. RSVG

- Retrospective review
- 148 infragenicular bypasses over 6-year period.
- Fem-BK pop secondary patency

<table>
<thead>
<tr>
<th>Fem-BK pop</th>
<th>1 year</th>
<th>3 year</th>
<th>5 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTFE</td>
<td>89.2%</td>
<td>70.9%</td>
<td>59.6%</td>
</tr>
<tr>
<td>RVSG</td>
<td>84.4%</td>
<td>84.4%</td>
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</tr>
</tbody>
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- Fem-tibial secondary patency

<table>
<thead>
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<th>Fem-Tibial</th>
<th>1 year</th>
<th>3 year</th>
<th>5 year</th>
</tr>
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<tbody>
<tr>
<td>PTFE</td>
<td>75.5%</td>
<td>61.1%</td>
<td>52.0%</td>
</tr>
<tr>
<td>RVSG</td>
<td>74.8%</td>
<td>69.8%</td>
<td>52.0%</td>
</tr>
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</table>

- Bottom line: mid and long-term patency is better with vein.


Heparin bonding

- Heparin has both anticoagulant and antiproliferative actions.
- Proprietary covalent end-point linkage to retain heparin on the ePTFE surface.
- Duration of action
  - Lasts 12 weeks in canine model
  - >8 years in human explant
- No systemic effect, HIT < 0.001%
- Cost: 8 mm × 80 mm supported ePTFE
  - Stretch = $1770
  - Heparin-bonded = $2660
Heparin-bonded PTFE

- Multicenter registry over 7 years concluding 2008
  - 425 patients with CLI underwent HB PTFE bypass
  - Mean ABI preop = 0.35
  - 36% of bypasses infrageniculate, 21% vein cuff
  - 27% on warfarin
  - Follow up: mean 24.5 months and available for 98% of pts
- Results at 36 months
  - Primary patency = 61%
  - Secondary patency = 70%
  - Both limb salvage and survival rates = 87%

J Vasc Surg 2010;51:1367-77

Heparin-bonded PTFE

- Retrospective Italian multicenter registry
  - 180 diabetics with CLI underwent HB PTFE bypass
  - Mean ABI preop = 0.35
  - All bypasses infrageniculate, 27% to tibioc
  - 23% received a distal cuff or patch
  - Follow up: mean 24.5 months and available for 98% of pts
- Results at 48 months
  - Primary patency = 46.3%
  - Secondary patency = 57.5%
  - Limb salvage = 75.4%

J Vasc Surg 2011;54(5):1332-8

Hybrid graft

- Stent graft attached to standard wall ePTFE graft
- Designed to reduce intimal hyperplasia
- For use in hemodialysis access
- Distal anastomosis in popliteal, hybrid/debranching procedures
  - 5 and 10 cm stent graft to 6, 7, 8, 9 mm graft.
  - All are 50 cm length

Infrapopliteal Prosthetic Graft Bypass

Conclusions

- The performance of autologous vein grafts is greatly superior to that of unmodified ePTFE.
- The results of ePTFE grafts with interposition vein patch/cuff are significantly better than those associated with unmodified ePTFE.
- The results of pre-cuffed ePTFE grafts are comparable to those of ePTFE with vein cuff.
- Early and mid-term results of heparin-bonded ePTFE grafts is promising and approach those of vein conduit.

The Effect of Anesthetic Choice on LE Bypass Outcomes
Regional vs. General Anesthesia

- Retrospective NSQIP review of 5,462 bypasses for CLI
- 4,768 general, 694 regional anesthesia
- Distal target = tibial 51%, popliteal 49%
- General anesthesia
  - Higher rate of resident involvement
  - Greater need for transfusion
  - Longer operative time
  - Involve prosthetic or composite vein bypass
- No difference in morbidity, mortality or LOS.

Ann Vasc Surg 27(2) 2013:199-207

Medical Therapies to Augment Patency

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Ann Vasc Surg 27(2) 2013:199-207

Aspirin

- PAD is a CAD equivalent, all patients should be on ASA for overall CAD risk reduction.
- Antiplatelet Trialists’ Collaboration showed a relative risk reduction of 43% in peripheral graft occlusion.
- Cochrane meta-analysis revealed a positive effect on primary patency at one year (OR = 0.59)
- Dose: 75-100 mg daily, started preoperatively.

J Vasc Surg 2010;52:825-33

CASPAR Results

- Limb related
  - No overall benefit of dual antiplatelet tx.
  - No difference in occlusion, reoccl, or above ankle amputation
- Systemic
  - Overall risk of death, MI or stroke was similar
  - Clopidogrel increased risk of bleeding (1.1% vs 1.2%)
- Prosthetic grafts (n = 253)
  - Clopidogrel provided a 35% relative risk reduction in primary outcome
    - Graft occlusion = 9% vs 3.2%; HR 0.63
    - Major amputation = 15% vs 9.1%; HR 0.48

J Vasc Surg 2010;52:825-33

Clopidogrel

- Clopidogrel and ASA in bypass Surgery for PAD (CASPAR) trial.
- Prospective, multicenter, randomized, double-blind, placebo controlled study.
- 851 pts randomized to ASA + clopidogrel or ASA + placebo within 2-4 days of surgery
  - Claudicants = 30%
  - Anastomosis to below knee popliteal = 73% (remainder crural/pedal, none above knee)
  - Prosthetic graft = 30%
- Primary outcome = graft occlusion or revascularization, amputation, bleeding or death

J Vasc Surg 2010;52:825-33

Other Perioperative Agents

Insufficient evidence to support the use of LMWH, IV heparin or Dextran perioperatively
Anticoagulation

Dutch Bypass Oral Anticoagulants trial
- 2690 pts randomized to VKA (INR 3-4.5) vs ASA
- No change in overall patency.
- Subgroup analysis suggested:
  • Oral anticoagulation improved vein graft patency
  • Aspirin improved prosthetic graft patency
- Benefit noted for VKA in vein bypasses at a 4.7% risk of major bleeding per year.

Lancet 2000;355:346-51

Anticoagulation

Veterans Affairs Cooperative trial
- 831 patients at 17 VA followed for 36.6 mo
- Vein or prosthetic bypass
- Randomize: warfarin + ASA (INR 1.4-2.8, 325 mg/d) vs ASA 325 mg/d
- Overall no patency benefit and higher mortality in warfarin arm.
- Warf + ASA improved assisted primary patency at 5 years in:
  • Prosthetic 6 mm Ax-Fem, Fem-Fem
  • Any prosthetic Fem-pop (AK) P=.012

J Vasc Surg 2002;35:413-21

Statins

- Improve patency
  • Retrospective, 172 patients (J Vasc Surg 2004;39:357-65)
  • Increased both primary assisted and secondary patency at 2 years (37 vs 87%)
  • No difference in perioperative serum cholesterol levels
- 3.7 fold increase in patency (J Vasc Surg 2004;39:357-65)
- Decrease perioperative CHD complications (Circulation 2005;112:587-92)

Conclusions

- Consider using the PREVENT III risk score to help predict one-year amputation free survival.
- Single segment, GSV > 3.5 mm is best
- Prosthetic, particularly the heparin-bonded PTFE grafts look promising.
- Medical treatment following bypass
  • All patients should be on a statin and ASA.
  • Add clopidogrel for prosthetic bypass.
  • Consider warfarin in high risk bypass.

Glass Pond, Rocky Mountain National Park