

Explaining the discrepancy between low
patency and higher limb salvage rates
after revascularization for CLI:
Does perfusion matter or not?

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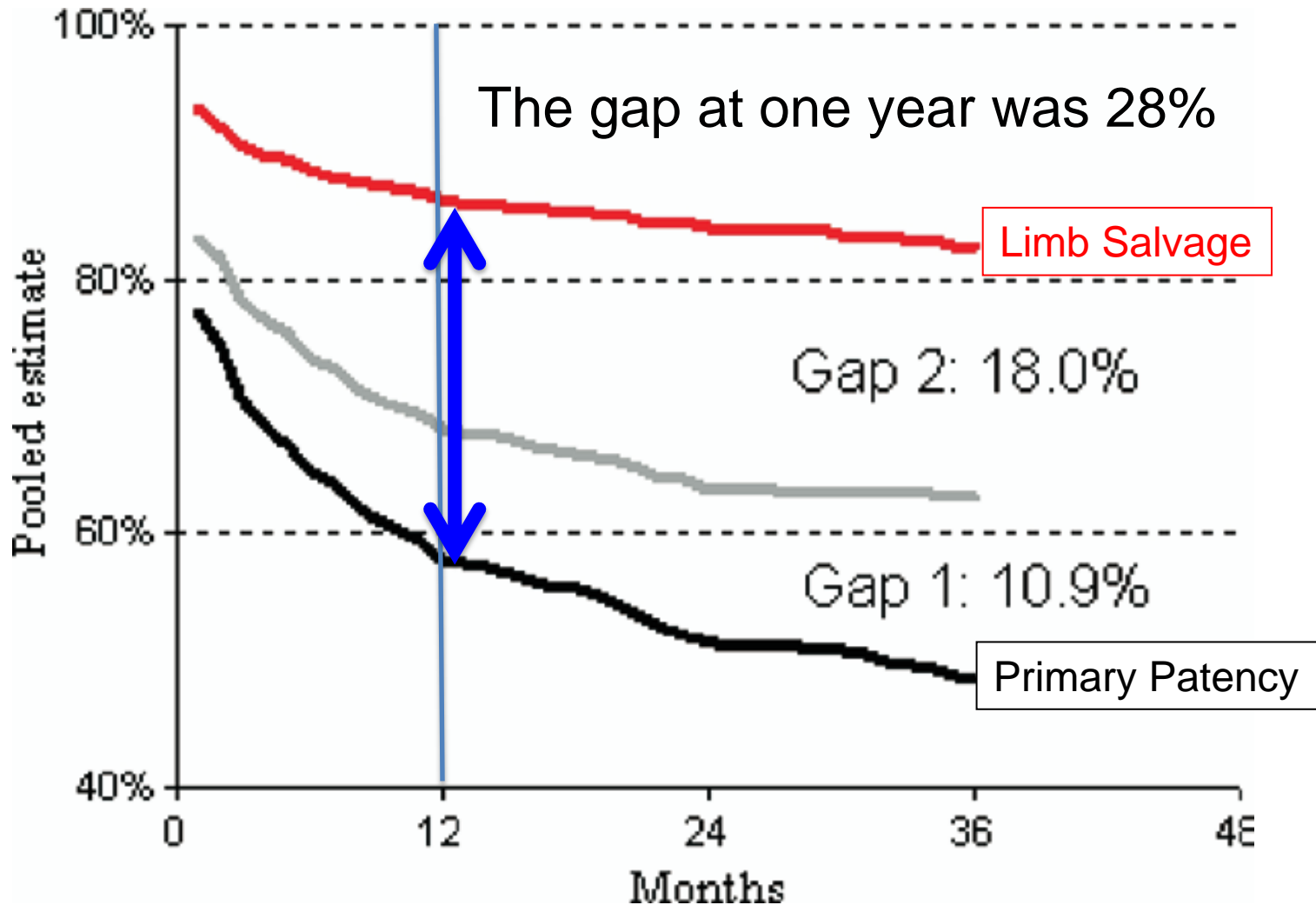
Disclosure

Peter A. Schneider

I have the following potential conflicts of interest to report:

- Scientific Advisory Board (non-paid): Cardinal, Abbott, Medtronic
- Royalty (modest): Cook
- Co-founder and Chief Medical Officer: Intact, Cagent

Why is Limb Salvage Higher than Patency?



Why is Limb Salvage Higher than Patency?

Assessment of Patency

- 2005-2015-39 studies
 - Patency and limb salvage with at least 1 year f/u
 - Minimum 50 patients

| Method | No. Papers Utilizing (%) | No. Patients Assessed (%) |
|---------------------|--------------------------|---------------------------|
| Physical exam + ABI | 8 (21%) | 1974 (31%) |
| ABI | 24 (62%) | 4365 (68%) |
| Doppler | 3 (8%) | 777 (12%) |
| Duplex | 26 (67%) | 4510 (70%) |
| CTA | 1 (3%) | 208 (3%) |
| Angiography | 21 (54%) | 3605 (56%) |

Does Perfusion Matter or Not?

Limb threat status is by determined by the development of a profound degree of ischemia.

Limb salvage depends on reversing or managing multiple factors in addition to improving perfusion.



Does Perfusion Matter or Not?

Yes, perfusion matters.

But...we should not expect one year patency rates and limb salvage rates to correlate.

Predictors of failure and success of tibial interventions for critical limb ischemia

Nathan Fernandez, MD, Ryan McEnaney, MD, Luke K. Marone, MD, Robert Y. Rhee, MD, Steven Leers, MD, Michel Makaroun, MD, and Rabih A. Chaer, MD, *Pittsburgh, Pa*

Why Is Limb Salvage Higher Than Patency?

75% limb salvage
vs
33% patency

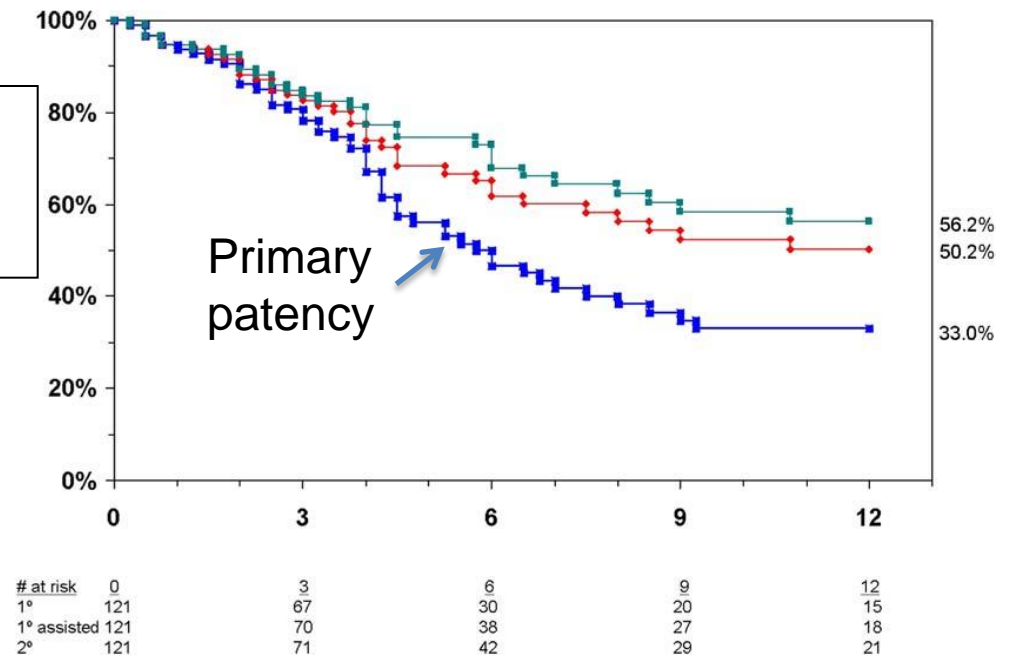
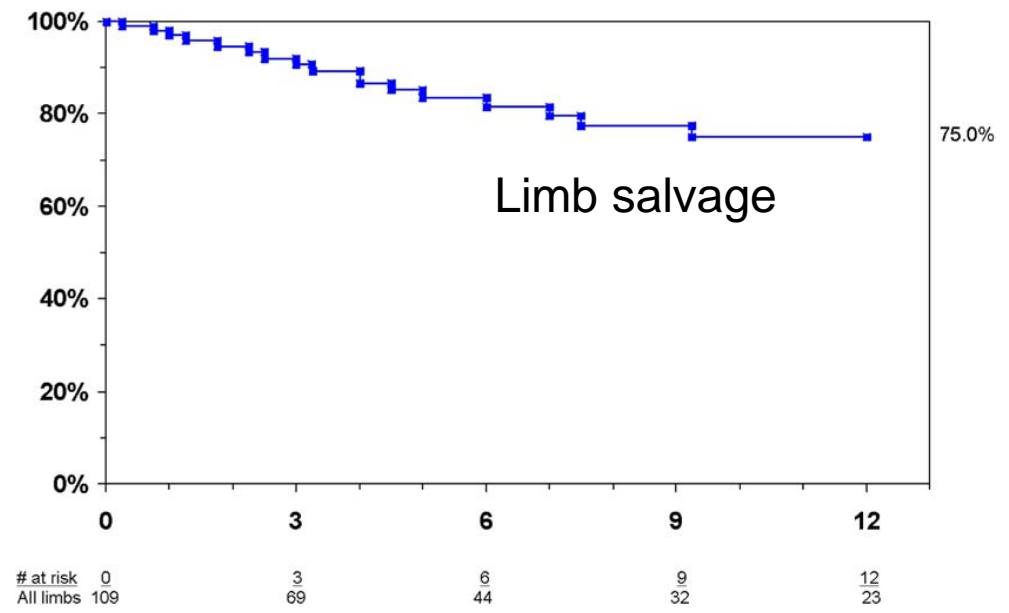


Fig 1. Patency in limbs undergoing tibial interventions (n = 121).



Why is Limb Salvage Higher than Patency?

| | Primary Patency (%) | Limb Salvage(%) | Gap |
|-------------------|---------------------|-----------------|--------------|
| Pitt (111) | 33 | 75 | 42 |
| MGH (409) | 64 | 85 | 24 |
| Leipzig (62) | 33* | 100 | 67 |
| In.PACT DEEP(358) | 60** | 93 | 33 |
| Cornell (106) | 64 | 87 | 23 |
| Range % | 33-64 | 75-100 | 23-67 |

Fernandez et al. J Vasc Surg 2010;52:834

Schmidt et al. CCI 2010;76:1047

Metzler et al. Ann Vasc Surg 2014;28:144

Conrad et al. J Vasc Surg 2011;53:1020

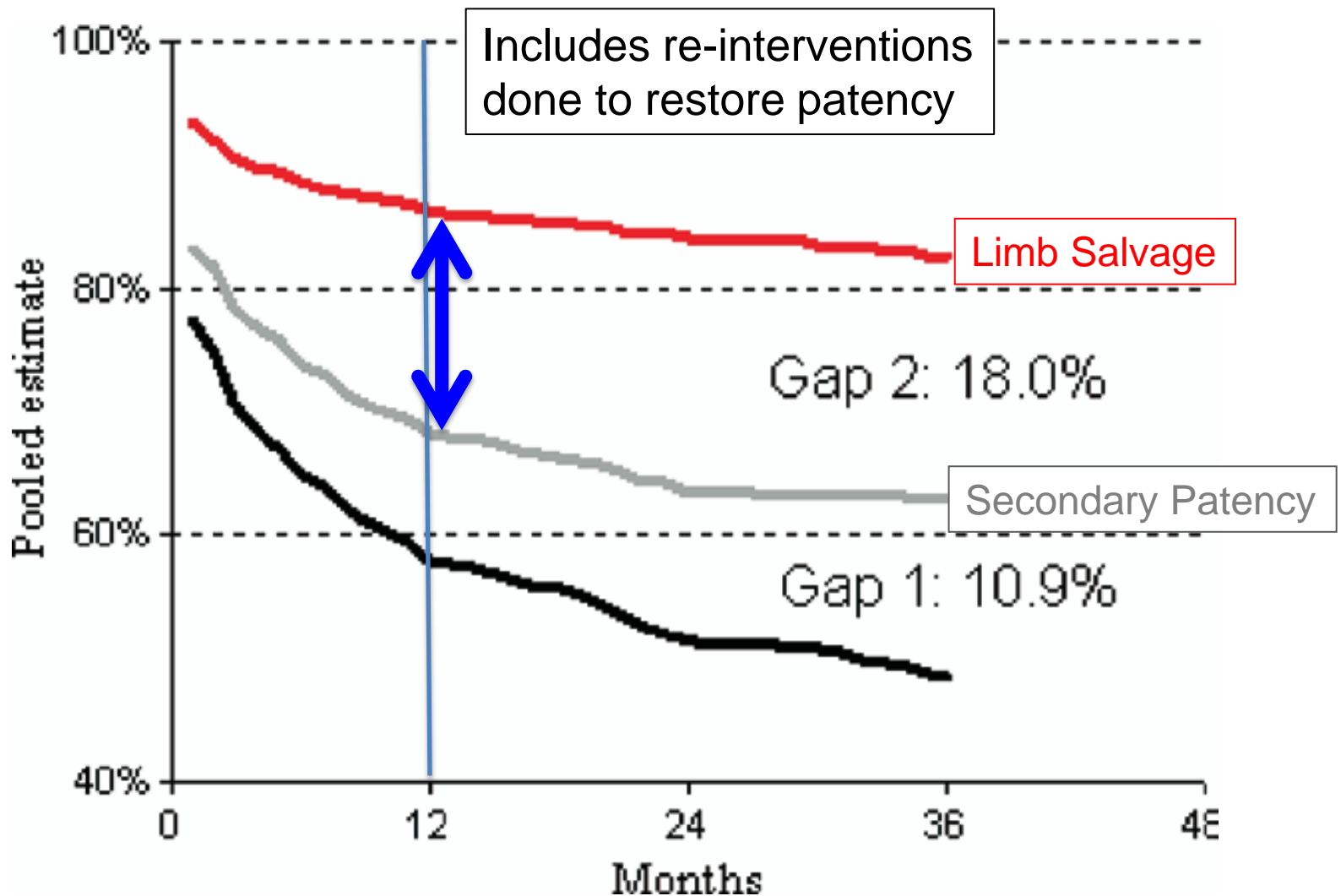
Zeller et al. JACC 2014;64:1568

Study Populations: REINTERVENTION

Why Is Limb Salvage Higher Than Patency?

- Those who have lost patency still potentially keep the limb if reintervention is prompt and successful.
- Re-intervention rate at 1 year: 13-50%.

Why is Limb Salvage Higher than Patency?



Why is Limb Salvage Higher than Patency?

| | Primary Patency (%) | Limb Salvage(%) | Gap | TLR (%) |
|-------------------|---------------------|-----------------|--------------|--------------|
| Pitt (111) | 33 | 75 | 42 | 50 |
| MGH (409) | 64 | 85 | 24 | 25 |
| Leipzig (62) | 33 | 100 | 67 | 50 |
| In.PACT DEEP(358) | 60 | 93 | 33 | 13 |
| Cornell (106) | 64 | 87 | 23 | 27 |
| Range % | 33-64 | 75-100 | 23-67 | 13-50 |

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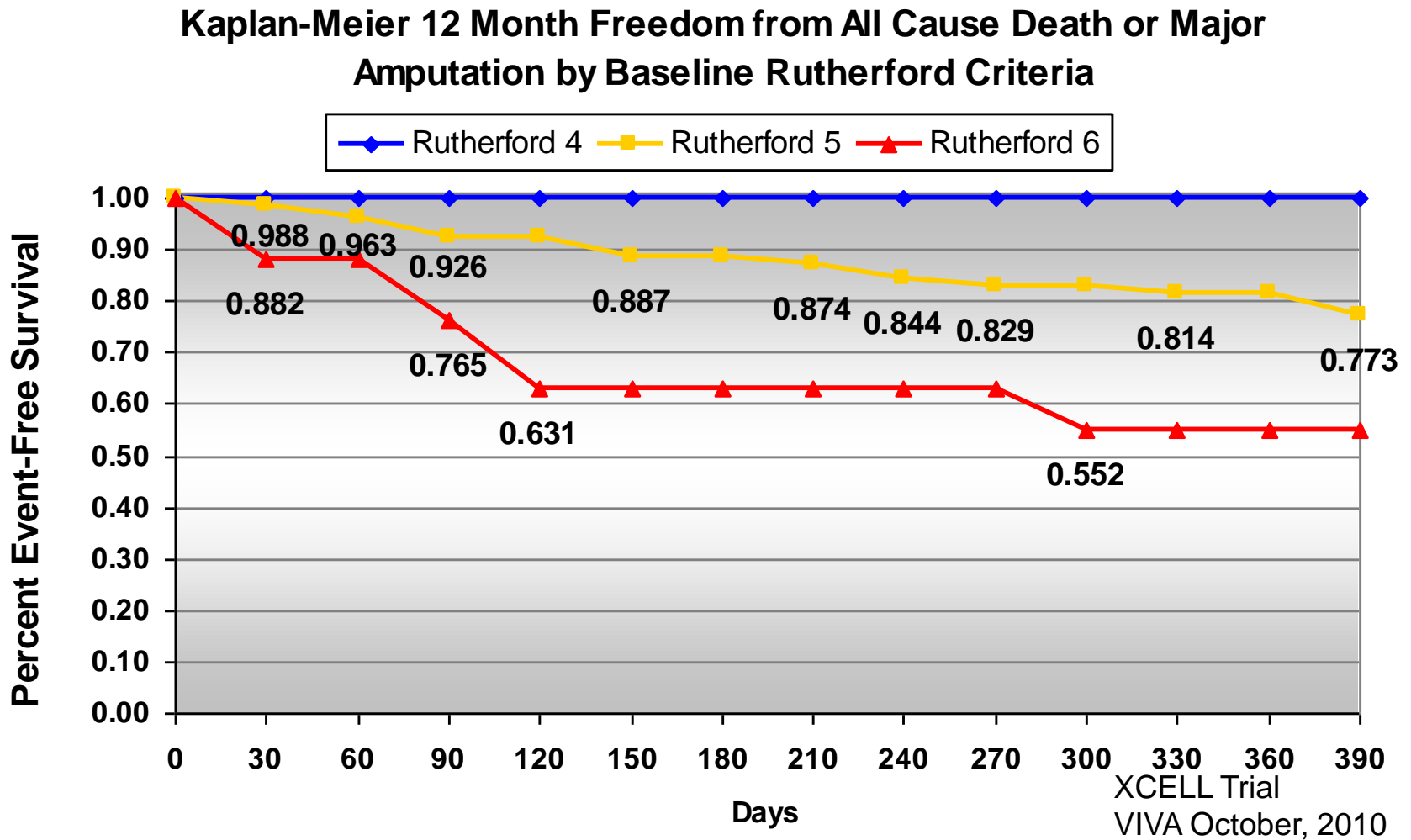
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No Tissue Loss=Low Likelihood of Limb Loss



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

Risk of leg amputation at 1 year

Wound

| | Ischemia – 0 | | | | Ischemia – 1 | | | | | Ischemia – 2 | | | | Ischemia – 3 | | | |
|-----|--------------|----------|----------|----------|--------------|----------|----------|----------|--|--------------|----------|----------|----------|--------------|----------|----------|----------|
| W-0 | VL | VL | L | M | VL | L | M | H | | L | L | M | H | L | M | M | H |
| W-1 | VL | VL | L | M | VL | L | M | H | | L | M | H | H | M | M | H | H |
| W-2 | L | L | M | H | M | M | H | H | | M | H | H | H | H | H | H | H |
| W-3 | M | M | H | H | H | H | H | H | | H | H | H | H | H | H | H | H |
| | fl- 0 | fl- 1 | fl- 2 | fl- 3 | fl- 0 | fl- 1 | fl- 2 | fl- 3 | | fl- 0 | fl- 1 | fl- 2 | fl- 3 | fl- 0 | fl- 1 | fl- 2 | fl- 3 |

Foot infection

Patients with no wound and no foot infection remain at a low or very low risk for amputation at 1 year.

VL=very low, L=low, M=moderate, H=high

Mills et al. J Vasc Surg 2014;59:220

Study Populations: REST PAIN

Why Is Limb Salvage Higher Than Patency?

- Resolution of rest pain syndrome correlates well with perfusion. But limb salvage does not correlate well.
- A loss of patency typically presents with recurrent symptoms and rarely immediately threatens the leg.
- Some included Rutherford 4 patients have diabetic neuropathic pain, not ischemic pain.
- The more R4 in a study, the less correlation between LS and patency.

Why is Limb Salvage Higher than Patency?

| | Primary Patency (%) | Limb Salvage(%) | Gap | Rest Pain | TLR (%) |
|-------------------|---------------------|-----------------|--------------|-------------|--------------|
| Pitt (111) | 33 | 75 | 42 | 17 | 50 |
| MGH (409) | 64 | 85 | 24 | 29 | 25 |
| Leipzig (62) | 33 | 100 | 67 | 26 | 50 |
| In.PACT DEEP(358) | 60 | 93 | 33 | 16 | 13 |
| Cornell (106) | 64 | 87 | 23 | 0 | 27 |
| Range % | 33-64 | 75-100 | 23-67 | 0-29 | 13-50 |

Fernandez et al. J Vasc Surg 2010;52:834

Schmidt et al. CCI 2010;76:1047

Metzler et al. Ann Vasc Surg 2014;28:144

Conrad et al. J Vasc Surg 2011;53:1020

Zeller et al. JACC 2014;64:1568

Why is Limb Salvage Higher than Patency?

| | Primary Patency (%) | Limb Salvage(%) | Gap | Rest Pain | TLR (%) | Rest Pain + TLR |
|-------------------|---------------------|-----------------|--------------|-------------|--------------|-----------------|
| Pitt (111) | 33 | 75 | 42 | 17 | 50 | 67 |
| MGH (409) | 64 | 85 | 24 | 29 | 25 | 44 |
| Leipzig (62) | 33 | 100 | 67 | 26 | 50 | 76 |
| In.PACT DEEP(358) | 60 | 93 | 33 | 16 | 13 | 29 |
| Cornell (106) | 64 | 87 | 23 | 0 | 27 | 27 |
| Range % | 33-64 | 75-100 | 23-67 | 0-29 | 13-50 | 27-76 |

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Why is Limb Salvage Higher than Patency?

| | Primary Patency (%) | Limb Salvage(%) | Gap | Rest Pain + TLR |
|-------------------|---------------------|-----------------|--------------|-----------------|
| Pitt (111) | 33 | 75 | 42 ← 67 | 67 |
| MGH (409) | 64 | 85 | 24 ← 44 | 44 |
| Leipzig (62) | 33 | 100 | 67 ← 76 | 76 |
| In.PACT DEEP(358) | 60 | 93 | 33 ← 29 | 29 |
| Cornell (106) | 64 | 87 | 23 ← 27 | 27 |
| Range % | 33-64 | 75-100 | 23-67 | 27-76 |

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Why is Limb Salvage Higher than Patency?

- When you add up the patients in the 2 subgroups where patency and limb salvage should not be expected to correlate, the totals are typically the same as or larger than the gap between patency and limb salvage.

Why is Limb Salvage Higher than Patency? Bypass Surgery for Limb Salvage

- More patients with tissue loss in bypass studies
 - Fewer rest pain patients
- Trend toward fewer re-interventions
- We should expect:

Better correlation between primary patency and limb salvage and a smaller gap for bypass than for endovascular.

Why is Limb Salvage Higher than Patency? Bypass Surgery for Limb Salvage

Meta-analysis of infrapopliteal angioplasty for chronic critical limb ischemia

Table II. Meta-analysis results of crural percutaneous transluminal angioplasty and popliteal-to-distal bypass^a

| <i>Result</i> | <i>1 month</i> | <i>6 months</i> | <i>1 year</i> | <i>2 years</i> | <i>3 years</i> |
|-------------------|----------------|-----------------|---------------|----------------|----------------|
| Primary patency | | | | | |
| PTA | 77.4 ± 4.1 | 65.0 ± 7.0 | 58.1 ± 4.6 | 51.3 ± 6.6 | 48.6 ± 8.0 |
| Bypass | 93.3 ± 1.1 | 85.8 ± 2.1 | 81.5 ± 2.0 | 76.8 ± 2.3 | 72.3 ± 2.7 |
| <i>P</i> | <.05 | <.05 | <.05 | <.05 | <.05 |
| Secondary patency | | | | | |
| PTA | 83.3 ± 1.4 | 73.8 ± 7.1 | 68.2 ± 5.9 | 63.5 ± 8.1 | 62.9 ± 11.0 |
| Bypass | 94.9 ± 1.0 | 89.3 ± 1.6 | 85.9 ± 1.9 | 81.6 ± 2.3 | 76.7 ± 2.9 |
| <i>P</i> | <.05 | <.05 | <.05 | | |
| Limb salvage | | | | | |
| PTA | 93.4 ± 2.3 | 88.2 ± 4.4 | 86.0 ± 2.7 | 83.8 ± 3.3 | 82.4 ± 3.4 |
| Bypass | 95.1 ± 1.2 | 90.9 ± 1.9 | 88.5 ± 2.2 | 85.2 ± 2.5 | 82.3 ± 3.0 |
| Patient survival | | | | | |
| PTA | 98.3 ± 0.7 | 92.3 ± 5.5 | 87.0 ± 2.1 | 74.3 ± 3.7 | 68.4 ± 5.5 |
| Bypass | NA | NA | NA | NA | NA |

NA, Estimates not available; PTA, percutaneous transluminal angioplasty.

^aValues are pooled estimate and standard error.

Why is Limb Salvage Higher than Patency? Bypass Surgery for Limb Salvage

| | Primary Patency | Limb Salvage | Gap |
|--------------|-----------------|--------------|-----|
| Endovascular | 58% | 86% | 28% |
| Open Bypass | 82% | 89% | 7% |

Romiti et al J Vasc Surg 2008;47:975.

| Bypass | Primary Patency | Limb Salvage | Gap |
|-------------------------|-----------------|--------------|-----|
| Reversed saphenous vein | 77% | 85% | 8% |
| In-situ | 82% | 91% | 9% |

Mills J. Surgical revascularization of infrainguinal occlusive disease. Includes all series 1981-2009 Rutherford 7th ed. 2010

Why is Limb Salvage Higher than Patency? Two Smaller Contributing Groups

- Loss of patency some time after wound healed.
- Tibial PTA failed but more proximal PTA site remained open.

Why is Limb Salvage Higher than Patency?

Conclusion

- Limb salvage is higher than primary patency.
- This is driven by inclusion of patients with;
 - No tissue loss/rest pain
 - Re-interventions for limb salvage
- Limb salvage should be expected to correlate with patency. The fact that these do not correlate, should not decrease the value of perfusion to an ischemic limb.

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