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NEXT GENERATION

Multidisciplinary European Endovascular Therapy

Efficacy of an **angiosome-directed versus indirect revascularisations** for wound healing in patients with diabetes and critical limb ischaemia: a literature review

Disclosure of Interest

Speaker name: Benedictine Y.C. Khor

Acknowledgements: Pamela Price, my dissertation supervisor who provided immense guidance throughout the preparations of this review

- I do not have any potential conflict of interest

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Critical Limb Ischaemia (CLI)

Fontaine Classification (Fontaine et al., 1954)		Rutherford Classification (Rutherford et al., 1997)	
Stage	**Clinical description**	**Category**	**Clinical description**
I	Asymptomatic	0	Asymptomatic
II	Intermittent claudication	1	Mild claudication
- IIa	Mild claudication		
- IIb	Moderate to severe claudication	2	Moderate claudication
		3	Severe claudication
III	Ischaemic rest pain	4	Ischaemic rest pain
IV	Ulceration or gangrene	5	Minor tissue loss (non-healing ulcer, focal gangrene with diffuse pedal ischaemia)
		6	Major tissue loss (extending above transmetatarsal level, foot no longer salvageable)

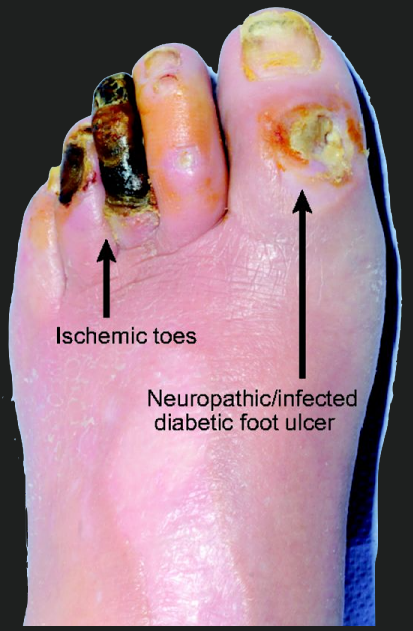

Figure: Nunan et al., 2014

CLI definition

The Trans-Atlantic Inter-Society Consensus **(TASC-II)** (Norgren et al., 2007) defines CLI as:

- the presence of ischaemic rest pain or tissue lesions, such as non-healing wounds, necrosis or gangrene,
- which typically presents at the **extremities** of the affected limb for more than two weeks.

- This is usually associated with haemodynamic quantification of:
  - ankle pressures <50–70 mm/Hg,
  - toe pressures <50 mm/Hg, or
  - $TcPO_2$ levels of <30 mm/Hg.

Current Practice

‘Best Vessel’ Strategy

- **Target vessel:** Guided by the least diseased artery as identified on angiography
- **Pros:** Best quality conduit
- **Cons:** Indirect perfusion, may require a good collateral supply to reperfuse site of ulceration

Persistence of ischaemic ulcerations **despite** technically successful revascularisations achieving the restoration of pedal pulses and vessel patency

(Carsten et al., 1998; Seeger et al., 1999; Attinger et al., 2006; Söderström et al., 2009; Simons et al., 2010; Forsythe et al., 2014).

The Angiosome Concept

Target vessel: Guided by **site of ulceration**

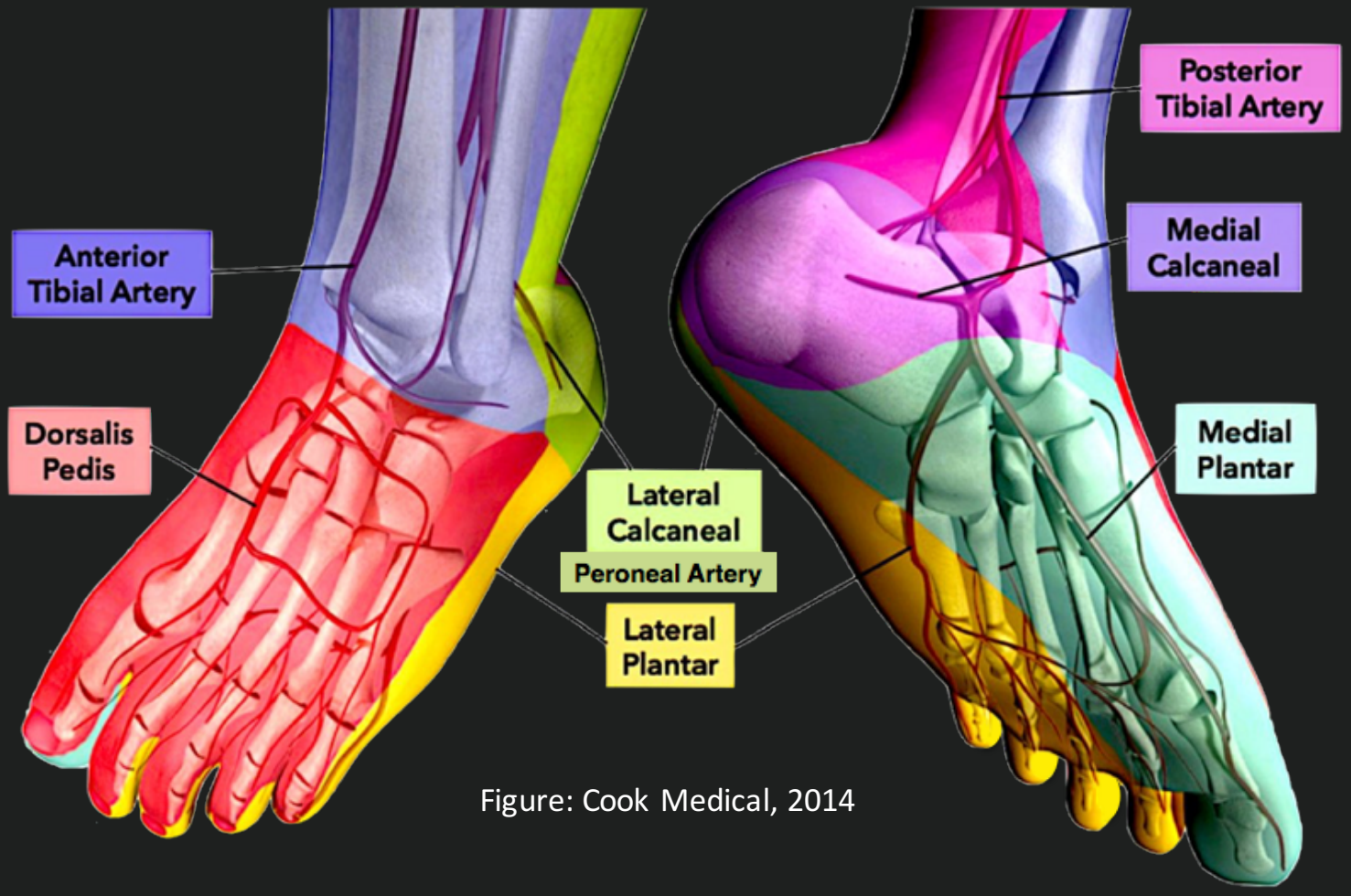

Figure: Cook Medical, 2014

Comparing the efficacy of:

Indirect / 'Best Vessel' strategy

- **Target vessel:** Guided by the least diseased artery as identified on angiography
- **Pros:** Best quality conduit
- **Cons:** Indirect perfusion, may require good collateral supply to reperfuse site of ulceration

Angiosome-directed strategy

- **Target vessel:** Guided by site of ulceration
- **Pros:** Direct perfusion from source artery, not dependent on collaterals
- **Cons:** May be required to recanalise a more **calcified** and **occluded** vessel, over one which might be more pliable and patent

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Peripheral Arterial Disease (PAD)

Comparison of PAD characteristics

(Boulton & Armstrong, 2006; Graziani et al., 2007; Setacci & Ricco, 2011; Forsythe et al., 2015)

	With diabetes	Without diabetes
Age of onset	Younger	Older
Disease progression	Aggressive	Gradual
Anatomical localisation	• Mainly distal • Distinctly infrapopliteal affliction, involving all three tibial arteries • Relative sparing of inframalleolar arteries & supragenicular arteries	• Mainly proximal • Lesions tend to affect femoral and aortic-iliac arteries more frequently than the distal arteries
Type of atherosclerotic lesion	• Stenosis < Occlusions • Diffuse, occurring over long segments	• Stenosis > Occlusions • Focal, occurring over short segments
Calcification	Commonly present	Absent
Collateral network	Poor	Unaffected

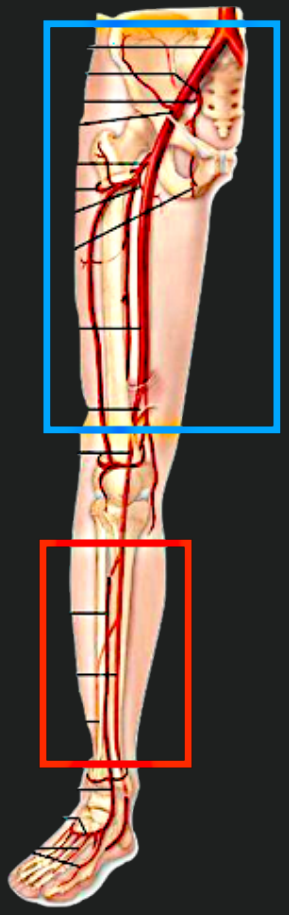


Figure: lower limb arterial tree
(Memorize, 2016)

Methods

8 databases	AMED, CINAHL, MEDLINE, ProQuest Health & Medicine Complete, ProQuest Nursing & Allied Health Source, The Cochrane Library, TRIP database, ScienceDirect
Search terms	S1 - “critical limb isch?emia” OR “isch?emi*” S2 - “peripheral arter* disease” OR “peripheral vascular disease” S3 - “diabetic foot” OR “diabet*” S4 - “bypass” OR “angioplasty” OR “endovascular” OR “revasculari?ation” OR “reconstruct*” S5 - “angiosom*” OR “direct revasculari?ation” OR “indirect revasculari?ation” S6 - S1 OR S2 OR S3 S7 - S4 AND S5 AND S6
Critical appraisal tool	Newcastle-Ottawa Scale

Methodological Rigour of Studies

	Fossaceca et al., 2013	Söderström et al., 2013	Acín et al., 2014	Lejay et al., 2014
Strengths / Limitations	**Strengths** ✓TASC-II diagnostic criterion satisfied* ✓Complete follow-up of all subjects ✓Diagnostic criteria of diabetes indicated ✓Subjects' duration of diabetes provided **Limitations** • Non-consecutive sample • Wound classification system not utilised • Presence of infection not documented • Omission of subjects' baseline characteristics	**Strengths** ✓TASC-II diagnostic criterion satisfied* ✓Complete follow-up of all subjects ✓Diagnostic criteria of diabetes indicated ✓Utilised wound classification system ✓Presence of infection accounted for ✓Consecutive sample ✓Propensity score **Limitations** • No data on subjects' duration of diabetes	**Strengths** ✓TASC-II diagnostic criterion satisfied* ✓Comparable inter-group baseline characteristics ✓Diagnostic criteria of diabetes indicated ✓Presence of infection accounted for ✓Consecutive sample **Limitations** • No data on subjects' duration of diabetes • Wound classification system not utilised • Drop-outs unaccounted • Patients with ESRD excluded	**Strengths** ✓TASC-II diagnostic criterion satisfied* ✓Complete follow-up of all subjects ✓Comparable inter-group baseline characteristics of subjects ✓Utilised wound classification system ✓Presence of infection accounted for ✓Consecutive sample **Limitations** • No data on subjects' duration of diabetes • No data on diagnostic criteria for diabetes
NOS Scores	6/9	8/9	5/9	7/9

• **Abbreviations:** End-Stage Renal Disease (ESRD); Newcastle-Ottawa Scale (NOS); Trans-Atlantic Inter-Society Consensus (TASC-II)
• * **Additional details:** TASC-II (Norgren et al., 2007)'s diagnostic criterion is for the clinical diagnosis of critical limb ischaemia to be confirmed with objective quantifications of haemodynamic compromise.

Findings

- Focusing on methodologically stronger studies (Söderström et al., 2013; Lejay et al., 2014), giving a representative sample of **280 subjects**

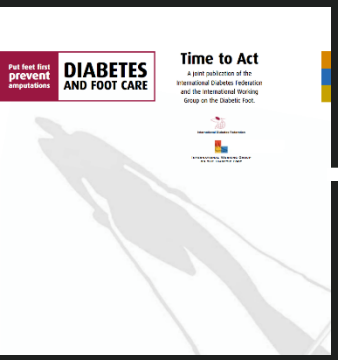
- Angiosome-directed revascularisations found to be **superior** to indirect revascularisations (p-values: <0.001 and 0.04)

- Results in a **nearly twofold increased probability** for subjects to achieve wound healing in 12 months (hazard ratios: 1.97; 95% confidence intervals, 1.34-2.90)

Clinical Relevance & Implications

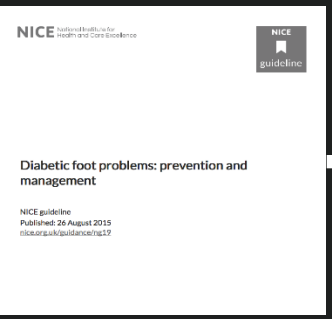
Focal point: to reduce avoidable lower-limb amputations, especially those relating to **diabetes and peripheral arterial disease (PAD)**

(All-Party Parliamentary Group (APPG) on Vascular Disease, 2015)



PAD is the **chief** contributing factor to non-healing diabetic foot ulcerations

(International Diabetes Federation & International Working Group on the Diabetic Foot, 2015)



Over 80% of diabetes-related amputations are **preceded** by a non-healing foot ulcer

(National Institute for Health and Care Excellence, 2015)

Within the limits of technical feasibility, it appears that **re-calibrating the revascularisation strategy to incorporate the angiosome concept may be more efficacious than an indirect approach** in optimising wound healing outcomes for patients with diabetes and critical limb ischaemia

Recommendations for future research

- Evidence for angiosome-directed revascularisations in a purely diabetic population is limited, but do appear promising and would merit from further investigation

  - To **rigorously assess and substantiate** the short- and long-term **safety and viability** of pursuing an angiosome-directed over an indirect strategy
  - Comply with the **European Wound Management Association's recommendations** *(Gottrup et al., 2010; Price et al., 2014)* to ensure **consistency** in outcome measurements and reporting
  - To **stratify patients according to disease type**, to aid in the development of **targeted** management strategies

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