New Insights into Microcirculation

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Thank you to
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What is the Microcirculation?

- Small arteries
- Arterioles
- Capillaries
- Venules
- Small veins
The Vascular Endothelium

- The endothelium is a delicate monolayer of cells that lines all blood vessels.
- It regulates:
  - the contractile and proliferative state of the underlying smooth muscle cells
  - the interaction of the blood vessel wall with the circulating blood (e.g., gateway to immune cells, hemostasis, etc)
The Vascular Endothelium
Microvascular Physiology

- Small arteries and arterioles dilate or contract to maintain a constant flow of blood
- Capillaries are able to regulate their flow by transmitting signals to upstream controlling arterioles
- A multitude of factors influence the contraction or relaxation of arterioles (such as innervation, insulin, melatonin, blood viscosity, metabolites), but a key factor is nitric oxide (NO)

Wiernsperger N, Rapin JR. Microvascular Diseases: Is A New Era Coming? 
*Cardiovasc Hematol Agents Med Chem* 2012; 10(2): 167-183
Capillary Blood Flow

- In addition to the arteriolar control of capillary blood flow, other key factors are at play
- These include:
  - hematocrit
  - blood viscosity
  - red blood cell deformability/aggregation

Microvascular Function and Health

“The fundamental role of microvessels is to supply target tissues with oxygen and nutrients; therefore it appears logical that microvascular disorders will impact on tissue function, given the close coupling between flow and metabolism.”

.........and in Addition

- Liver disease in general
- Kidney disease
- Neuropathies/neuralgias
- Restless leg syndrome
- Osteoarthritis
- Retinal diseases
- Poor healing of any tissue
- Soft tissue injury
- Intervertebral disc damage
- Recovery from ischemic damage
- Antiaging
Heart Disease and Microcirculation

- Coronary microvascular dysfunction is under intense investigation because of the growing awareness of its importance.
- For example, in patients with chest pain with a normal angiogram, coronary flow reserve (a measure of microvascular health) is a comprehensive indicator of cardiovascular risk.

Lee DH, Youn HJ, Choi YS et al. Coronary flow reserve is a comprehensive indicator of cardiovascular risk factors in subjects with chest pain and normal coronary angiogram. Circ J 2010; 74(7): 1405-1414
The Liver and Microcirculation

- There are major changes in the microcirculation in the liver with age
- These include:
  - increased endothelial cell thickness
  - reduced numbers of pores (fenestrations)
- This is thought to contribute to dyslipidemia, vascular disease, liver degeneration and poor drug metabolism

Diabetes and Microcirculation

- Diabetic microangiopathy is probably the best known clinical expression of microvascular disease
- It comprises retinopathy, nephropathy and neuropathy
Chicken or Egg?

- As just mentioned, type 2 diabetes (T2D) causes microvascular disease
- But there is a growing school of thought that microvascular dysfunction is the fundamental CAUSE of insulin resistance
- Leading of course to T2D

Chicken or Egg?

“These data indicate that various estimates of microvascular dysfunction were associated with incident T2DM and, possibly, impaired fasting glucose, suggesting a role for the microcirculation in the pathogenesis of T2DM.”

The Indian Paradox

- The prevalence of T2D in India is relatively high and with poor glycemic control (average HbA$_{1C}$ 9.2%)

- Yet eye complications (such as retinopathy) are only 16.6%\(^1\)

- Compared to Europe, Japan, the US and Australia at around 30%\(^2\)

The Indian Paradox

- Could it be the many spices in their diet, especially Turmeric, Cayenne and Ginger, that support microcirculatory health?

- The physiomedicalists described Ginger as a ‘diffusive stimulant’ directly pointing to its effect on microcirculation
Gotu Kola and Microcirculation

- Two controlled trials have investigated the activity of Gotu Kola actives (triterpenoids) in patients with microvascular damage due to diabetes.

- The largest trial involved 100 patients with or without neuropathy, and compared the extract with placebo over 12 months and also 40 healthy controls\(^1\)

- It was significantly more effective at improving microcirculatory measures and edema

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Gotu Kola and Microcirculation

- A trial in 50 patients compared Gotu Kola actives to placebo or no treatment for 6 months
- Significant improvements in measures linked to microscopic vascular damage, including capillary permeability

Ginkgo and Microcirculation

- A single dose of standardised Ginkgo extract (112.5 mg) resulted in a significant increase in blood flow in nail capillaries in healthy volunteers\(^1\)
- Another study demonstrated increased blood flow to the forearms of volunteers\(^2\)
- This confirms the ability of Ginkgo to enhance microcirculatory flow

Grape Seed and Microcirculation

- Numerous clinical trials using doses of between 100 and 150 mg/day of OPCs from Grape Seed have demonstrated a beneficial effect on capillary resistance and capillary permeability.

- For example, 100 mg/day of OPCs was administered to elderly patients with capillary fragility. Very good results were achieved in 67%, good in 17%, and moderate in 13%.

Garlic and Microcirculation

- Garlic (particularly as the fresh-crushed raw clove or as an allicin-releasing powder) is good for both the microcirculation and microcirculatory flow\(^1\)
- For example, in a controlled clinical trial a single 900 mg dose of Garlic powder significantly increased capillary skin perfusion by 55%

Garlic and Microcirculation

- Another study found that Garlic powder (600 mg/day) administered for 7 days increased calf blood flow by approximately 15%

Bilberry and Microcirculation

- In open trials, bilberry extract improved symptoms caused by decreased capillary resistance (microvascular bleeding, bruising and fecal occult blood)\(^1\)
- Reduced the microcirculatory changes induced by cortisone therapy in patients with asthma and chronic bronchitis\(^2\)
- Improved diabetic retinopathy with a marked reduction or even disappearance of hemorrhages\(^3\)

1 Piovella C, Curri BS, Piovella M et al. *Therapia Angiol* 1979; **35**: 119
2 Carmignani G. *Lotta Contro La Tubercle Malattie Polm Soc* 1983; **53**: 732
3 Orsucci PL, Rossi M, Sabbatini G et al. *Clin Ocul* 1983; **4**: 377
Beets and Microcirculation

- Beets are one of the richest sources of nitrate.
- It is now realised that a specific pathway in the body can make nitric oxide from dietary nitrate; the nitrate-nitrite-nitric oxide pathway.
- This has profound implications for microcirculatory and endothelial health, and for regulating blood pressure.

Morgan M. Beet, Greens & Herbs for Health & Vitality. *Nutritional Perspective* 2013; 38: 1-7
Cocoa is Healthy!

- There are several studies suggestive of cocoa’s positive effect on the microcirculation and endothelium.
- In a clinical trial, the impairment of endothelial function caused by a glucose challenge was reduced by dark chocolate, but not white chocolate\(^1\)
- Dark chocolate reduced endothelial dysfunction in breath-hold divers\(^2\)

1 Grassi D, Desideri G, Necozione S et al. *Hypertension* 2012; 60(3): 827-832
Green Tea and Endothelial Health

- Green Tea (2 weeks) improved forearm endothelial dysfunction in smokers\(^1\)
- Significant increase in plasma nitric oxide\(^1\)
- Green Tea (4 weeks) improved flow mediated dilatation (from 5.7 ± 2.7% to 8.7 ± 3.5%) in patients with chronic kidney disease\(^2\)

The 5-Point Dietary Plan

1. Boost dietary nitrate: green leafy vegetables, but especially beets as juice or a supplement
2. Increase cocoa intake: 85% chocolate, 20 g/day or 2/3 oz
3. Increase berry anthocyanin intake: 2 to 3 oz/day of blueberries, strawberries, raspberries and blackberries
4. Raw crushed Garlic: ½ to 1 clove/day
5. Increase herbs and spices: especially Green Tea (3 to 4 cups/day), Turmeric and Ginger
Disc Injury

- The 5-Point Dietary Plan
- Gotu Kola Complex
- St John’s Wort if there is nerve entrapment
Retinopathy

- The 5-Point Dietary Plan
- Bilberry 6000mg
- Gotu Kola Complex
Erectile Dysfunction

- The 5-Point Dietary Plan
- Korean Ginseng
- Tribulus Forte
- Ginkgo
  or
- Gotu Kola Complex
Chronic Venous Insufficiency

- The 5-Point Dietary Plan
- Horsechestnut Complex
- In extreme cases and with ulceration:
  - Echinacea Premium
  and
- Gotu Kola Complex
Thank You