

Restricted microvascular blood flow in skeletal muscle after an oral glucose challenge in healthy humans

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Increased plasma insulin levels during a euglycaemic hyperinsulinaemic clamp (Clerk *et al.*, 2006) or with a mixed meal (carbohydrate, protein and fat) (Vincent *et al.*, 2006) stimulates an increase in microvascular perfusion in skeletal muscle. This microvascular insulin action augments skeletal muscle glucose disposal by increasing the delivery of insulin and glucose to the myocyte. This action is markedly impaired in insulin resistance (Clerk *et al.*, 2006; Keske *et al.*, 2009). The aim of the current study is to determine whether the clinically used oral glucose challenge (OGC) is able to elicit equivalent increases in microvascular perfusion in skeletal muscle as we have previously shown using mixed meal or insulin clamp. Overnight fasted healthy volunteers (49 ± 5 yr, 1F, 7M; mean ± SEM) without a first or second degree relative with type 2 diabetes, underwent an OGC (50g glucose x 1h). Participants had normal: BMI (21.37 ± 2.6), blood glucose (4.7 ± 0.1 mM), plasma insulin (3.6 ± 0.7 mU/L), HbA1c (5.4 ± 0.1 %), total cholesterol (4.8 ± 0.3 mM), LDL (3.1 ± 0.3 mM, calculated using the Friedewald Formula), HDL (1.4 ± 0.1 mM) and triglyceride (0.8 ± 0.2 mM) levels. Following the OGC, circulating glucose increased 1.7-fold

	Baseline	1h OGC
Blood glucose (mM)	4.7 ± 0.1	8.1 ± 0.4†
Brachial artery diameter (mm)	4.05 ± 0.15	4.17 ± 0.18
Brachial artery blood flow (ml/min)	57.3 ± 5.1	115.0 ± 26.0*
Microvascular blood volume (AI)	1.19 ± 0.26	0.94 ± 0.10
Microvascular blood flow (AI/s)	0.14 ± 0.03	0.10 ± 0.02*
Large artery stiffness (cm/s)	7.18 ± 0.48	7.14 ± 0.46
Central systolic blood pressure (mmHg)	116.2 ± 4.8	113.1 ± 4.1 [#]
Central diastolic blood pressure (mmHg)	79.8 ± 2.9	77.3 ± 2.6*

Brachial artery blood flow (assessed by 2D Doppler ultrasound) increased 2-fold following the OGC (Table). Contrary to expectation, forearm skeletal muscle microvascular blood flow (assessed by contrast-enhanced ultrasound) decreased following the OGC (Table). Central blood pressure (assessed by Mobile-O-Graph) decreased modestly following the glucose load, while large artery stiffness was unaffected. Thus, an OGC in healthy people induces large artery vasodilation, while impairing microvascular blood flow in skeletal muscle. We conclude that impaired microvascular function following an OGC leads to decreased insulin and glucose delivery to myocytes, and may underestimate muscle insulin sensitivity in healthy people.

Clerk LH, Vincent MA, Jahn LA, Liu Z, Lindner JR, Barrett EJ. (2006). Obesity blunts insulin-mediated microvascular recruitment in human forearm muscle. *Diabetes* **55**, 1436-42.

Vincent MA, Clerk LH, Lindner JR, Price WJ, Jahn LA, Leong-Poi H, Barrett EJ. Vincent *et al.* (2006). Mixed meal and light exercise each recruit muscle capillaries in healthy humans. *Am J Physiol Endocrinol Metab* **290**, E1191-7.

Keske MA, Clerk LH, Price WJ, Jahn LA, Barrett EJ. (2009). Obesity blunts microvascular recruitment in human forearm muscle after a mixed meal. *Diabetes Care* **32**, 1672-7.