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## CARDIOVASCULAR FLASHLIGHT

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# Rosiglitazone reduces ischaemia-reperfusion injury in patients with the metabolic syndrome

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In animals, thiazolidinediones reduce ischaemia-reperfusion injury. A clinical meta-analysis raised suspicion that rosiglitazone increases the incidence of myocardial infarction (Nissen *et al.*, *N Engl J Med* 2007;356:2457–2471). However, human data on a possible benefit on infarct size (i.e. ischaemia-reperfusion injury) are not available. Therefore, we investigated the effect of rosiglitazone on ischaemia-reperfusion injury in 10 insulin resistant participants without hyperglycaemia. We used a thoroughly validated human *in vivo* model to quantify ischaemia-reperfusion injury in skeletal muscle by annexin-A5-scintigraphy (Rongen *et al.*, *Circulation* 2005;111:173–178). At the end of each treatment period (rosiglitazone 4 mg b.d. vs. placebo), the participants were subjected to 10 min of forearm ischaemia, combined with standardized intermittent handgripping. At reperfusion, 500 MBq <sup>99m</sup>Tc-annexin-A5 was administered intravenously. Annexin-uptake (counts per pixel) was measured in thenar muscle 1 h post-reperfusion using a gamma camera. Ischaemia-reperfusion injury was quantified as the percentage difference in uptake between experimental and control side (annexin-targeting). Rosiglitazone reduced annexin-targeting from 8.4% (median; range 0.6–49%) to 4.7% (0.7–20%) ( $P = 0.037$ ). We present the first human *in vivo* data on the beneficial effects of rosiglitazone on ischaemia-reperfusion injury. This observation puts the disputed elevation in myocardial ischaemic events during rosiglitazone treatment in perspective.

Panel A. Study design.

Panel B. Individual plots of the effects of rosiglitazone on <sup>99m</sup>Tc-annexin-targeting in insulin resistant subjects.

Panel C. Typical <sup>99m</sup>Tc-annexin-uptake one hour after reperfusion at the end of the placebo period. Left: control hand; right: post-ischaemic hand. Counts increase from blue to yellow.

Panel D. Same patient, but at the end of the rosiglitazone treatment period.

