

**A49**

**Nitrate tolerance-induced deterioration of the ischemic adaptability of the heart**

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**Introduction:** We tested whether postconditioning limited infarct size in rabbits with haemodynamic nitrate tolerance.

**Methods:** Male rabbits made tolerant to the hypotensive response to 30 µg/kg intravenous nitroglycerin (NG) by a preceding one-week exposure to transdermal NG (0.07 mg/kg/h) were subjected to 35 min coronary occlusion (test ischemia) followed by 3 h of reperfusion with the following additional interventions: no intervention (NI); postconditioning pacing (PPC): five cycles of 5 min periods of rapid ventricular pacing (500 b.p.m.), or postconditioning coronary occlusion (PCO): five cycles of 5 min coronary occlusion with 10 min inter pacing/interocclusion intervals, applied after the end of the test ischemia. These protocols were applied in both nitrate-tolerant and non-tolerant animals. Infarct size expressed as a percentage of area at risk (I/R) was determined by triphenyltetrazolium chloride staining, left ventricular cyclic nucleotides were determined by radioimmunoassay from samples out of the area at risk, 75 min after the test ischemia.

**Results:** In non-tolerant animals both PPC and PCO reduced the I/R compared to the NI group. When animals had been made nitrate-tolerant, the I/R was significantly higher in the NI group compared with non-tolerant animals and the beneficial effect of the PPC or PCO on the I/R disappeared.

**Conclusions:** We conclude that (i) nitrate tolerance blocks postconditioning induced by either PPC or PCO, (ii) PPC is more effective post-conditioning challenge than PCO, and (iii) nitrate tolerance per se reduces the capability of the heart to tolerate an ischemic insult.