

Abnormal Vasomotor Function of Porcine Coronary Arteries Distal to Sirolimus-Eluting Stents

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Objectives: To determine vasomotor functional responses of conduit coronary artery distal to bare-metal (BMS), polymer-only (POLY), and sirolimus-eluting (SES) stents, in a clinically relevant animal model.

Background: Drug-eluting stents (DES) reduce in-stent restenosis, and also affect neointima formation and vascular remodeling in downstream coronary segments. Whether distal artery vasomotor function is also influenced by DES has not been determined.

Methods: Pigs (n=12) received coronary stent implant and hearts were harvested at one month. Arterial segments ≥ 15 mm distal to stents were excised and studied in an organ-chamber apparatus. Endothelium-dependent and -independent relaxation and contraction to classical agonists were measured. **Results:** SES showed increased lumen area and reduced neointima; abnormal vasomotor function of conduit arteries distal to SES was also observed.

Contraction to endothelin-1 was significantly enhanced for SES compared to both BMS and POLY. Endothelium-dependent relaxation to a maximal dose of substance P was attenuated for SES compared to both BMS and POLY ($46 \pm 6\%$ vs. $71 \pm 3\%$ and $78 \pm 3\%$, respectively, $P < 0.001$). Endothelium-independent relaxation to sodium nitroprusside was potentiated for SES, compared to BMS and POLY ($100 \pm 5\%$ vs. $69 \pm 7\%$ and $77 \pm 5\%$, respectively, $P = 0.02$).

Conclusions: Stent-based local delivery of sirolimus profoundly inhibited neointima formation but caused vasomotor dysfunction in distal conduit vessel segments. These observations suggest that distal coronary vasospasm may be more readily evoked in the presence of DES and contribute to pathophysiological sequelae.