Suppression of Coronary Artery Stent Inflammation by Colchicine Decreases Stent Restenosis, as Assessed by Serial in vivo Optical Molecular-structural Imaging

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Background: Restenosis of coronary stents causes substantial morbidity. Inflammation drives restenosis by activating smooth muscle cells to form obstructive neointima. Recent data suggests that colchicine, an anti-proliferative and anti-inflammatory agent, may reduce clinical stent restenosis. Here we assessed the effects of colchicine on in vivo stent-induced inflammatory protease activity and subsequent restenosis using serial intravascular molecular-structural near-infrared fluorescence (NIRF)-optical coherence tomography (OCT) imaging.

Methods: Rabbits implanted with clinical-grade bare-metal stents (3.5x12 mm) received oral colchicine 0.6 mg or placebo daily (N=5 rabbits, 15 stents per group) and were imaged at 2 and 6 weeks with intravascular NIRF-OCT 24 hours following ProSense VM110 (4 mg/kg IV; ex/em 750/780 nm) for molecular NIRF imaging of cathepsin protease inflammatory activity. Neointimal formation was measured every 400 μm by coregistered structural OCT. Stents were analyzed by ex vivo fluorescence microscopy, histology, and cathepsin mRNA expression.

Results: In controls, NIRF inflammation at 2 weeks was significantly enhanced at the stent edges (edge 32.6±7.3 vs. mid 20.1±2.6 nM; p<0.0001) and corresponded to greater stent edge ΔOCT neointimal growth between 2 and 6 weeks (edge 0.61±0.25 vs. mid 0.33±0.13 mm2; p<0.01), providing strong prediction of early NIRF inflammation for subsequent restenosis by OCT (r=0.72; p=0.001). Colchicine significantly decreased 2-week NIRF inflammation (stent TBR: control 2.42±0.10 vs. colchicine 1.69±0.11; p<0.0001), and neutralized the stent edge 6-week neointimal increase observed in controls (colchicine ΔOCT edge 0.05±0.05 vs. mid 0.02±0.03 mm2; p=0.21). Ex vivo analyses corroborated the in vivo results.

Conclusion: We demonstrate that in vivo NIRF inflammatory protease activity predicts stent locations that develop greater restenosis, and that colchicine, an FDA-approved agent, decreases stent-induced inflammation and subsequent restenosis in vivo. Intravascular NIRF-OCT is a novel translatable approach to predict site-specific coronary stent restenosis based on the local inflammatory profile and monitor the effects of anti-restenosis therapeutics.

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