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Abstract: Inflammation drives atherosclerosis complications and is a promising therapeutic target for plaque stabilization. At present, it is unknown whether local stenting approaches can stabilize plaque inflammation in vivo. Here, we investigate whether everolimus-eluting stents (EES) can locally suppress plaque inflammatory protease activity in vivo using intravascular near-infrared fluorescence (NIRF) molecular imaging. Balloon-injured, hyperlipidaemic rabbits with atherosclerosis received non-overlapping EES and bare metal stents (BMS) placement into the infrarenal aorta (n = 7 EES, n = 7 BMS, 3.5 mm diameter x 12 mm length). Four weeks later, rabbits received an injection of the cysteine protease-activatable NIRF imaging agent Prosense VM110. Twenty-four hours later, co-registered intravascular 2D NIRF, X-ray angiography and intravascular ultrasound imaging were performed. In vivo EES-stented plaques contained substantially reduced NIRF inflammatory protease activity compared with untreated plaques and BMS-stented plaques (P = 0.006). Ex vivo macroscopic NIRF imaging of plaque protease activity corroborated the in vivo results (P = 0.003). Histopathology analyses
revealed that EES-treated plaques showed reduced neointimal and medial arterial macrophage and cathepsin B expression compared with unstented and BMS-treated plaques. EES-stenting stabilizes plaque inflammation as assessed by translational intravascular NIRF molecular imaging in vivo. These data further support that EES may provide a local approach for stabilizing inflamed plaques.

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