Multiparametric molecular imaging provides mechanistic insights into sympathetic innervation impairment in the viable infarct border zone.

Abstract: Impaired catecholamine handling in the viable infarct border zone may play an important role in ventricular remodeling and lethal arrhythmia. We sought to get further biologic insights into cardiac sympathetic neuronal pathology after myocardial infarction, using multiple tomographic imaging techniques. In a porcine model of myocardial infarction (n = 13), PET and MR imaging were performed after 4-6 wk and integrated with electrophysiologic testing and postmortem histology. PET with the physiologic neurotransmitter (11)C-epinephrine, which is sensitive to metabolic degradation unless it is stored and protected in neuronal vesicles, identified a defect exceeding the perfusion defect (defined by (13)N-ammonia; defect size in all animals, 42 ± 12 vs. 35% ± 12% of left ventricle, P< 0.001). In a subgroup of 7 animals, defect of the metabolically resistant catecholamine (11)C-hydroxyephedrine was smaller than epinephrine (41 ± 8 vs. 47% ± 6% of left ventricle, P = 0.004), whereas defect of a third catecholamine, (11)C-phenylephrine, which is sensitive to metabolic degradation, was similar to epinephrine (48 ± 6 vs. 47% ± 6%, P = 0.011 vs. perfusion defect). Histology confirmed the presence of nerve fibers in the infarct border zone. Tagged MR imaging identified impaired peak
circumferential wall strain and wall thickening in myocardial segments with epinephrine/perfusion mismatch (n = 6). Confirmatory of prior work, inducible ventricular tachycardia was associated with a larger epinephrine/perfusion mismatch (n = 11). In the viable infarct border zone, neuronal vesicular catecholamine storage and protection from metabolic degradation are more severely altered than catecholamine uptake. This alteration may reflect an intermediate state between normal innervation and complete denervation in advanced disease.