**PROTEASE-ACTIVATED RECEPTOR-2 RELAXATION OF RAT AORTAS VASODILATION IN METABOLIC SYNDROME**

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Metabolic syndrome describes the clinical condition of an individual that presents a number of cardiovascular disease risk factors, including obesity, hyperlipidemia, insulin-resistance and hypertension. Low-grade systemic inflammation is also recognized as part of metabolic syndrome. In various tissues, local cellular release of proteases like trypsin, mast cell beta-tryptase, kallikrein, and coagulation factors VIIa and Xa, can activate PAR2 (protease-activated receptor-2) to regulate production of mediators of inflammation and/or cause vasodilation. Using SHRSP.Z-Leprfa/IzmDmcr rats (SHRSP.ZF) with metabolic syndrome, we demonstrated that PAR2-mediated nitric oxide (NO)-dependent vasodilation is sustained until 20 weeks of age (wks), but attenuated at 30 wks in aortas from SHRSP.ZF. In the current study, we examined age-related changes in the mechanism of PAR2-mediated relaxation of aortic vascular smooth muscle. Specifically, we measured protein and mRNA expression of PAR2, endothelial NO synthase (eNOS), and soluble guanylyl cyclase, PAR2 agonist-induced cGMP accumulation and aortic ring relaxations in tissues from SHRSP.ZF at 10, 20, and 30 wks. We found PAR2 mRNA and protein expression were similar in aortas of rats at 10 and 20 wks, but were less at 30 wks. eNOS content was similar in aortas of rats at all ages. In contrast, soluble guanylyl cyclase protein content in aortas of rats at 20 and 30 wks were less than in rat aortas at 10 wks. cGMP accumulation induced by PAR2-activating peptide, 2-furoyl-LIGRLO-amide, was similar in aortas of rats at 10 and 20 wks, but less in rat aortas at 30 wks. Aortic ring relaxations in response to cGMP-analog were impaired in rats at 30 wks. These results suggest that attenuation of relaxation pathway via PAR2 activation on endothelial cells, accompanying with reduced response to NO in smooth muscle cells, is involved in the impairment of PAR2-mediated vasodilation with ageing in SHRSP.ZF.