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THE ROLE OF VASCULAR PEROXIDE 1 IN SPONTANEOUSLY HYPERTENSIVE RAT LEFT VENTRICULAR REMODELLING

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Objectives To test the role of vascular peroxide 1 (VPO1), a newly identified hame-containing peroxidase in left ventricular remodelling in spontaneously hypertensive rats.

Methods Twelve 24-week-old male spontaneously hypertensive rats (SHR) served as SHR group, and 12 age and sex matched Wistar Kyoto rats (WKY) were selected as control group. Systolic blood pressure was measured before experiment. After performing echocardiography analysis, hearts were isolated. Pathological changes of myocardial tissue were measured by HE staining, myocardial collagen was measured by Masson staining, and the expression of VPO1, MMP-2, MMP-9 and TIMP-2 was detected by immunohistochemistry and western blot. Rat heart-derived H9c2 cells were treated with angiotensin II, the cell surface area and the mRNA level of atrial natriuretic peptide, brain natriuretic peptide were measured. Expression of VPO1, MMP-2 and gelatinolytic activity of pro-MMP-2 and the concentration of HOCl was measured. The effect of VPO1 RNA interference on cardiomyocytes hypertrophy, HOCl generation, pro-MMP-2 activity and MMP-2 expression were observed. Furthermore, the direct effects of HOCl on pro-MMP-2 activity and MMP-2 expression were also examined.

Results Blood pressure in SHR was significantly higher compared with WKY, increased concentric left ventricular hypertrophy, myocardial cells hypertrophy while the expressions of VPO1, MMP-2, and TIMP-2 protein were significantly up-regulated were found in SHR. In cultured cells, treatment with angiotensin II significantly induced hypertrophy and increased the gelatinolytic activity of pro-MMP-2 and MMP-2 expression while unregulated VPO1 expression and HOCl production. Silencing VPO1 expression significantly suppressed angiotensin II-induced hypertrophy and increased MMP-2 activity concomitantly with decreased HOCl production. Moreover, treatment with HOCl also markedly increased the gelatinolytic activity of pro-MMP-2 and MMP-2 expression.

Conclusions VPO1 participating in the extracellular matrix remodelling by activate MMP-2 via HOCl formation, and therefore play an important role in development of left ventricular remodelling.