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Effects of angiotensin II intervention on MMP-2, MMP-9, TIMP-1, and collagen expression in rats with pulmonary hypertension

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ABSTRACT. This study investigated the effects of angiotensin II (AngII) intervention, using captopril and losartan, on the expression of matrix metalloproteinase-2 (MMP-2), MMP-9, tissue inhibitor of metalloproteinase-1 (TIMP-1), and collagen in rats with pulmonary hypertension, in an effort to understand mechanisms underlying pulmonary vascular remodeling. A total of 40 male Sprague-Dawley rats were randomly divided into normal group, model group, captopril group, and losartan group. After 5 weeks, the mean pulmonary arterial pressure (mPAP), right ventricular index, and neointima formation in each group were determined. Immunohistochemical analysis was performed to determine the degree of pulmonary arterial muscularization as well as MMP-2, MMP-9, and TIMP-1 protein expression in lung tissue. Real-time fluorescent quantitative PCR was

used to detect *MMP2*, *MMP9*, *TIMP1*, *COL1A1*, and *COL4A1* mRNA expression. Picro-sirius red staining was performed to detect collagen protein expression. Neointima formation was observed in the model group. Moreover, the mPAP, right ventricular index, degree of arterial muscularization, and collagen deposition, as well as mRNA and protein expression of *MMP2*, *MMP9*, and *TIMP1* were significantly higher than those in the other groups ($P < 0.05$). The mPAP, right ventricular index, degree of arterial muscularization, and mRNA and protein expression in the captopril and losartan groups were significantly decreased compared with those of the model group ($P < 0.05$). AngII regulates MMP-2, MMP-9, and TIMP-1 expression and affects collagen deposition. Thus, this hormone is involved in pulmonary vascular remodeling, indicating a possible mechanism that can be targeted in pulmonary hypertension intervention.

Key words: AngII; MMP-2; MMP-9; Pulmonary hypertension; TIMP-1

