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**QILIQIANGXIN INHIBITS THE DEVELOPMENT OF CARDIAC HYPERTROPHY, REMODELLING, AND DYSFUNCTION DURING 4 WEEKS OF PRESSURE OVERLOAD IN MICE**

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**Objectives** Qiliqiangxin (QL), a traditional Chinese medicine, has been used in the treatment of chronic heart failure. However, whether QL can benefit cardiac remodelling in the hypertensive state is unknown. We here examined the effects of QL on the development of cardiac hypertrophy through comparing those of losartan in C57BL/6 mice underlying transverse aorta constriction for 4 weeks.

**Methods** QL and losartan were administrated at 0.6 mg and 13.4 mg kg<sup>-1</sup>, respectively. Cardiac hypertrophy, function, and remodelling were evaluated by echocardiography, catheterisation, histology, and examination of specific gene expression and ERK phosphorylation. Cardiac apoptosis, autophagy, tumour necrosis factor  $\alpha$ /insulin-like growth factor-1, and angiotensin II type 1 receptor expression and especially the proliferation of cardiomyocytes and phosphorylation of ErbB receptors were examined in vivo to elucidate the mechanisms.

**Results** Transverse aorta constriction for 2 weeks resulted in a significant cardiac hypertrophy, which was significantly suppressed by either QL or losartan treatment. At 4 weeks after transverse aorta constriction, although the development of cardiac dysfunction and remodelling and the increases in apoptosis, autophagy, tumour necrosis factor  $\alpha$ /insulin-like growth factor-1, and angiotensin II type 1 receptor expression were abrogated comparably between QL and losartan treatments, QL, but not losartan, enhanced proliferation of cardiomyocytes, which was paralleled with downregulation of CCAAT/enhancer-binding protein  $\beta$ , upregulation of CBP/p300-interacting transactivator with ED-rich carboxy-terminal domain 4, and increases in ErbB2 and ErbB4 phosphorylation. Furthermore, inhibition of either ErbB2 or CBP/p300-interacting transactivator with ED-rich carboxy-terminal domain 4 abolished the cardiac protective effects of QL.

**Conclusions** QL inhibits myocardial inflammation and cardiomyocyte death and promotes cardiomyocyte proliferation, leading to an ameliorated cardiac remodelling and function in a mouse model of

pressure overload. The possible mechanisms may involve inhibition of angiotensin II type 1 receptor and activation of ErbB receptors.