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论著

基质金属蛋白酶及其组织型抑制剂活性及表达失衡与高血压性左心室重塑的关系

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摘要 目的： 探讨慢性压力负荷增高时，大鼠左心室（LV）基质金属蛋白酶（MMPs）/组织型基质金属蛋白酶抑制剂（TIMPs）失衡与LV重塑的关系。方法：40只6周龄雄性卒中易感性自发性高血压大鼠（SHR-SPs）作为研究对象，10只同周龄雄性Wistar-Kyoto（WKY）大鼠作为对照。6个月后，以Millar压力容积导管评价2组大鼠的在体LV血流动力学，并对2组大鼠的心脏进行组织病理学、明胶酶谱和免疫印迹法分析。结果：反映LV收缩与舒张功能的血流动力学参数在2组间有显著差异（P＜0.05）；SHR-SPs心脏胶原容积分数、血管周胶原面积/管腔面积、心肌横断面积、心室壁动脉中膜面积/管腔面积均增高（P＜0.05）；心肌MMP-2活性、蛋白含量及TIMP-1蛋白含量在SHR-SPs中明显增高（P＜0.05）。结论：慢性压力超负荷能够导致心脏细胞外基质代谢失调及MMPs/TIMPs系统失衡，继而产生心室腔扩张、LV收缩与舒张功能障碍。

关键词 高血压 细胞外基质 基质金属蛋白酶 金属蛋白酶类组织抑制剂

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Altered activity and expression of MMPs/TIMPs are associated with functional and structural left ventricular remodeling in hypertensive rats

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Abstract

<FONT face=Verdana>AIM: To investigate the relationship between matrix metalloproteinases and tissue inhibitors of matrix metalloproteases imbalance with functional and structural left ventricular (LV) remodeling in the hypertensive rats.
METHODS: 6-week-old male stroke-prone spontaneously hypertensive rats (SHR-SPs,n=40) served as the hypertensive heart disease model,and age-matched male Wistar-Kyoto (WKY) rats (n=10) were used as control.After 6 months,the rats in two groups were anesthetized for invasive hemodynamic measurement by Millar pressure-volume (P-V) conductance catheter.Then the rats were sacrificed and hearts were dissected for morphological analysis,gelatin-zymography and Western blotting analysis.
RESULTS: Left ventricular (LV) hemodynamic parameters showed the systolic and diastolic dysfunction in SHR-SPs compared with that in control group (P<0.05).Collagen volume fraction,ratio of perivascular collagen area to luminal area,myocardial cross-sectional area and the medial area to luminal area ratio of the SHR-SPs were all increased remarkably (P<0.05).LV matrix metalloproteinase-2 (MMP-2) activities,MMP-2 and tissue inhibitors of matrix metalloprotease-1 (TIMP-1) protein level in SHR-SP were notably higher than those in control group (P<0.05).
CONCLUSION: Chronic pressure-overload is capable of inducing imbalances of cardiac ECM and MMPs/TIMPs system,both imbalances induce LV dilation,cardiac systolic and diastolic dysfunction.</FONT>

Key words Hypertension Extracellular matrix Matrix metalloproteinases Tissue inhibitor of metalloproteinases

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