The effects of ischemia/reperfusion on matrix metalloproteinases in rat hearts

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Matrix metalloproteinases (MMPs) are a family of Zn^{2+} and Ca^{2+}-dependent endopeptidases involved in remodeling of extracellular matrix. MMP-2 has been also shown as a primary mediator of the acute mechanical dysfunction of the heart after ischemia/reperfusion (I/R). The aims of the study were to investigate the influence of I/R on MMP-2 and to study the effects of wortmannin (WT) and LY294,002 (LY), specific inhibitors of PI3K/Akt kinase pathway, on modulation of MMP-2 activities after ischemic preconditioning (IP, cycles of short I/R). In the study isolated Langendorff-perfused rat hearts subjected to protocols of test I/R and/or IP were used. WT or LY were infused before and during the reperfusion phases of IP. The levels and activation of proteins were determined by immunoblot assay. The MMP activities were measured by zymography. We found that ischemia induced activation of tissue pro-MMP-2 with maximum reached after 15 min of ischemia. During prolonged ischemia and the following reperfusion the activities of this form of MMP-2 declined. Short ischemia and reperfusion that led to increased cardiac tolerance against prolonged I/R reduced MMP-2 activities and induced also an activation of Akt kinase. The application of both WT and LY was connected with inhibition of IP-mediated Akt kinase activation and modulation of MMP-2 activities. Our results suggest that MMP-2 may be involved in the responses of rat hearts to ischemia and point to possible relationship between Akt kinase and modulation of MMP-2 activities in rat hearts.

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