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CALPAIN ACTIVATION CONTRIBUTES TO MYOCARDIAL APOPTOSIS INDUCED BY ISCHEMIA-REPERFUSION

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Background Calpain is a family of cytoplasmic cysteine proteases activated by calcium ions. The mechanistic link between apoptosis and activation of calpain remains unclear. Apoptotic mechanism has been implicated in myocardial ischemia-reperfusion (I/R) injury.

Aim The aim of this study was to investigate the role of calpain in adult cardiomyocyte apoptosis induced by I/R.

Methods Male wild type mice were randomly divided into control and PD150606 groups. Mice were subjected to myocardial ischemia by occlusion of the left anterior descending coronary artery for 45 min and reperfusion for 3 h (I/R). Terminal deoxynucleotidyl transferase d-UTP nick end labeling (TUNEL) staining was performed using an In Situ Cell Death Detection kit on paraffin heart sections (5 mm). Hoechst 33342 was used as a counter-stain. Adult mouse cardiomyocytes were isolated and cultured, then subjected to ischemia for 1 h, and reperfusion for 3 h. The survival of cardiomyocytes, activity of calpain and caspase-3, cytoplasmic DNA fragments and cytochrome c concentrations were determined. Results Compared to control, the numbers of TUNEL-positive nuclei were significantly increased in the peri-infarct area in I/R mice ($p < 0.05$). Compared to normal cultured cardiomyocytes, the survival of the cells significantly decreased, however the activation of calpain and caspase-3, and cytoplasmic DNA fragments and cytochrome c concentrations were significantly increased in simulated I/R ($p < 0.05$). These effects of I/R on cardiomyocytes were alleviated by calpain inhibitor PD150606 ($p < 0.05$).

Conclusion Calpain inhibitor PD150606 decreases myocardial apoptosis induced by I/R. Our data suggest that calpain activation may play a critical role in the development of myocardial I/R.