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Objectives Calpains have been implicated in myocardial ischaemia-reperfusion (I/R) injury. The mitochondrial permeability transition pore (mPTP) subsequently triggers apoptotic cell death during I/R. However, the mechanistic link among calpain activity, mPTP opening and apoptosis in myocardium during I/R remains to be elucidated.

Aim This aim of this study was to investigate whether the activation of calpain in I/R cardiomyocytes is associated with alterations in mPTP and subsequent apoptotic cell death.

Methods Primary cultured neonatal mouse cardiomyocytes were deprived of oxygen and glucose to simulate ischaemia, and restored oxygen and sugar supply to simulate reperfusion (simulated I/R injury). To determine the influence of calpain activity on mPTP and apoptosis, cells were pretreated with PD150606 (PD, a specific calpain inhibitor). Apoptosis in cardiomyocytes was determined by TUNEL-staining and caspase-3 activity analysis. To identify the activated calpain isoform implicated in myocardial I/R injury, the autolysis of the N-terminal domains of the catalytic subunit of m- and m-calpain in cardiomyocytes were detected by immunoblot analysis. mPTP opening in cardiomyocytes was assessed by using the calcein–cobalt method and mitochondrial membrane potential (Δym) by imaging cells loaded with JC-1.

Results Reperfusion following ischaemia, rather than ischaemia, led to the autolysis of the N-terminal domains of the catalytic subunit of m-calpain in cardiomyocytes. However, the autolysis of the N-terminal domains of the catalytic subunit of m-calpain in cardiomyocytes was not observed in the investigation. The percentage of TUNEL-positive cardiomyocytes and caspase-3 activity was significantly less in the PD (20.38%±2.23% and fold of changes, 1.43±0.13) compared with the untreated I/R (31.48% ±1.65% and fold of changes, 2.21±0.17) group. Moreover, pD pretreatment of cardiomyocytes dramatically suppressed the opening of mPTP and the loss of Δym caused by I/R.

Conclusions Myocardial I/R can lead to the activation of m-calpain, which subsequently triggers apoptotic cell death by inducing mPTP opening.

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μ-CALPAIN MEDIATES MYOCARDIAL APOPTOSIS DURING ISCHAEMIA-REPERFUSION VIA MITOCHONDRIAL PERMEABILITY TRANSITION PORE OPENING

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