

## EFFECT OF CALPAIN INHIBITION ON MYOCARDIAL INFARCTION FOLLOWING LOCAL ISCHEMIA AND REPERFUSION

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This study was performed to test the protective effectiveness of a novel water-soluble and cell-permeable calpain inhibitor when administered before or after local ischemia. Isolated rabbit hearts were perfused in an open working Langendorff heart system. After a steady state period of 20 min, the ramus interventricularis was blocked for 60 min, and reperfused for 120 min. The calpain inhibitor A-705253 ( $K_i = 27 \pm 2.5$  nM) from Abbott/Ludwigshafen/Germany was added to the perfusion fluid: series (A) of experiments before the closure, series (B) after the reopening of the coronary vessel. Results: The area of necrosis/infarction was  $77.9 \pm 2.3\%$  of the area at risk in controls without calpain inhibition in series A ( $n=12$ ), respectively  $72.7 \pm 4.0\%$  in series B ( $n=8$ ). Preischemic administration of A-705253 ( $n=8$ ) reduced the area of infarction most effectively ( $p<0.001$ ) to  $49.3 \pm 3.9\%$  ( $n=8$ ) with an inhibitor concentration of  $10^{-8}$  mol/l. Even with postischemic inhibitor application ( $n=8$ ) area of infarction could be reduced significantly ( $p<0.01$ ) to  $48.3 \pm 2.3\%$ . The experiments imply a major role of calpains in myocardial ischemia and reperfusion injury.

Key words : Ischemia, Reperfusion, Calpain