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**THE COMBINATION THERAPY OF CILOSTAZOL AND ISCHEMIC POSTCONDITIONING PROTECTS AGAINST ISCHEMIA-REPERFUSION INJURY IN NON-DIABETIC AND DIABETIC RAT HEARTS WITH LONG-TERM ATORVASTATIN TREATMENT**

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**Objective** This study aims to investigate if the combination therapy of cilostazol and ischemic postconditioning (Ipost) could protect the non-diabetic and diabetic rat hearts against reperfusion injury after long-term atorvastatin treatment.

**Methods** Non-diabetic and diabetic rats were randomly assigned to six groups: (1) nonconditioning, (2) Ipost, (3) atorvastatin (2 mg/kg/day for 2 weeks), (4) atorvastatin and Ipost, (5) atorvastatin and cilostazol (20 mg/kg cilostazol once before reperfusion), (6) atorvastatin, cilostazol, and Ipost. Infarct size, haemodynamics and expression of Akt and eNOS were examined.

**Results** Long-term atorvastatin treatment without or with Ipost didn't decrease reperfusion injury in non-diabetic and diabetic rat hearts. However, the cardioprotective effects were shown in the group of statin, cilostazol and Ipost ( $25.0 \pm 4.9\%$  and  $31.1 \pm 5.5\%$  in non-diabetic and diabetic hearts), but not in the group of statin and cilostazol ( $44.8 \pm 4.76\%$  and  $57.7 \pm 5.2\%$ ). Western blot results revealed that Akt and eNOS phosphorylation were detected in the combination treatment of cilostazol and Ipost after long-term statin treatment.

**Conclusions** The combination therapy of cilostazol and Ipost could reduce reperfusion injury via increasing Akt and eNOS phosphorylation in statin-treated non-diabetic and diabetic hearts.