

# Extracorporeal Cardiac Shock Wave Therapy Markedly Ameliorates Ischemia-Induced Myocardial Dysfunction in Pigs in Vivo

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**Background**—Prognosis of ischemic cardiomyopathy still remains poor because of the lack of effective treatments. To develop a noninvasive therapy for the disorder, we examined the in vitro and vivo effects of extracorporeal shock wave (SW) that could enhance angiogenesis.

**Methods and Results**—SW treatment applied to cultured human umbilical vein endothelial cells significantly upregulated mRNA expression of vascular endothelial growth factor and its receptor Flt-1 in vitro. A porcine model of chronic myocardial ischemia was made by placing an ameroid constrictor at the proximal segment of the left circumflex coronary artery, which gradually induced a total occlusion of the artery with sustained myocardial dysfunction but without myocardial infarction in 4 weeks. Thereafter, extracorporeal SW therapy to the ischemic myocardial region (200 shots/spot for 9 spots at  $0.09 \text{ mJ/mm}^2$ ) was performed ( $n=8$ ), which induced a complete recovery of left ventricular ejection fraction ( $51 \pm 2\%$  to  $62 \pm 2\%$ ), wall thickening fraction ( $13 \pm 3\%$  to  $30 \pm 3\%$ ), and regional myocardial blood flow ( $1.0 \pm 0.2$  to  $1.4 \pm 0.3 \text{ mL} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$ ) of the ischemic region in 4 weeks (all  $P < 0.01$ ). By contrast, animals that did not receive the therapy ( $n=8$ ) had sustained myocardial dysfunction (left ventricular ejection fraction,  $48 \pm 3\%$  to  $48 \pm 1\%$ ; wall thickening fraction,  $13 \pm 2\%$  to  $9 \pm 2\%$ ) and regional myocardial blood flow ( $1.0 \pm 0.3$  to  $0.6 \pm 0.1 \text{ mL} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$ ). Neither arrhythmias nor other complications were observed during or after the treatment. SW treatment of the ischemic myocardium significantly upregulated vascular endothelial growth factor expression in vivo.

**Conclusions**—These results suggest that extracorporeal cardiac SW therapy is an effective and noninvasive therapeutic strategy for ischemic heart disease. (*Circulation*. 2004;110:3055-3061.)

**Key Words:** angiogenesis ■ contractility ■ hibernation ■ ischemia ■ regional blood flow

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