Results After cold stress treatment, ox-LDL, hs-CRP and IL-8 (all $p<0.05$ vs control group)were significantly increased; pronounced intimal thickening, plaque formation and angiogenesis in plaques increased significantly ($p<0.05$ vs control group); plaque lipid cores were greater and plaque fibrous caps were thinner; less collagen fibers while more macrophages were observed ($p<0.05$ vs control group); higher instability scores were obtained($p<0.05$ vs control group); the expression of endoplasmic reticulum stress markers GRP78, CHOP increased significantly ($p<0.05$vs control group). In vitro, we found that macrophages could be induced to transform into foam cells by ox-LDL in dose dependent way, while JNK inhibitor mitigated this effect ($p<0.05$ vs 100 mg/l group). ER stress marker protein GRP78 and CHOP increased markedly ($p<0.05$ vs 100 mg/l group). Inhibition of JNK phosphorlation resulted in decrease in level of apoptosis and caspase 3 ($p<0.05$ vs 100 mg/l group)

Conclusions The ER stress-JNK-mediated apoptosis in macrophages contributes to the instability of atherosclerotic plaques by cold stress.

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THE ENDOPLASMIC RETICULUM STRESS-JNK PATHWAY-MEDICATED APOPTOSIS IN MACROPHAGES CONTRIBUTES TO THE INSTABILITY OF ATHEROSCLEROTIC PLAQUES INDUCED BY COLD STRESS

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Objectives To elucidate whether and how the endoplasmic reticulum(ER) stress-JNK pathway in macrophages is involved in the instability of atherosclerotic plaques induced by cold stress.

Methods Forty male New Zealand white rabbits fed on high-fat diet for 2 weeks following by balloon injury of abdominal aorta were randomly divided into two groups: Cold-stress group and control group. Cold-stress group were exposed to cold (4°C) for 1 h per day for 20 weeks. The animals were sacrificed and then the pathological changes of atherosclerotic plaques were evaluated. Ultrasonography, contrast-enhanced ultrasonography and immunohistochemistry were used to evaluate IMT (intima-media thickness), angiogenesis and macrophage infiltration. Instability of plaque was evaluated with protocol designed instability score chart. Serum levels of blood lipid, ox-LDL, hs-CRP and IL-8 were determined by ELISA. GRP78 and CHOP expression were determined by western-blot. In vitro, macrophages were stimulated by different concentration (25 mg/l, 50 mg/l, 100 mg/l) of ox-LDL. And sp600125 was used to inhibit the phosphorylation of JNK. After 24 h, the intracellular lipid accumulation in macrophage was determined by Oil Red O staining. The indicator of endoplasmic reticulum stress GRP78, CHOP and JNK, p-JNK and Caspase-3 expression were determined by the western-blot analysis.