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**Title:** Protective effects of keratinocyte growth factor-2 on warm ischemia reperfusion lung injury in rats

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**Body:** Introduction: Ischemia reperfusion injury manifests as acute lung injury due to the injury of both the endothelium and epithelium. Keratinocyte growth factor-2 (KGF-2) was previously demonstrated to play an important role in the repair of alveolar epithelial damage. Recently, it was also reported to help maintain the barrier function of capillary monolayers. Objective: Investigate the potential effects of KGF-2 on ischemia reperfusion-induced lung injury and the related mechanisms. Methods: KGF-2 (2.5-10mg/kg) was administered intratracheally to rats 3 days before surgery. Then the left lung in rats was subjected to ischemia for 60 minutes and reperfusion for 180 minutes. Lung morphology, blood gas analysis, total cell number and protein concentration in the bronchoalveolar lavage fluid were measured. The protective effects of KGF-2 on endothelial cells and related mechanisms were evaluated in vitro. Results: Pre-treatment with KGF-2 effectively inhibited lung edema, inflammatory cell infiltration, protein exudation and the release of inflammatory cytokines.

In vitro study demonstrated that KGF-2 could inhibit endothelial cell apoptosis, enhance migration, and maintain the integrity of the blood-gas barrier. Phosphoinositide 3-kinase inhibitors can attenuate the protective effect of KGF-2 in endothelial cells. Conclusion: KGF-2 may serve as a candidate novel therapy in ischemia reperfusion induced lung injury.