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Oral Communication Abstract
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N-3-oxododecanoyl homoserine lactone induces receptor-interacting protein kinase 1-dependent apoptosis in synergy with lipopolysaccharide in endothelial cells

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Objectives: Endothelial dysfunction is associated with the initiation of sepsis-associated organ failure. Bacterial quorum-sensing molecules act as pathogen-associated molecular patterns; however, the effects of quorum-sensing molecules on endothelial cells remain less understood. This study investigated the molecular mechanisms of quorum sensing molecule-induced cell death and their interaction with lipopolysaccharide (LPS) in human umbilical vein endothelial cells.

Methods: Endothelial cells were treated with N-3-oxododecanoyl homoserine lactone (3OC12-HSL) and LPS derived from *Pseudomonas aeruginosa*.

Results: Treatment with 3OC12-HSL reduced cell viability in a dose-dependent manner, and co-treatment with 3OC12-HSL and LPS enhanced cell death. Terminal deoxynucleotidyl transferase deoxyuridine triphosphate nick end labeling assay revealed an increase in apoptotic cell death following 3OC12-HSL treatment; furthermore, co-treatment with 3OC12-HSL and LPS enhanced apoptosis. Western blotting revealed that treatment with 3OC12-HSL activated the receptor-interacting protein kinase 1 (RIPK1) pathway, leading to an increase in the levels of cleaved caspase 8 and 3. Moreover, co-treatment with 3OC12-HSL and LPS increased the levels of caspase 3 and 8. In addition, we found that treatment with necrostatin-1, an RIPK1 inhibitor, reduced cell death and ameliorated the activation of the RIPK1-dependent apoptotic pathway in 3OC12-HSL-treated cells.

Conclusions: 3OC12-HSL in synergy with LPS induced endothelial cell apoptosis via the activation of the RIPK1 pathway. Inhibition of RIPK1 may act as a therapeutic option for preserving endothelial cell integrity in patients with sepsis by disrupting the toxicity of quorum-sensing molecules.