Autophagy in sepsis:
Mechanisms, potential roles and therapeutic applications

Autophagy, an important host mechanism for removal of intracellular bacteria and pathogens, has recently emerged as an important mediator of programmed cell death pathways. An apparent conundrum is that autophagy acts both in cytoprotection and in cell death. The pro-survival function of autophagy has been demonstrated at the cellular and organ level in different contexts. In contrast, there is also evidence that over-stimulation of autophagy can lead to cell death possibly through activating apoptosis. The interplay between autophagic and apoptotic pathways has also emerged as a crucial decision-making process in determining the initiation of programmed cell death. In endotoxin administration, infection, or ischemia-reperfusion injury, autophagy has been generally suggested to be a cell-survival response that can limit cellular damage and cell death. However, the role of autophagy in sepsis is still not clearly defined. Based on currently available experimental data, deregulation of autophagy has been suggested to contribute to immune cell death, myocardial dysfunction, and lung injury during sepsis. The functional significance of autophagy by using pharmacological agents has also revealed that treatment with rapamycin (autophagy inducer) protected against immune cell death and cardiac dysfunction during sepsis, possibly through inhibition of apoptosis. Accordingly, autophagy may unveil novel therapeutic approaches for treating patients with sepsis or sepsis-related organ dysfunction.