Postinjury Inflammation and Organ Dysfunction

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KEYWORDS

• Organ dysfunction • Postinjury inflammation • SIRS • CARS • SARS • PICS

KEY POINTS

- The development of organ dysfunction (OD) is related to the intensity and balance between trauma-induced simultaneous, opposite inflammatory responses.
- Early proinflammation via innate immune system activation may cause early OD, whereas early antiinflammation, via inhibition of the adaptive immune system and apoptosis, may induce immunoparalysis, impaired healing, infections, and late OD.
- Patients discharged with low-level OD may develop the persistent inflammation-immunosuppression catabolism syndrome (PICS), which may cause an indolent death.
- The incidence of multiple organ failure (MOF) has decreased over time, but MOF remains morbid, lethal, and resource intensive. Single OD, especially acute lung injury, remains frequent.
- At this time, treatment of OD is limited, and prevention via adequate resuscitation, ventilation, and nutritional support remains the mainstay strategy.

HISTORICAL PERSPECTIVE: EVOLVING CONCEPTS ON THE PATHOGENESIS OF MULTIPLE ORGAN FAILURE

As advances in prehospital and acute hospital care conquered the so-called golden hour, multiple organ failure (MOF) emerged as the leading cause of late trauma death.[1–3] Eiseman and colleagues[4] coined the term MOF in 1977, with a clinical description of 42 patients with progressive organ dysfunction (OD). By the 1990s, Moore and colleagues[5]

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proposed that MOF was a bimodal phenomenon. In the 1-event model, a massive traumatic insult induces intense systemic inflammation response syndrome (SIRS) and precipitates OD. In the 2-event model, patients initially resuscitated into moderate SIRS become vulnerable to a second activating event (infections, embolism, transfusions, secondary operations, etc.) during the so-called compensatory antiinflammatory response syndrome (CARS) and could develop late MOF.

Modern hypotheses propose that injury triggers simultaneous, opposite responses: the proinflammation response (SIRS) and the antiinflammation response, previously misnamed compensatory (CARS) (**Fig. 1**).[6] OD is related to the intensity and the balance between these opposing trauma-induced inflammatory responses. Severe SIRS, a proinflammation via activation of the innate immune system, causes early OD, whereas early antiinflammation, via inhibition of the adaptive immune system and apoptosis, limits proinflammation and creates a preconditioned state to protect against second hits and hasten healing. When countering unbalanced proinflammation, persistent antiinflammation leads to the severe systemic antiinflammatory response syndrome (SARS; a more appropriate term than CARS), setting the stage for immunoparalysis, impaired healing, infections, and late OD.[6,7] This process was confirmed in a 2011 study by the Inflammation and Host Response to Injury Large-Scale Collaborative Research Program (Glue Grant) showing that alterations in the genomic expression of the classic inflammatory and antiinflammatory responses occurred simultaneously.[8]

As MOF began to recede as a result of aggressive prevention, a new OD phenotype emerged among patients discharged after lengthy intensive care unit (ICU) stays to long-term facilities, where they developed a persistent inflammation-immunosuppression catabolism syndrome (PICS).[7] Although the phenotypes and epidemiology of postinjury OD have changed considerably over the past 20 years, it remains morbid, lethal, and resource intensive, as described later.[9]

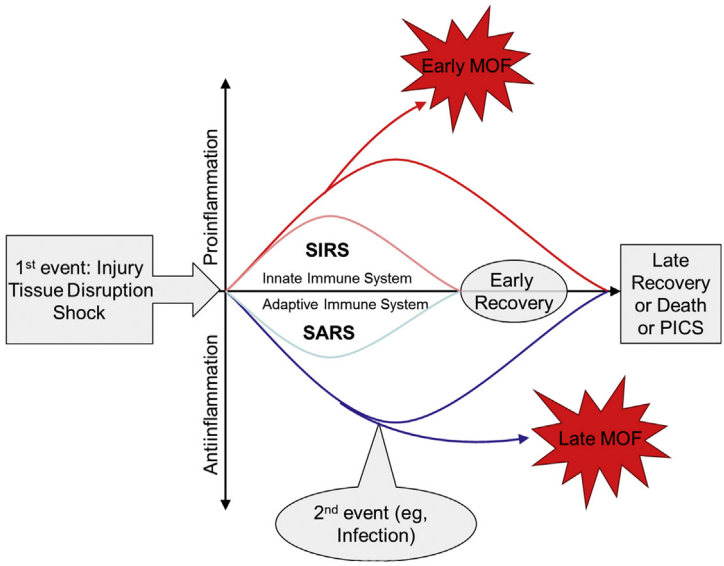

Fig. 1. Theoretic framework for postinjury MOF: The synchronous immunoinflammatory model. PICS, persistent inflammation-immunosuppression catabolism syndrome; SARS, systemic antiinflammatory response syndrome.