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## **SYSTEMIC INFLAMMATION AFTER MYOCARDIAL INFARCTION**

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## Editorial

SIRS, the systemic inflammatory response syndrome, is defined by the presence of 2 or more of the following criteria: Heart rate >90 beats/min, respiration rate >20 breaths/min, body temperature >38 or <36 °C or leukocyte count >12 or <4 x 10<sup>9</sup>/l (1). In this issue of Critical Care Medicine, van Diepen and colleagues analyzed the charts of 1843 patients with ST-elevation myocardial infarction (STEMI). They found, that SIRS was present on admission in 25.0% of the patients (2). In comparison to patients without SIRS, their risk for death, cardiogenic shock, heart failure or stroke during the following 90 days was substantially higher (21.6% vs 11.9%, p<0.001). Each additional SIRS criterion was statistically associated with an increased risk for adverse outcome, with heart rate being the strongest prognosticator of all 4 SIRS criteria. At 24 hours, 8.1% of STEMI patients fulfilled 2 or more SIRS criteria, and the frequency of adverse events was 21.7% compared to 10.1% (p<0.001) in patients without SIRS. Mortality was higher among patients with SIRS at either time-point. Thanks to this study, the SIRS criteria can now be used as easily available risk assessment tools in the clinical management of patients with myocardial infarction.

Clearly, SIRS parameters can develop in STEMI patients as a result of hemodynamic deterioration. A large myocardial infarction will impair cardiac output and cause cardiogenic shock. Heart and respiration rates will increase in order to compensate for low stroke volume and metabolic acidosis, respectively. These physiological alterations are triggered by the sympathetic autonomous nervous system, which is stimulated by hemodynamic compromise, chest pain and anxiety. Adrenergic hormones also facilitate the detachment of white blood cells from the endothelium, increasing the numbers of circulating neutrophils during acute stress.

Another cause for SIRS in STEMI patients is, of course, a concomitant infection. A retrospective analysis of the SHOCK trial revealed, that 13% of patients with myocardial infarction complicated by cardiogenic shock were suffering from a culture positive infection (3). The predominant pathogens were *Staphylococcus aureus*, *Klebsiella pneumonia* and *Pseudomonas aeruginosa*. Patients with infections had a lower systemic vascular resistance suggesting that sepsis-induced vasodilation contributes to the shock state. Patients with infections also required longer durations of mechanical ventilation and hospital stay. Invasive interventions such insertion of central venous catheters increased the risk of concomitant infections. Others have postulated bacterial translocation of the gut as a source for inflammation in patients with heart failure (4).

However, it is important to note that inflammation can be initiated without any underlying

infection. Inflammation in STEMI patients can be triggered by the release of damage associated molecular patterns (DAMPs) from the necrotic myocardium. DAMPs are intracellular structures and include, among others, high mobility group box group 1 (HMGB1) proteins, mitochondrial components and heat shock proteins (5). Such danger signaling molecules are probably also discharged from underperfused tissues during cardiogenic shock. Subsequently, DAMPs are recognized by cells of the innate immune system, which in turn activate an intracellular cascade and finally switch on genes encoding for cytokines such as interleukins (IL) and tumor necrosis factor (TNF) alpha (6). These inflammatory mediators are released into the circulation, promoting local and, at sufficient concentrations, systemic inflammation. While the goal of local inflammation is the repair of damaged cardiac and non-cardiac tissues, systemic inflammation alerts the jeopardized organism and deploys adaptive mechanisms.

Last but not least, clinicians should realize that inflammatory mediators such as TNF alpha, IL-6 and nitric oxide reversibly depress myocardial contractility (7-9), potentially leading to heart failure (10, 11). However, myocardial depression reduces cellular oxygen expenditure in a condition, in which myocardial oxygen supply is impaired, creating a new balance between cellular energy generation and consumption (12). Consequently, the cells at risk might survive in a viable, but non-contracting state (hibernating myocardium) (13). Hence, inflammation-induced myocardial depression can be viewed as an adaptive mechanism in patients with coronary artery disease and impaired myocardial perfusion. When coronary flow is re-established, the viable cells have the potential for full functional recovery.

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