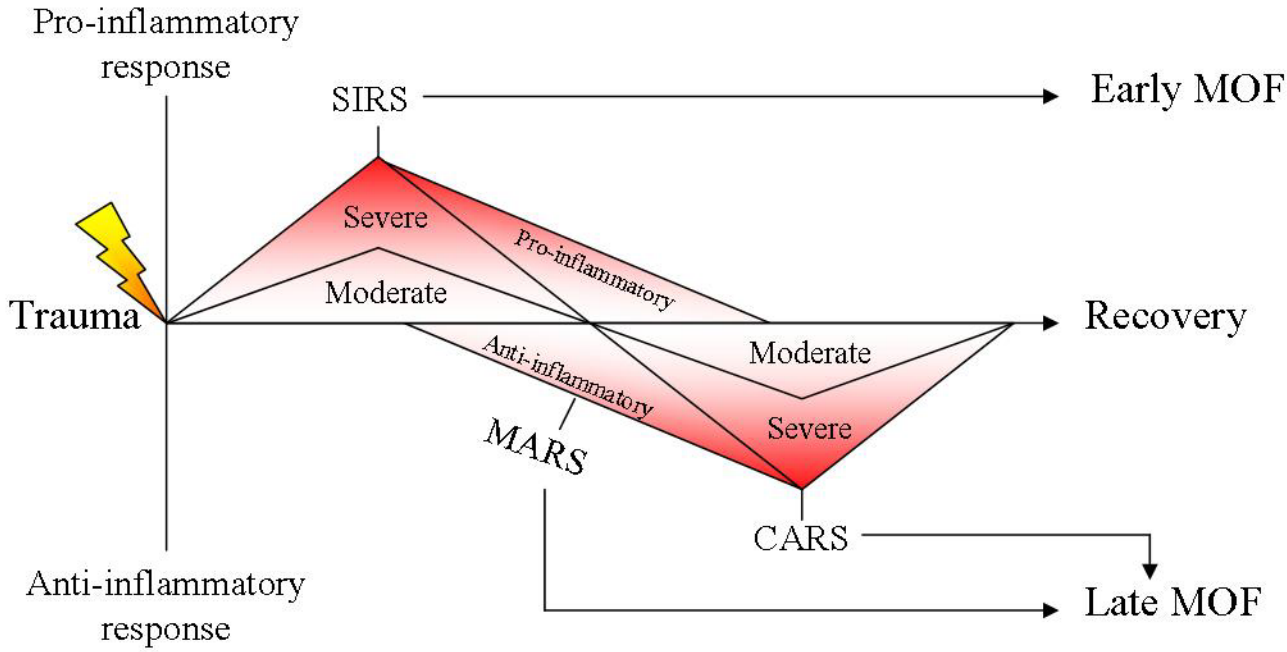

Figure 1

Biphasic model of organ failure. Depiction of the biphasic model of organ failure (MOF), originally coined by Moore[8]. The relative degree of immune activation is displayed on an arbitrary scale on the vertical axis. The horizontal axis indicates the time following trauma. When injury is sustained, a systemic pro-inflammatory response (SIRS) is evoked which can lead to the early version of MOF. At a later stage a compensatory anti-inflammatory response syndrome (CARS) or mixed antagonist response syndrome (MARS) can lead to immune paralysis and subsequently, the late form of organ failure.

Rolling

Rolling is regulated and controlled by selectins. These proteins undergo interactions with ligands on endothelial cells, which slow down the leukocytes at this surface [22]. E-selectin, which can bind carbohydrate molecules, is presented on endothelial cells and are involved in the initial contact between endothelial cells and leukocytes. Leukocytes express L-selectin on their surface and is important in secondary tattering, a process in which attached leukocytes provide adhesion for other leukocytes. As a result, leukocytes bind directly to each other and thus enhance the effect of the homing process [23]. L-selectin is shed after interaction with the endothelium and integrins take over to regulate the next step in the transmigration process. Some authors have reported a correlation between decreased L-selectin expression on leukocytes and the incidence of SIRS or early MOF, indicating to a relation between the degree of neutrophil activation and the development of complications occurring during the pro-inflammatory phase [24,25]. The shed molecules can be found as soluble factors in serum (sL-selectin). Consequently, the activation level of the neutrophil population is associated with the level of sL-selectin in the blood. Maximum sL-selectin levels in serum are found 6 hours after trauma, giving an indication on the time when the highest amount of neutrophils have lost their L-selectin to migrate to the tissue [26].

Adhesion

Integrins are involved in the adhesion of leukocytes to the endothelium. The integrin amβ2, or MAC-1 (CD11b/CD18) and the ligand ICAM-1 (intercellular adhesion molecule 1) form a high affinity stationary connection between leukocyte and endothelium. This is in contrast to the low affinity, reversible binding of selectins. Functional integrins are only expressed upon activation of the neutrophil and are necessary for an adequate transmigration process [27]. An increased expression of MAC-1 is found on neutrophils from patients who were admitted with an ISS > 16 as compared to traumapatients with an ISS < 16, indicating to activated neutrophils after injury [26]. Increased expression of MAC-1 is also found in experimental models and patients who received large amounts of blood products for resuscitation [28]. In contrast, during late organ failure a decreased expression of MAC-1 is found on neutrophils from patients who died from the consequences of sepsis as compared to patients who survived [29]. These results are congruent with the decreased