Systemic inflammatory responses in cardiac surgery

Stefan G. De Hert, MD, PhD
Department of Anesthesiology
Division of Cardiothoracic and Vascular Anesthesiology
Academic Medical Center
University of Amsterdam
Professor of Anesthesiology and Chair of the Division
Meibergdreef 9
1100DD Amsterdam
The Netherlands
Email: s.g.dehert@amc.uva.nl

Inflammation represents the response of the body to tissue injury and is in normal circumstances a controlled humoral and cellular response that will lead to wound healing and control of infection. In some instances this response may become exaggerated, ultimately leading to additional tissue injury and the development of organ dysfunction. Cardiac surgery may provoke such an inflammatory response with important clinical implications, in up to 20 % of the operated patients. Such a response may be activated by the extent of the surgical trauma, by hypothermia, blood loss and blood transfusion, and others. In the case of cardiac surgery additional factors such as contact activation, ischemia-reperfusion injury, and possibly endotoxemia may contribute to the development of a systemic inflammatory response. Key components in the development of such a response include activation of the complement system, the cytokine cascade, the coagulation – fibrinolytic cascade, and the neutrophil – endothelium interaction.

Deleterious effects of a systemic inflammatory response may occur at any organ level. Major cardiac events such as cardiac death, acute myocardial infarction, and heart failure appear to occur in up to 10 % of coronary surgery patients. Pulmonary complications such as acute lung injury occur in up to 3 % of the patients, while frequencies of up to 13 % for renal dysfunction and even up to 45 % for hepatic dysfunction have been reported.

Preoperative risk stratification may help to identify patients, susceptible to develop severe systemic inflammatory responses after cardiac surgery. Such factors include
preoperative morbidity such as cardiac failure and diabetes, the anticipated complexity of the surgery but also the presence of particular genotypes that appear to be associated with a higher risk of postoperative complications.

Perioperative hemodynamic instability may increase postoperative morbidity and mortality. There is strong clinical evidence that postoperative splanchnic hypoperfusion is associated with the development of complications at other organ levels such as acute respiratory distress syndrome. Gastric mucosal acidosis is indicative for inadequate oxygenation of the splanchnic tissue and seems to be rather common after cardiopulmonary bypass even in the absence of overt hemodynamic instability. It seems to be a highly sensitive predictor for complications which is independent of other clinical risk factors even in lower risk surgery. It seems therefore that maintaining hemodynamic stability and minimizing postoperative splanchnic ischemia may reduce postoperative complications.

The potential influence of anesthetic techniques is not yet clear. Locoregional techniques may reduce perioperative stress but it remains to be definitively determined whether such effects also improve patient outcomes. Many of the drugs used for anesthesia and analgesia have been shown to demonstrate immunomodulatory effects. Propofol has been shown to act as a radical oxygen species scavenger. In addition it alters the balance between pro- and anti-inflammatory cytokines in favor of the anti-inflammatory part, and it impairs several aspects of the white blood cell activation. Some of these effects are also observed with its solvent, intralipid, but other seem to be directly related to propofol. Thiopental and ketamine have also been reported to attenuate the inflammatory response, but to a lesser extent than propofol while midazolam seems to have little effect on host defense mechanisms. Opiates have several effects on the immune system, which are mediated both indirectly through the central nervous system and directly by interacting with the cellular immune system. Recent observations indicate that substituting epidural anesthesia for postoperative opioids is associated with a substantial reduction of cancer recurrence. Local anesthetics apparently exhibit an anti-inflammatory activity that may be helpful in modulating the surgery-induced stress response. Volatile anesthetic agents have organ protective effects related to a preconditioning and a postconditioning effect. In addition they have been shown to reduce the inflammatory response by different mechanisms. Finally, clonidine also has an anti-inflammatory action, mediated through $\alpha_2$-adrenoreceptor activation but it does not appear to influence the perioperative stress response during cardiac surgery. Overall, although there is substantial evidence that anesthetic agents affect the immunomodulatory response, the potential impact on clinical outcome in cardiac surgery remains to be determined.
Other perioperative factors that may influence the perioperative inflammatory response include the extracorporeal circulation technology, the composition of the priming solution, and the type of cardioplegia. With regard to the type of surgery, it seems that indices of inflammation appear to correlate mainly with the overall severity of illness rather than with a specific surgical procedure. Allogenic blood transfusion appears to exacerbate the proinflammatory response to cardiac surgery. The effects of autotransfusion seem less impressive. Although shed mediastinal blood contains high concentrations of different inflammatory elements, autotransfusion in the postoperative period did not cause a measurable elevation in cytokines.

It should be noted that a controlled, self-limiting inflammatory response to cardiac surgery is an integral an essential part of postoperative recovery that helps in preventing perioperative infection and promoting wound healing. Only when the inflammatory response gets out of control, a significant immune-mediated morbidity and mortality may occur.

Different therapeutic approaches have been attempted to prevent such uncontrolled perioperative inflammatory responses to occur. A first approach consists in decreasing the effects of contact activation. This can be obtained by minimizing the exposure to the extracorporeal circuit and by improving circuit biocompatibility. While such techniques usually seem to be associated with lower levels of circulating markers of inflammation, their beneficial effects on clinical outcome remain to be definitively established. A second approach is directed towards minimizing the deleterious effects of ischemia-reperfusion injury by administration of compounds that have been shown to decrease such injury. These compounds include free radical scavengers, anti-oxidants, serine protease inhibitors, specific anesthetic agents and others. Finally, attempts to decrease the risk of perioperative endotoxemia include selective digestive decontamination, enteral nutrition and immuno-nutrition and maintenance of adequate splanchnic perfusion. In addition to these approaches, administration of specific anti-immune therapy strategies have been proposed such as hemofiltration, leucocyte depletion, and others. Finally supportive strategies such as different types of renal replacement therapies and various modalities of mechanical ventilation may have an effect on the course of the postoperative inflammatory response after cardiac surgery. However, while many of these therapeutic approaches seem to be attractive from pathophysiological point of view and even were proven to be successful in some experimental settings, their clinical applicability and usefulness, largely remain to be established.
Recommended literature


* Hollmann MW, Durieux ME: Local anesthetics and the inflammatory response. Anesthesiology 200; 93: 858 - 75


