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Inflammatory response and extracorporeal circulation

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Patients undergoing cardiac surgery with extracorporeal circulation (EC) frequently develop a systemic inflammatory response syndrome. Surgical trauma, ischaemia–reperfusion injury, endotoxaemia and blood contact to nonendothelial circuit compounds promote the activation of coagulation pathways, complement factors and a cellular immune response. This review discusses the multiple pathways leading to endothelial cell activation, neutrophil recruitment and production of reactive oxygen species and nitric oxide. All these factors may induce cellular damage and subsequent organ injury. Multiple organ dysfunction after cardiac surgery with EC is associated with an increased morbidity and mortality. In addition to the pathogenesis of organ dysfunction after EC, this review deals with different therapeutic interventions aiming to alleviate the inflammatory response and consequently multiple organ dysfunction after cardiac surgery.

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Introduction

During cardiac surgery, extracorporeal circulation (EC) enables surgeons to treat a wide range of heart diseases while circulation and oxygenation of human blood are maintained by machines. While the first successful cardiopulmonary bypass (CBP) during a ventricular septum repair in 1953 by Gibbon was still an experimental procedure, CPB has in the meantime emerged as a well-established procedure, used worldwide in more than half a million people per year [1,2]. Blood trauma and the creation of embolic particles were initially common adverse effects of EC. However, through the development of new biomaterial technologies and implementation of pharmacologic drugs, these potential side effects were reduced, linked to a rapid improvement of patients' outcome. Nevertheless, despite the encouraging successes, patients undergoing cardiac surgery continue to frequently develop post-operative complications arising from the inappropriate activation of inflammatory pathways [3].

Inflammation is the response of the organism to several noxious stimuli. During cardiac surgery, different stimuli, such as blood exposition to the nonendothelial surface of the CPB, ischaemia–reperfusion injury and endotoxaemia, may trigger an inflammatory response. The activation of humoral and cellular cascades leads to an increase of pro-inflammatory cytokines in the circulating blood and to enhanced leucocyte recruitment [4]. The resulting systemic inflammatory response syndrome (SIRS) is associated with post-operative complications including myocardial dysfunction, respiratory failure, acute kidney injury (AKI), neurologic dysfunction, bleeding disorders and, finally, multiple organ failure (MOF). MOF is strongly associated with increased morbidity and mortality rates among patients undergoing cardiac surgery.

Mediators of the inflammatory response

Coagulation linked to inflammation

In the vascular system, endothelial cells produce pro- and anticoagulation factors, which together maintain the equilibrium of blood fluidity. The exposure of blood components to artificial surfaces within the extracorporeal circuit leads to an activation of coagulation cascades. These pathways, classically divided into an intrinsic and extrinsic pathway, consist of a series of enzyme cascades and lead to the generation of activated thrombin (Fig. 1) [5].

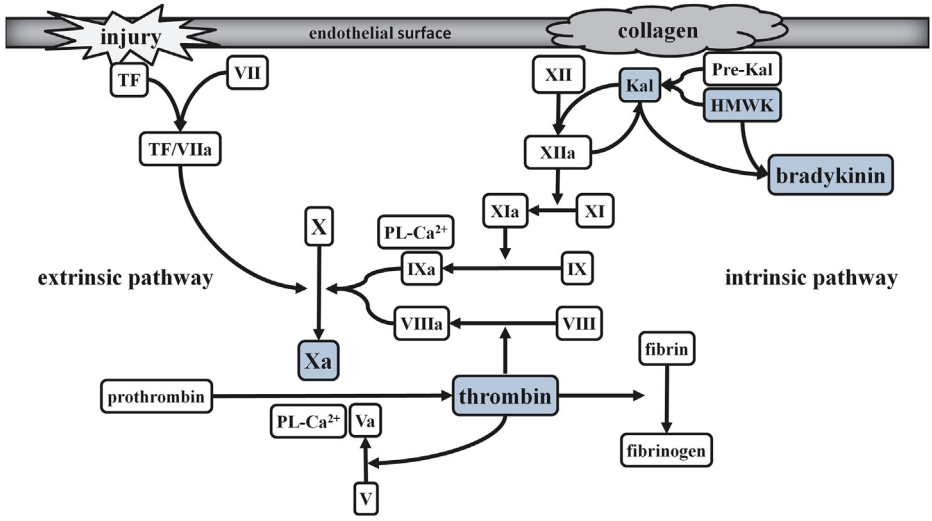

Fig. 1. Schematic overview of the intrinsic and extrinsic coagulation pathway. Coagulation factors that contribute to inflammatory cell activation are coloured blue. TF, tissue factor; Pre-Kal, prekallikrein; Kal, kallikrein; HMWK, high molecular weight kininogen; PL, phospholipids; and coagulation factors, V,VII, VIII, IX, X, XI and XII (a indicating active form).