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Ischemia-modified albumin and adenosine plasma concentrations are associated with severe systemic inflammatory response syndrome after cardiopulmonary bypass

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Abstract

Purpose: Severe systemic inflammatory response syndrome (SIRS) occurring after cardiopulmonary bypass (CPB) is a common cause of mortality during cardiac surgery. These syndromes are characterized by vasoplegia and ischemia-reperfusion phenomenom. Adenosine is a strong endogenous vasodilating agent, which may be involved in blood pressure failure during CPB induced by severe SIRS. Ischemia-modified albumin (IMA) is considered as a sensitive marker of tissue ischemia.

We examined whether the IMA or adenosine plasma concentrations (APCs) change during a severe SIRS-induced blood pressure failure during CPB.

Materials and Methods: Plasma concentration and IMA (median [range]) were measured before, during, and after surgery in 86 patients who underwent coronary revascularization under CBP and were correlated to postoperative clinical course.

Results: Preoperative APC values (1.45 [0.52-2.11] μmol L^{-1} vs 0.36 [0.12-0.66] μmol L^{-1}) and IMA (144 [91-198] IU mL^{-1} vs 109 [61-183] U mL^{-1}) were significantly increased in patients presenting postoperative severe SIRS. Mean durations of mechanical ventilation, stay in the intensive care unit, and requirement of vasoactive drugs were significantly higher in patients with higher APC and IMA, but APC was the best predictive marker a postoperative severe.

Conclusions: Adenosine plasma concentration and IMA concentration are associated with postoperative severe SIRS after CPB.

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1. Introduction

Systemic inflammatory response syndrome (SIRS) encompasses clinical symptoms observed after various infectious or noninfectious insults. After cardiopulmonary bypass (CPB), this inflammatory syndrome can result in organ dysfunction (severe SIRS) such as myocardial reperfusion damage, lung injury, and generalized profound vasodilation, thus increasing postoperative morbidity and mortality [1–3].

No specific marker has yet been identified to predict the development of SIRS. Cardiac troponin I (cTnI) measurement is routinely performed after cardiac surgery, but the significance of its rise remains controversial [4–6]. A number of recent studies have shown that ischemia-modified albumin (IMA) could be a potential marker of tissue ischemia [7–10]. Ischemia-modified albumin results from the modification of the N-terminus cobalt binding sites of albumin caused by the release of free radicals from ischemic tissue [7]. The IMA concentration increases only a few minutes after the beginning of even a minimal ischemic process, and its concentration is correlated with the size of the ischemic tissue [7]. Ischemia-modified albumin is thus a candidate marker of transient myocardial [8,9] or nonmyocardial ischemia [10]. However, IMA concentrations have never been studied after CPB.

Adenosine may participate in hemodynamic disturbance in severe SIRS after cardiac surgery [11,12]. Adenosine is a ubiquitous nucleoside that comes from ATP dephosphorylation and is released in the case of oxidative stress or during ischemia [13–15]. Previously, it was shown that the increase in adenosine plasma concentration (APC) may participate in the blood press drop during vasoplegia that precedes severe SIRS [11]. Thus, the aim of this prospective clinical study was to investigate the influence of SIRS on APC, cTnI, and IMA concentrations in patients after cardiac surgery with CPB.

2. Methods

This study protocol was approved by our institutional ethics committee, and informed consent was obtained from each patient included in the study.

2.1. Patients

Eighty-six adult patients with no active infection, inflammatory disease, or pulmonary hypertension undergoing coronary artery surgery under CPB were prospectively and consecutively included in the study for months.

Patients who had been treated with papaverine, dipyridamole, or immunosuppressive or antibiotic agents during the preceding 6 weeks were not included. Patients with plasma albumin concentration under 20 g/L or with cirrhosis were not included.

Symptomatic patients with 1 or more stenotic coronary arteries (>70%) underwent coronary revascularization. Patients with recent myocardial infarction (<1 month) were excluded. Acute myocardial infarction was defined using the universal definition [16].

Perioperative acute myocardial infarction was also defined as an increase in cTnI greater than 5× 99th percentile the upper reference limit plus either new pathological Q waves or new bundle-branch block or angiography evidence [16].

Preoperative renal function was assessed by baseline creatinine clearance, calculated according to the Cockroft-Gault formula [17].

2.2. Management of anesthesia and surgery

Patients were premedicated with 0.05 mg kg^{-1} of orally administered oxazepam the night and 1 hour before surgery. After preoxygenation, anesthesia was induced with 0.05 mg kg^{-1} of intravenous midazolam (Hypnovel; Roche Laboratories, Neuilly sur Seine, France), 0.3 mg kg^{-1} of etomidate (Etomidate-Lipuro; P Braun, Boulogne, France), 0.3 μg kg^{-1} of sufentanil (Sufenta; Solvay Pharma Suresnes, France), and 0.5 mg kg^{-1} of atracurium (Tracrium; Glaxo-Wellcome, Mayenne, France). Anesthesia was maintained with an infusion of 0.5 μg kg^{-1} h^{-1} of sufentanil and 0.5 mg kg^{-1} h^{-1} of atracurium (under train-of-four monitoring). Sevoflurane (Sevorane; Abbott, Rungis, France) was administered to obtain a maximal alveolar concentration of 0.5 to 1.5. Lungs were mechanically ventilated via an endotracheal tube. Tidal volume was set between 6 and 8 mL kg-^{1} of ideal body weight, respiratory rate was fixed to obtain an $Etco_2$ between 30 and 40 mm Hg. Prophylactic antibiotics were administered intravenously, with 1.5 g of cefamandole (Céfamandole; Panpharma, Fougères, France) given 10 minutes before induction and then 750 mg given every 2 hours during surgery.

Mild hypothermic (34°C) nonpulsatile CPB was performed after administration of intravenous heparin (300 IU kg^{-1}), always using the same model of membrane oxygenator (BARD Quantum; Bard Limited, Crawley, UK) and a roller pump (COBE Optima Cardiovascular, Inc, Arvada, Co). A blood flow of 2.4 L min^{-1} m^{-2} was maintained, with the aim of keeping arterial blood pressure between 50 and 75 mm Hg during the entire CPB. Myocardial preservation was achieved with intermittent infusion of colloid-crystalloid solution (Buckberg; FRESENIUS Laboratories, Kabi, Sevres, France).

During CPB, vasoplegia was considered to have occurred if the mean arterial pressure was less than 50 mm Hg, with a duration of more than 5 minutes despite a normal blood flow rate of 2.4 L min^{-1} m^{-2}.

For patients treated with preoperative antiplatelets agents (such as aspirin), tranexamic acid was administered before CPB with an intravenous loading dose of 15 mg kg^{-1} and was associated with a priming dose of 0.5 g and a continuous intravenous perfusion of 1 g h^{-1} during CPB (or 0.5 g h^{-1} in patients with preoperative creatinine clearance less than 60 mL min^{-1}).

To avoid any surgical bias, surgery was performed by the same surgeon and was standardized.