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ORIGINAL ARTICLE

Effect of Haemodynamic Changes on Epithelium-related Intestinal Injury in Off-pump Coronary Surgery

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Objectives Intestinal injury is thought to play a central role in the occurrence of multiorgan dysfunction after on-pump coronary surgery. Clinical benefits of off-pump revascularisation remain, however, controversial.

Material and Methods Hepatic enzymes and plasmatic IL-6, IL-8 and intestinal-type fatty acid binding protein (I-FABP) were determined in 20 patients (age 65–75) undergoing either on-pump ($n = 10$) or off-pump ($n = 10$) coronary surgery. Haemodynamic and biochemical parameters, catecholamine and volume therapy were monitored.

Results Central venous pressure (CVP) was significantly higher in the off-pump group during and 12 h after operation (9.5 ± 1.35 vs. 6.21 ± 0.63 mmH_2O, $p = 0.012$). Higher GGT and GLDH levels occurred in the off-pump group and correlated with the elevated I-FABP levels at 24 h (935.8 ± 83.7 vs. 370.4 ± 67.7 pg/mL, $p < 0.001$). CVP correlated with I-FABP peak values (Pearson's coefficient 0.852). IL-6 and IL-8 were released to a lower extent in the off-pump group compared to on pump ($p < 0.05$) at 24 h (139.3 ± 27.7 vs. 279.4 ± 56.2 and 15.3 ± 7.4 vs. 38.5 ± 13.8 pg/mL) and at 72 h post-operatively (4.5 ± 2.1 vs. 30.1 ± 12.1 and 7.8 ± 1.2 vs. 17.1 ± 5.2 pg/mL).

Conclusions While inflammatory activation is reduced with CPB avoidance, elevated CVP during off-pump surgery is followed by temporary postoperative enterocyte damage that may threaten the normal function of the gastrointestinal system and lead – in certain groups of high risk patients – to irrecoverable injury.

Keywords Off-pump • Splanchnic ischaemia • Central venous pressure • Inflammation

Introduction

The gut is one of the first organs undergoing ischaemic injury during haemodynamic stress. Therefore, gastrointestinal integrity is an excellent predictor [1] of outcome after cardiac surgery.

Cardiopulmonary bypass associated complications in general, including generalised systemic inflammatory response, cerebral dysfunction, myocardial depression or haemodynamic instability were thought to be avoided by off-pump coronary artery bypass grafting (OPCAB). Nonetheless, although OPCAB demonstrated to be a safe and effective procedure, it did not eliminate the potential of significant perioperative organ injury; the magnitude remains comparable to ONCAB (on-pump coronary artery bypass). Not only the Octopus trial [2], but also Puskas et al. [3,4] and Angelini et al. [5] demonstrated equivalent inhospital and 30-day outcomes, as well as similar long-term outcomes for ONCAB and OPCAB. OPCAB either resulted in a significant reduction in mortality, or myocardial infarction and stroke [6].

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The central role of impaired gut barrier function in driving the systemic inflammatory response syndrome and multisystem organ failure after ONCAB and OPCAB surgery have been previously demonstrated. Velissaris et al. [1] showed that despite superior global oxygen flux associated with beating-heart revascularisation, gastric mucosal hypoxia occurred to similar extents in OPCAB and ONCAB with worsening trends for the OPCAB patients during the postoperative period. Moreover, Ascione et al. [7] suggested that the function of the small intestine was worse after surgery with OPCAB than with ONCAB; oppositely, pancreatic function was worse with ONCAB than with OPCAB, while hepatic metabolic function did not differ in the type of surgery at the end of the operation; however, all functions recovered to similar levels by day 5.

The mechanisms of functional hypoperfusion of visceral organs, which might lead to visceral injury and induction of systemic inflammatory response syndrome during OPCAB, are still poorly understood and no reliable specific biochemical markers to detect intestinal injury are currently available. Interleukin-6 is an early component of acute phase reaction during ischaemia reperfusion of the intestine that is released in the splanchnic system depending on the intensity of the surgical trauma and is closely involved in the pathogenesis of multiple organ failure [8]. It directly controls endothelial cell injury and initiates neutrophiles adhesion. Interleukin-8 was shown to mediate the inflammation process at a later phase of ischaemia reperfusion injury through modulation of neutrophile infiltration and sequestration [9]. Infiltrating neutrophiles contribute substantially to local inflammation by releasing myeloperoxidase and generating reactive oxygen species. Interleukin-10 thought to be produced in the hepatosplanchnic system [10] was recently shown to peak early after initiation of cardiopulmonary bypass and return to baseline levels before the end of the extracorporal support [11], which makes it less interesting as a possible marker of postoperative intestinal damage. Intestinal-type fatty acid binding protein is a small cytoplasmic protein mainly expressed in the epithelial mucosal cells of the intestinal villi. As recently revealed, it is highly sensitive to both early epithelial cell injury [12] and post-reperfusion cell recovery [13]. These unique characteristics make it a possible marker for nonocclusive transient intestinal ischaemia associated with cardiac surgery.

The aim of the present study was to investigate the relationship between haemodynamic changes, visceral injury and systemic inflammatory response in ONCAB and OPCAB patients in order to establish possible quantifiable predictors of visceral injury after coronary grafting.

Material and Methods

Data from 20 patients with normal cardiac, renal, hepatic and cerebral function undergoing either conventional on-pump or off-pump first-time coronary artery revascularisation were analysed in this study. Exclusion criteria were recent acute myocardial infarction, unstable angina pectoris, peripheral arterial occlusive disease, diabetes mellitus and chronic occlusive pulmonary disease.

Anaesthetic Protocol and Medication

All procedures were performed electively under disoprivan, sufentanil and pancuronium anaesthesia, following a fixed anaesthetic protocol. Premedication was achieved with diazepam 10–15 mg. Peripheral venous and radial arterial cannulae were inserted under local anaesthesia. General anaesthesia was induced with 2.5 µg/kg sufentanil, 0.1 mg/kg midazolam. Relaxation prior to endotracheal intubation was achieved with 0.1 mg/kg pancuronium. A pulmonary artery catheter was introduced into the right internal jugular vein. Cefuroxim 1500 mg was administered i.v. Heparin was administered to maintain activated clotting times >250 s in off-pump surgery and >400 s in on pump procedures. In order to maintain filling pressures and cardiac output, mean arterial pressure was held between 60 mmHg and 70 mmHg by administration of volume, and optimisation of heart rate and rhythm. Inotropic support was started with norepinephrine at cardiac index <2.2 L/min m^2. When the cardiac index remained marginal (<2.0 L/min m^2) after primary support, low-dose epinephrine was the next drug of choice.

Surgical Procedure

After performing total sternotomy, surgical preparation of arterial and venous conduits was performed in all patients. Coronary grafting was performed similarly. In the ONCABG, cannulation of the aorta and right atrium was done and nonpulsatile CPB in normothermia was performed using a roller pump (Stockert) and membrane oxygenator (Terumo-Vaskutek). Pump flow was maintained at 2.4 L/min m^2. Cardioplegia in the on pump group was achieved by antegrade administration of Brettschneider solution. During CPB, MAP was allowed to vary between 45 and 60 mmHg. In the OPCABG group, MAP was allowed to vary between 55 and 80 mmHg during the bypass implantation. Blood pressure deviations were corrected with norepinephrine and nitroglicerine in both groups. Alpha-Stat regulation of blood pH was similarly used in both groups.

Data Assessment

Haemodynamic monitoring and blood sampling was performed during the operation as follows: before induction of anaesthesia (preinduction), at the beginning of distal anastomoses, at the end of the distal anastomoses and at the end of proximal anastomosis.

Post-operatively blood gas analyses were performed at 4 h intervals during the first 24 h. Venous blood samples for laboratory and special measurements were taken before the operation, immediately after the operation, and 24 h and 72 h after the operation. Plasma was stored at −20 °C until assay. Time point registration of the haemodynamic data, arterial blood gas analyses and perioperative venous blood sampling are represented in Fig. 1. Venous whole