Lung Injury and Protection During Cardiopulmonary Bypass

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Summary

The cardiopulmonary bypass machine supports the respiratory and circulatory functions of the body while surgery is being performed upon the heart. The basic cardiopulmonary bypass circuit consists of oxygenator, pump and reservoir which are connected by tubes for the purpose of converting the patient's low pressure, venous blood into "arterialized" blood and returning it to the arterial system of the patient.

It has been recognized that CPB is associated with a systemic inflammatory response, and occasionally leads to major organ dysfunction. This has been termed post-pump syndrome, however; the exact mechanisms involved in PD following CPB have not yet been fully clarified. Recent researches have underlined importance of some of the humoral and cellular mechanisms involved. Neutrophils, monocytes, and macrophages undergo activation resulting in local and systemic secretion of humoral inflammatory mediators.

On the humoral level activation of complement, secretion of cytokines, and the production of surface adhesion molecules result in activation of neutrophils and macrophages which in turn resulting in further secretion of enzymes such as proteases and oxygen free radicals which induce direct lung injury. When endothelial cells are activated by cytokines, complement and ischemia-reperfusion, they begin to produce surface adhesion molecules which help further adhesion and activation of neutrophils. This pathophysiological process leads to disruption of endothelial and epithelial integrity, and allows albumin, plasma and activated neutrophils to enter the interstitial and alveolar space causing tissue edema and reducing pulmonary compliance and blood oxygenation.

Physiological disturbance in the lungs can be categorized grossly into abnormal gas exchange and poor lung

List of Abbreviations

ABP	Arterial blood pressure
ACT	Activated clotting time
AIDs	Autoimmune diffecincy syndrome
ALI	Acute lung injury
ARDS	Acute respiratory distress syndrome
BA	Bronchial artery
BAL	Broncho-alveolar lavage
CABG	Coronary artery bypass graft
cAMP	Cyclic adenosine monophosphate
CO_2	Carbon dioxide
CPAP	Continuous positive airway pressure
COPD	Chronic obstructive pulmonary disease
CPB	Cardio pulmonary bypass
CPR	Cardiopulmonary resuscitation
ECC	Extracorporeal circulation
EDRF	Endothieln derived releasing factor
FiO_2	Fraction of inspired oxygen
FRC	Functional residual capacity
FVC	Forced vital capacity
I:E	Inspiration : expiration
ICU	Intensive care unit
IL	Inter leukin
iNOS	Inducible form of nitric oxide synthase
LIP	Lower inflection point
LPS	Lipopolysaccharide
LT	Leukotriene
MAC	Membrane-attaking complex
MDA	Malnodialdhyde
MMP	Matrix metalloproteinase

List of Abbreviations (Cont.)

MOF	Multiorgan faliure
NO	Nitric oxide
NSAID	Non steroidal anti-inflammatory drugs
NTG	Nitroglycrine
PA	Pulmonary artery
PAF	Platelt activating factor
PAO_2	Alveolar oxygen tension
PaO_2	Arterial oxygen tension
PCV	Pressure controlled ventilation
PD	Pulmonary dysfunction
PEEP	Positive end expiratory pressure
PFC	Perflurocarbon
PG	Prostaglandins
PMNs	Polymorph nuclear cells
PVC	Polyvinyl chloride
PVR	Pulmonary vascular resistance
SIRS	Systemic inflammatory response syndrome
SNP	Sodium nitroprusside
TEE	Transesophogeal echocardiography
TNF	Tumor necrosis factor
T-PA	Tissue plasminogen activator
TX	Thromboxane
V/Q	Ventilation perfusion
VALI	Ventilator associated lung injury

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Introduction

Postoperative lung injury is one of the most frequent complications of cardiac surgery that impacts significantly on healthcare expenditures and is largely believed to result from the use of cardiopulmonary bypass (CPB) **(Berry et al., *1993*).**

Despite the improvement in CPB techniques as well as postoperative intensive care, impaired pulmonary function is a well-documented complication of CPB resulting in increased morbidity and mortality **(Menasche and Edmunds, 2006).**

CPB is associated with a whole-body inflammatory response. The contact of blood components with the artificial surface of the bypass circuit causes activation of complements, upregulation of cytokines and adhesion molecules, and production of oxygen-derived free radicals. The pathogenic consequences are adhesion of complement-activated neutrophils to endothelial cells, neutrophil migration into the extravascular spaces and oxygen derived free radical-mediated pulmonary damage. Injured endothelial cells are vulnerable to the cytokine-mediated inflammatory cascade **(Apostolakis et al., 2009)**.

The "post-bypass lung" is characterized by increased intrapulmonary shunt, atelectasis, increased alveolar-to-arterial oxygen partial pressure difference ($AaDO_2$), increased extravascular lung water and decreased compliance. Major causes of post-bypass lung are the reduced or absent blood flow through the lungs during CPB and entry of blood into pleural spaces during surgery **(Altmay et al., 2006).**

It is clear that many factors are involved in the detrimental effects of CPB in all organs and especially in the lungs. Therefore, substantial improvements in the process of CPB can be only obtained when a multi-factorial approach is

followed, directed at both material-dependent and material-independent factors **(Gott et al., 1998).**

Since the inflammatory response of CPB is multifactorial, a combined therapeutic approach should be implemented to avoid the attenuation of the clinical sequelae. On the one hand, the abrogation of CPB by using off-pump techniques alone is not possible in many cases, and on the other hand, this technique alone does not seem to fully alleviate postoperative lung dysfunction. So modifications of CPB techniques, such as the utilization of heparin-coated circuits, use of ultra-filtration techniques, hemodilution techniques, or the use of additional perfusion techniques during cardiopulmonary bypass may be useful as lung ischemia during bypass leads to activation of inflammatory response. All this mechanisms may be beneficial for reduction in the observed activation of systemic inflammatory response syndrome (SIRS) or the scavenging of various pro-inflammatory cytokines **(Tschernko et al., 2002).**

Aim of the work

The aim of this work is to review the pathophysiological, histological and inflammatory changes in the lungs during cardiopulmonary bypass and the sequelae of these changes and how to protect the lungs from injury caused by this process.

Basic Setup and Physiology of Extracorporeal Circulation

Extracorporeal Circulation (ECC):

Extracorporeal circulation is the circulation of blood outside the body through a hemodialyzer for removal of substances usually excreted in the urine, or through an extracorporeal circulatory support unit **(**heart-lung machine) for carbon dioxide-oxygen exchange. ECC is the procedure in which blood is taken from a patient's circulation to have a process applied to it before it is returned back to the circulation **(Paparella et al., 1999).**

Cardiopulmonary Bypass (CPB).

Cardiopulmonary bypass is a form of extracorporeal circulation. It is a technique that temporarily takes over the function of the heart and lungs during surgery, maintaining the circulation of blood and the oxygen content of the body. The CPB pump itself is often referred to as the **heart–lung machine** or "the pump". CPB pumps are operated by perfusionists in association with surgeons who connect the pump to the patient's body **(Paparella et al., 2002).**

Components of CPB Machinne:

The CPB circuit for cardiac surgery consists of a venous drainage line, a venous reservoir, an oxygenator-heat exchanger, a pump, and an arterial return line**.** In addition, there is a suction line that provides drainage from intracardiac chambers ("vent" line). Additional adjuncts include a cardioplegia delivery-system, an arterial line filter, various in-line monitors and blood gas analyzers, and temperature monitors. The CPB machine includes many additional

components such as a membrane oxygenator, and heat exchanger into one unit. A microfilter-bubble trap is added to the arterial line. Depending on the operation various suction systems are used to return blood from the surgical field, cardiac chambers and/or the aorta again to the machine. Aspirated blood passes through a cardiotomy reservoir and microfilter before returning to the venous reservoir. Optionally, but increasingly recommended, field blood is washed in a cell saver system and returned to the perfusate as packed red cells. In addition to adjusting pump flow, partial and occluding clamps on venous and arterial lines are used to direct and regulate blood flow **(Gravlee et al., 2000).**

Total bypass indicates that all the venous return from superior and inferior venae cavae, and the coronary sinus is drained to the oxygenator, and no blood is pumped by the right ventricle to the lung.

Partial bypass means that some of the blood return is still pumped by both right and left ventricles like in case of femoral bypass. In case of total bypass, although all the venous return is bypassed from the right ventricle, 2% to 5% of cardiac output is drained to the left ventricle. This is the physiologic shunt from the bronchial and pleural veins **(Paparella et al., 1999).**

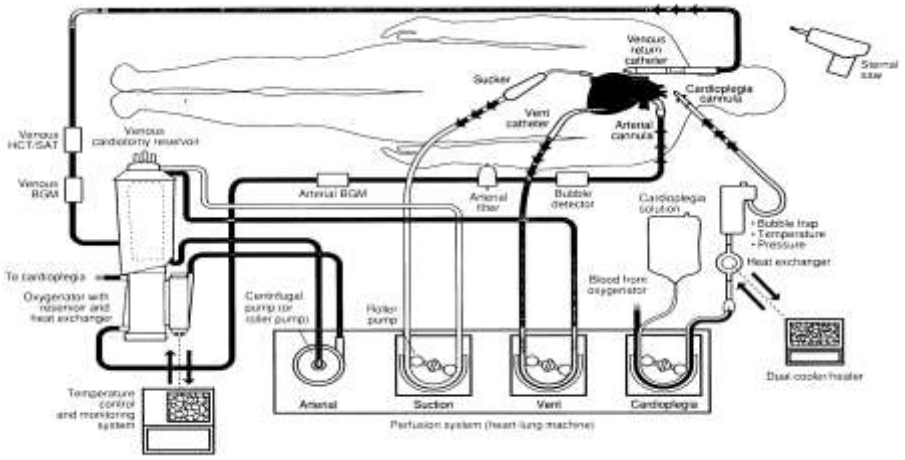

Fig. (1): Diagramatic representation of the CPB machine From **(Leonard, 1998).**

I-Venous Cannulation and Drainage:

Venous blood usually enters the circuit by gravity into a venous reservoir placed 40 to 70 cm below the level of the heart. The amount of drainage is determined by central venous pressure, the height differential, resistance in cannulae, tubing, and connectors, and absence of air within the system.

Size of cannulae is determined by patient size, anticipated flow rate, and catheter flow characteristics and resistance. Three basic approaches for central venous cannulation are used: bicaval, single atrial, or cavoatrial. Bicaval cannulation and caval tourniquets are necessary to prevent bleeding and air entry into the system when the right heart is entered during CPB. Because of coronary sinus venous return, caval tourniquets should not be tightened without decompressing the right atrium. Bicaval cannulation without caval tapes is often preferred to facilitate venous return during exposure of the left atrium and mitral valve.

Single venous cannulation is adequate for most aortic valve and coronary artery surgery.

Negative pressure is sometimes applied to the venous lines to provide assisted venous drainage using a roller pump or centrifugal pump, or by applying a regulated vacuum to a closed hard-shell venous reservoir (vacuum-assisted venous drainage, VAVD).This may permit use of smaller diameter catheters and may be helpful when long, peripheral catheters are used **(Davila et al.,2001).**

Complications Associated with Venous Cannulation:

These include atrial arrhythmias, atrial or caval tears and bleeding, air embolization, injury or obstruction due to catheter malposition, and inadvertent decannulation. Placing tapes around the venae cavae may lacerate branches, nearby vessels (e.g., right pulmonary artery), or the vena cava itself. Before or after CPB, catheters may compromise venous return to the right atrium from the body. Venous catheters and/or caval tapes may displace or compromise central venous or pulmonary arterial monitoring catheters. Any connection between the atmosphere and cannula intake ports may entrain air and lead to an air lock or gaseous microembolism. Assisted venous drainage (AVD) increases the risk of air entrainment (**Jones et al., 2002).**

Finally, improperly placed purse-string sutures may obstruct the vena cava when tied (**Jones et al., 2002).**

Causes of Low Venous Return:

Low venous pressure, hypovolemia, drug- or anesthetic-induced venous dilatation, inadequate differential height between heart and reservoir, too small cannula size, cannula kining from any cause, air locks, or excessive flow resistance in the drainage system are possible causes of