Review

What is the Role of Leukocyte Depletion in Cardiac Surgery?

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Leukocytes play an important pathogenic role in ischaemia-reperfusion injury. During cardiopulmonary bypass, leukocyte filters have the potential to remove leukocytes, thereby reducing contact of activated leukocytes with the endothelium of target organs. Improvement in the safety and efficacy of commercially available leukocyte filters in recent years has led to their increasing use in cardiac surgery. However, the benefits have been inconsistent. Current evidence suggests that leukocyte depletion may not have a significant impact in low risk elective coronary artery bypass grafting but may be beneficial in valve surgery and high-risk cardiac surgery. High-risk surgical groups that may benefit from leukocyte filtration are those with left ventricular hypertrophy (LV mass > 300 g), poor ejection fraction (EF < 40%), chronic obstructive airways disease (predicted FEV1 < 75%), prolonged ischaemia (cross clamp time > 120 min or cardiac transplantation), paediatric cardiac surgery and patients in cardiogenic shock requiring emergency coronary artery bypass grafting. Future trials should be powered to detect important clinical end points and be designed to avoid premature exhaustion of the filter.

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Introduction

In recent years, the role of leukocyte filtration in cardiac surgery had been extensively evaluated. However, the outcomes have been variable with some studies demonstrating a benefit, some showing no effect and still others demonstrating detrimental effects. In this review we summarise the current state of knowledge of the effect of leukocyte filtration in cardiac surgery and we believe explain and resolve the controversy by separating out two groups of studies. One group of studies of low risk coronary bypass surgery shows little or no clinical benefit from leukocyte filtration. The other group of studies of valve replacement or high-risk cardiac surgical procedures shows fairly consistent benefits in terms of improved cardiac function and accelerated recovery of the patient.

We performed Ovid Medline, National Library of Medicine PubMed database searches and obtained articles from references listed in individual published journals. Searches were made for relevant publications in English using the terms 'leukocyte depletion', 'leukocyte filtration', 'cardiopulmonary bypass', 'coronary bypass graft', 'valvular surgery', 'paediatric', 'blood transfusion', 'transplantation' and the combinations of the terms listed. In general the highest quality clinical studies available

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Abbreviations: AXR, aortic cross-clamp; CABGs, coronary artery bypass grafts; CI, cardiac index; CPB, cardiopulmonary bypass; CRP, C-reactive protein; EF, ejection fraction; FEV1, forced expiratory volume (1 s); IABP, intra-aortic balloon pump; ICAM, intercellular adhesion molecule; ICU, intensive care unit; IL, interleukin; LV, left ventricle; LD, leukocyte depletion; LDTC, leukocyte depleted terminal cardioplegia; LF, leukocyte filtration; MPO, myeloperoxidase; MDA, malondialdehyde; OI, oxygenation index (arterial oxygen tension/inspired oxygen fraction); PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedged pressure; PMNE, polymorphonuclear elastase; PRCT, prospective randomised control trial; PVR, pulmonary vascular resistance; TNF-alpha, tumour necrosis factor-alpha; RI, respiratory index; RBC, red blood cell; Trop, troponin; WBC, white blood cell count

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(Level 2 - Randomised Controlled Clinical Trial) were reviewed.

Filtration and Filter Ratings

Filtration involves the separation of particles from a fluid. Filters can be subdivided into two classes, depth filters and surface filters, by the manner in which they achieve separation. In a depth filter, particles become attached and removed from a fluid as it flows through long tortuous passages. Depth filters are thick and are constructed from porous materials such as wool, paper, glass fibre or asbestos. Surface filters, also called membrane filters, retain particles on the upstream side of a porous matrix as the fluid flows through it. Membrane filters are used for critical applications such as sterilising and dialysis.

Pore sizes are usually specified in micrometres (μm) and refer to the smallest size of a particle retained by the filter media to a stated degree of efficiency. The degree of efficiency is stated as either 'absolute' or 'nominal'. An absolute pore size rating describes a defined pore size whereby any particle greater than the specified size will be retained with 100% efficiency. In contrast, at the nominal pore size rating, the majority, but not 100% of the particles are removed. The conditions that affect the nominal filter efficiency include differential pressure (pressure difference between the inlet and outlet), viscosity of the liquid, porosity of the membrane and effective filter area (a larger filter area allows faster flow rates). Nominal rating is usually used for depth filters.

Leukocyte Filtration

Leukocyte filtration is the process whereby leukocytes are removed from the blood by passage through a filtration device. In 1928 Alexander Fleming used cotton wool to remove leukocytes from small amounts of blood.[1] However, it was not until 1972 that the first commercial filter was used to remove leukocytes from packed red cells. This first generation filter was constructed of a column, tightly packed with cotton wool.[1] Current filters are composed of a polyester fibre material packed in a special configuration to maximise cellular contact. The filter material (cotton, nylon, microfibre) or its surface properties may be modified by an appropriate coating to alter the surface tension or electrostatic charge. A positive surface charge attracts leukocytes to adhere to the fibre surface.[1] Viable red blood cells, lymphocytes, granulocytes and platelets differ in their relative adhesiveness to different filter fibre materials. Hence, specific filters exist to remove leukocytes, platelets or infective material. In the setting of leukocyte filtration, combinations of adhesive and mechanical sieve properties of the filter contribute to the removal of leukocytes.

In the late 60s and early 70s, the idea of leukocyte filtration emerged when physicians identified blood aggregates in the blood used for transfusion. These aggregates were known to be harmful to patients receiving transfusions. Leukocytes may cause various unwanted reactions such as non-haemolytic febrile transfusion reactions and alloimmunisation that in turn can lead to platelet refractoriness, urticaria, anaphylaxis and transfusion associated graft versus host disease. Leukocytes may also act as host cells for the replication of certain virus such as the Epstein–Barr virus.[2]

The Inflammatory Response to Cardiopulmonary Bypass (Complement and Leukocytes)

Cardiopulmonary bypass (CPB) has been shown to induce an inflammatory response by means of complement activation, endotoxin release, leukocyte activation along with up-regulation of adhesion molecules and release of inflammatory mediators (e.g. reactive oxygen species [ROS], arachidonic acid metabolites, cytokines, platelet activating factor, nitric oxide and endothelins)[3] (Fig. 1). This complex inflammatory cascade contributes to the development of post-operative complications of the respiratory, renal, neurological and gastro-intestinal systems. This is in addition to the ischaemia-reperfusion injury caused to the heart and possibly the lungs.

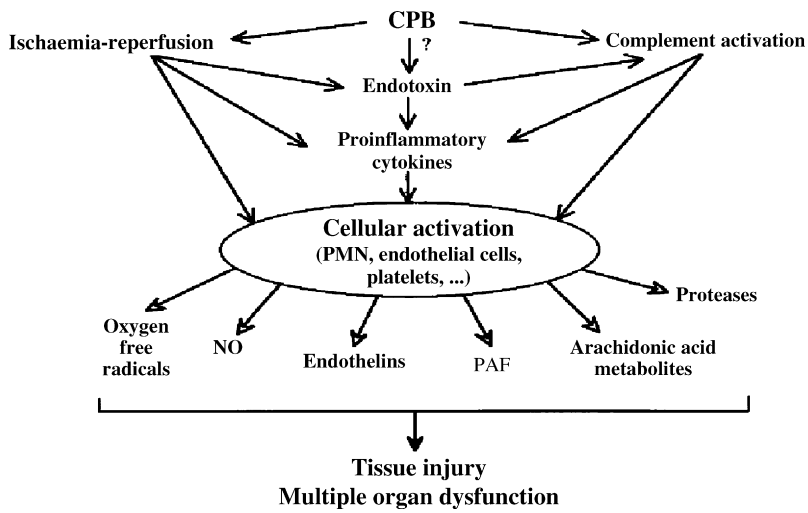

Figure 1. *The inflammatory response to cardiopulmonary bypass (CPB). After Wan et al. 1997 with permission*[3].