

The significance of the intra- and postoperative inflammatory cytokine filtration

Commentary

Cardiopulmonary bypass (CPB) is the technique, where the functions of the heart and the lung are temporarily taken over by a machine during surgery, in order to maintain the circulation of blood and the oxygen supply to the body. Usually, CPB is used in open heart and coronary bypass surgeries, as it is difficult to operate on a beating heart. In addition, CPB can be used during other thoracic surgeries if the patient, while being operated, becomes hemodynamically unstable, in association with hypoxia, progressive hypercarbia, and/or persistent low pH (<7.2).¹

In the Toronto general hospital, CPB is initiated in 35% of cases of bilateral lung transplant. CPB may be initiated in the following cases.²

- i. Patients with reduced pulmonary vascular bed
- ii. Patients with pulmonary arterial hypertension
- iii. Patients undergoing lobar transplantation
- iv. Patients undergoing combined thoracic and cardiac surgery
- v. During lung transplant, if the native diseased lung is unable to maintain oxygenation, while the first lung being implanted
- vi. During the implantation of the second lung (in bilateral lung transplantation), when the newly implanted first lung receives all the cardiac output, but unable to function properly due to the development of edema.

Disadvantages of CPB can be summarized as^{1,2}

- i. Hemodilution, heparinization, and platelet dysfunction, leading to coagulopathy
- ii. RBCs trauma, leading to hemolysis
- iii. Complement and leukocytes activation, leading to a systemic inflammatory response

Cardiothoracic surgery involving CPB is also associated with ischemic reperfusion injury (IRI), which activates the TLR4- Pyk2-NFκB pathway and results in increased production of pro-inflammatory cytokines. Stimulation of TLR4 with lipopolysaccharides, *in vitro*, showed significant increase in cytokine production (TNFα within 1-2hours, IL1β within 2-3hours, and IL6 within 4-6hours).^{3,4}

IRI is associated with increased reactive oxygen species production and inhibition of KATP channels, which results in inflammasomes activation and increased IL1β and IL18. Both cytokines are able to induce IL6. In addition, TNFα increases with the onset of perfusion, which might explain the significant post-operative increase of this cytokines.⁵ However, co-treatment of astrocytes and microglial cells *in vitro* with lipopolysaccharides and IL6 resulted in the down regulation of TNFα and IL1β production, and the enhancement of LPS- induced release of IL10.⁴

Anne Burke-Gaffney, and her colleagues, reported the independent post-operative enhancement of Slit2-Robo4 signaling pathway and IL10.⁵ Such independency might be explained by the notion that; the

Volume 4 Issue 4 - 2016

Mohamed SA Mohamed

Universitat zu Koln, Germany

Correspondence: Mohamed SA Mohamed, Universitat zu Koln, Deutz-Kalker Str. 118, 50679, Cologne, Germany, Email mohammed.shehatta1@gmail.com

Received: June 03, 2016 | **Published:** June 16, 2016

activation of TLR4 through the IRI of cardiopulmonary bypass, as well as other surgical injuries, results in signaling that leads to the up-regulation of various inflammatory cytokines. However, with the rise of the levels of those cytokines, indirect feedback mechanisms will be directed towards the attenuation of their production, and giving the immune regulatory mechanisms the upper hand.^{3,4} As the Slit2-Robo4 signaling pathway has been identified as anti-inflammatory, its up-regulation together with IL10 would be expected, however, without being dependent on each other.

On the practical side, the uncontrolled post-operative increase in cytokines is not favored as they may be involved in kidney, liver, lung and or other organs injury. Accordingly, filtration of cytokines during cardiac and thoracic surgery requiring CPB might be of great value to decrease their circulating levels, which might correlate with better post-operative outcome. In addition, with a profound IRI injury during organ transplantation, which is augmented by the direct contact between the donor's and the recipient's antigens and immune cells, the stimuli for the cytokine production are intense and last longer, leading to the possibility of reaching a level of cytokine storm, which by itself could result in a massive uncontrolled systemic inflammatory response syndrome (SIRS), leading to multiple organ dysfunction syndrome (MODS) and or multiple organ failure (MOF).⁶

Accordingly, monitoring the levels of the circulating inflammatory cytokines following transplant and exposing the transplant patients to post-operative cytokine hemofiltration (e.g. at 24hours post-operative) might lead to a significant improvement of the patient's general condition and decreased incidence of post-operative complications (for example, IL6 correlates with the 30-day mortality after lung transplant, and IL8 correlates with the incidence of primary lung graft dysfunction).⁷ Clinical studies should be conducted to confirm the application of the above mentioned recommendations.

Acknowledgements

None.

Conflicts of interest

The intellectual properties included in this manuscript belong

solely to the author. Reproduction or use of any of them requires the written permission of the author.

- i. No funding was provided for the development of this work.
- ii. The author welcomes funding cooperation for experimental and clinical studies.

References

1. McRae K. Anesthesia for intrathoracic transplantation. In: Cheng DCH, et al. editors. *Perioperative care in cardiac anesthesia and surgery*. Philadelphia, USA: Lippincott, Williams & Wilkins; 2006. p. 49–63.
2. Boasquevisque CH, Yildirim E, Waddell TK, et al. Surgical techniques: lung transplant and lung volume reduction. *Proc Am Thorac Soc*. 2009;6(1):66–78.
3. Zhao H, Anand AR, Ganju RK. Slit2–Robo4 Pathway Modulates Lipopolysaccharide–Induced Endothelial Inflammation and Its Expression Is Dysregulated during Endotoxemia. *J Immunol*. 2014;192(1):385–393.
4. Minogue AM, Barrett JP, Lynch MA. LPS–induced release of IL–6 from glia modulates production of IL–1 β in a JAK2–dependent manner. *J Neuro inflammation*. 2012;9:126.
5. Burke–Gaffney A, Svermova T, Mumby S, et al. Raised plasma robo4 and cardiac surgery associated acute kidney injury. *PLoS ONE*. 2014;9(10):e111459.
6. Tisoncik JR, Korth MJ, Simmons CP, et al. Into the eye of the cytokine storm. *Microbiol Mol Biol Rev*. 2012;76(1):16–32.
7. Kaneda H, Waddell TK, de Perrot M, et al. Pre–implantation multiple cytokine mRNA expression analysis of donor lung grafts predicts survival after lung transplantation in humans. *Am J Transplant*. 2006;6(3):544–551.