

## Do we really know why cardiac surgery is still affected by substantial inflammatory reaction?

Modern cardiac surgery was born in early fifty's with the use of the heart lung machine. This machine allowed to bypass the heart and the lung, draining the blood from the right atrium, oxygenating and pumping it into the ascending aorta. In this way the heart could be stopped and protected and it was possible to perform operations on a still and empty heart. Surgical techniques and technology development are greatly improved in the last year, allowing complex cardiac operation with low risk, but still the cardiopulmonary bypass have an impact on the pathophysiology of the kidney, lung, brain and in general on the coagulative and inflammatory pathways. The traditionally advocated reasons of these issues are several: the circulation of the blood in an external tubing system leading to an activation of the coagulation, the contact with the air, the suction of blood from the cavities, the trauma of blood components caused by the roller pump. We found a new possible cause of these coagulative and inflammatory disorders during the cardiopulmonary bypass: the microembolization of mesothelial cells sucked from the surgical field. Clearly, the mesothelial cells are generally present on the pleura, pericardium and their related fluids, but never in the blood. In our recent publication, perfusion 2016, we demonstrated that surgical maneuver of sucking blood from the pleura or from the pericardium, very common during the cardiac procedures, lead to a strong exfoliation of the mesothelial cells from the serosae. Those cells mix with the blood in the heart lung machine and are finally pumped in the aorta. And from the aorta the mesothelial cells reach all the organs (Fig. 1).

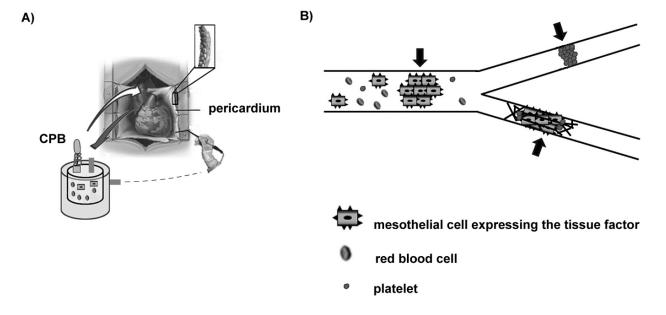


Fig. 1. Cartoon explaining the hypothesis of mesothelial cells microembolization. (A) Mesothelial cells exfoliating from the pericardium are sucked from the surgical field, get mixed with the blood of the CPB and are re-injected in the systemic circulation. (B) Activated mesothelial cell, aggregated in clusters, embolize in the micro vessels (arrows) and cause vessel thrombosis.

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We moreover found that immediately after the aspiration of the blood from pleura and pericardium thousands of mesothelial cells embolize in the peripheral arterial blood, and several of those cells tend to create macro emboli with a mean size of 80  $\mu$ m (the mean size of the single mesothelial cells is 30  $\mu$ m) (Fig. 2). It has been previously demonstrated that activated mesothelial cells are able to trigger the coagulative cascade, furthermore, given the mean size of the capillaries (6  $\mu$ m), is easy to suppose that the mesothelial cells, single or aggregate, embolize and occlude the capillaries, with consequent arteriolar thrombosis, organ damage and inflammatory reaction. Clearly, the more blood the organs receive, the higher is the risk of damage: not surprisingly those organ are lungs, kidneys and brain.

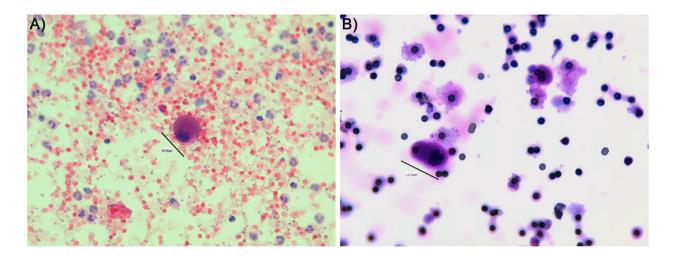


Fig. 2. (A), Cytological smear of peripheral blood, showing a circulating non-hematologic cell with a diameter of 35,68 μm (Hematoxylin and eosin staining, magnification 200X). (B), A circulating non-hematologic cell with a diameter of 42 μm, isolated by ScreenCell filtration system, the black dots are the pores of the filters, (8 μm in diameter) (Hematoxylin and eosin staining, magnification 200X).

To assess if the mesothelial cells have actually an impact on the coagulation, we performed an *invitro* test (ROTEM ™, Intem and Extem test), with blood contaminated by mesothelial cells and found that both the extrinsic and the intrinsic pathway were deranged compared with the non –contaminated controls.

In conclusion, we found that mesothelial cell microembolization can play a role in the postoperative complications following cardiac surgery. Further studies are needed to evaluated the real clinical impact of our finding and possible preventive strategies.

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## **Publication**

Circulating non-hematological cells during cardiopulmonary bypass: new findings in cardiac surgery procedures.

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