Title: Alpha-2 Agonists and Ischemia-Reperfusion Injuries in Free Flap Surgeries: A Narrative Literature Review

Author(s): Dallemagne Max, Lebussy Kilian

Hospital/Institute: (complete address)

Cliniques universitaires Saint-Luc, Université catholique de Louvain

Avenue Hippocrate 10, 1200 Bruxelles

The objective of this narrative literature review is to evaluate the potential of alpha2-agonists in preventing injuries caused by ischemia-reperfusion phenomenon and their role in modulating microcirculation during reconstructive surgeries involving free flaps

# **Background:**

Alpha-2 agonists are commonly used molecules in clinical practice in the operating room and intensive care units due to their sedative and opioid-sparing properties. Recent research has demonstrated their potential in preventing inflammatory processes during sepsis, cardiac surgeries, and mitigating microcirculatory alterations during surgical stress. These findings prompt us to consider the use of these molecules in reconstructive surgeries involving free flaps. Every free flap surgery faces the challenge of ischemia-reperfusion, resulting in cellular damage, activation of pro-inflammatory pathways, and circulatory disturbances.

#### **Methods:**

We referred to publications found on PubMed, Google Scholar, and the Cochrane database. The terms used include "adrenergic alpha-2 receptor agonists," "microcirculatory," "ischemia-reperfusion," "free flap surgery," "dexmedetomidine," and "clonidine." The search period extends from 2010 to the year 2022. The publications used include both human and animal studies. Case reports and articles dealing with other alpha2 agonists were not considered.

## **Results:**

In in vitro and animal studies, alpha2 agonists, mainly dexmedetomidine, have shown promise in reducing proinflammatory processes and microcirculatory alterations after ischemia-reperfusion (1). From an inflammatory perspective, they decrease the production of IL-6, TNF-alpha, and Il-1B. They also inhibit pro-apoptotic pathways and activate anti-apoptotic pathways. They decrease oxidative phenomena, enhance antioxidant pathways, and regulate NO production. From a microcirculatory perspective, there is an improvement in flap perfusion indices; lower cellular edema and necrosis rates, as well as better flap viability, are observed(2). There are no human studies focusing on the prevention of ischemia-reperfusion injuries by alpha2-agonists in free flap surgery. However, a study on healthy volunteers demonstrate that clonidine improves endothelial function and modulates inflammatory processes after reperfusion of a limb subjected to hypoxia(3).

### **Conclusions:**

This narrative literature review suggests that alpha-2 agonists may protect free flaps from the deleterious effects of ischemia/reperfusion. They may also reduce microcirculatory alterations. While these findings have been demonstrated in animal studies, larger clinical studies in humans are necessary to confirm their efficacy.

### **Declaration of interests:**

None

## **Fundings:**

None

# **References:**

1: Gencay, I., Boybeyi, O., Unlu, G., Yazici, I., Aydin, G., & Buyukkocak, U. (2019). Dexmedetomidine as an Alternative Anesthetic Agent for Flap Surgery : An Intravital Evaluation in the Cremaster Muscle Flap. Journal of Craniofacial Surgery, 30(8), 2469-2472. https://doi.org/10.1097/SCS.0000000000005850

-	2: Fang, M., He, J., Ma, X., Li, W., & Lin, D. (2020). Protective effects of dexmedetomidine on the survival of random flaps. Biomedicine & Pharmacotherapy, 128, 110261. https://doi.org/10.1016/j.biopha.2020.110261
-	3: Gourdin, M., Dubois, P., Mullier, F., Chatelain, B., Dogné, JM., Marchandise, B., Jamart, J., & De Kock, M. (2012). The Effect of Clonidine, an Alpha-2 Adrenergic Receptor Agonist, on Inflammatory Response and Postischemic Endothelium Function During Early Reperfusion in Healthy Volunteers: Journal of Cardiovascular Pharmacology, 60(6), 553-560. https://doi.org/10.1097/FJC.0b013e31827303fa