Commentary: Postconditioning of the injured spinal cord: Can we do more?

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Central Message

Spinal cord stimulation postconditioning is mediated through $\alpha 7nAChR$ microglia inhibition and enhances neuronal survival and neurologic function in a rabbit model of spinal cord injury.

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Spinal cord injury (SCI) is still one of the most devastating complications of aortic surgery. It occurs in as many as 20% of patients after open and endovascular thoracoabdominal aortic aneurysm repair and is associated with poor long-term outcomes and increased health care costs.^{1,2} Accumulating evidence from multicentric registry data analyzing clinical outcomes after aortic arch surgery with modern hybrid stent grafts, also known as the frozen elephant trunk (FET) procedure, suggests the occurrence of postprocedural SCI in as many as 7% of patients, thereby calling into question the deliberate use of the FET procedure.³ SCI occurred in 6.5% of 170 patients after the FET procedure in the international, multicenter registry for the E-vita OPEN PLUS hybrid stent graft (JOTEC GmbH Hechingen, Germany).⁴ Similarly, a recently published article in the *Journal* from the International Aortic Arch Surgery Study Group reported an SCI rate of 6.3% after the FET procedure.⁵

The underlying mechanisms of SCI after aortic surgery are not yet fully understood. As a consequence, current therapeutic strategies largely focus on various perioperative and intraoperative measures to prevent or limit the effects of spinal cord ischemia and subsequent reperfusion injury. These measures include sufficient cooling of the core body temperature, avoidance of prolonged duration of lower body circulatory arrest, blood pressure management, cortisone application, selective antegrade cerebral perfusion, and continuous cerebrospinal fluid drainage.⁶⁻⁸ Furthermore, surgical strategies mainly have the target of preserving collateral blood supply to the spinal cord. Avoidance of extended stent coverage of aortic segments or the left subclavian artery, reinsertion of the segmental artery in thoracoabdominal aortic aneurysm repair, and achievement of an optimal distal landing zone (higher than T7 to T10) during the FET procedure have all been linked to a decrease in the incidence of SCI.^{3,7,8} The introduction of the spinal cord collateral network concept by Griep and coworkers^{9,10} and its recent clinical translation of preconditioning the paraspinal arterial

collateral network perfusion system by minimally invasive selective segmental artery coil embolization before thoracoabdominal aortic aneurysm repair¹¹ represent another important step toward decreasing SCI in this high-risk patient cohort.

This issue of the *Journal* presents the results of a very interesting basic science report by Li and coworkers¹² that adds another important piece in the puzzle of understanding the underlying mechanisms of delayed SCI after aortic surgery. Li and coworkers¹² focused on the postconditioning effects of spinal cord stimulation (SCS) in a rabbit model of transient spinal cord ischemia triggered by a balloon occlusion of the infrarenal aorta for 28 minutes with subsequent reperfusion. Spinal cord stimulation (2 Hz for 30 minutes through an epidural electrode) at the onset of reperfusion and then daily for 1 week attenuated ischemia-reperfusion injury by inhibition of proinflammatory microglia activation, enhancing neuronal survival and neurologic function of the spinal cord. Most importantly, Li and coworkers¹² found that the neuroprotective effects of SCS in delayed SCI were mediated through $\alpha 7$ nicotinic acetylcholine receptor ($\alpha 7nAChR$) microglia inhibition. This finding was supported by the fact that the aforementioned positive neuroprotective effects of SCS were largely blunted in animals that received serial subarachnoid injections of a selective irreversible $\alpha 7nAChR$ antagonist.

Li and coworkers¹² are to be congratulated for their excellent basic research work on this highly complex and clinically relevant topic. They have elucidated a relevant mechanism of SCI in complex aortic surgery and potentially provided a target for future pharmacologic therapies that specifically target microglia inhibition through $\alpha 7$ nAChR agonists. Although it may be premature to reach a final conclusion for clinical practice on the basis of this experimental work, it seems intriguing to speculate that a therapeutic combination of spinal cord preconditioning and postconditioning (including minimally invasive selective segmental artery coil embolization, SCS, or $\alpha 7$ nAChR agonists) may diminish SCI and its detrimental clinical sequelae for patients undergoing surgery for complex aortic disease. Further experimental evidence is needed, perhaps from larger animal models, under conditions that more closely reflect the clinical setting of extensive aortic repair (including longer durations of thoracoabdominal spinal cord ischemia, persisting malperfusion, and postreperfusion treatment regimen) to confirm the promising results of this excellent work.

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