Advances in spinal cord protection for complex aortic repairs

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Spinal cord ischemia (SCI) and subsequent paraplegia remains the most dreaded obstacle for complex thoracoabdominal aortic interventions, occurring in up to 20% of patients undergoing extent II repair. Although aneurysm extent, location, presence of dissection, and urgency confer risk, SCI still occurs in roughly 4% of elective nondissected short-segment aortic repairs.^{1,2} This relatively high incidence in low-risk patients underscores the humbling and indiscriminate nature of postoperative paraplegia.

The contemporary approach to spinal cord protection is based on optimizing spinal cord hemodynamics through cerebrospinal fluid drainage, permissive hypertension, and preservation of cord perfusion vessels. Perfusion support will remain a mainstay of treatment for high-risk procedures and for patients exhibiting spinal cord deficits; however, the metabolic tolerance of the cord remains at odds with the recovery of blood flow through the collateral network. Emerging frontiers are focusing on expanding the spinal cord's ability to tolerate ischemia and, more importantly, optimizing perfusion techniques, enhancing recovery of the cord, and maximizing the dynamic nature of the collateral arterial network.^{3,4}

EXPANDING ISCHEMIC TOLERANCE

The focus of most spinal cord injury translational research is on identifying methods to increase the spinal cord's tolerance of transient ischemia. Although there have been many operative advances in reducing the overall surgical ischemic insult, it has not been eliminated. Spinal cord ischemia-reperfusion injury results in a bimodal pattern of neurologic injury thought to be due to an initial ischemic insult that activates a secondary inflammatory insult during reperfusion.⁵ An ongoing question in ischemia tolerance research is how to preserve injured yet viable neurons during the secondary reperfusion insult and subsequent loss by apoptosis.

Erythropoietin (EPO) holds significant promise among pharmacologic treatments, with established anti-inflammatory and neuroprotective effects in murine models of ischemic stroke and contusive spinal cord injury.⁶ EPO

A patient with Marfan's syndrome presenting with an expanding intercostal patch aneurysm. His initial operation was complicated by postprocedural weakness, which recovered. He had 4 large intercostals coming off the patch, all of which would be taken with thoracic endovascular aortic repair (TEVAR) coverage of the patch (A). Therefore, we coiled 2 of the intercostals (B) at 2 weeks before TEVAR, which excluded the others (C). The patient exhibited no weakness or signs of spinal cord injury, demonstrating the feasibility of this approach.

Central Message

Advances in spinal cord protection are working to expand ischemia tolerance, optimize perfusion, and maximize the collateral network.

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has been proven to improve functional outcomes and reduce neuronal loss in multiple animal models of ischemic injury, including in our own laboratory's murine model of spinal cord ischemia-reperfusion injury using a thoracic aortic cross-clamp.⁶⁻⁹ The mechanism of EPO in ischemia-reperfusion injury relies on a specific tissue protective receptor that is unique from the hematopoietic receptor^{8,9} in that it activates antiapoptotic pathways and is thought to preserve neurons throughout the reperfusion phase of injury.

Another important focus of ischemia-reperfusion injury research is in dampening the severity of the reperfusion insult. Microglia play a significant role in enhancing the inflammatory signaling that follows neurologic ischemia.⁷ Inhibitors of microglial activation, such as alpha 2 receptor agonists and Toll-like receptor 4 receptor antagonists, have promising data from animal models that support their efficacy in improving functional and cellular outcomes.¹⁰⁻¹²

Although these agents have shown promising results, it is unlikely that multi-institutional randomized trials will be supported by the pharmacologic industry. Nonetheless, the importance of these adjuncts cannot be overemphasized, given that emergent cases may be limited to these treatments alone.

PRECOLLATERALIZATION

For many years, Griep and colleagues^{4,13,14} have focused on characterizing changes in blood supply to the spinal cord occurring after different types of aortic repair. They measured spinal cord perfusion pressure (SCPP) following sacrifice of intercostal and lumbar arteries in a porcine model of SCI and demonstrated a 24- to 48-hour reduction in SCPP following sacrifice of all intercostal and lumbar arteries, analogous to the injury induced by thoracoabdominal aneurysm repair. Remarkably, SCPP returned to normal levels by 48 hours despite no intercostal or lumbar artery reimplantation, suggesting augmentation of existing collateral arterial vasculature acutely by arteriogenesis. That study and similar efforts have advanced our understanding of the dynamic nature of spinal cord blood supply and the ability to manipulate and augment cord perfusion.

Consequently, manipulation of the collateral network as a means of arteriogenic preconditioning has progressed in animal models, and is now being used in clinical practice as means of preventing SCI during high-risk procedures. Surgeons have begun temporally spreading out the sacrifice of direct spinal cord inflow sacrifice by staging full aortic exclusion through both open and hybrid techniques^{4,13,14}; for instance, the proximal to mid-descending can be stented before the eventual open completion. Another approach has been the creation of graft fenestrations to intentionally perfuse the aneurysm sac, with coverage of the fenestration done at a later date.

The anatomy of the aneurysm dictates the extent of staging, however. The real future of staging collateralization focuses on the intercostal and lumbar arteries rather than on the aneurysm. The segmental feeders can be occluded directly with consistent control of the extent of sacrifice with serial embolization of intercostal or lumbar arteries. In fact, the first-in-man experience of segmental arterial coil embolization to prevent spinal cord was published in the *Journal* earlier this year.¹⁵⁻¹⁷ This preemptive sacrifice of spinal cord blood flow in a region that inevitably will be sacrificed for the aneurysm repair allows for distribution of the overall ischemic insult over time and for augmentation of the arterial collateral network before additional loss of segmental arteries.

Surgeons at our institution also have performed this procedure before repair of an extent II aneurysm. This technique has proven safe to date, but the need for research remains in terms of how to occlude these vessels, how many vessels to take at a time, how long to wait between sacrifices to allow perfusion recovery, and how to decide which collaterals to take first.

SUMMARY

In summary, paraplegia following complex aortic surgery remains a devastating complication that has been

improved on in past decades but seems to have hit a ceiling in terms of the inability to further reduce its occurrence. Current advances in collateral network manipulation and ischemia tolerance adjuncts hold significant promise in finally affecting improvement in patient outcomes and reduction of this postoperative complication. Further research on spinal cord ischemia injury is warranted to examine the potential benefits and limitations of these approaches.

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