cord remains at risk beyond the initial ischemia trigger. KATP channels are inward rectifiers, and opening thereof provides ischemic protection via hyperpolarization and suppression of neuronal activity in the classic preconditioning model. Both drug dose-dependent responses as well as time point of administration might further impact treatment efficiency. Additional mechanistic understanding of KATP downstream pathways is warranted to ultimately delineate its role.

Nevertheless, the aforementioned results are remarkable. Improving tolerance of the spinal cord to ischemic insults on a cellular level has the potential to be a game changer and may become an essential tool in the arsenal of the aortic surgeon. We look forward to hearing more from this group, and others, as they strive to carry work like this bench to bedside.

See Article page e90.

Commentary: A little help from the bench to cut risk of paraplegia?

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Although open aortic repair is associated with substantial postoperative complications, spinal cord deficit (ie, paraplegia and paraparesis) may be the most devastating one. Regarding Crawford's lifetime experience with 1509 thoracoabdominal aortic aneurysm (TAAA) repairs, as presented

Illustration of the spinal cord.

CENTRAL MESSAGE

Preventing spinal cord deficit requires a multimodal approach.

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in the late 1990s by Svensson and colleagues,¹ the rate of postoperative spinal cord deficit was a staggering 31% after the most extensive form of such repair, the Crawford extent II TAAA repair. Since the Crawford era, the rates of spinal cord deficit have dramatically decreased; rates of temporary and permanent spinal cord deficit were 2.4% and 5.4%, respectively, across all extents of TAAA repair, and for extent II repair, the rate of permanent spinal cord deficit was 8.0%.² How were surgeons able to reduce the

likelihood of developing postoperative spinal cord deficit? There has been an ongoing refinement of surgical technique that is based on the recognition that protecting the spinal cord is essential to preventing paralysis; these efforts have resulted in gradual improvements in contemporary outcomes across many aortic centers.³ The use of a multimodal approach⁴ to TAAA repair that includes cerebrospinal fluid drainage, left heart bypass, maintaining an adequate mean arterial pressure, and revascularization of intercostal arteries,⁵ as well as additional measures⁶ that may include motor-evoked potential monitoring,⁷ systemic or targeted hypothermia, the use of intrathecal papaverine with cerebrospinal fluid drainage,⁸ or other pharmacologic agents,⁹ appears to have collectively reduced the risk of paraplegia. Furthermore, many of these adjuncts have been adopted in endovascular aortic repair, which also carries an enhanced risk of spinal cord deficit but is without simple methods to revascularize the intercostal arteries.

In this issue of the *Journal*, Ikeno and colleagues¹⁰ from the University of Colorado explore pharmacologically induced tolerance to spinal cord deficit using a murine model. Specifically, using several robust murine models, they investigate the role of direct and indirect activation of mitochondrial ATP-sensitive potassium channels in the prevention of spinal cord ischemia. Mice were pretreated with a 3-day course of different combinations of pharmaceutical agents (eg, nicorandil, diazoxide, carboxy-PTIO), followed by inducing spinal cord ischemia through cross-clamping of the aorta for 7 minutes. Results measured by functional tests and immunohistochemistry were impressive—nicorandil significantly preserved motor function.

However, questions remain. First, the age of the tested mice was young (ie, 3–4 months old), and as we all know, patients undergoing aortic repair of the distal aorta tend to be older. Younger mice have a different physiology than older ones, not to mention a lack of atherosclerotic plaque that is so prevalent in typical patients undergoing distal aortic repair. Second, all experiments were conducted in normothermic circumstances (37°C–38°C), whereas most open distal aortic repairs are performed under mildly hypothermic (32°C) or profoundly hypothermic ($\leq 18^\circ\text{C}$) conditions. Temperature is well-established to significantly influence and change the cellular metabolism of the acutely sensitive tissue of the spinal cord. Third, the authors studied one mode of development for spinal cord deficit—the ischemic–reperfusion pathway; in clinical practice, the development of spinal cord deficit is multifaceted and involves ischemic and embolic pathways and may also

present immediately after repair or in a delayed fashion (within a few days after initially being determined to be free of any related concern).

Postoperative spinal cord deficit is complex; prevention of this life-altering complication necessitates the use of multiple strategies. Although the rates of spinal cord deficit have been reduced in recent decades, there remains a duty to further decrease the rate of this debilitating and life-altering complication. The use of nicorandil appears effective in mitigating ischemic–reperfusion injury to the spinal cord and may be a welcome addition to existing multimodal protection strategies. Attempts by the authors to define and explore preventative measures and investigate possible pharmacologic agents present an interesting venue for further investigation. Nicorandil appears a promising possible addition to the armamentarium of surgeons and may have very practical applications in reducing risk during endovascular aortic repair.

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