What vasopressor promotes better spinal cord perfusion after traumatic spinal cord injury? A direct comparison of norepinephrine and phenylephrine in a porcine model of SCI.

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Introduction
Current clinical guidelines for acute SCI recommend elevating the mean arterial blood pressure (MAP) to increase spinal cord perfusion, which is typically achieved with vasopressors such as norepinephrine (NE) and phenylephrine (PE). While both are effective at raising the MAP, it is unclear which of these two vasopressors actually promotes better perfusion within the spinal cord. These drugs differ in their pharmacologic properties and therefore potentially have different effects on spinal cord blood flow (SCBF), oxygenation (PO2), and downstream metabolism after injury. Using a porcine model of thoracic SCI, we evaluated how these vasopressors influenced intraparenchymal SCBF, PO2, hydrostatic pressure, and metabolism within the spinal cord adjacent to the injury site.

Methods
Yorkshire pigs underwent a contusion/compression SCI at T10 and were randomized to receive either NE (n=9) or PE (n=9) for MAP elevation of 20 mm Hg, or no MAP augmentation (n=4). Prior to injury, a combined SCBF/PO2 sensor, a pressure sensor, and a microdialysis probe were inserted into the spinal cord adjacent to T10 at two locations: a 'proximal' site and 'distal' site, 2 mm and 22 mm from the spinal cord injury, respectively. Measurements were made both during sustained compression and after decompression, to simulate the clinical conditions during which acute SCI patients typically have MAP augmentation.

Results
At the proximal site, NE and PE resulted in little improvement in SCBF during cord compression. Following decompression, NE resulted in increased SCBF and PO2, while decreased levels were observed for PE. However, both NE and PE were associated with a gradual decrease in the L/P ratio after decompression. PE was associated with greater hemorrhage through the injury site than control animals.

Figure 1 - spinal cord intraparenchymal monitoring of blood flow, oxygenation, and metabolism
(a) Schematic drawing and (b) surgical set-up illustrating the fixation device, which is secured rigidly via the pedicle screw/rod construct to the spinal column. The device has three independently drilled channels through which the SCBF/ PaPO2 (left), pressure (right) and microdialysis (middle) probes are inserted. The final location of the sensor tips are approximately 0.2 cm and 2.2 cm away from the edge of the impactor. * Spinal cord injury hemorrhage.

Figure 2 - Spinal cord perfusion and hemorrhage after norepinephrine and phenylephrine MAP augmentation
Norepinephrine promotes better spinal cord perfusion than phenylephrine after acute SCI, both during sustained compression and after decompression (top panel). Area measurements of hemorrhage taken from axial sections of spinal cord tissue 800 um apart (bottom panel) show that the amount of hemorrhage tends to be increased in both the PE and NE group compared to the control animals. The extent of hemorrhage in PE animals is significantly greater than control.

Conclusions
Combined, our results suggest that NE promotes better restoration of blood flow and oxygenation than PE in the traumatically injured spinal cord, thus providing a physiologic rationale for selecting NE over PE in the hemodynamic management of acute SCI. However, the increased hemorrhage observed in the spinal cord with the vasopressors serves as a warning of the potential adverse consequences of MAP augmentation.

Learning Objectives
Norepinephrine promotes better blood flow and oxygenation within the injured spinal cord, as compared to phenylephrine.

MAP augmentation with phenylephrine results in greater hemorrhage within the spinal cord.