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Commentary: Cell therapy for spinal regeneration—implications for recovery after complex aortic surgery

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Spinal ischemia–reperfusion injury is a dreaded complication affecting some patients after complex aortic surgery, causing paraplegia and loss of quality of life.[1] Contemporary neuroprotection strategies will optimize spinal cord perfusion, pressures, and temperature but do not address postischemic injury by enhancing neurorepair and regeneration.[2] Cellular therapy for spinal regeneration may provide a unique approach to preserve postoperative quality of life.

In this issue of *JTCVS Open*, Nakai and colleagues[3] investigate the therapeutic potential of human bone marrow mesenchymal stromal cells (hBM-MSCs) in spinal ischemia–reperfusion injury in a novel murine model. Spinal ischemia–reperfusion injury was induced by clamping both the aortic arch distal to the left carotid and the proximal left subclavian artery for 5 minutes. Intravenous administration of hBM-MSCs was performed 2 hours after reperfusion. Histology showed localization of hBM-MSCs in the spinal cord, lung, spleen, and kidney. Motor functional recovery was enhanced in the cellular treatment group, accompanied by improved lumbar spinal cord motor neuron density. Reverse transcription polymerase chain reaction results also showed a transcriptional shift in the spinal cord favoring anti-inflammatory and angiogenic pathways. Overall, the authors highlight the potential reparative capacity of hBM-MSC therapy after spinal cord ischemia.

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CENTRAL MESSAGE

Cell-based regenerative strategies may provide unique avenues for postoperative repair of ischemic spinal cord injuries and preserve quality of life after complex aortic interventions.

This study provides the first step toward the use of novel, cell-based treatments to address spinal ischemia–reperfusion injury after complex aortic surgery. While the data are exciting, there are important limitations. Systemic delivery of cells may limit regional engraftment at the site of interest and decrease effectiveness. Cells homing to other organs off-target could have serious side effects. The underlying cell and molecular mechanisms mediating the observed functional benefits are also unclear. Understanding whether hBM-MSCs require direct contact with the spinal cord, if they differentiate into key cell populations, or if paracrine release of reparative biomolecules is key for further development. Nonetheless, the data demonstrate the value of exploring this novel cellular therapy.

The future of ischemic spinal cord repair and regeneration is promising. Targeted administration by direct injection, intrathecal delivery, or by arterial fluoroscopic catheter approaches may be capable of delivering cell therapies without sequestration outside the target organ. Understanding mechanisms for postischemic spinal cord repair, such as critical paracrine mediators, may also facilitate future acellular therapies. Acellular repair can mitigate key barriers of stem cell therapy, such as donor-cell availability, engraftment variability, and numerous regulatory challenges.[4,5] Biomaterials from extracellular matrix or synthetic origins have been shown to provide bioactive factors that upregulate endogenous mechanisms of repair or act as a base to improve cell engraftment.[6-9] Further exploring optimal administration strategies and better defining reparative mechanisms may facilitate targeted patient-specific strategies that will protect and enhance the quality of life of patients undergoing complex aortic surgery.

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