

Article information: <https://dx.doi.org/10.21037/jss-22-116>

Reviewer 1

Comment 1: *The authors do not provide evidence that spinal drains are essential in TEVAR*

Response: While the placement of a spinal drain is not required in every patient undergoing TEVAR, patients considered for prophylactic CSF drain placement are those deemed at high risk for spinal cord ischemia. A study by Suarez-Pierre et al of 1, 292 propensity-matched pairs of patients (2,584 total patients) from the Vascular Quality Initiative TEVAR registry found that spinal drain placement was associated with a reduced risk of SCI (1.5% vs 2.5%; risk-adjusted odds ratio [OR], 0.47; 95% confidence interval [CI], 0.24-0.89; P = .02). In this study, among patients undergoing thoracic and thoracoabdominal endovascular aortic repair, preoperative placement of a spinal drain, compared with no drain, was associated with reduced risk of SCI. Cerebrospinal fluid drainage as a rescue measure was found not to provide the same protection offered by routine preoperative placement.

Reference: *Suarez-Pierre A, Zhou X, Gonzalez JE, et al. Association of preoperative spinal drain placement with spinal cord ischemia among patients undergoing thoracic and thoracoabdominal endovascular aortic repair. J Vasc Surg 2019;70:393-403. 10.1016/j.jvs.2018.10.112*

Additionally, a retrospective, single-center review of 85 patients, performed from January 2014 to December 2019 by Chaudhary et al, concluded that the use of prophylactic CSF drain placement reduced the rate of spinal cord injury to approximately 2%, whereas the overall incidence of SCI in the literature is between 4-9% for all patients. Each institution should evaluate their own risk of spinal cord drainage and determine whether the strategy is appropriate on an individual basis. Patients are considered high risk if undergoing >20 cm aortic coverage, coverage of the lower third of the thoracic aorta, pararenal or type IV thoraco-abdominal aortic aneurysm with planned coverage of >5 cm above the celiac artery, a history of previous abdominal aortic aneurysm repair or surgery, or occlusion of the left subclavian artery or internal iliac arteries.

Reference: *Chaudhary O, Sharkey A, Schermerhorn M, Mahmood F, Schaefer M, Bose R, et al. Ann Vasc Surg 2020*

Response to reviewer comment in the text: Line 71 we have added “While the placement of a spinal drain is not required in every patient undergoing TEVAR, patients considered for prophylactic CSF drain placement are those deemed at high risk for spinal cord ischemia. A study by Suarez-Pierre et al of 1, 292 propensity-matched pairs of patients (2,584 total patients)

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Comment 2: The authors do not compare outcomes between anesthesiologist and IR placed spinal drains

Response: To date, there is no head-to-head comparison study to assess outcome differences between anesthesiologist and IR placed spinal drains. A possible reason for this stems from the fact that IR placed drains are usually undertaken after unsuccessful attempts by anesthesiologists or failure by the anesthesiologist to successfully place the drain. Such a comparative study would be welcome and likely need to be multi-centered, prospective and randomized to be of maximal benefit. There is literature showing patient satisfaction scores with IR placed drains are high due to the prone position and lower volume of CSF fluid loss during the procedure.

Comment 3: The authors simply present their institutional protocol and opinion as a review

Response: There was no intention by the authors to present our institutional approach as a review. There is a lack of consensus for the optimal management of lumbar drain catheters and each institution should evaluate their own risk of spinal cord drainage and determine whether the strategy is appropriate on an individual basis.

Reviewer 2

Comment 1: In your recommendation you do not state what to do in a case of difficulty of placement at the beginning of the case. You mention: previous difficulty, anticipated difficulty during preoperative assessment, multiple prior attempts, and post-operative coagulopathy. You do not state what your opinion is on the right course of action in an event where the patient is in the room getting poked, but no dice. Earlier in the manuscript you mention this problem but do not offer any final recommendations for this particular situation and why.

Response: Failure to successfully place the lumbar drain in the operating room requires discussion between the surgeon and the anesthesiologist. We recommend an urgent consultation with IR and to transport the patient under general anesthesia to interventional radiology for placement under fluoroscopic guidance. Preoperative planning to include informing IR of a potential need for their assistance is advisable. Less attractive options that need to be discussed and considered are to proceed without the drain or to emerge from anesthesia and abort the procedure with a plan for elective surgery with elective drain placement by IR on another date.

Response to the reviewer comment in the text: Line 77 we have added “We recommend an urgent consultation with IR and to transport the patient under general anesthesia to interventional radiology for placement under fluoroscopic guidance.”

Comment 2: Please comment on use of point-of-care ultrasonography (POCUS) for aid of placement. POCUS has been used successfully by OB anesthesiologists for epidurals and spinal for many years now. Is there any data or expert opinion on POCUS of spinal anatomy preoperatively or right before the lumbar drain placement? If not, should it be routinely used to improve the success rate?

Response: A 2011 literature review incorporating 7 review articles, 5 RCTs, 27 observational cohort studies, 14 case reports and 2 technical articles, by Chin et al, ‘*Ultrasonography of the Adult Thoracic and Lumbar Spine for Central Neuraxial Blockade*’ concluded that while ultrasound-guided neuraxial blockade is a useful technique that can be used to accurately identify intervertebral levels, estimate depth to the epidural space, and locate an appropriate interlaminar space for needle insertion, the authors stated that “we do not believe the technique should supplant the traditional surface landmark-based techniques of spinal and epidural anesthesia; these are simple, safe, and effective”. We agree with the findings of this literature review.

Reference: Chin et al, *Ultrasonography of the Adult Thoracic and Lumbar Spine for Central Neuraxial Blockade* Anesthesiology 2011; 114:1459 – 85

Additionally, a more recent 2021 systematic review of randomized controlled trials with meta-analysis and trial sequential analysis (see reference below), sought to compare the efficacy, efficiency and the safety of pre-procedural ultrasound to landmark palpation in the non-obstetric adult population. In all, 18 randomized controlled trials with 1800 patients were included in this review. Pre-procedural ultrasound increased the total time taken (mean difference 110.8 s; 95% CI, 31.01 to 190.65; P = 0.006; I² = 96%; moderate quality of evidence) and subgroup analyses revealed no influence of the predicted difficulty of the neuraxial procedure on outcomes. The authors concluded that the use of pre-procedural ultrasound for neuraxial procedures in the non-obstetric adult population did not enhance the first pass success rate and increased the total time taken to a clinically insignificant extent.

Reference: Onwochei D, Nair G, Young B, Desai N. *Conventional landmark palpation versus preprocedural ultrasound for neuraxial procedures in nonobstetric patients: A systematic review with meta-analysis and trial sequential analysis of randomised controlled trials.* European Journal of Anaesthesiology. 2021 Aug;38(Suppl 2):S73-S86.

As stated by the reviewer, POCUS has been used by obstetric anesthesiologists for neuraxial blockade for several years. However, while it is true that POCUS has been used successfully by OB anesthesiologists for epidural/spinal placement, and anecdotally there may be instances when POCUS helps with epidural placement, society guidelines do not recommend the ultrasound technique over the conventional landmarks technique. The authors agree with this approach.

Response to the reviewer comment in the text: Line 131 we have added the following text “A recent 2021 systematic review of randomized controlled trials with meta-analysis and trial sequential analysis sought to compare the efficacy, efficiency and the safety of pre-procedural ultrasound to landmark palpation in the non-obstetric adult population. Pre-procedural ultrasound increased the total time taken and subgroup analyses revealed no influence of the predicted difficulty of the neuraxial procedure on outcomes. ¹². Line 186 we have added an additional reference.

Comment 3: Line 79. You identify that "intuitively" that are some reasons why TEVARs may have less concern for SCI. Very recently, new data are coming about about different pathophysiology between SCI in open repairs and TEVARs. Please include these in your discussion. Does not need to be long, 1-2 sentences, but the mention of potentially different pathophysiology is paramount

Response: We removed the word “intuitively” from the manuscript. In light of the recent research data in the reference below, based on behavior, MRI, histopathological and metabolome comparisons, the results in the published animal research referenced below provide evidence that the mechanisms of spinal cord injury from endovascular repair seem to be drastically different to those from open repair. We have included this in the text of our manuscript.

Reference: Awad, H., Tili, E., Nuovo, G. *et al.* Endovascular repair and open repair surgery of thoraco-abdominal aortic aneurysms cause drastically different types of spinal cord injury. *Sci Rep* 11, 7834 (2021).

Response to the reviewer comment in the text: Line 79 the word “intuitively” has been removed from the text. Line 186 we have added the reference Awad, H., Tili, E., Nuovo, G. *et al.* Endovascular repair and open repair surgery of thoraco-abdominal aortic aneurysms cause drastically different types of spinal cord injury. *Sci Rep* 11, 7834 (2021).

Comment 4: Authors mention different pharmacologic therapeutics. Please also mention use of naloxone infusions and evidence behind them.

Response: SCI in TEVAR can be significantly reduced by using proactive intraoperative and postoperative neuroprotective interventions that prolong spinal cord ischemic tolerance and increase spinal cord perfusion and oxygen delivery. Numerous interventions have been postulated to preserve spinal cord integrity. Naloxone infusion during aortic surgery has been hypothesized to decrease SCI. Naloxone infusions up to 1ug/kg/hr in addition to bolus doses of mannitol and methylprednisolone have been associated with some spinal cord protection. However, these patients required greater quantities of opioid analgesics and experienced higher postoperative pain scores compared with patients not managed with naloxone. The mechanism of action of naloxone may be mediated by the effect on the excitatory amino acid glutamate which increases during ischemic events and is associated with neuronal cell toxicity. Glutamate inhibition could explain the neuroprotective effects of naloxone. In addition, endogenous opioids may reduce microcirculatory blood flow following injury to the spinal cord. Animal stroke models indicate improved blood flow and outcome in patients who received naloxone during an ischemic event. Evidence suggests the role of kappa receptors in SCI, with minimal delta receptor involvement. Naloxone may also reduce proteolysis, neutrophil superoxidase release and fluctuations in calcium movement across membranes.

Acher C, Marks E, Wynn M *Intraoperative neuroprotective interventions prevent spinal cord ischemia and injury in thoracic endovascular aortic repair* J Vasc Surg 2016 Jun;63(6):1458-65.

Johnson E, Nguyen J, Oyler D, Davenport D, Endean E, Tyagi S *Naloxone Continuous Infusion for Spinal Cord Protection in Endovascular Aortic Surgery Leads to Higher Opioid Administration and More Pain*, J Cardiothorac Vasc Anes Volume 35, Issue 4, April 2021, Pages 1143-1148

Olsen P, Hoffman C, Green M *Naloxone Infusion During Thoracic Endovascular Aortic Aneurysm Repair to Prevent Spinal Cord Injury* J Cardiothorac Vasc Anesth 2018 Apr;32(2):e37.

Response to the reviewer comment in the text: Line 112 we have added the following text - Naloxone infusions up to 1ug/kg/hr in addition to bolus doses of mannitol and methylprednisolone have been associated with some spinal cord protection. However, these patients required greater quantities of opioid analgesics and experienced higher postoperative pain scores compared with patients not managed with naloxone. Glutamate inhibition could explain the neuroprotective effects of naloxone. Evidence suggests the role of kappa receptors in SCI, with minimal delta receptor involvement. Naloxone may also reduce proteolysis, neutrophil superoxidase release and fluctuations in calcium movement across membranes.

Comment 5: Any role of hyperbaric therapy for SCI? Maybe worth one sentence regarding potential future direction. A center from Toronto might have some anecdotal success.

Response: Hyperbaric oxygen therapy significantly increases levels of vascular endothelial growth factor (VEGF), which is essential for promoting angiogenesis and neuroprotection. It helps restore blood supply in the spinal cord by increasing vascular density, which promotes neuronal protection and functional recovery. As such, it has been described in several case reports as part of the multimodal treatment for spinal cord ischemia including as adjunct rescue treatment for patients with spinal cord injury that were refractory to traditional medical management.

Reference: Parotto M, Ouzounian M, Fedorko L, Oreopoulos G, Lindsay T, Katznelson R. Hyperbaric oxygen therapy for spinal cord ischaemia after complex aortic repair - a retrospective review. *Anaesthesiol Intensive Ther.* 2018;50(2):103-109.

Response to reviewer comment in the text: line 114 we have added the following – Hyperbaric oxygen therapy has been described in several case reports as part of the multimodal treatment for spinal cord ischemia, including as adjunct rescue treatment for patients with spinal cord injury refractory to traditional medical management.

Comment 6: Why do you capitalize anesthesiology?

Response: We did not have any reason for capitalizing the word anesthesiology. We have reformatted the text to remove same.

Response to reviewer comment in the text: lines 23, 32 and 124 we have removed the capital A and replaced the letter with a lower case a.