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EDITORIAL

What should we do against delayed onset paraplegia following TEVAR?

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Spinal cord ischemic injury remains the most devastating complication following the repair of descending thoracic or thoracoabdominal aneurysm. Despite the use of various strategies to prevent spinal cord ischemia, its risk and accompanying neurological deficits have not changed appreciably since it was first reported in 1956 by Adams and Van Geertruyden [1]. In a large series of patients undergoing thoracic or thoracoabdominal aortic aneurysm repair, it ranged from 4.4 to 16 % [2–4].

The traditional repair of descending thoracic aortic aneurysm with thoraco-laparotomy requires aortic cross-clamping and is associated with considerable morbidity and mortality rates despite the significant advances in perioperative critical care and anesthetic, neuro-monitoring [5] and surgical techniques [6–8]. Because endovascular treatment, compared to conventional surgery, is associated with a decrease in hospital mortality and postoperative morbidity, the use of stent-grafts has already changed the treatment of lesions of the descending thoracic aorta, and endovascular repair has been an alternative to traditional repair. Endovascular treatment was also expected to potentially reduce the incidence of ischemic spinal cord injury; however, the rate was reported to be 0–12 % [9–11], which is comparable to that of surgical series (2.7–13.8 %) [12, 13].

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One of the main reasons that the risks associated with spinal cord injury have not decreased is that our understanding of the mechanisms of injuries associated with spinal cord ischemia and reperfusion remains poor. Clinically, ischemic spinal cord injury can present with dense motor deficits on emergence from anesthesia (immediate paraplegia) or it can present in a delayed fashion with progressive lower extremity weakness (delayed paraplegia). Interestingly, in a prospective observation study, Maeda et al. [14] showed that a greater percentage of patients with ischemic spinal cord injury following thoracic endovascular aneurysm repair (TEVAR) had a delayed paraplegia (66.7 %) than following traditional treatment (16.7 %). Similar results were also reported by Ullery et al. [15]. Thus, it is expected that as TEVAR increases in the future, so will the incidence of delayed onset paraplegia.

Whereas the mechanism responsible for delayed paraplegia is incompletely understood, several studies show the presence of apoptosis and caspase-3 activation in the spinal cord of animals exhibiting delayed onset paraplegia [16, 17]. And one experimental study using caspase-3 knockout mice has provided definitive evidence that caspase-3 activation is required for the development of delayed paraplegia following spinal cord ischemia [18]. These observations have important clinical implications suggesting the preventive effects of caspase-3 inhibition against spinal cord ischemia resulting from surgery (including TEVAR). However, due to their toxicity [19], caspase inhibitors are not yet available in clinical practice. Additionally, following spinal cord ischemia, delayed neurological dysfunction occurs in 2 phases, correlating to increases in inflammatory chemokine release and microglial activation [20], and toll-like receptor 4-mediated microglial activation in the spinal

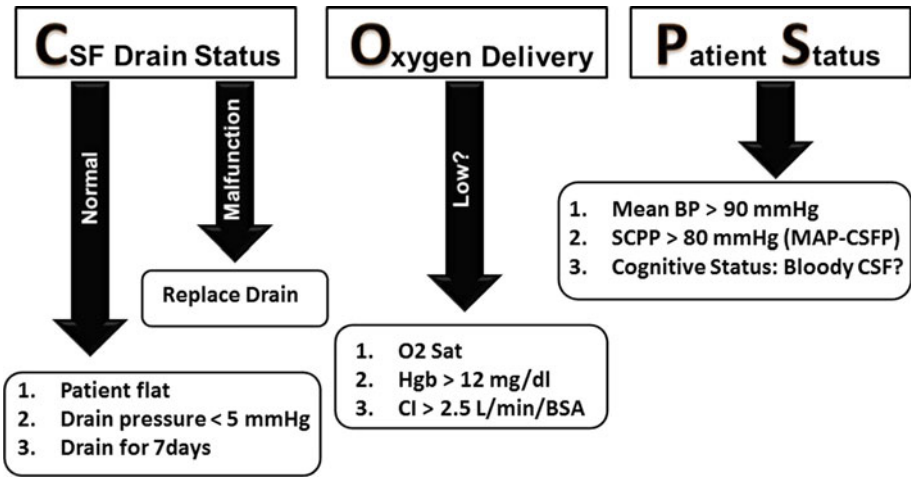

Fig. 1 Treatment of delayed neurological deficits: the "COPS" Protocol. *CSF* cerebrospinal fluid, *Hgb* hemoglobin, *CI* cardiac index, *MAP* mean arterial pressure, *SCPP* spinal cord perfusion pressure

cord is critical in the mechanism of delayed paraplegia [21]. According to a recent experimental study [22], minocycline, which potentially attenuates the activation of microglia, represents a clinically relevant pharmacologic tool to reduce the risk of paraplegia in patients undergoing TEVAR. However, as far as I know, any clinical trials to prove their neuroprotective effect have not yet shown up. Unfortunately, although perioperative cerebrospinal fluid drainage (CSFD) was shown in a randomized clinical trial to reduce the total rate of paraplegia after aortic surgery, it could not provide significant reduction of the incidence in delayed onset paraplegia [23]. In other words, we do not, as yet, have a certain preventable method for delayed onset paraplegia.

Postoperative factors that may incite delayed onset paraplegia were reported to include hypotension, systemic inflammatory response syndrome, sepsis, cardiac dysrhythmias or cardiac failure, and diminished oxygen delivery caused by anemia, hypoxia, and low cardiac output [24]. In the past two decades, Svensson et al. [4] emphasized the importance of maintaining adequate blood pressure postoperatively for collateral circulation of the spinal cord. Of interest to us, Estrera et al. [25] recently proposed a treatment protocol (CSFD status/oxygen delivery/patient status; COPS) for delayed neurological paraplegia after aortic surgery, whereby CSFD is maintained for 3 days postoperatively to keep CSF pressure less than 10 mmHg with a limit of 15 ml/h when the patient is neurologically intact. If delayed neurological deficits occur, then the CSF is drained to maintain a pressure of <5 mmHg without limit (Fig. 1) [25]. I do believe that this COPS protocol can enhance the "collateral network" to perfuse the spinal cord in patients undergoing TEVAR and thereby decrease the risk of delayed onset paraplegia after TEVAR.

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