Contemporary Spinal Cord Protection During Thoracic and Thoracoabdominal Aortic Surgery and Endovascular Aortic Repair: A Position Paper of the Vascular Domain of the European Association for Cardio-Thoracic Surgery

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Abstract  Ischemic spinal cord injury (SCI) remains the Achilles heel of open and endovascular descending thoracic and thoracoabdominal repair. Recently, neurological outcome has improved coincidentally with the introduction of neuroprotective measures. However, permanent paraplegia remains the most devastating complication.

The aim of this position paper is to provide physicians with broad information regarding spinal cord blood supply, to share strategies foreshortening intraprocedural spinal cord ischemia and to describe strategies to increase spinal cord tolerance to transitory ischaemia, diagnostic and therapeutic strategies to detect ischemia and augment spinal cord blood perfusion will be described.

This manuscript is meant to support physicians caring for patients in need of any kind of thoracic or thoracoabdominal aortic repair in decision making algorithms in order to understand, prevent or reverse ischemic spinal cord injury.

Information has been extracted from focused publications available in PubMed database being cohort studies, experimental research reports, case reports, reviews, short series and meta-analyses. Individual chapters of this position paper were assigned and after delivery harmonized by CE, EW and MC. Consequently, further writing assignments were distributed within the group and delivered in August 2014. The final version was submitted to the EJCTS for review in September 2014.

Classes of recommendation

Class I
Definition
Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
Suggested wording to use- is recommended/ is indicated

Class II
Definition
Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.

Class IIa- weight of evidence/opinion is in favour of usefulness/efficacy
Suggested wording to use- should be considered

Class IIb- Usefulness/efficacy is less well established by evidence/opinion
Suggested wording to use- may be considered
Class III

Definition
Evidence or general agreement that the given treatment or procedure is not useful/effective and in some cases may be harmful.
Suggested wording to use- is not recommended

Levels of evidence
Level of evidence A- data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B- data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C- consensus of opinion of the experts and/small studies, retrospective studies, registries.
Abbreviations in the text

DTA- descending thoracic aorta
TAAA- thoracoabdominal aneurysm
SCI- spinal cord injury
TEVAR- thoracic endovascular aortic repair
SA- segmental arteries
CSF- cerebrospinal fluid
MAP- mean arterial pressure
SSEP- somatosensory evoked potentials
MEP- motor evoked potentials
ASA- anterior spinal artery
PSA- posterior spinal artery
SCPP- spinal cord perfusion pressure
IOM- intraoperative neurophysiological monitoring
LHB- left heart bypass
COPD- chronic obstructive pulmonary disease
CVP- central venous pressure
IRP- intercostal reimplantation
ICA- intercostal artery
EP- evoked potentials
Epi-MEP- epidural motor evoked potentials
CMAP- compound muscle action potentials
NIRS- near infrared spectroscopy
MISACE- minimally invasive selective segmental artery coil embolization
Summary and Background

Over half a century after the first successful surgery for aneurysms of the descending thoracic (DTA) and thoracoabdominal aorta (TAAA) by Etheredge (in 1955) and De Bakey (in 1956), ischemic spinal cord injury (SCI) remains the most devastating complication after repair of any modality. In 1993 Svensson described the risk of paraplegia after open surgery according to the ‘Crawford classification’—(Table I) 15% of type I, in 31% of type II, 7% of type III and 4% of type IV aneurysm patients suffered postoperative paraplegia. In the past two decades, the neurological outcome of open DTA/TAAA repair has improved coincidently with the introduction of several neuroprotective adjuncts and cerebrospinal fluid drainage (1-9). In spite of numerous strategies designed to reduce the risk of SCI its occurrence is relevant (1,3,4,10-15).

Thoracic endovascular aortic repair (TEVAR) offers a less-invasive approach diminishing the magnitude of the repair-associated injury by avoiding thoracotomy and aortic cross-clamping, minimizing perioperative end-organ ischemia and the insult to the respiratory system but is still associated with a significant risk of SCI.

In 2007, Coselli presented the largest open repair series so far of 2286 patients reflecting a significant improvement in spinal cord protection with 3.3% for type I, 6.3% for type II, 2.6% for type III and 1.4% for type IV TAAAs— the current benchmark for endovascular repair. Paraplegia is an individual disaster with profound impact on early mortality, longevity and health care cost, and eventually a significant socioeconomic issue (16,17). Conrad et al stratified SCI after open and endovascular DTA/TAAA repair by deficit severity and determined its impact on early and late survival: the 30-day mortality was significantly higher in patients with SCI (and varied with the severity of the SCI); 5-year mortality more than doubled with SCI and reached 100% amongst patients with flaccid paralysis (18).

The final goal to eliminate SCI has not yet been reached. Since ischemic SCI is multifactorial in origin, contemporary spinal cord protection requires an integrated strategy and a multimodality approach. The successful treatment of the—often old and frail—patient with an extensive aortic pathology remains a challenging task for all members of the multidisciplinary aortic team.
Common risk factors for paraplegia/paraparesis after DTA/TAAA repair are: 1. Aneurysm extent (related to the number of segmental arteries (SA) compromised, e.g. occluded, sacrificed or reimplanted during repair), 2. Location, aneurysms affecting the lumbar region (with less robust collateralization as compared to the thoracic region where intercostal arteries provide instant backup flow originating e.g. from both mammaries) 3. Extended aortic cross-clamp times during open repair—particularly when adding prolonged (normothermic, or only mild to moderately hypothermic) distal circulatory arrest to segmental inflow compromise (19-21)– while deep hypothermic circulatory arrest and distal aortic perfusion might be protective (19,22-27) and 4. Perioperative hypotension (e.g. after weaning from CBP (28), or during the early postoperative period (e.g. during temporary atrial fibrillation) (29,30)—might be a widely underestimated risk factor responsible for a significant number of cases of postoperative ischemic injury resulting in delayed-onset paraplegia: up to 83% of all patients developing paraplegia after open repair and 87% of cases after endovascular repair, respectively (19,29,31-35).

After TEVAR and open repair a ‘post-implantation syndrome’may aggravate the risk for delayed paraplegia (36). Recent advances in the understanding of the anatomy and physiology of the collateral network supplying the spinal cord have lead to a new experimental strategy of the ‘staged repair (37,38). This strategy has been validated in a large retrospective analysis and might be applicable to open and endovascular repair and particularly suitable for hybrid repairs. None-the-less, reoperative DTA/TAAA repair might be significantly safer with hypothermic circulatory arrest for two reasons: it protects the cord from intraoperative ischemic insults by decreasing metabolism, secondly, it lowers the incidence of postoperative hemodynamic instability resulting from intraoperative visceral ischemia (23,25,29).

Based on these considerations contemporary concepts for perioperative spinal cord protection involve: 1. The maintenance of high-normal /moderately elevated arterial pressure; 2. The drainage of cerebrospinal fluid and 3. The reattachment of critical SAs in open repair (particularly if staging is not an option) (5,13,29,39-43). The prevention of spinal cord ischemia requires the knowledgable use of these adjuncts and a thorough understanding of the anatomy and physiology of spinal cord blood supply, the appropriate monitoring modalities and the characteristics of haemodynamic support, surgical and interventional techniques, and their interaction.
Introduction

Aortic disease, including DTA and TAAA, is the 12th leading cause of overall death in the United States: between 43,000 and 47,000 patients die annually in the United States from diseases of the aorta and its branches (44). While the exact numbers for Europe are not readily available, an estimated 110,000 to 125,000 Europeans die annually from aortic disease. The natural history of DTA/TAAA is devastating and five-year survival range from 13% to 50% (45-48). The majority of patients with DTA/TAAA are in their 60’s, 70’s, and 80’s and have difficulties in tolerating the physiological insult of open surgical repair. In Europe probably fewer than 5000 (<2000 in the U.S.) DTA/TAAA per year are treated, with a hospital mortality rate of up to 20% and a one-year survival of only 60 to 70%; as a consequence, probably 4 out of 5 patients with DTA/TAAA decline (or are not even offered) surgery because it is anticipated that they will have a prohibitive operative mortality and morbidity.

TEVAR and open repair both severely compromise the blood supply to the spinal cord: either by extensive SA-sacrifice during surgery, the simultaneous SA-occlusion with the deployment of covered stentgrafts or the interruption of collateral perfusion during aortic cross clamping (or with large bore sheaths in place during prolonged endovascular procedures) leaving the hypogastric arteries not being perfused and the collateral network thus being deprived of its major distal inflow source. Accordingly, the major risk factors for ischemic SCI during TAA/A-repair are: 1. The extent of aortic graft replacement or endovascular covering (i.e. the complexity of the repair) 2. The presence of acute aortic dissection—particularly, with extensive, acute SA-malperfusion due to the formation of a false lumen and 3. The degree of urgency (i.e. limited time for proper planning, no option for staging or even lack of maintainance of perioperative hemodynamic instability). The risk may vary between 4-7% after TEVAR for DTA, 2-28% after elective descending aortic surgery and up to 40 % after emergency repair of extensive TAAAs. [Table II].

The impact of prior distal aortic operations—i.e. abdominal aortic aneurysm resection—on SCI risk after reoperative surgery for more proximal aortic disease affecting the descending or thoracoabdominal aorta has been the focus of controversial expert debates. Large retrospective series suggest a decreased risk of acute SCI, also supported by experimental evidence and the concept of a ‘staged repair’—while others discuss an increase in paraplegia / paraparesis risk (37,38,49-51). The key to understanding the pathophysiology behind reoperative repair might be to understand how the previous repair affected the collateral inflow—i.e. if the hypogastrics have been sacrificed or the left subclavian has been overstented, the risk of a subsequent repair might be increased.
The pathophysiology of spinal cord injury in DTA/TAAA-surgery is essentially an ischaemia-infarction model caused by a variety of mechanisms. It has been assumed that injury arises primarily as a consequence of two mechanisms: 1. An intraoperative insult after temporary interruption of spinal cord blood supply during surgery of duration sufficient to irreversibly damage cell bodies and nerve tracts in the spinal cord. 2. The second insult was thought to occur postoperatively: permanent reduction of blood supply secondary to sacrifice of critical blood vessels – the thoracic (intercostal) and lumbar SAs – to a level incompatible with cord viability.

While the first pathomechanism primarily affects open surgical repair, the second mechanism also is limiting endovascular repair due to the sudden simultaneous occlusion of SA inflow when a covered stentgraft is deployed percutaneously and perfusion to the hypogastric arteries supplying distal collateral inflow may be compromised by large bore sheaths during the procedure. Starting with aortic cross-clamping or circulatory arrest during open aortic repair and followed by the sacrifice or exclusion of SA. During TAAA-repair arterial blood supply to the spinal cord is acutely reduced possibly triggering edema and subsequently an increased production of cerebrospinal fluid (CSF). Elevated CSF pressure generates a gradient hindering arterial blood to enter the spinal canal and arterial blood supply to the spinal cord is progressively reduced leading to a vicious circle of progressive ischemic injury.

Significant progress has been made in understanding the paraspinal and intraspinal arterial collateral network supporting the spinal cord during depreviation of major sources of direct arterial blood supply (37,52). Contemporarily strategies to prevent acute SCI in DTA/TAAA surgery or TEVAR primarily aim for minimizing the duration of ischemia during surgery by means of improving perfusion pressure and flow as well as tissue oxygen delivery, and enabling early detection of spinal cord ischaemia to permit immediate intervention. Intraoperatively, numerous adjuncts have been implemented to reduce SCI. Currently, left heart bypass, cerebral spinal fluid (CSF) drainage, reimplantation of the most important SAs, hypothermia, and maintenance of an adequate mean arterial pressure (MAP) are thought to be effective measures. Electrophysiological assessment is helpful in detection of ischemia in the monitored neural tracts, the use somatosensory evoked potentials (SSEP) or motor evoked potentials (MEP) has been studied extensively in thoracoabdominal aortic surgery and TEVAR. Additionally, these methods might be able to detect situations of marginal blood flow resulting in neuronal dysfunction 1. At a time when the neurons are still salvageable and the insult is potentially reversible and 2. Allowing for guidance of therapeutical interventions to relieve acute ischemia.
This article reviews the multiple factors involved in the development of SCI resulting in paraplegia/paraparesis following DTA/TAAA surgery, TEVAR and hybrid approaches, the clinical experience with different approaches to decrease the risk of spinal cord ischaemia, and the neuroprotective measures lowering the incidence of spinal cord ischaemia.
Spinal Cord Blood Supply

Arterial blood supply to the spinal cord is provided by the anterior spinal artery (ASA) arising cranially from both vertebral arteries to supply its anterior portion. A pair of posterior spinal arteries (PSA) also arising from the vertebral arteries supplies the posterior spinal cord. Caudally, the ASA receives arterial collateral blood from the internal iliac arteries and the sacral artery, and from the inferior mesenteric artery. Additional supply is provided by paired intercostal and lumbar SAs that originate from the descending thoracic and abdominal aorta.

Two different paradigms are used to explain the elusive nature of spinal cord circulation, one based on anatomic (direct, segmental supply) and the other on less anatomic and rather dynamic demand depending (collateral) blood supply (42). A thorough understanding of the anatomy of the blood supply of the spinal cord appears essential for developing strategies to prevent spinal cord injury. Direct visualization of these vessels is arduous and most surgeons therefore continue to rely on a few classic anatomic studies. The most influential of these has been the treatise by Albert W. Adamkiewicz (1850–1921), whose meticulously detailed drawings suggest that the most important input to the ASA is a single dominant branch of a SA in the lower thoracic or upper lumbar region, which is now often referred to as the artery of Adamkiewicz, who in 1881 published his thesis entitled ‘Die Blutgefäße des menschlichen Rückenmarks’ at the University of Krakau (53). His concept became the accepted doctrine for over a century – and the rationale to justify reimplantation of intercostals and lumbar arteries in TAAA surgery – even after Guy Lazorthes in 1971 postulated a new concept he had developed since the 60’s, based on three main arteries, each arising from several regional segmental arteries, supplying the cervical, thoracic and lumbo-sacral region of the spinal cord (54-56).

The clinical relevance of these concepts is controversial: the proponents of Adamkiewicz’ argue that SA reimplantation during TAA/A repair is the best possible strategy for preserving spinal cord blood supply (57-62). Despite various painstaking and inventive attempts to avoid ischemic SCI with this approach, there continues to be a definite seemingly irreducible incidence of paraplegia and paraparesis after treatment of extensive TAAA (59,62-64). Furthermore, reattaching intercostal or lumbar SAs—a daunting undertaking during open surgical repair—is not possible with current endovascular techniques. (Table II summarizes the incidence of paraplegia / paraparesis after both – open surgical and endovascular repair).
Imaging techniques to identify SAs considered critical to spinal cord function are controversial. In the 1990s, selective intercostal angiography was introduced to preoperatively identify the artery of Adamkiewicz (57,59). Then radiologic imaging technology evolved and Noijiri et al proposed preoperative detection of the artery of Adamkiewicz using intraarterial computed tomographic angiography (65). Recently, it became possible to identify what was thought to be the artery of Adamkiewicz using magnetic resonance angiography (66-69).

Within the spinal canal, there is an axial network of small arteries that connect with each other as well as with major arteries that supply the spinal cord (37). Blood supply to the spinal cord is even more complex and pathologically modified in patients with aortic diseases. In almost 25% of these patients, most SAs are occluded and spinal cord integrity is maintained by an extensive collateral network in which lumbar arteries and the pelvic circulation are responsible for main blood supply. Reimplantation of SAs increases aortic x-clamp time and possibly aggravates intraoperative spinal cord hypoperfusion due to blood loss via backbleeding. Probably a substantial percentage of reimplanted SAs occlude early. Alternative surgical techniques for reimplantation include latero-lateral aortic patch reimplantation or the use of small bypasses such as vein grafts or prostheses.

The alternative paradigm suggests- in addition to the radicular arteries- the spinal cord also has a complex collateral circulation. It is hypothesised that there is also an axial network of small arteries in the spinal canal, perivertebral tissues, and paraspinal muscles that receives input from the subclavian, internal thoracic, lumbar and hypogastric arteries [Figures I-III]. These small arteries are connected with each other and with the ASA and PSA providing blood flow to the spinal cord. This network can increase blood flow from one source when another is impaired. Conversely, steal effect can occur - spinal cord blood flow can be reduced if an alternative lower resistance pathway becomes patent elsewhere in the circulation. The concept of collateral circulation is most probably the reason why the maintenance of high arterial blood pressure and cardiac index may reduce spinal cord ischaemia in TAAA surgery.

Reimplantation of significant patent intercostal arteries has been associated with lower paraplegia rates (43). However, if a particular branch is small or occluded, a great deal of time may be spent without benefit – possibly even causing harm to the spinal cord increasing the risk of intraoperative SCI. Intercostal reimplantation may jeopardise spinal cord blood flow by back bleeding. Even after successful revascularisation of a dominant SA, symptomatic spinal cord injury may be observed. On the contrary, intercostal reimplantation may jeopardise spinal cord blood flow by back bleeding. By using ligation or clipping of SA (preferably prior to opening the aneurysm sack), the blood flow is directed to the spinal cord by collateral vessels and the need for revascularisation becomes
futile. Therefore it might be more important to consider the superior and inferior supply of the spinal cord via the subclavian arteries and internal iliac network (e.g. the hypogastric arteries). At least unilateral internal iliac artery perfusion should be strictly maintained. Careful consideration is also warranted in the treatment of common and internal iliac aneurysms particularly if an iliac stentgraft is utilized. A branched stentgraft should be used if possible—otherwise proximal embolization, e.g. with Amplatzer plugs seems to give (at least) less buttock ischemia. However, patients with poor pelvic circulation are critically dependant on the above-mentioned specific intercostal vessels. In these cases, reimplantation of critical intercostals (Th8 - L4) may be considered.
The duration of aortic cross-clamping has a close relationship to the risk of neurological complications. For this reason, one major objective of surgery is to keep the overall ischaemic time short.

Open TAAA repair starts by placing a cross-clamp on the proximal and distal aorta to isolate partially (sequential or staged repair) or totally the diseased segment. Unless distal aortic perfusion via extracorporeal circulation support is initiated there is no or only minimal blood flow below the cross-clamp. Spinal cord perfusion is sustained only via vertebral, cervical and subclavian arteries. Thus, spinal cord perfusion pressure (SCPP = radicular artery end pressures minus the greater of venous or cerebrospinal fluid pressures) may be compromised (70,71). Important arteries arising from the aortic aneurysm sac are no longer perfused. In case of back bleeding, the steal phenomenon will additionally reduce both collateral network pressure and thereby perfusion pressure of the ASA. Therefore, it is important to avoid back bleeding instantly by oversewing (or preferably prior to aneurysm sac opening by clip occlusion); blocking of the corresponding SAs with small catheters after opening the aneurysm is another option (with caution in patients with connective tissue disease) if an island repair is planned. A novel approach termed “minimally invasive segmental artery coil embolization” (MISACE) is an elegant alternative recently introduced as an option allowing for endovascular staging to precondition spinal cord blood supply, avoid “steal” and type II endoleaks and shorten cross clamp time. Several methods have been used to provide reperfusion on the one hand and avoid back bleeding of these arteries on the other hand. One approach is to preserve a fragment of the back wall of the aneurysm where large SA arise and use it during aortic reconstruction with the idea to restore critical perfusion. Another approach is to attach critical SAs via a second prosthesis into the aortic prosthesis. Furthermore, to prevent significant steal via back bleeding, non-critical arteries are occluded with surgical clips from outside or oversewn from inside. A common mistake is to aim for reimplantation of the vigorous ‘back bleeders’—but these are the arteries that are sufficiently collateralized—rather than those SA that do not bleed back. As the time required for reimplantation all segmental vessels possibly increases the risk of paraplegia, IntraOperative neurophysiological Monitoring (IOM) may direct the surgeon during sequential cross-clamping and provide information about which vessels are essential for sufficient spinal cord perfusion. However, the success of this strategy is controversial and the paraplegia rates with this strategy have not proven to be superior.
Because of the key role of pelvic circulation mainly provided by the hypogastric arteries, many patients are critically dependant on distal (retrograde) perfusion from left heart bypass (LHB; femoral artery bypass. Partial LHB provides a controlled perfusion of the distal aorta by directing blood from the left atrium to the distal descending aorta or femoral artery. Flow is controlled by the centrifugal pump, while some institutions even use a complete circuit with a membrane oxygenator. During partial LHB with a proximal aortic cross-clamp, the distal aortic cross-clamp can be moved from proximal to distal as repair of the descending aorta progresses to minimise end organ ischaemia, a technique that has been termed ‘sequential repair’ by Dr Coselli. A large amount of retrospective data suggests that the use of LHB in extensive TAAA reduces the risk of ischaemic complications. The absence of an oxygenator in the LHB system necessitates less heparinisation, which is associated with considerable reduction in bleeding. It effectively improves oxygenation during one-lung ventilation, especially as vascular surgery patients frequently are smokers with chronic obstructive pulmonary disease (COPD) (72). In addition, LHB allows for selective perfusion of mesenteric branch vessels through separate balloon-blocked catheters. Summarised, LHB facilitates both afterload reduction as well as cooling and rewarming, avoids vasodilators, increases distal aortic pressure for patients dependent on caudal vessels, reduces an increased CSF pressure, and decreases the risk of visceral and spinal cord ischaemia by permitting selective organ and segmental artery perfusion. However, LHB does not appear to be the ultimate advance for all cases: this especially applies to Crawford TAAA Classification Type I and II patients, where the rate of spinal cord dysfunction is not reduced.
Strategies to Increase the Spinal Cord Tolerance to Transitory Ischaemia

The highly metabolic grey substance of the spinal cord is more sensitive to ischaemia than the white substance. Under normothermic conditions, the central nervous system hardly tolerates ischaemia, manifesting neuronal dysfunction and injury within 5 min after the cessation of blood flow. When incomplete ischaemia is produced, paraplegia generally does not occur with an aortic cross-clamping time of less than 15 minutes. As cross-clamp time is prolonged, the risk of paraplegia gradually increases. It is important to note, that the risk of spinal cord injury is closely related to the body core temperature during lower body circulatory arrest, initiated with placing the cross clamp: Kamiya and colleagues from the Hannover group found a six-fold increase in the incidence of ischemic spinal complications in their subgroup analysis of patients undergoing prolonged distal circulatory arrest at only moderate hypothermia (73). Experimentally, the safe period of distal arrest has been shown to be widely overestimated and irreversible spinal cord ischemia at 28 Celsius occurs earlier than expected (74). The only intervention in humans that has consistently proven to be effective in protecting the central nervous system from ischaemia during absence of blood flow is hypothermia (75-77). Additionally, delayed postoperative rewarming might have a positive effect on the ischemia tolerance of the spinal cord and therefore is part of the postoperative protocol at some institutions (however, there is not yet enough clinical evidence or prospective randomized data to proof this concept.)

The protective effect of hypothermia is thought to be primarily a consequence of the decreased metabolic demands associated with reduced spinal cord oxygen consumption. But hypothermia may also protect the cell by stabilising membranes and attenuating the inflammatory and excitotoxic responses to ischaemia during reperfusion. Further protection of the spinal cord tissue has been attempted with regional spinal cord hypothermia (epidural cooling) (64). However, besides contamination issues, responsive hyperperfusion and consecutive development of edema is feared by some after cooling is ended.

In addition to lowering oxygen consumption, the risk of intraoperative spinal cord ischaemia may be avoided or minimised by improving oxygen delivery via an increase of spinal cord perfusion pressure. Demand side interventions prolong ischaemic tolerance by decreasing oxygen demand (barbiturates and hypothermia), while reducing the levels of neurotoxins released during ischaemia and/or their deleterious effects (naloxone and hypothermia) The spinal cord may be directly protected against neuronal injury at the cellular level by reducing hyperemic and inflammatory responses (hypothermia, steroids and free radical scavengers). Supply side interventions increase spinal cord
blood supply and tissue oxygen delivery by maximizing collateral blood flow to the spinal cord, reducing spinal fluid pressure, increasing arterial blood pressure and cardiac index during and after the repair, preventing steal and guaranteeing a sufficient oxygenation during aortic cross-clamping. The observation that similar reductions in paralysis can be achieved by combining different therapies basically reflects the complexity of spinal cord blood supply and neuronal injury.
Strategies to Augment Spinal Cord Perfusion

As previously elaborated on, spinal cord perfusion during aortic surgery depends on 1. The ASA flow from radicular vessels arising above the proximal cross-clamp and supplied by proximal aortic pressure, and 2. From vessels arising from the aorta below the distal cross-clamp, depending on distal aortic perfusion via LHB or CPB with oxygenator and from the central venous and CSF pressure. During proximal aortic cross-clamping, MAP increases considerably and needs pharmacological correction to control left ventricular afterload. The elevated cerebral blood pressure during proximal aortic cross-clamping may result in an overproduction of CSF and an elevation of CSF pressure. Elevated CSF pressure further reduces SCPP. If CSF pressure exceeds both ASA and PSA pressure, the spinal cord blood flow is ceased and oxygen supply interrupted- the spinal cord is suffering ischaemia. Full or partial recovery from delayed postoperative paraplegia after open or endovascular TAAA repair has been reported and emphasizes the effectiveness of acute interventions to improve spinal cord perfusion, if applied instantly. Postoperative events such as hypotension due for instance to haemorrhage or increased CSF pressure may also increase the risk of paraplegia after open and endovascular TAAA repair. Therefore, maintaining adequate spinal cord perfusion by increasing arterial pressure and augmenting cardiac output, together with preventing hypotension, lowering CSF pressure, and reducing central venous pressure (CVP), is important for the prevention of spinal cord ischaemia.

CSF production rises during ischaemia causing an increased CSF pressure appearing soon after cross-clamping. To minimise spinal cord ischaemia, CSF drainage is used to maintain a low CSF pressure while improving net perfusion pressure. The physiological basis for lumbar CSF drainage is given by SCPP being a direct function of MAP minus lumbar CSF pressure (or alternatively central venous pressure). Therefore, an increased CSF pressure decreases SCPP. Draining CSF has the potential to increase SCPP by decreasing CSF pressure. Experiences during open surgical DTA/TAAA repair have shown that this intervention has a positive effect on neurological outcome. In general, introduction of a CSF catheter is performed preoperatively but can also be performed postoperatively when neurological symptoms develop. It is highly advisable to insert a CSF drain in all patients undergoing TAA/A surgery or thoracoabdominal EVAR and measure CSF pressure for at least 48 hours postoperatively. If CSF pressure was allowed to rise postoperatively in combination with a period of blood pressure instability immediately beforehand, late onset spinal cord dysfunction due to spinal cord edema may occur. CSF should be drained into a sealed reservoir to achieve a CSF pressure of 10 mmHg, some institutions alternatively aim for the preoperative ‘opening pressure’ immediately after CSF cath placement as an individual baseline pressure of the patient. CSF drainage appears to be
a safe method even in patients subjected to full anticoagulation for extracorporeal circulation. Complications associated with this technique occur in up to 1% of patients and include intracranial hypotension, subdural haematoma, intracranial haemorrhage, remote cerebellar haemorrhage, spinal headache, persistent CSF leak, intraspinal haematoma, catheter fracture, meningitis, and direct spinal cord injury. Some institutions insert the CSF catheter on the evening prior to surgery to avoid or ameliorate bleeding complications. The most serious complications appear to be associated with intracranial hypotension from rapid or too much CSF drainage. Precautions, such as continuous measurement of CSF pressure, controlled intermittent CSF drainage, and assessment of coagulation function, decrease the risks associated with CSF drainage.

Augmentation of MAP or in combination with CSF drainage is another technique for the treatment of spinal cord ischaemia. In general, vasopressor agents such as norepinephrine are administered to maintain a MAP of 80–100 mmHg to ensure a SCPP of at least 70 mmHg. A more recent clinical study suggested that failure to maintain a patient’s individual preoperative arterial baseline pressure during the early postoperative period after TAA/A repair is strongly associated with delayed postoperative paraplegia (29). MAP can be further increased in 5 mmHg steps in case of persisting SCI. When arterial pressure increases, it is also important to assure a satisfying cardiac output and to guarantee an optimal oxygen delivery (control of hemoglobine). In addition, maintaining a normal or reduced during arterial pressure augmentation may also be important for maximizing SCPP. Inconsistent arterial pressure control may also partly explain the controversy surrounding the effectiveness of CSF drainage as an exclusive decrease of CSF pressure without additional arterial pressure control may limit the ability to improve spinal cord perfusion. Hypotension from bleeding or other causes is often associated with the onset of SCI after TAAA repair. Nevertheless, clinical observations suggest that SCI may as well contribute to hypotension due to generalized vasoplegia. In some patients, spinal cord ischaemia-associated hypotension is caused by neurogenic shock with autonomic dysfunction. In this situation, hypotension may not be the cause but represent an early sign of spinal cord ischaemia and the beginning of a vicious cycle. An immediate treatment of hypotension associated with spinal cord ischaemia is necessary to prevent permanent paraplegia. Finally, arterial pressure should be monitored carefully when antihypertensive therapy is resumed after successful open or endovascular TAA/A repair to avoid unintentional hypotension. Nitroprusside derivatives should be strictly avoided due to possible AV-shunting. The benefits of postoperative arterial pressure increase must be weighed against the risk of bleeding and the risks associated with temporary arterial pressure elevation. Anaesthetic staff needs to be well trained in the management of TAAA surgery and the postoperative patient to prevent large variations of blood pressure during and early after the procedure. Equally, an intensive care unit that is familiar with all aspects of postoperative care after
TAA/A repair is very important to provide maximal haemodynamic stability. Many patients with late onset paraplegia have a documented period of instability prior to symptoms.

Spinal cord perfusion can be surgically augmented by reattachment of segmental arteries into the vascular graft, if the surgeon respects the anatomic paradigm that direct segmental blood flow is the most important intervention to reduce paraplegia risk. Large segmental arteries with little or no back bleeding may be particularly important for spinal cord perfusion. Alternatively, occlusion or oversewing of strong back-bleeding segmental arteries has been advocated to improve spinal cord perfusion by preventing arterial steal effect and shortening intraoperative ischemic time (3). As most reports combine intercostal reimplantation (IRP) with other strategies it is hard to determine how much reattachment of intercostal arteries (ICA) contributes on its own to improved results, even though it is frequently presented as the factor primarily responsible for reducing paraplegia.

On the other side, a significant reduction of the risk of paralysis without IRP was obtained by increasing ischaemic tolerance and maximising collateral circulation to the spinal cord. Significantly, this technique maintains high proximal arterial blood pressure during aortic occlusion. These findings show that spinal cord infarction can almost always be prevented without any IRP if ischaemic protection and collateral circulation to the spinal cord are sufficient (3). Although this approach considerably reduced immediate paralysis, delayed paralysis still occurred in a few patients days to weeks after surgery (29). The occurrence of delayed paraplegia shows the limitations of perioperative ischaemic protection and of the maintenance of collateral circulation strategies to prevent infarction (29). Recent advances in magnetic resonance angiography have permitted a more precise imaging of the ASA and the expected most important SAs in patients with TAAA. It provides a method to anatomically identify SA for potential reimplantation. Non-selective IRP may also be protective by additionally increasing perfusion pressure in the collateral circulation and feeding the greater radicular artery. This suggests that any SA can supply blood to the spinal cord and may evolve into collateral circulation to the ASA. In patients with reduced collateral circulation, reimplanting any SA in the critical zone of T8 to L1 may permanently increase perfusion pressure in the collateral network. This may be the important factor to avoid spinal cord infarction, not whether specific identified intercostals are reimplanted.

Techniques that rely on extensive IRP based on changes in evoked potentials (EP) may be successful not because intercostals identified by ischaemic changes were reimplanted, but because reimplanting so many intercostals increased perfusion pressure in the collateral circulation. By
reimplanting SA as an aortic button using a side clamp after the distal anastomosis is completed, it is possible to achieve high SA patency without significantly increasing aortic occlusion times. These findings suggest that factors related to spinal cord ischaemia as well as collateral circulation account for most of the paralysis risk in TAAA surgery and that IRP, although not necessary to prevent paraplegia in most patients, is critically important in a few. Since we do not yet know how to identify the few patients who will be paralysed without IRP, it is important to reimplant SA only without substantially increasing intraoperative spinal cord ischemic time, surgical morbidity and mortality, even in those who would not be paralysed without IRP in order to maximize the benefit for the few who would be.

In TEVAR, it is not possible to preserve blood flow in segmental arteries. If the left subclavian artery requires coverage by the endovascular stentgraft to facilitate complete exclusion of the aneurysm or to allow for a better proximal landing zone, subclavian arterial flow should be preserved by prior transposition of the subclavian artery onto the left common carotid artery. Another approach to preserve left subclavian artery flow in TEVAR is to perform a left carotid to subclavian bypass graft with ligation or coil embolisation of the proximal left subclavian artery stump. Maintaining blood flow in the left subclavian artery is important for spinal cord perfusion as its branches supply the ASA.

*Meanwhile there is substantial evidence available supporting routine preservation of the left subclavian artery (78,79)*
Strategies to Detect Spinal Cord Ischaemia

Early detection of spinal cord ischaemia is important as it permits early intervention before ischaemia evolves to infarction. SSEP and MEP are established methods of spinal cord monitoring during TAAA surgery and endovascular repair. The clinical objectives for SSEP / MEP monitoring are to ensure adequate spinal cord perfusion throughout the procedure, to identify critical vessels for reimplantation, and to establish a MAP adequate for spinal cord perfusion. Decreased EP amplitudes have proven to correlate with spinal cord ischaemia, but the sensitivity and specificity of these techniques for detection of spinal cord ischaemia remains to be determined. Intraoperative changes or loss of EP signals are not always caused by spinal cord ischaemia. A functioning peripheral nerve is required to generate both SSEP and MEP signals. Therefore, peripheral nerve ischaemia from any cause will affect the associated SSEP or MEP amplitudes. Vascular malperfusion of a lower extremity can cause a loss of peripheral EP in the absence of spinal cord ischaemia if blood flow to the limb is significantly impaired. Lower extremity malperfusion may be caused by aortic dissection itself, atheroembolism or most commonly by arterial cannulation of the femoral artery for extracorporeal circulation. Similar to malperfusion, aortic cross-clamping without distal aortic perfusion results over time in fading EP signals from the lower extremities. Acute intraoperative stroke may also produce EP changes. They can be distinguished from changes caused by spinal cord ischaemia by comparing signals recorded at different sites along the neural conduction pathway. Stroke is associated with selective loss of cortical signals and typically affects the EP from both upper and lower extremities.

SSEP recordings measured via the sensory cortex can be affected by ischaemia of the peripheral nerves, the spinal cord, the brainstem, the sensory cortex, and additionally by technical and anaesthesiological factors. An advantage of SSEP monitoring is that it is relatively safe to perform and easy to interpret by comparing the amplitude and latency of SSEP recorded from the upper and lower extremities. The fidelity of SSEP is improved with neuromuscular blockade under general anaesthesia. Although high concentrations of inhaled anaesthetics, thiopental, or propofol can attenuate cortical SSEP signals, a balanced general and inhaled anaesthetic provides consistent conditions for intraoperative SSEP monitoring. Anatomically, the SSEP travels cephalad via the peripheral nerve and enters the dorsal roots of the spinal cord corresponding to the stimulated nerve. It traverses the dorsal horn and ascends the spinal cord via the dorsal spinal cord that mediates proprioception and vibration. A potential limitation of SSEP monitoring is that spinal cord ischaemia confined to the anterior spinal cord may cause a selective motor deficit with intact sensation. In this situation, SSEP monitoring may fail to detect spinal cord ischaemia. This anatomic picture is likely an oversimplification, because SSEP from the lower extremity is thought to include a contribution from the spinocerebellar pathways that
are located deeper in the spinal cord. Since the latter contribution is vascularised by the ASA, it is possible that the SSEP may respond to selective anterior ischaemia by the effect on this component of the pathway. Alternatively, anterior ischaemia may steal blood from the posterior perfusion, leading to SSEP changes. As SSEP are primarily a white substance pathway in the spinal cord and largely devoid of synaptic connections, they may react less sensitive than MEP pathways that include synapses. However, SSEP recorded in the spinal cord are known to be sensitive to hypotension and have been used to gauge deliberate hypotension during TAAA surgery. The sensitivity of SSEP to distal perfusion has resulted in substantial false-positive changes. As aortic cross-clamping compromises perfusion of the anterior spinal cord and results primarily in motor deficits, it is not surprising that SSEP monitoring during TAAA surgery with distal aortic perfusion has not reduced the incidence of neurological deficits.

Monitoring of motor pathways, particularly in case the function of alpha motor neurones is included, is a sensitive measure of anterior spinal cord function. To ensure that only motor pathways are stimulated, electrical or magnetic stimulation of the cerebral cortex is used to produce descending volleys of activity in the corticospinal tracts. Following the pathway of motor function, MEP elicited through transcortical electrical stimulation appears to be a more specific monitor. Transmission may be evaluated by recording from the distal spinal cord using epidural recordings (evoked spinal cord volley, epi-MEP), from a peripheral nerve (neurogram) or from muscles (compound muscle action potentials, CMAP). Unfortunately, epi-MEP are less sensitive to the degree of spinal cord ischaemia because they do not involve the anterior horn cell and their axons are less sensitive to ischaemia than grey matter.

MEP monitoring has been used to identify SAs critical for reattachment following the acute loss of lower extremity MEP signals during TAAA repair. Study of MEP during surgery may guide the physician in determining the optimum postoperative blood pressure. In patients with a significant risk of spinal cord ischaemia, sequential cross-clamping of the aorta may identify the critical segments of the aorta that provide important blood supply to the spinal cord. MEP may therefore be used to guide the need and level of intercostal and lumbar SA reattachment. Although this method of monitoring spinal cord function may be useful in studying the effectiveness of adjuncts to improve the risk of paraplegia, it sometimes provides false-positive results. Particularly since the neurological function of the spinal cord may be affected by anaesthetic agents that potentially depress the synaptic function of the cerebral cortex and spinal grey substance. Although epidural anaesthesia or analgesia can be used for endovascular or open TAAA repair, it is important to distinguish the effects of central neuroaxial blockade by local anaesthetics from spinal cord ischaemia. In particular, the amplitude of MEP is sensitive to neuromuscular blocking agents and many general anaesthetic agents. General anaesthetic
regimens utilising intravenous infusions of remifentanil, ketamine, propofol, or etomidate without neuromuscular blockade or carefully controlled incomplete neuromuscular blockade are often required to maintain satisfactory MEP signals during operation.

Recently, near infrared spectroscopy (NIRS) has been successfully introduced into a clinical pilot study to non-invasively detect spinal cord ischemia during open thoracic/thoracoabdominal repair. Sensitivity and response time are promising but further research has to validate this method experimentally and clinically to define its role in relation to neurophysiological monitoring to detect spinal cord ischemia. 80
TEVAR - Special Considerations

Thoracic endovascular aortic repair (TEVAR) of thoracic aneurysms or TAAA has made us rethink the pathophysiology of spinal cord ischaemia. Coverage of the thoracic aorta without revascularisation of SAs feeding the spinal cord was expected to produce higher rates of spinal cord ischaemia than actually observed. TEVAR may be performed with CSF drainage. Other adjuncts believed to be necessary in avoiding spinal ischaemia such as revascularisation of important intercostals branches cannot be employed and still, paraplegia rates are low supporting the collateral network concept (and the strategy of SA sacrifice in open TAA/A repair). TEVAR has less influence on the patient’s perfusion physiology, ensures cardiovascular stability, and offers shorter or no organ ischaemic periods as aortic cross-clamping is not necessary during TEVAR, thereby avoiding distal hypotension (except for the duration of large bore sheaths placed in the iliac arteries during the procedure) and negative effects on spinal cord perfusion associated with open TAAA surgery. Distal aortic perfusion remains uninterrupted, guaranteeing a continuous blood flow to the spinal cord and excluding a steal effect via segmental arteries after opening the aneurysm. Delayed paraplegia may occur due to (micro) embolism caused by atherosclerotic debris or blood clots flushed into spinal cord vasculature after being mobilized from the aneurysm sac during partial and/or temporary perfusion which may occur in type II endoleaks.

Reperfusion injury after open surgical aortic replacement can occur when cytotoxic metabolites formed during cross-clamping reach the reimplanted segmental arteries. Considering avoidance of SCI after TEVAR it must be remembered that the extent of repair is of importance to determine the risk of spinal cord ischaemia. The low risk of paraplegia in TEVAR compared with open TAAA surgery is multifactorial. If series contain patients with a shorter length of covered aorta they will inevitably show lower rates of spinal cord ischaemia. Likewise, when a dissected aorta is stented, retrograde perfusion of the false lumen via communications in the membrane maintains intercostal artery blood supply. This is clearly not a phenomenon that occurs after surgical repair and complete exclusion of the lesion. The length of the aorta covered is also relevant when the case of synchronous or dumbbell-shaped aneurysms is considered. Here, a staged approach is sensible to allow vital formation of collaterals to the spinal cord. Surprisingly, the coverage of large sections of segmental arteries with TEVAR leads to a low incidence of spinal cord ischaemia. One possible explanation is the above-mentioned uninterrupted distal aortic perfusion as.

However, the issue of spinal cord ischaemia still remains with TEVAR because of 1. The inability to revascularise covered segmental arteries, 2. A brief period of hypotension for TEVAR
deployment 3. The risk of emboli from aortic atheromatous lesions persists and 4. Possibly due to compromise of distal perfusion due to large bore sheaths used for stent-graft deployment during the procedure. Consequently, paraplegia remains the most devastating complication in TEVAR. Independent proven risk factors for the development of delayed onset paraplegia are 1. Perioperative MAP of less than 70 mmHg, 2. CSF drainage complications, 3. Previous abdominal aortic aneurysm repair (if the hypogastrics have been compromised), 4. Significant preoperative renal insufficiency, 5. Left subclavian artery coverage without revascularisation, and 6. The use of three or more stent-grafts (reflecting length of the covered segments as well as lengths of the procedural time). However, others have shown that the impact of of simultaneous closure of two independent arterial spinal-cord supplying vascular territories (in particular in combination with intraoperative hypotension) is the most important risk factor for symptomatic spinal cord injury irrespective of covered length or previous aortic repair- underscoring the importance of the collateral network concept (81). A thorough consideration of the risk profile in patients requiring TEVAR remains essential. Careful haemodynamic monitoring is vital and prophylactic measures for spinal cord protection should be considered in patients whose thoracic aortas require extensive coverage and those with other independent risk factors.

When TEVAR is performed in patients with chronic atherosclerotic aneurysm in contrast to the ones with acute aortic dissection, collaterals may have developed with time and are able to compensate for acute SA occlusion. Many studies have underlined the importance of these individual collateral arterial networks supplying the spinal cord in patients undergoing thoracic or thoracoabdominal endovascular aortic repair. Neurophysiological monitoring is viewed as an effective method to detect spinal cord ischaemia during these procedures (82). In patients with deteriorating SSEP or MEP, a decrease in SCPP and / or CVP as well as an increase in MAP is obligatory to ensure sufficient collateral spinal cord perfusion.

Recently, an approach to enhance collateralization has been reported being minimally invasive selective segmental artery coil embolization before TEVAR or open repair (MISACE) (83). The method seems to be effective but extensive clinical work has to be done before a recommendation can be made.
Summary

In the past, the community of aortic surgeons has been fundamentally divided by their respective hypotheses as to the cause of paraplegia after TAA/A repair. Those who were convinced that paraplegia is the consequence of chronic hypoperfusion after sacrifice of segmental arteries critical to spinal cord blood supply reimplant segmental arteries, trading prolonged intraoperative spinal cord ischemia for the achievement of arguably superior postoperative perfusion (10,63,84–89). Others were convinced that the blood supply to the spinal cord depends upon a highly variable collateral system capable of perpetuating sufficient spinal cord perfusion even after radical sacrifice of (almost all) segmental arteries under stable hemodynamic conditions encourages others to forego reimplantation, shortening intraoperative spinal cord ischemia by cutting down aortic cross clamp time (3,90).

Reimplantation remains the most widespread strategy for preserving spinal cord function. In 2000, Jacobs and associates reported a significant reduction of neurological complications— to 2.3% — with the monitoring of MEP in a series of 170 patients with TAAA, using a reimplantation approach with left heart bypass and CSF drainage (91). Van Dongen et al reported a 4.2% rate of postoperative paraplegia in a series of 118 patients, using hypothermia, LHB and a reimplantation strategy guided by MEP and SSEP monitoring (84). In 2002, Dong et al reported a 5.4% paraplegia rate in a series of 56 TAA/A operations utilizing MEP and SSEP monitoring with a reimplantation approach. The majority of studies sought to prevent ischemia by reimplanting segmental arteries with particular focus on the area between T7 and L2, believing that paraplegia is the consequence of hypoperfusion after sacrifice of critical spinal cord arteries (10,63). Several studies have attempted to demonstrate the arguable superiority of that approach. In contrast, in 1994 and 1996, paraplegia rates as low as 3% in DTA/TAAA repair without intersegmental artery reimplantation were described both in a series of 110 by Acher, and in 95 consecutive patients by Griepp et al (90,92).

In 2004, Ohtsubo proposed the selective perfusion of the Artery of Adamkiewicz to prevent intraoperative spinal cord ischemia (93). Dr Furukawa from Dr. Morita’s group in Japan in their most recent paper proposed a sophisticated, integrated intraoperative approach: selective intraoperative perfusion of the identified artery to prevent ischemia during aortic cross-clamping, temporary clamping of segmental arteries during aortic cross clamping to prevent steal once the aneurysm sack is opened (along with neuroprotective adjuncts like CSF drainage and high systemic blood pressure) and
reconstruction of those SA deemed relevant for the supply of the Artery of Adamkiewicz to restore native spinal cord perfusion (94). Although only a very small series, 44% of the reconstructed SA were occluded in postoperative follow-up, and the only case of paraplegia occurred in the group with SA reconstruction (94). Dr Acher, a former proponent of SA sacrifice who had switched to a very sophisticated reimplantation strategy in 2005 using preoperative magnetic resonance angiographic localization to identify the Artery of Adamkiewicz has stated recently (in December 2010) that “it remains unclear whether intercostal reimplantation reduces paraplegia risk, as we had initially proposed” (43,90).

Paraplegia is a multifactorial problem with several aetiologies, contributing factors and underlying aortic pathologies and may vary considerably among different patient collectives and according to the respective institutional protocol. No single spinal cord protecting method is currently capable to provide absolute safety. Included are spinal cord injuries as a consequence of the deterioration of the aorta, ischaemic injuries from loss of distal aortic perfusion, ischaemic injuries from loss of critical intercostal and lumbar vessels during the procedure, and other perioperative factors such as hypotension that result in a delayed paraplegia. Advanced contemporary surgical and anaesthetic methods include reduction of aortic cross-clamp times, TEVAR, retrograde perfusion techniques via partial LHB, hypothermia, reattachment of segmental arteries, lumbar CSF drainage, arterial pressure augmentation, and intraoperative neurophysiological monitoring and have improved the safety of thoracic and TAAA repair.

The objective is to rapidly identify the ischaemic condition and restore spinal cord perfusion with an attempt to minimise the duration of spinal cord ischaemia. However, even the combination of these various techniques does not abolish the problem. The practice of stenting the thoracic aorta and excluding the important spinal cord arteries with relatively low rates of paraplegia suggests that an exclusively anatomical basis concerning spinal cord ischaemia is not a realistic scenario and that the actual individual functionality of the patient’s collateral network, anaesthetic stability and duration of ischaemia seem to play a major role. Despite all these advances and an improved understanding of spinal cord perfusion, spinal cord ischaemia and infarction causing postoperative paraplegia or paraparesis remains an important and debilitating complication of all thoracic and thoracoabdominal aortic operations- be it open or endovascular repair. The seriousness and mortality associated with this complication justifies the routine clinical application of techniques to prevent and treat spinal cord ischaemia. It would be more than welcome to gain evidence by randomized controlled trials to eventually develop widely acceptable algorithms to prevent this most devastating individual tragedy and significant health care issue.
Clinical experience supports the efficacy of arterial pressure augmentation and lumbar CSF-drainage for the treatment of delayed onset paraplegia caused by spinal cord ischaemia when applied immediately after appearance of neurological signs in patients undergoing endovascular or open TAAA repair. Concerning intraoperative monitoring: Is EP monitoring mandatory to achieve success in thoracic and TAAA surgery? The answer is probably 'no' because spinal cord problems are multifactorial. EP answers to a variety of physiological factors that alter neuronal function and viability. To rely only on EP will not solve the problem. MEP recorded from the muscles seems to offer the quickest response to spinal cord ischaemia and the best prognostic information. Therefore, clinical experience has chosen it to be the best adjunct to decision-making to improve spinal cord perfusion and to determine the effectiveness of these manoeuvres.

Based on current literature, we aimed at formulating the below-mentioned recommendations to prevent, diagnose and treat spinal cord injury.

Recommendations for prevention

1) CSF drainage should be considered in patients undergoing TEVAR at high risk for spinal cord injury. IIaC (this panel of experts)
2) CSF drainage is recommended in patients undergoing open thoracic or thoracoabdominal repair. IB (5)
3) Primary subclavian artery revascularization should be considered in patients undergoing TEVAR. IIaC (78,79)
4) CSF drainage should be continued for at least 48 hours after TEVAR or open thoracic or thoracoabdominal repair. IIaC (this panel of experts)
5) In case of feasibility, staging of segmental artery occlusion may be considered (secondary distal extension after frozen elephant trunk repair repair, MISACE) IIbC (this panel of experts)

Recommendations for diagnosis

1) MEP/SSEP may be considered as an intraoperative tool for detecting spinal cord ischaemia in patients undergoing open thoracic or thoracoabdominal repair. IIbC (84,91)
2) MEP/SSEP may be considered as an intraoperative diagnostic tool for detecting spinal cord ischaemia in patients undergoing TEVAR at high risk for spinal cord injury. IIbC (82)
Recommendations for treatment

1) In patients sustaining spinal cord injury after TEVAR or open thoracic/thoracoabdominal repair, blood pressure elevation—ideally above the individual preoperative mean arterial blood pressure—to at least 80mmHG should be aimed for. IIaC (this panel of experts)

2) CSF drainage (if not already present), aiming for adequate hemoglobin levels (>10mg/dl) as well as aiming for hemodynamic stability (correction of postoperative atrial fibrillation) should be considered. IIaC (this panel of experts)

3) Administration of glucocorticoids to reduce spinal cord edema may be considered as an adjunctive therapy. IIbC (this panel of experts)

Summarizing, our knowledge upon the etiology of spinal cord injury has improved and differences between open surgery and TEVAR have been realized and formulated. Future research will further provide us with knowledge upon etiology, prevention, detection and treatment of spinal cord injury.
### Table I

<table>
<thead>
<tr>
<th>Crawford Classification</th>
<th>DTA</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open Surgical</td>
<td>1-7%</td>
<td>0-24%</td>
<td>0-22%</td>
<td>0-13%</td>
<td>0-2%</td>
</tr>
<tr>
<td>Endovascular</td>
<td>1-10%</td>
<td>10%</td>
<td>19%</td>
<td>5%</td>
<td>3%</td>
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</tbody>
</table>

Table I: The Crawford Classification of TAA/As classifies aneurysms involving the descending thoracic and abdominal aorta according to anatomic extent highlighted in red. Aneurysm extent and type of surgical repair influence the risk of spinal cord ischaemia. CCT = Crawford Classification Type; Risk of spinal damage in percent
### Table II

**Contemporary incidence of ischemic SCI with permanent dysfunction according to aneurysm extent – reported by international centers of excellence in aortic repair**

<table>
<thead>
<tr>
<th>Year</th>
<th>N</th>
<th>Incidence of ischemic SCI with permanent dysfunction according to aneurysm extent</th>
<th>Technical / perioperative management</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>DTA</strong></td>
<td><strong>Thoracoabdominal / Crawford</strong></td>
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<td></td>
<td></td>
<td><strong>Technical / perioperative management</strong></td>
<td><strong>Segmental arteries</strong></td>
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<td></td>
<td></td>
<td><strong>Type I</strong></td>
<td><strong>CSF drainage</strong></td>
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<td></td>
<td></td>
<td><strong>Type II</strong></td>
<td><strong>Neuromonitoring</strong></td>
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<tr>
<td></td>
<td></td>
<td><strong>Type III</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Type IV</strong></td>
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#### Endovascular (TEVAR)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Year</th>
<th>N</th>
<th>Incidence of ischemic SCI with permanent dysfunction according to aneurysm extent</th>
<th>Technical / perioperative management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greenberg et al.</td>
<td>22</td>
<td>2008</td>
<td>352</td>
<td>1% 10% 19% 5% 3%</td>
<td><strong>occluded</strong></td>
</tr>
<tr>
<td>Gravereaux et al.</td>
<td>95</td>
<td>2001</td>
<td>53</td>
<td>5.7% #  #  #  #</td>
<td><strong>occluded</strong></td>
</tr>
<tr>
<td>Conrad et al.</td>
<td>18</td>
<td>2008</td>
<td>105</td>
<td>7% #  #  #  #</td>
<td><strong>occluded</strong></td>
</tr>
<tr>
<td>Bavaria et al.</td>
<td>90</td>
<td>2007</td>
<td>140</td>
<td>3% #  #  #  #</td>
<td><strong>occluded</strong></td>
</tr>
<tr>
<td>Feezor et al.</td>
<td>97</td>
<td>2008</td>
<td>326</td>
<td>10% #  #  #  #</td>
<td><strong>occluded</strong></td>
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<tr>
<td>Stone et al 98</td>
<td></td>
<td>2006</td>
<td>74</td>
<td>10.4%*** #  #  #  #</td>
<td><strong>occluded</strong></td>
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</table>

#### Open Surgery

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<th></th>
<th></th>
<th>Year</th>
<th>N</th>
<th>Incidence of ischemic SCI with permanent dysfunction according to aneurysm extent</th>
<th>Technical / perioperative management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greenberg et al.</td>
<td>22</td>
<td>2008</td>
<td>372</td>
<td>1% 14% 22% 10% 2%</td>
<td><strong>reimplanted or bypassed</strong></td>
</tr>
<tr>
<td>Conrad et al.</td>
<td>18</td>
<td>2008</td>
<td>471</td>
<td>7% 24% 20% 13% 2%</td>
<td><strong>reimplanted T9-L1, if patent</strong></td>
</tr>
<tr>
<td>Fehrenbacher et al.</td>
<td>22*</td>
<td>2010</td>
<td>343</td>
<td>1% 4.3% 5.4% 3.1% 0%</td>
<td><strong>reimplanted T8 – celiac axis</strong></td>
</tr>
<tr>
<td>Coselli et al.</td>
<td>11*</td>
<td>2007</td>
<td>2286</td>
<td># 3.3% 6.3% 2.6% 1.4%</td>
<td><strong>reimplanted in 61%</strong></td>
</tr>
<tr>
<td>Bavaria et al.</td>
<td>96</td>
<td>2007</td>
<td>94</td>
<td>14% $$ #  #  #  #</td>
<td>~</td>
</tr>
<tr>
<td>Zoli et al.</td>
<td>99</td>
<td>2010</td>
<td>609</td>
<td>2.3% 2.5% 11.5% 3.9% 2.2%</td>
<td><strong>total sacrifice</strong></td>
</tr>
<tr>
<td>Sundt et al.</td>
<td>30</td>
<td>2011</td>
<td>99</td>
<td>3% $$ #  #  #  #</td>
<td><strong>reimplanted, T9-L1</strong></td>
</tr>
<tr>
<td>Schepens et al.</td>
<td>100</td>
<td>2009</td>
<td>571</td>
<td># overall paraplegia 5.3%, paraparesis 3%</td>
<td><strong>Reimplanted, T8-L1</strong></td>
</tr>
<tr>
<td>Safi et al.</td>
<td>39</td>
<td>2005</td>
<td>1106</td>
<td>~ ~ 10.7% ~ ~</td>
<td><strong>no reimplant in 61%</strong></td>
</tr>
<tr>
<td>Stone et al.</td>
<td>98</td>
<td>2006</td>
<td>83</td>
<td>7.2%*** #  #  #  #</td>
<td>~</td>
</tr>
</tbody>
</table>
Table II. Contemporary incidence of ischemic SCI with permanent dysfunction according to aneurysm extent – reported by international centers of excellence in endovascular (TEVAR) and open surgical aortic repair. Perfusion-, temperature- and the anesthesiological perioperative management for open repair varied significantly amongst reference centers, e.g.: Sundt et al: DHCA @ 18°C; Schepens et al.: moderate hypothermia @ 32C, DHCA only if proximal clamping impossible, Zoli et al: full cardiopulmonary bypass, partial cardiopulmonary bypass, left heart bypass and DHCA. Legend: * = 'at the discretion of the treating Physician'; # = excluded; + = Intraoperative epidural cooling (EC) to 25°C to 27°C until reperfusion of the lower extremities; ** = singularly operated in DHCA, SA reimplant, no CSF drain(!); ++ = selective perfusion (balloon catheters) to the celiac and superior mesenteric arteries, renals intermittently with 4°C crystalloid, left heart bypass in 40%, 60% clamp-and-sew’ 32°C to 34°C; ## = delayed paraplegia secondary to persistent hypotension, comparison is not representative as patient characteristics are not uniform, e.g. urgent / emergent procedures – see original data for details; $$ = The Gore TAG non-randomized multi-center trial: significantly higher incidence of symptomatic aneurysms (38% vs 21%, P=.007) in the surgical control group, in the majority historically and retrospectively acquired; surgeons performing the open procedures had various surgical backgrounds, there was a variable volume of thoracic aortic surgery performed in each contributing center, and a variable use of spinal cord protection techniques. E.g., in the open repair group 75% of the paraplegic pts died in hospital; ^^ = overall 3.3% (N=36); *** = DTA pts treated for degenerative pathology excluding ruptures; ~ = not reported.
<table>
<thead>
<tr>
<th>INSULT</th>
<th>EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Prolonged) aortic cross-clamping</td>
<td>Acute loss of direct (SAs) and indirect (collateral network) cord perfusion</td>
</tr>
<tr>
<td>Decrease in mean arterial pressure (e.g. due to anesthesia, CPB)</td>
<td>Insufficient spinal cord perfusion pressure (resulting in acute, generalized malperfusion of the cord)</td>
</tr>
<tr>
<td>Increase in CSF-pressure</td>
<td>Counteracts spinal cord perfusion pressure triggering a 'spinal compartment syndrome'</td>
</tr>
<tr>
<td>Loss of critical SAs</td>
<td>Acute loss of direct spinal cord perfusion</td>
</tr>
<tr>
<td>Insufficient distal perfusion pressure (on-pump/ no-pulsatility)</td>
<td>Inadequate distal inflow to the collateral network</td>
</tr>
<tr>
<td>Arterial Steal Phenomenon via patent SAs after opening the aneurysm sack</td>
<td>Reduced SCPP → edema of the spinal cord</td>
</tr>
<tr>
<td>Reperfusion injury after cross-clamping</td>
<td>Spinal cord edema (beginning 'vicious cycle')</td>
</tr>
<tr>
<td>Postoperative thrombosis of spinal cord perfusing arteries</td>
<td>May be responsible for delayed paraplegia (e.g. after TEVAR)</td>
</tr>
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<table>
<thead>
<tr>
<th>TEVAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEVAR covering of left subclavian artery, intercostal and segmental lumbar arteries, internal pelvic arteries, sacral arteries</td>
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<tr>
<td>Previous distal aortic surgery</td>
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<tr>
<td>Severe peripheral vascular disease</td>
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Table II: Mechanisms of spinal cord ischaemia in open thoracic aortic repair and during thoracic endovascular aortic repair (TEVAR).
### Table IV

<table>
<thead>
<tr>
<th><strong>Minimising Spinal Cord Ischaemia Time</strong></th>
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<tbody>
<tr>
<td>Multi-segmental, sequential reconstruction of the aorta</td>
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<tr>
<td>Stepwise or staged or sequential clamping of the aneurysm (anatomy permitting)</td>
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<tr>
<th><strong>Increasing Tolerance to Ischaemia</strong></th>
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<tr>
<td>Deliberate utilization of mild systemic hypothermia</td>
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<tr>
<td>Optional deep hypothermic circulatory arrest and/or selective spinal cord hypothermia by epidural cooling</td>
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<tr>
<td>Pharmacological neuroprotection/ischemic preconditioning (‘staged repair’)</td>
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<tr>
<th><strong>Augmenting Spinal Cord Perfusion</strong></th>
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<tr>
<td>Deliberate proximal and distal hypertension</td>
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<tr>
<td>Lumbar cerebrospinal fluid (CSF) drainage</td>
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<tr>
<td>Reimplantation of segmental arteries</td>
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<tr>
<td>Preservation of subclavian artery and internal iliac artery flow/ left heart bypass/distal aortic perfusion</td>
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<tr>
<th><strong>Early Detection of Spinal Cord Ischaemia</strong></th>
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<tr>
<td>IOM (MEP and SSEP)</td>
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<tr>
<td>Fast track concept and serial postoperative neurological examination</td>
</tr>
</tbody>
</table>

Table III: Strategies to prevent and treat spinal cord ischaemia. IOM = intraoperative neurophysiologic monitoring; MEP = motor evoked potentials; SSEP = somatosensory evoked potentials.
Figure 1: Spinal cord blood flow and perfusion pressure during thoracic aortic occlusion. The changes (arrows) represent the response to aortic cross-clamping per se. ▲ = increase; ▼ = decrease; ICP = intracranial pressure.
Figure IIa: Blood supply to the spinal cord. Schematic drawing of the spinal cord with indications of areas supplied by the posterior and the anterior spinal arteries. Radicular arteries are variable in location. The inflow to spinal arteries is divided into three main supply units: zone of marginal blood supply. ASA = Arteria spinalis anterior (anterior spinal artery); PSA = Arteriae spinales posteriores (posterior spinal artery); PICA = posterior inferior cerebellar artery; SA = segmental arteries; ICA = intercostal arteries; LA = lumbal arteries.
Figure I: Anatomy of the collateral network from experimental casts, sagittal (A) and dorsal (B) views. Macroscopic appearance of the pair of dorsal segmental vessels at L1. The dorsal process is removed. In A, the X designates the paraspinous muscular vasculature providing extensive longitudinal arterioarteriolar connections in A and B; the triangle indicates iliopsoas muscle; the double arrow indicates anterior spinal artery from 37.

Figure II: Relationship of the anterior spinal artery (ASA) and the repetitive epidural arcades in a Yorkshire pig model. V indicates the epidural venous plexus. Anterior to the extensive venous plexus, 4 arteriolar branches (yellow arrows) contribute to 1 circular epidural arcade. This pattern is repeated at level of each vertebral segment. These vascular structures connect segments side to side as well as longitudinally. Green arrows designate the anterior radiculomedullary artery, which connects directly with the anterior spinal artery. From Etz et al.
Figure III: A schematic diagram of the blood supply to the spinal cord demonstrates the relationships, relative sizes, and the interconnections among the segmental arteries (SAs), the anterior radiculomedullary arteries (ARMAs), the epidural arcades, and the anterior spinal artery (ASA). The longitudinal anastomoses along the dorsal processes of spine as well as dorsal communications (interstitial connections) between the right and the left branches of segmental arteries are also shown, from 37.
Figure IV:  

- **Left upper panel:** physiological somatosensory evoked potentials (SSEP)  
- **Right upper panel:** pathophysiological SSEP  
- **Left lower panel:** physiological motor evoked potentials (MEP)  
- **Right lower panel:** pathophysiological MEP
References


