Electrophysiologic Monitoring During Surgery to Repair the Thoraco-Abdominal Aorta

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Summary: Prevention of paraplegia during the repair of thoraco-abdominal aortic aneurysms and dissections present a substantial challenge to the operative team. The value of intraoperative electrophysiological monitoring (IOM) is to identify spinal cord ischemia that occurs during the procedure and guide the intraoperative management to reduce the risks of paralysis. The usefulness of IOM techniques requires an understanding of spinal cord blood flow and the spinal cord physiology, the surgical technique and their interaction. This paper will integrate these factors to review the laboratory and clinical experience with somatosensory evoked responses (SSEP) and motor evoked potentials (MEP) during thoraco-abdominal aorta surgery.

Key Words: Aortic aneurysm, Surgery, Somatosensory evoked potentials, Motor evoked potentials.

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Intraoperative spinal cord monitoring (IOM) during surgery on the thoraco-abdominal aorta (TAA) has been of an area of significant inquiry due to the substantial incidence of paraplegia after surgery. The reported incidence varies from 0.5% with aortic coarctation repairs, where the procedure is short and the patient usually has well-developed collateral circulation, to nearly 48% with emergency repairs of extensive thoraco-abdominal degenerative lesions (Connolly, 1998; Crawford et al., 1986). It is clear that the risk of perioperative paralysis varies due to a substantial number of factors including the segment of the aorta that is diseased. Crawford classified the aneurysms into four types with the highest incidence of paralysis with types I and II where aortic involvement includes all of the descending and some of the ascending thoracic aortic arch (Crawford et al., 1991) (Fig. 1). There has been substantial interest in using IOM to reduce the incidence of paralysis by identifying conditions causing spinal cord ischemia and recognizing when intraoperative management improves perfusion thereby reducing the risk of permanent spinal cord injury. This article will review the anatomic and physiologic factors contributing to paralysis and the experience, both experimental and clinical, with electrophysiological monitoring as an adjunct to surgery.

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MECHANISMS OF SPINAL CORD INJURY WITH TAA SURGERY

Paraplegia results from a variety of mechanisms that ultimately lead to spinal cord ischemia (Table 1). Some of these mechanisms include generalized ischemia, inadequate distal perfusion pressure, and the loss of critical radicular arteries including the arteria radicularis magna. IOM can detect the onset of ischemia and determine the effectiveness of treatment used to reduce the ischemia. Actions that reduce the risk of neural injury by correcting the ischemia or increasing the tolerance of the spinal cord to ischemia can extend surgical time. Unfortunately, even when intraoperative ischemia is corrected, apoptosis or new postoperative ischemic events may still lead to delayed paraplegia.

SPINAL CORD BLOOD SUPPLY

To fully understand the application of IOM to surgery on the thoraco-abdominal aorta, it is useful to review the blood supply of the spinal cord. The spinal cord is supplied by the anterior spinal artery (AntSA) which perfuses the anterior two-thirds to four-fifths of the spinal cord, including the motor tracts and the anterior horn cells. Two posterior spinal arteries (PostSA) supply the remaining portions of the cord, including the dorsal columns and a small part of the posterior funiculi. The PostSA, and to some degree the AntSA, runs the length of the spinal cord; however, the AntSA is not continuous, especially in the midcervical, upper thoracic, and a narrowed region just cephalad to the lumbar enlargement. An anastomotic vascular ring surrounds the spinal cord and provides some shared blood flow between the anterior and posterior spinal arteries.

Once in the spinal cord, the spinal cord blood flow is auto-regulated similar to the brain (Hickey et al., 1995). As such, the normal spinal cord will attempt to maintain spinal cord blood flow over a perfusion pressure from approximately 50 to 150 mm Hg above the normal spinal fluid pressure (CSFP). If the perfusion pressure falls below this range, which can be caused by reduced arterial pressure or increased cerebral spinal fluid pressure, autoregulation of blood flow fails and spinal cord blood flow is directly dependent on perfusion pressure. Failure of autoregulation inevitably leads to ischemia.

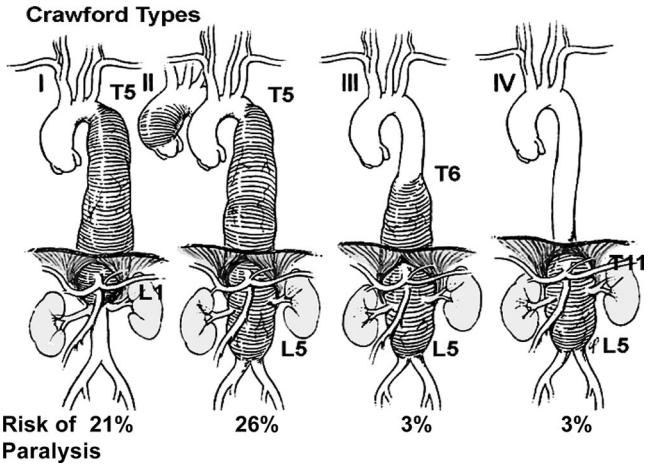

FIGURE 1. Crawford classification of thoraco-abdominal aortic aneurysm. Type I begins below the subclavian arteries and can involve the cervical and thoracic segmental arteries supplying blood flow to the anterior spinal artery (AntSA). The aneurysm does not extend into the abdomen and may not involve the Arteria radicularis magna (ARM). Type II can include the entire thoracic aorta, possibly dissecting into the aortic valve and extending into the abdominal aorta. It may involve all the segmental arteries perfusing the AntSA. Type III begins at T6 and does not involve the segmental arteries providing blood flow to the AntSA but may extend to the iliac arteries to involve the ARM which provides 75% of the blood flow to the anterior spinal cord. Type IV begins below the diaphragm. In 70% of patients it will not involve the ARM. The risk of paraplegia is highest in types I and II. Adapted from Crawford (1991), with permission.

TABLE 1. Proposed Mechanisms of Ischemic Spinal Cord Injury in Aorta Surgery

Generalized spinal cord ischemia from aorta cross-clamping
Inadequate perfusion from caudal arterial supply (inadequate bypass)
Loss of critical radicular arteries with surgery (including arteria radicularis magna)
Hypoperfusion from decreased spinal cord perfusion pressure
Increased CSF pressure
Decreased spinal arterial pressure
Embolization of plaque or thrombi intraoperatively
Reperfusion injury after aortic cross-clamping
Postoperative arterial thrombosis
Apoptosis

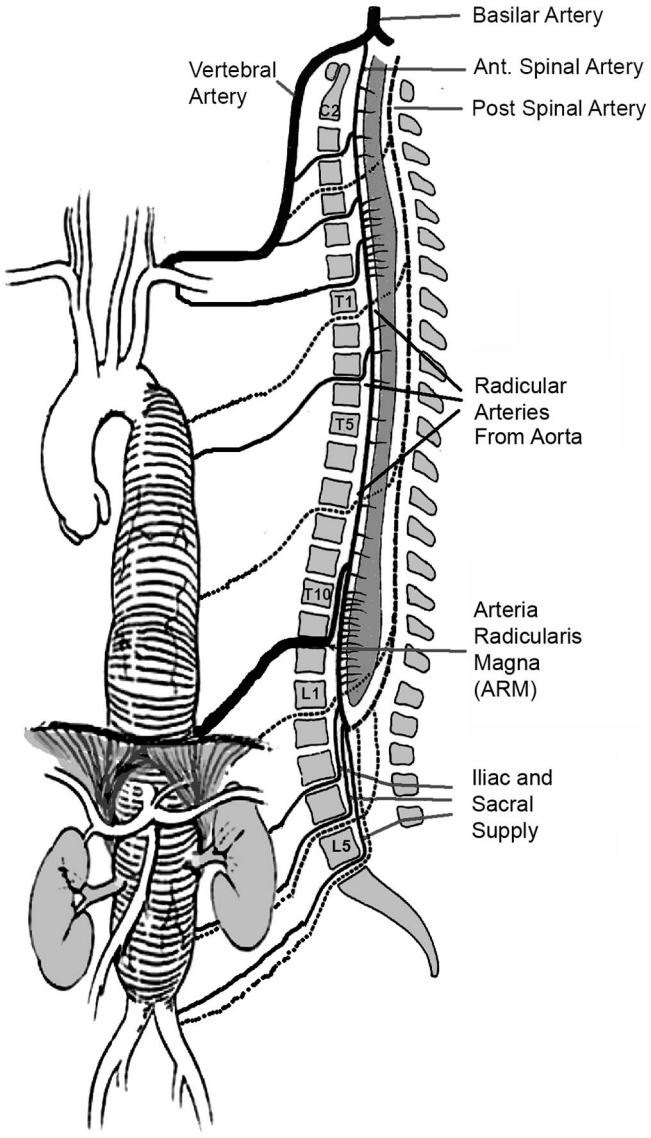

FIGURE 2. Blood supply to the spinal cord originates from the vertebral arteries and is fed by two to eight radicular arteries arising from the subclavian and intercostal arteries and from the lateral sacral and iliac arteries. One radicular artery (arteria radicularis magna) is larger than the others and supplies the lumbar enlargement). Adapted from Crawford (1991), with permission.

The AntSA and PostSA arise in the cephalad region from the vertebral arteries and descend along the spinal cord receiving radicular perforators from the aorta (Fig. 2). The AntSA and PostSA receive blood flow from only a few dominant radicular blood vessels. Although 62 radicular arteries are present in the embryo (one at each vertebral level) only 2 to 8 remain in the adult to provide blood flow to the AntSA and these segmental arteries originate from the aorta and travel via different routes (Djindjian et al., 1970). In the cervical region 2 or 3 segmental arteries arise from the cervical or subclavian arteries. The thoracic cord usually has only 1 to 3 anterior segmental arteries arising from the aorta making it susceptible to ischemia because collateral flow must travel a long distance before receiving flow from other major vessels. The region between T4 and T7 is thought to be the least well supplied region of the spinal cord and it is particularly vulnerable to ischemia. This explains the higher risk of paralysis in patients with disease of the thoracic segment of the aorta (Crawford types I and II).

Segmental arteries supplying the AntSA are not identical in size; one anterior segmental artery is larger than the others and is typically derived more from the left intercostals than the right. This artery is referred to as the "arteria

radicularis magna" (ARM or Artery of Adamkiewicz) and supplies the lumbar enlargement of the spinal cord. The location of the ARM is variable with the artery arising in 75% of patients from intercostal arteries at T9-T12, in 15% of patients at T5-T8 and in 10% of patients at L1 to 2 from the aorta or iliac artery. If ARM arises in the T5-T9 region a second artery may be found in the caudal area (conus medullaris artery). The ARM supplies about 75% of the blood flow to the AntSA, making it critical to spinal cord blood supply.

The developmental changes which result in loss of radicular arteries in the thoracic and lumbar regions lead to a vascular anatomy in the adult which is highly variable. In addition, patients with aortic aneurysms and degenerative vascular disease have additional variability. Over time patients may develop collateral circulation since existing arteries may be gradually occluded by mural thrombi or arterial plaques. Hence, in patients with TAA, a meshwork of collateral blood vessels develops and the lumbar arteries (L3-L5) and the pelvic circulation become the main blood supply to the spinal cord in almost a quarter of the patients (Jacobs et al., 2002a; Jacobs et al., 2002b). This also explains why the distal perfusion of the aorta is critically important during aorta cross-clamping in some patients. These factors, coupled with the narrowing of anterior spinal artery just cephalad to the ARM, result in three vascular regions; the cervical region, the superior thoracic region, and the caudal region (T5 to conus medullaris).

In some patients, the radicular perforators from the PostSA are critically important to spinal perfusion because of wide spacing between AntSA vessels creating watershed regions of interrupted and poor blood supply. In these regions the interruption of any perforator may lead to critical ischemia of the spinal cord. When present, these critical arteries are most commonly found between T8 and L4; the number of critical vessels in the surgical area (T5-L5) has been found to range between 1 and 5 (Adams and Van Geertruyden, 1956; Djindjian et al., 1970; Jacobs et al., 2002a). In patients who are dependant on these vessels, critical intercostals need to be identified and reimplanted to reduce the incidence of operative paraplegia. Unfortunately they usually cannot be identified preoperatively by angiography making functional testing with IOM critical for preservation of spinal cord blood flow (Djindjian et al., 1970; Jacobs et al., 2002a). This loss of critical segmental perforators is also seen in some aortic dissections or as a consequence of ischemia due to an intraaortic balloon (Scott and Sancetta, 1949; Tyras and Willman, 1978).

With the ARM supplying 75% of blood flow and being in the region at risk for loss of critical perforators, it is extremely important to reimplant the ARM (Jacobs et al., 2002a; Kuniyoshi et al., 2003; Ogino et al., 2006; van Dongen et al., 2001). The key importance of reimplanting the ARM is shown in several studies where the location of critical reimplanted arteries mirrors the location of the ARM (Jacobs et al., 2002a; Kuniyoshi et al., 2003; Ogino et al., 2006; van Dongen et al., 2001). Further, when critical radicular arteries are disconnected from the aorta during surgery and not reconnected, retrograde flow may clause a steal of blood from the AntSA (Wan et al., 2001). The incidence of paraplegia is directly related to the length of aorta excluded from bypass and cardiac perfusion by aortic cross-clamping. Steal can be minimized by the concept of stepwise cross-clamping of the aorta; this can determine which vessels are critical to spinal cord perfusion so that they may be reimplanted. This also allows only a small segment of the cord to be at risk for vascular steal phenomena. The importance of these radicular arteries was recognized as early as 1958 when experiments in dogs (and later in monkeys) demonstrated that the interruption of a critical radicular vessel could result in paraplegia and that reimplantation could prevent it (Fried et al., 1969; Spencer and Zimmerman, 1958). Clinical reports in patients with TAA and intraaortic balloons has substantiated these findings (Scott and Sancetta, 1949; Tyras and Willman, 1978).

In summary, the blood supply to the spinal cord is critically dependant on a mesh work of blood vessels supplied cephalad from the vertebral arteries, at the caudal end from sacral and iliac arteries, and from radicular perforators from intercostal arteries along the surgical site (which include the ARM). No consistent vascular pattern is seen in all patients and spinal cord dependency on specific vascular regions varies. For example, in some patients the entire aorta can be excluded (without reimplantation of intercostals vessels) with no postoperative paraplegia. In others, the key role of the pelvic circulation requires bypass to provide retrograde distal perfusion from atrial-femoral or femoral veno-atrial bypass. Finally, others are critically dependant on specific intercostal vessels. The role of IOM is to assist in identifying the specific ischemic risk factors in each patient and guide the corrective measures to reduce neurologic risk.

MONITORING STRATEGY DURING TAA SURGERY

To better understand the role of IOM, it is useful to consider the surgical procedure in stages and consider the strategy for electrophysiologic monitoring to reduce the risk of paralysis associated with these maneuvers (Gloviczki, 2002). The repair starts by placement of a cross-clamp on the aorta to the isolate the diseased segment. Unless bypass procedures are initiated there will be no blood flow in the radicular and caudal arteries below the cross-clamp. All spinal cord perfusion will come from the vertebral arteries. The long distance and small caliber of vessel will markedly reduce AntSA and PostSA blood flow. The cross-clamp in the thoracic aorta also causes a critical elevation of blood pressure proximal to the clamp with accompanying elevations in cerebrospinal fluid (CSF) pressure. The increased CSF pressure can further reduce spinal cord perfusion pressure (SCPP) [SCPP = spinal arterial pressure minus spinal CSF pressure] compounding the reduction of spinal cord blood flow (Connolly, 1998). When the spinal CSF pressure exceeds the pressure in AntSA and PostSA, no spinal cord blood flow occurs and the incidence of paraplegia is 100% (Blaisdell, 1962).

Global spinal cord ischemia can occur just with thoracic cross-clamping. Highly metabolic spinal cord gray matter is more sensitive to ischemia than the white matter such that the resulting spinal cord necrosis is primarily in lamina 3 to 10 (Kobrine et al., 1979; Machida et al., 1988; Machida et

al., 1990). The spinal cord is similar to the brain in that the amount of residual blood flow and the duration of the hypoperfusion determines the time to irreversible injury. For the spinal cord, complete ischemia in animals results in infarction in about 8 minutes (Connolly, 1998) However, in partial ischemia paralysis generally does not occur with an aortic cross-clamping time of less than 15 minutes; as cross-clamp time increases, a gradual increase in paralysis occurs until at approximately 60 minutes of cross-clamp time the incidence of paralysis is nearly 100% (Katz et al., 1981; Livesay et al., 1985). Consequently, many surgeons use segmental aortic cross-clamping and attempt to have the aortic segment cross-clamped for no more than 30 to 40 min. Unfortunately, the actual ischemic time the cord will tolerate varies between patients (Robertazzi and Cunningham, 1998). Brief periods of no flow have produced paraplegia, whereas some patients tolerate much longer periods, reportedly as long as 46 minutes (Adams and Van Geertruyden, 1956; Crawford et al., 1970).

To help reduce the ischemic risk, surgeons can place a shunt between the proximal and distal aorta. This bypass of blood reduces the proximal hypertension and also reduces the increased CSFP. It also facilitates better distal spinal cord perfusion for patients who are dependant on the caudal vessels. However, a passive shunt is dependent on cardiac function and may not produce adequate distal blood pressure and spinal perfusion pressure. Thus proximal to distal bypass techniques (eg, axillo-femoral, left pulmonary vein–femoral artery) are often used to provide perfusion of distal vessels (Jacobs et al., 2002a). Although a bypass perfusion pressure of 60 to 70 mm Hg is generally accepted as adequate, the pressure necessary to effectively perfuse critical vessels is not known in any given patient without functional testing provided by IOM. In some reports the adequate pressure was as high as 90 to 110 mm Hg (de Haan and Kalkman, 2001; Dong et al., 2002). When adequate, these distal perfusion techniques have been reported to reduce the risk of paralysis to about 10% from the inherent risk of 30% to 50% with cross-clamping alone (Wan et al., 2001).

Isolation of a segment of the aorta by the placement of a second cross-clamp reduces or eliminates the blood flow into the radicular arteries of the isolated segment. If any of these arteries are critical to adequate spinal cord perfusion, this will result in spinal cord ischemia and can lead to infarction. Several methods have been utilized to provide reperfusion of these arteries. One approach is to preserve the back wall of the aneurysm where the intercostal arteries arise and use it in the aortic reconstruction thus restoring critical perfusion (Connolly, 1998). This technique may not be feasible; other techniques have been developed to identify and implant the arteries in the repaired aorta segment. Because of its importance, some surgeons attempt to identify the ARM preoperatively to ensure that it is reimplanted into the aortic graft. Preoperative ARM identification is possible in 85% of cases by angiography. Simply reimplanting the ARM further reduces the risk of paralysis from 10% to 5% to 6% (Svensson et al., 1994; Wan et al., 2001). If it cannot be identified, some surgeons reimplant all intercostals in the T8-T12 range (Connolly, 1998). Unfortunately, studies have documented that many critical arteries cannot be visually identified. Monitoring provides a method to identify critical vessels during sequential cross-clamping of intercostal vessels to determine if reconstruction of an excluded vessel is necessary for perfusion.

During cord ischemia, time is critical and the time required to reimplant all vessels could increase the risk of paraplegia by prolonging the ischemic time. Monitoring can direct the surgeon by providing information about which vessel needs to be reimplanted and which vessels are not essential for cord perfusion. The net effect of this is seen in one study where the risk of paralysis was 14% when more than 10 intercostals were not reimplanted and 3.6% when less than 10 were not reimplanted (Galla et al., 1999; Guerit et al., 1999). Not surprisingly, the use of perfusion below the cross-clamp reduced the risk of paralysis to 10%. It is further reduced to 5% simply by reimplanting intercostal arteries, the radicular vessels and the vessels that comprise the ARM (Connolly, 1998).

Another technique used to reduce the risk of spinal cord ischemia is the use of CSF drainage to maintain a low CSF pressure (CSFP). The reduction in CSFP improves the net perfusion pressure (SCPP). Intraoperative monitoring can assist in identifying the critical CSFP that improves perfusion (Jacobs et al., 1999b; Jacobs et al., 2000).

In short, the goal of the surgical technique is to optimize the perfusion and reduce the overall ischemic time of the spinal cord. Hence, the surgeon must work expeditiously during the cross-clamp time. The value of intraoperative electrophysiological neuromonitoring is to promptly identify spinal cord regions that are ischemic while the insult is reversible and then guide the interventions to correct the ischemia and reduce the risk. Electrophysiologic techniques have been applied successfully to these surgeries and have reduced the risk of intraoperative paralysis.

APPLICATION OF INTRAOPERATIVE MONITORING TO TAA SURGERY

Since SSEP monitoring has been available since the 1980s, the largest clinical experience is with SSEP monitoring during aortic surgery. SSEP involves repetitive stimulation of peripheral nerves (such as the posterior tibial nerve at the ankle) and recording of the electrical response in the epidural space (epi-SSEP) or over the cerebral sensory cortex. With aortic surgery this technique can identify ischemia of the neural tract including the peripheral nerve, the white matter tracts of the dorsal columns, and ischemia in the brainstem or cerebral cortex. Of note, this pathway includes only white matter tracts in the spinal cord; synapses occur in the brain at the cervico-medullary junction, thalamus and cortex.

Some of the earliest dog studies demonstrated that the cortical SSEP could be used to guide the adequacy of bypass perfusion techniques. In one study, when the distal perfusion pressure, provided by left pulmonary vein to femoral artery bypass, was 70 mm Hg the cortical SSEP was maintained and the spinal cord remained adequately perfused (Laschinger et al., 1983a). When distal perfusion was $<$40 mm Hg, a slow

decay of the cortical SSEP occurred, with decreased amplitude and increased latency, that began 15 to 20 minutes after aortic cross-clamping with complete loss within 25 minutes. Tracings returned within 10 minutes if perfusion returned: in this case with bypass pressures above 60 mm Hg. Paraplegia was not seen if the cortical SSEP was maintained. In an attempt to identify critical radicular vessels, animal studies found that the cortical-SSEP was lost within 7 to 10 minutes of occlusion of critical intercostal vessels (Laschinger et al., 1987). The critical vessels varied among animals with no single reliably identifiable region between the subclavian and low lumbar region that contained the critical vessels. Spinal cord blood flow measurements corroborated the ischemia detected by cortical SSEP changes.

These studies in animals laid the groundwork for SSEP use in humans. Since 1987 clinical experience with the SSEP has paralleled the experimental observations in animals. A slow onset of cortical SSEP change (>15 minutes) indicates peripheral nerve ischemia. Isolated events such as from the bypass cannula in the femoral artery occluding flow to the leg are the most frequent of peripheral nerve ischemia. If the change occurs within 15 minutes it has been assumed to be of spinal cord origin, either from inadequate distal aorta perfusion or loss of critical intercostals. Thus, clinicians have used the SSEP to determine if bypass was necessary, if the pressure of bypass was adequate, and if it was safe to exclude a specific radicular artery.

One of the earliest human studies using the SSEP was done by Cunningham and Laschinger (1982). They observed four patterns of change in the SSEP depending on the mechanism of ischemia (Fig. 3). A type I pattern was when the SSEP was altered in 3 to 4 minutes after proximal cross-clamping of the aorta with complete loss in 8 to 9 minutes.

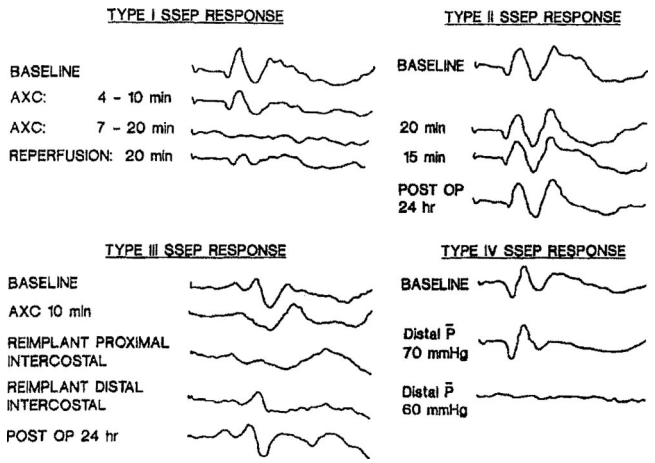

FIGURE 3. Type I intravenously somatosensory evoked potential changes during aortic cross-clamping in surgery on the thoraco-abdominal aorta. Type I is seen with inadequate distal perfusion pressure. Type II is where perfusion is adequate with cross-clamping. Type III is seen with the loss and reimplantation of a critical radicular artery. Type IV shows the dependency on adequate bypass perfusion pressure. Reproduced from Robertazzi and Cunningham (1998), with permission.

This pattern was thought to be indicative of inadequate perfusion of the spinal cord from distal arterial supply. This emphasized the value of bypass perfusion. The SSEP did appear to identify the adequacy of distal perfusion. In subsequent observations with an uncorrected type I SSEP response, usually caused by bypass perfusion <60 mm Hg, the incidence of paraplegia was 37.5% if the SSEP was absent for >30 minutes and the SSEP had not recovered to baseline amplitude and latency within 50 minutes of reperfusion (Robertazzi and Cunningham, 1998). A type II pattern, where the SSEP did not change after aortic clamping suggested adequate spinal perfusion was present.

The ability of the SSEP to identify critical intercostal vessels was identified as a type III pattern. Here, the SSEP was maintained after aortic cross-clamping but was significantly altered when a critical intercostal artery was clamped. The SSEP was restored when the critical intercostal was reimplanted. Other studies report similar changes; rapid reperfusion of critical intercostal vessels returns the cortical SSEP and appears to reduce the risk of paraplegia (Cunningham et al., 1982; Laschinger et al., 1982; Laschinger et al., 1983b). A type IV pattern, where a gradual "fade out" reduction in amplitude but not latency of the SSEP over 30 to 50 minutes, is considered characteristic of lower extremity hypoperfusion. Although this pattern may not signal spinal cord ischemia, it prevents further monitoring (Meylaerts et al., 1999). This may signal the need to reorient the bypass cannula.

However, the SSEP has not been completely reliable in always predicting paralysis since it monitors proprioception and vibration pathways in the posterior spinal cord. The SSEP has limited ability to determine if the ischemia involves motor function and if the corrective measures have prevented paralysis (de Haan and Kalkman, 2001). In some cases SSEP loss has been correlated with motor outcome and many studies show a consistently high correlation of ischemic injury with SSEP loss (Elmore et al., 1992). For example, rapid SSEP signal loss (within 3 to 5 minutes) after cross-clamping has signaled ischemia and subsequent ischemic intervals exceeding 30 minutes correlated with an incidence of a neurologic deficit in 70% of patients (Cunningham et al., 1998; Laschinger et al., 1987; Robertazzi and Cunningham, 1998). Further, the postoperative incidence of paraplegia was directly related to the duration of SSEP loss, usually 40 to 60 minutes.

These and other studies suggest that the SSEP can be used to gauge the adequacy of spinal cord perfusion with bypass shunting and identify critical intercostal vessels. However, as also stated, the SSEP change does not always correlate with paralysis since isolated injury in the spinal motor pathways are not always reflected in the sensory pathways of the SSEP (Galla et al., 1999). Large series have shown a high SSEP false-positive (40% to 67%) and false-negative rate (13%) (Crawford et al., 1988; de Haan and Kalkman, 2001). Although several studies have shown an improved outcome using SSEP monitoring, care should be taken to recognize the limitations in accuracy and slow response to ischemia seen with the SSEP (Dawson et al.,

1991; de Mol et al., 1990; Grabitz et al., 1996; Griepp et al., 1996; Schepens et al., 1994).

With the advent of reliable motor evoked potential monitoring, clinical inquiry turned toward transcranial motor evoked potential (MEP) monitoring. MEP includes stimulation of the motor cortex by electrical (MEP) or magnetic ((mag)MEP) means and recording in the epidural space (epi-MEP) or in muscles where a compound action potential (cmap-MEP) occurs. The neural pathway originates in the pyramidal cells of the motor cortex and descends in the spinal white matter tracts of the cortical-spinal tract until it synapses in the anterior horn cells of the spinal cord gray matter. From there, the response travels the peripheral nerves to the muscles. This differs from the SSEP in that the response can detect ischemia in the antero-lateral white matter tracts, the spinal gray matter, and the peripheral nerve and muscles. MEP is of particular interest since aortic occlusion in dogs demonstrated that the predominant injury from spinal cord ischemia is gray matter necrosis (Crawford et al., 1991; Reuter et al., 1992).

Beginning in 1997 research using MEP in animal models examined the effectiveness of using cmap-MEP to detect and predict spinal cord injury from aortic cross-clamping and radicular artery occlusion. In a pig study, magnetically elicited cmap-MEP was used to evaluate spinal cord ischemia (Qayumi et al., 1997). One group of animals (A) had aortic cross-clamping only; this resulted in the loss of cmap-MEP response within 2 minutes. After a 25- to 30-minute occlusion, cmap-MEP response recovered within 29 to 40 minutes. The neurologic response was variable in this group. Group B had all intercostal arteries ligated with no aortic cross-clamping. In this group the MEP was retained for 4 h and neurologic outcome was good. In group C, the animals had all posterior arterial branches from the aorta to the spinal cord ligated and aortic cross-clamping. These animals had immediate loss of MEP and the responses never returned. Neurologic recovery in group C was variable. These results suggest cmap-MEP is useful for detecting ischemia, but cmap-MEP like SSEP lacked absolute prediction of postoperative neurologic function.

Lips et al. (2002) correlated histology of the spinal cord and cmap-MEP change in a model of permanent spinal cord ischemia using temporary or permanent clip occlusion of all radicular arteries. The absence of cmap-MEP signals exceeding 1 h consistently resulted in paraplegia and spinal cord infarction; loss of the cmap-MEP for 30 minutes resulted in infarction of 20% of the gray matter volume. Histologic, neurologic, and cmap-MEP results had good correlation. If prompt restoration of the cmap-MEP occurred, a good outcome was seen with no infarction. The time for recovery of cmap-MEP correlated with the extent of gray matter infarction confirming the time relationship with ischemia and injury.

Early small clinical reports supported cmap-MEP as an effective way to detect spinal cord ischemia; failure of surgical manipulations to promptly regain cmap-MEP predicted probable paralysis (de Haan et al., 1997; Dong, MacDonald, et al., 2002a). In one study of 20 patients, cmap-MEP was used to guide operative interventions of left heart bypass, increasing bypass pressure and intercostal vessel reimplantation (de Haan, 1997). In this series the MEP response correlated with outcome. Other studies corroborated these findings concluding that MEP is an effective monitor for spinal cord ischemia (Dong et al., 2002b; Jacobs et al., 1999b; Jacobs et al., 2002a; Meylaerts et al., 1999; van Dongen et al., 2001). In one study of 130 patients with Crawford type I and II disease, 29% of patients had sudden loss of MEPs with aortic cross-clamp. Increasing the distal bypass perfusion pressure from 60 mm Hg to 66 mm Hg caused a return of the cmap-MEP (Jacobs et al., 2000). When progressive proximal segments were isolated, 28% of type I patients and 67% of type II patients had rapid decreases in MEP signals indicating critical intercostal arteries needed reimplantation. Figure 4 depicts MEP responses seen during relative hypoperfusion of the spinal cord. In this study no patient awoke with paraple-

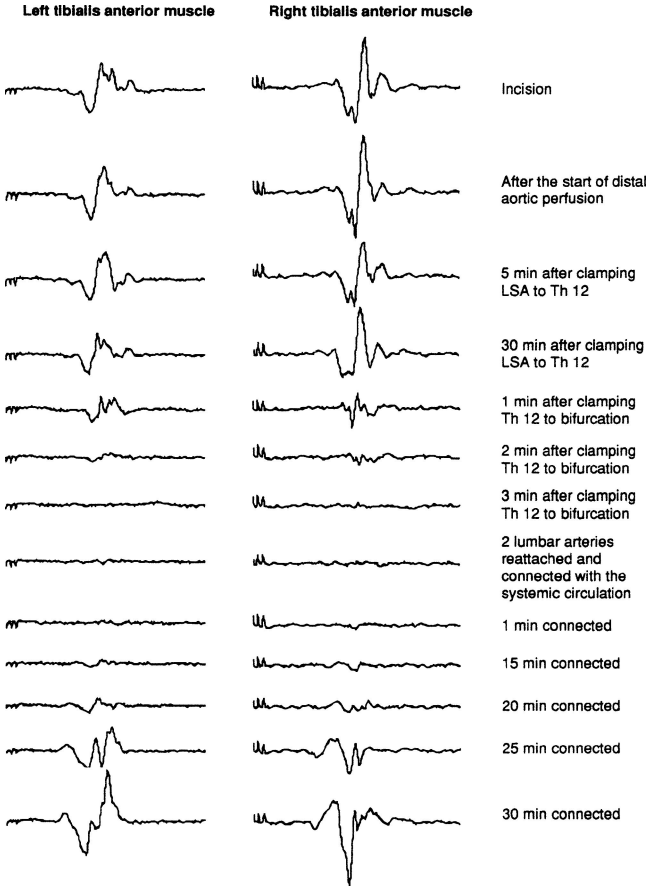

FIGURE 4. Effect of ischemia on cmap-MEP response and recovery after reperfusion during a type I1 TAA resection. During the thoracic part of the operation no tc-MEP changes were observed and eight intercostal arteries were ligated. During the abdominal part of the operation tc-MEP changes were observed within 2 minutes after placement of the clamps between T-12 and the bifurcation. Two large lumbar arteries were identified and reattached to the graft. MEPs returned 15 minutes after the blood flow in the reattached lumbar arteries was restored. Reproduced from deHaan and Kalkman (2001), with permission.

gia, 0% incidence of paraplegia, and MEPs were used to identify the need for increased distal perfusion or reimplantation of critical radicular arteries.

Another human study consisted of 210 patients who had left heart bypass, CSF drainage and cmap-MEP monitoring (Jacobs et al., 2002b) Surgical interventions included increasing distal perfusion pressure followed by identification and reimplantation of critical vessels. Cross-clamping of the proximal and distal aorta resulted in cmap-MEP response loss in 91 patients. The losses were corrected by increasing the bypass pressure (27 patients), selective grafting (16), or reimplantation (47) of critical vessels. On average, three to five vessels were implanted. Eighteen patients did not have visible vessels for reimplantation. Eleven patients had cmap-MEP changes when bypass was stopped temporarily, suggesting a critical contribution by the pelvic circulation. Only one patient awoke paraplegic (0.4%); this occurred after a complete and uncorrectable loss of cmap-MEP response. This as well as other later studies support cmap-MEP as a valuable adjunct to reduce paralysis (Jacobs et al., 2000; Kawanishi et al., 2007).

Although false negatives with MEP monitoring have occurred (ie, immediate postoperative paralysis with preserved intraoperative MEP), most studies show an excellent correlation of outcome with MEP (de Haan and Kalkman, 2001). All studies, both clinical and experimental, have reported a very rapid response, within 2 to 4 minutes, to ischemic conditions. This rapid response provides more useful feedback in the intraoperative environment where time is critical in determining outcome. These clinical studies suggest that MEP monitoring provides significant additional reductions in paraplegia.

APPLICATION OF EPIDURAL RECORDINGS SSEP AND MEP IN AORTA SURGERY

Because cortical SSEP and MEP restrict use of inhalational agents (low dose, SSEP, very low dose or none, MEP) and neuromuscular blockade (MEP), recording the epidural responses to standard stimulation has been investigated. Using this technique cortical stimulation to produce a MEP would be performed and spinal cord responses recorded via an epidural electrode placed below the area at risk for ischemia. Similarly for SSEP, an accessible mixed motor sensory nerve (eg, posterior tibial nerve) would be stimulated and a spinal cord response recorded above the area at risk. The spinal cord can also be directly stimulated with an epidural electrode (SCEP) and spinal cord responses recorded by a second epidural electrode so that the response travels through the area of ischemic risk. Unfortunately, the specific neural tracts used in SCEP monitoring are not known, but, like the epidural recordings with MEP and SSEP they are likely white matter axonal tracts without synapses. In all cases the goal is to stimulate and record in such a manner as to have the signal pass through the area of spinal cord at risk for ischemia but avoid the cerebral cortex and muscles that limit the anesthetic choices.

Unfortunately, epi-SSEP has not been demonstrated to provide reliable information on the effectiveness of therapeutic interventions in aorta surgery. In a dog study epi-SSEP were used to predict outcome in three treatment groups; aortic cross-clamp alone, aortic cross-clamp plus CSF drainage and aortic cross-clamp with aorto-femoral shunt (Elmore et al., 1992). The frequency of epi-SSEP loss varied between the treatment groups but was highly associated with paraplegia (92%). However, the loss with subsequent return of epi-SSEPs did not correlate with neurologic outcome. Many paraplegic dogs demonstrated return of the epi-SSEP. In the same study all dogs that lost epi-MEP response (mean time after the onset of occlusion was 25 minutes) were paraplegic or paraparetic. Several paraplegic animals did not loose their epi-MEP response, resulting in a predictive accuracy of only 16%. This suggests that the epidurally recorded MEP is sensitive to spinal cord ischemia but is not sufficiently predictive of paralysis. The epi-MEP may actually be less sensitive to ischemia than the epi-SSEP (Elmore et al., 1991). In dogs, when the epi-MEP was compared with the descending SCEP (Shokoku et al., 1993) during proximal aortic cross-clamp and bilateral subclavian artery occlusion, the epi-MEP had a more rapid amplitude loss than SCEP suggesting the epi-MEP is more sensitive to ischemia than SCEP.

Paralleling these animal studies are a few human clinical studies with a small number of patients (Grossi et al., 1988; Matsui et al., 1994; North et al., 1991). In general, the epi-MEP responded rapidly to ischemia or reperfusion of critical vessels with amplitude decreasing by 50% within 20 minutes. SCEP and epi-SSEP were less responsive to ischemia and the amplitude did not demonstrate significant change during critical artery reconstruction. In one patient who awoke with paralysis, the epi-MEP decreased beginning at 10 minutes and disappeared at 40 minutes after cross-clamp placement; these authors concluded the ischemic time for permanent spinal cord injury is 40 minutes. In clinical reports the epi-SSEP and epi-MEP were more sensitive than the SCEP to spinal ischemia and the epi-SSEP was very sensitive to distal bypass perfusion pressure (Sueda et al., 2000). In another human study of 18 patients undergoing aorta surgery, the SCEP was used as well as the cortical-SSEP to enable the continuation of spinal cord monitoring after the loss of cortical-SSEP responses from peripheral nerve ischemia (North et al., 1991). Based on the SCEP, critical intercostals were reimplanted or additional CSF draining performed. Those patients with bypass who retained SCEPs and cortical-SSEPs did not sustain paralysis. The one patient who lost both cortical-SSEPs and SCEPs within 10 minutes of cross-clamping awoke with paralysis. This study may suggest that the loss of SCEP and cortical-SSEPs correlates with neurologic outcome and that SCEP may be useful without bypass when cortical-SSEPs were lost from peripheral nerve ischemia. The use of SCEPs for reimplantation has also been successful. Like the SSEP, patients who experience immediate loss of SCEP usually have paralysis; however, some patients with paralysis have the SSEP or SCEP return highlighting the lack of predictive power of therapeutic maneuvers, a crucially important use of IOM. This means that although the SSEP and SCEP are sensitive to ischemia that results in paralysis, the true effectiveness of corrective mea-

sures cannot be effectively gauged, making their ability to prevent paralysis limited.

Overall, the limited evidence suggests epi-SSEP and epi-MEPs are less sensitive than other techniques, notably cmap-MEP and probably SSEP, in appraising spinal cord ischemia. The tracts being monitored by epidural electrodes do not involve the synapses in the anterior horn cell and axons appear less sensitive to ischemia than gray matter (Elmore et al., 1992). The slow disappearance of epidural recordings with spinal cord ischemia results in a delay makes them too slow to use as a warning for necessary surgical interventions (de Haan and Kalkman, 2001). In comparison to the large studies available for SSEP and cmap-MEP, the studies with epidural responses are small and do not have the statistical power to assess differences or reliability of these monitoring techniques.

COMPARISON OF SSEP AND MEP IN AORTA SURGERY

Large and small clinical studies have found that when comparing SSEP and MEP there is a relatively long delay (7 to 30 minutes) between the onset of ischemia and the disappearance of SSEP whereas the MEP generally changes comparatively quickly, 2 to 5 minutes (de Haan et al., 1998; Dong et al., 2002a, 2002b; Meylaerts et al., 1999; Weigang, Hartert, et al., 2005, 2006). Many studies comparing SSEP and cmap-MEP have results similar to a study by Meylaerts, Jacobs, et al. (1999) of 38 patients with type IV aortic aneurysms. Here the alarm criteria used were a change of cmap-MEP amplitude to $<$25% of pre–cross-clamp baseline, SSEP amplitude decrease to $<$50% of baseline, or SSEP latency increase to $>$10% of baseline. Thirteen patients experienced immediate MEP changes during segmental artery clamping and 11 were corrected by reanastomosis of critical intercostal arteries. The average recovery time of the MEP was 18 minutes. SSEP changes were only seen during 2 of these events with the SSEP change occurring 10 minutes after the cmap-MEP change and the SSEP recovery 20 minutes after MEP recovery. The most important finding was that SSEP changes were not associated with MEP changes; 2 SSEP changes were associated with arterial pressure decreases and 11 SSEP changes did not appear to be associated with blood pressure or aortic cross-clamp. At the conclusion of surgery all MEP responses had recovered but over 80% of patients still had SSEP alterations; no paraplegia was seen. Some patients had gradual SSEP decline during the procedure without a temporal change related to perfusion. Only 22% of the cmap-MEP changes were seen in the SSEP. This may be due to rapid correction of ischemia as detected by the cmap-MEP with correction before SSEP alteration, suggesting SSEP offers little additional information.

In a clinical study involving 118 patients using cortical-SSEP and cmap-MEP, only 5 of 42 patients with MEP changes had corresponding cortical-SSEP change, supporting evidence that cmap-MEP was the more sensitive technique and best correlated with paraplegia (van Dongen, Schepens, et al., 2001). Although no paraplegia was seen immediately after surgery, the 5 patients who developed paraplegia postoperatively all had altered intraoperative cmap-MEP recordings and most had persistent cmap-MEP amplitude reduction at skin closure. This suggests an increased relative risk of paralysis of 21 times when the cmap-MEP had amplitude loss greater than 50% 5 minutes after cross-clamping. In a study by van Dongen, Schepens, et al. (2001) of 188 patients with SSEP and MEP monitoring, persistence cmap-MEP loss was highly associated with paraplegia (odds ratio, 30.9), but not all patients with persistent MEP loss were paraplegic on awakening.

Clearly the effectiveness of the monitoring and some of the differences between the SSEP, MEP and epidural recorded responses relate to the specific neural tracts being monitored and their responsiveness to ischemia. Based on the available data (including the studies above), the time to electrical alteration and failure of various neural tissues is shown in Table 2. The cerebral cortex is the most sensitive to ischemia with a loss of EEG activity at 20 seconds after inadequate perfusion. The spinal cord gray matter is next most sensitive to ischemia with loss of synaptic activity at 1 to 2 minutes, whereas conduction in sensory and motor white matter tracts show alteration in activity in 3 to 6 minutes (SSEP tract) or 11 minutes (motor tract) and loss of conduction at 7 to 18 minutes (SSEP) or 11 to 17 minutes (MEP). The white matter tracts of the sensory and motor systems are about equal to each other in sensitivity to ischemia (de Haan and Kalkman, 2001; Guerit et al., 1996; Kobrine et al., 1979). The peripheral nerve causes the loss of SSEP and MEP conduction after 20 to 30 minutes of ischemia. Here, electrophysiologic abnormalities from leg ischemia are thought to be due to temporal dispersion of the conducting fibers (Nielsen and Kardel, 1981).

The second issue pertains to the prediction of outcome. When focusing on motor outcome, the MEP has the greater predictive power since it actually measures function in the cortical-spinal tract (CT). However, since only 5% of the CT fibers are involved in the response, the correlation is not exact (Sala et al., 2004). Further, a variety of other descending tracts are needed for coordinated motor function so losses in associated tracts may hamper motor function despite maintenance of adequate function in the CT (Sala et al., 2004). SSEP also has the drawback that ischemia in the anterior spinal region that supplies the motor tracts may not be seen in the posteriorly located SSEP tracts. The differences in arterial blood supply, AntSA versus PostSA, produce a differential

TABLE 2. Time to Electrical Alteration or Failure in Selected Spinal Neural Tissues

Tissue	Time to Alteration	Time to Electrical Failure
Cerebral cortex		20 seconds
Spinal gray matter		1–2 minutes
White matter (sensory)	3–6 minutes	7–18 minutes
White matter (motor)	11 minutes	11–17 minutes
Peripheral nerve		20–45 minutes

From collected sources (Connolly, 1998; Cunningham et al., 1982; Cunningham et al., 1987; Czermak et al., 2004; de Haan et al., 1998; de Haan and Kalkman, 2001; Guerit et al., 1996; Jacobs et al., 2000).

TABLE 3. Comparison of Somatosensory Evoked Potential (SSEP) and Motor Evoked Potential (MEP) Monitoring in Aorta Surgery

	SSEP	MEP
Pathway	Proprioception	Motor
Spinal Artery	Anterior	Posterior
Time (white matter)	7–18 minutes	11–18 minutes
(gray matter)	- No -	1–2 minutes
Post op use?	Yes	(magnetic only)
Anesthesia	Mod. restrictions	Restrictive
NMB	Allowed	- No -
False-positive*	67%	Low
False-negative*	13%	Low
Improved outcome	Yes	Yes

NMB = neuromuscular blockade use.

vulnerability to ischemia. Hence, the loss of the SSEP and MEP act as a surrogate for the entire functional aspect of the spinal cord.

As seen above, there are advantages and disadvantages of each electrophysiological technique (Table 3). MEP has the advantage that it is more responsive to spinal cord ischemia and restoration of flow because of its inclusion of the spinal gray matter. It also has a higher correlation with outcome (paralysis) since it is monitoring the motor pathways. However, the SSEP has the advantage of less restrictive anesthesia requirements and the ability to monitor patients postoperatively.

APPLICATION OF MONITORING FOR AORTIC STENT PLACEMENT

Deployment of endovascular aortic grafts has expanded to include thoracic aortic aneurysms. This procedure has the advantages of being a less invasive procedure and a shorter ischemic time for distal tissues (Czermak et al., 2004). This technique is rapidly replacing open surgical procedures in some elective situations. However the problem of ischemic injury is made difficult with these techniques since it is both more difficult to evaluate for critical radicular arteries and impossible to reimplant these arteries. Consequently, paraplegia has been described as a complication of endovascular sent placement (Mitchell et al., 1999). Test occlusion before permanent stenting can be a valuable method for changing the management approach. Test occlusion requires effective IOM techniques to appraise imminent spinal cord injury.

This approach was reported by Bafort et al. (2002) in a single patient who was deemed to be at excessive risk for open surgery. In this patient axillo-femoral bypass was used to prevent distal ischemia. Balloon occlusion of the aorta was done both proximal and distal to the aortic segment to be stented. Transesophageal echocardiography was used to confirm absence of flow in the occluded segment. SSEP monitoring assessed spinal cord ischemia during a 15-minute test occlusion. The patient did not experience SSEP change and did not have paraplegia. This technique is similar to the method reported by Ishmaru et al.(1998), who used a removable endograft for test occlusion.

More recently a study designed to evaluate the benefit of MEP and SSEP reported on 21 patients undergoing endovascular stent graft deployment in patients with aneurysms of the thoracic and thoraco-abdominal aorta (Weigang et al., 2006). SSEP and cmap-MEP monitoring was used to detect spinal cord ischemia. Patient management included mild systemic hypothermia (34 to 35 degrees Centigrade) and CSF fluid drainage to maintain normal CSF pressure. Three of the 21 patients (14%) exhibited short-term loss and recovery of MEP and SSEP after the deployment of the removable self-expanding endoprosthesis. Neurophysiological monitoring was viewed as an effective method to detect spinal cord ischemia. In patients who did not recover the SSEP or cmap-MEP, open surgical intervention during the endovascular graft placement to reimplant critical vessels could be then used. In all cases the MEP reacted more quickly than the SSEP. The authors note that should changes have been persistent, open surgery might have been necessary to remove the stent, place a prosthesis with reanastomosis of critical arteries. This technique allows patients viewed as high risk for paraplegia to attempt endovascular therapy and avoid the higher risk surgical procedure. The advantages of endograft placement, no aortic cross-clamping, continuous distal perfusion, and no reperfusion injury, may substantially reduce the risk of hypoperfusion seen in surgical procedures.

LONG-TERM OUTCOMES AND IOM

Clearly the goal of IOM and surgical intervention is to fully correct spinal cord ischemia before any lasting injury. However, even partial correction of ischemia may have value. First, as seen in the study by Lips et al. (2002) and confirmed in experimental models such as those by Jones et al. (1981) irreversible injury is a product of both time and severity of ischemia. Studies show that the time to irreversible injury is related to the residual blood flow; increasing the residual blood flow increases the time before irreversible injury occurs. Hence, the early identification of ischemia by IOM and immediate efforts to improve spinal cord blood flow may increase the allowable operative time. Some postoperative paralysis is undoubtedly due to postoperative complications or apoptosis, programmed cell death that is triggered by intraoperative ischemia. In the latter, ischemia leads to free radical production, mitochondrial injury, protein C activation, and excessive intracellular Ca^{2+} leading to apoptosis or programmed cell death despite the fact that the cell may initially recover (Lo et al., 2005; Lopez–Neblina et al., 2005; Polster et al., 2004). Improvement in spinal cord blood flow reducing the severity of the ischemia may help prevent the triggering of apoptosis and delayed injury.

Preischemic conditioning, the concept of reducing ischemic cellular death by producing repeated carefully limited ischemia, has been suggested for improving outcomes during aortic surgery similar to possibilities in cortical or myocardial surgery. IOM may be a way of assessing the degree of conditioning ischemia and providing a accurate end marker for "preischemic conditioning" (Contreras et al., 2005;

Svensson, 1998). In a dog study, Contreras et al. (2005) used SSEP to define the ischemic time and the recovery of the spinal cord from the ischemic insult. In these animals the aorta was cross-clamped until the cortical SSEP was reduced in amplitude by 60%, the trigger to initiate reperfusion. Reperfusion continued until full SSEP recovery. Three cycles of ischemia-reperfusion occurred before the ischemic insult. In this model, post ischemic neurologic evaluation showed reduced paralysis in the animals that were preconditioned when compared with control animals. This technique remains untested in humans.

Not all delayed injury may be prevented since it may result from a postoperative events including postoperative occlusion of a critical artery by vasoconstriction, platelet aggregation or delayed arterial thrombosis. Postoperative injury may also be related to post surgical hypotension, spinal cord edema, or debris emboli into critical vessels. Hence the appearance of postoperative paraplegia can be significantly delayed with injuries resulting in paraplegia not occurring until postoperative day 21 (Crawford et al., 1988; Fuchs et al., 2003; Griepp et al., 1996; Wan et al., 2001). In the intraoperative environment, some of these patients who have delayed onset paralysis were shown to be dependant on a critical minimum blood pressure. This suggests there may be a role for monitoring in the postoperative period to guide the blood pressure management particularly when clinical observation is not adequate or possible (Guerit et al., 1999). Hypertension in all patients can cause problems in the graft suture lines, cause myocardial stress and injury as well as spinal cord edema and paralysis. Alternately, relative hypotension may contribute to spinal cord ischemia that could be corrected. During the immediate postoperative period when the patient is still deeply sedated from residual anesthesia, the IOM could be continued to guide therapy. Once a patient begins to awaken, transcranial electrical MEP may be painful and therefore unacceptable. A clinical examination will be valuable once the patient is awake; however, in the transition period the SSEP or transcranial magnetic MEP may allow continued spinal cord monitoring.

CONCLUSION AND FUTURE APPLICATIONS

Despite advances in our understanding of the spinal cord ischemic injury, paraplegia remains a dreaded complication from the treatment of TAA aneurysm, surgery or endovascular graft placement. Animal and clinical experiences suggest that electrophysiologic monitoring can be an effective adjunct to surgery on the thoraco-abdominal aorta to reduce the incidence of postoperative paraplegia. The application of neurophysiological monitoring has assisted in clinical management through improved intraoperative decision making leading to dramatic reductions in paraplegia. Delayed paraplegia remains a major complication of TAA aneurysm treatments.

Inherent in these observations is that spinal cord dysfunction is a multifactorial problem with many etiologies and contributing factors that are patient specific (Gloviczki, 2002). Some of these include degree of aortic deterioration preexisting and intraoperative ischemic injury from loss of distal aortic perfusion and loss of critical segmental vessels. Whereas IOM provides a means to identify spinal cord ischemia, changing medical management such as glucose control, improved bypass techniques, intrathecal papaverine, and opiate antagonists are being evaluated to further reduce spinal cord injury (Fig. 5). IOM could play a critical role in evaluating these evolving management techniques.

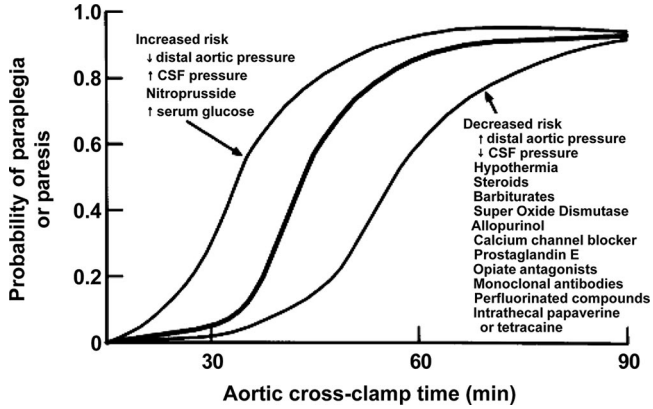

FIGURE 5. Probability of paraplegia and management maneuvers that are suggested to improve or increase the risk of paraplegia in thoraco-abdominal surgery. Reproduced from Gloviczki (2002), with permission.

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