Spinal Cord Protection During Surgical Procedures on the Descending Thoracic and Thoracoabdominal Aorta

Review of Current Techniques

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During the past 3 decades significant advances have been made in the surgical treatment of diseases affecting the aorta. Despite these important advances paraplegia remains a devastating complication of procedures on the thoracic and the thoracoabdominal aorta.1-6 Paraparesis and paraplegia occur as a direct result of interruption of blood flow to the spinal cord during these procedures. A number of techniques have been advocated for the prevention of spinal cord ischemic injury. This article will present our current understanding of the extent of this problem, the mechanism of injury, and the methods that have been devised to reduce the frequency of paraplegia after procedures on the descending aorta.

INCIDENCE OF SPINAL CORD ISCHEMIC INJURY

Paraparesis and paraplegia can result after surgical procedures on the thoracic and abdominal aorta. The incidence of spinal cord injury seems to correlate with the extent of the aorta which is resected and whether the area of resection encompasses the peridiaphragmatic aorta. Table 1 summarizes the incidence of spinal cord ischemic injury (SCI). The frequency of SCI ranges from 0.2% after elective repair of an abdominal aortic aneurysm to as high as 40% in the setting of acute dissection or rupture involving the descending thoracic or thoracoabdominal aorta.7-11 Similarly, in thoracoabdominal aortic aneurysms, SCI correlates with the length of the thoracic aorta which is involved.1 In Crawford type 4 thoracoabdominal aneurysms, where most or all of the abdominal aorta is replaced, SCI is seen in 1% of the patients. On the other hand, in Crawford Type 2 thoracoabdominal aneurysms, where most or all of the descending thoracic and abdominal aorta is replaced, the incidence of SCI is as high of as 21%. The risk of SCI is increased significantly in the presence of a dissection in the setting of a thoracoabdominal aneurysm. Perioperative hypotension, long period of aortic cross-clamping, increased cerebrospinal fluid (CSF) pressure, sacrifice of critical intercostal or lumbar arteries, and the extent of aortic disease.12-14

BLOOD SUPPLY OF THE SPINAL CORD

During embryologic development, 62 radicular arteries supply the spinal cord. Most of these arteries undergo degeneration in the embryo. By birth, 10 to 23 radicular arteries fuse to form the paired posterior spinal arteries. These vessels are continuous throughout the length of the spinal cord and supply blood to the posterior one third of the spinal cord. On the other hand, by birth a single anterior spinal artery is formed by 6 to 8 radicular arteries. This single vessel supplies the anterior two thirds of the spinal cord. There are no communicating branches between the anterior and posterior spinal arteries.15-17

Unlike the continuous posterior spinal arteries, the anterior spinal artery is discontinuous and supplies the spinal cord in a segmental fashion. The segmental...
distribution of the anterior spinal artery is highly variable. The anterior spinal artery receives blood in a segmental fashion from the left vertebral artery, the thyrocervical trunk, the intercostal arteries, and the lateral sacral artery. Only a fraction of the segmental arteries reach the spinal cord. The superior cord to the level of T2 is supplied by three to five anterior radicular arteries, the mid-thoracic cord has up to one radicular artery and the lower thoracic, and lumbar spinal cord is supplied by three to five anterior radicular arteries including the artery radicularis magna (ARM). The major radicular supply to the anterior spinal artery in the thoracic and upper abdominal region is provided by the ARM, known as the arteries of Adamkiewicz. Although in the majority of instances ARM originates from the descending aorta between the levels of T-9 and T-12, there is significant variability in the origin of this artery.18,19 In 50% of instances ARM has a left-sided origin.20 In an animal model, there was a 70% incidence of paraplegia with ligation of the ARM.21 The combination of the variable origin of the feeding vessels, the segmental nature of the blood supply to the anterior spinal artery, and the discontinuous blood supply of the spinal cord by the anterior spinal artery, accounts for the failure to reliably predict the frequency of SCI after operations on the descending aorta.

Consequences of Aortic Occlusion

Oclusion of the aorta results in distal hypotension with a resultant decrease in the perfusion pressure of the spinal cord. In a baboon model, Svensson and Loop3 have demonstrated a decrease from 20 mL/100 g tissue/min to 1.8 mL/100 g tissue/min in lumbar and thoracic spinal cord blood flow after aortic cross-clamping for 60 min. With 60 min of spinal cord blood flow at 10 mL/100 g tissue/min no paraplegia was observed. On the other hand, when spinal cord blood flow was reduced to 4 mL/100 g tissue/min, all animals became paraplegic. This and many other studies have shown a requirement for a minimum amount of blood flow to prevent paraplegia. Irrespective of the mechanism, a decrease in spinal cord blood flow results in neural ischemia. At normothermia mitochondrial oxidative phosphorylation stops after 3 to 4 min resulting in depletion of the adenosine triphosphate (ATP) stores, and failure of the ATP-dependent membrane pumps, which regulate intracellular calcium homeostasis.22 The increasing levels of intracellular calcium activate the release of cytoplasmic enzymes that damage DNA and structural proteins. Furthermore, increasing intracellular calcium results in production of xanthine oxidase, which mediates free radical production during reperfusion and release of neurotoxic amino acids aspartate and glutamate.23 With reperfusion, xanthine oxidase in the presence of reduced nicotinamide adenine dinucleotide phosphate converts molecular oxygen to the superoxide radical. The free radical damage DNA, degrade cellular structural elements, cause a loss of membrane integrity, and increase the ratio of vasoactive prostaglandins. The production of prostaglandins further compounds the ischemia by resulting in vasospasm and microvascular thrombosis.

The blood flow to the spinal cord during aortic occlusion is supplied by vessels proximal to the cross-clamp. With aortic occlusion, the aortic pressure above the clamp rises. The proximal aortic hypertension results in an increase in cardiac afterload and an increase in CSF pressure.

The risk of paraplegia during aortic surgery is determined by the interaction of four independent processes: (1) decrease in spinal cord blood flow; (2) rate of neuronal metabolism; (3) postischemia reperfusion injury; and (4) postreperfusion blood flow. A number of techniques have been proposed to decrease the risk of SCI after procedures on the descending aorta: expeditious surgery, preservation of intercostal arteries, distal aortic perfusion, drainage of CSF, pharmacological agents, metabolic agents, identification of vascular supply, somatosensory evoked potentials, motor evoked potentials, and hypothermia. These techniques address one or a combination of the determinants of paraplegia.

Expeditious Surgery

In 1910, Alexis Carrel established a safe aortic cross-clamp time to be between 10 to 15 min during experimental surgery on the aorta.24 Clinically the “clamp and go” technique was the first method used in the repair of aneurysms of the thoracic and thoracoabdominal aorta. Livesay et al14 showed the risk of paraplegia to increase from 3 to 11% with cross-clamp times higher than 30 min. Svensson and colleagues2 also determined the aortic cross clamp time to be an independent predictor of SCI. Other studies, however, have failed to show a clear relationship between cross-clamp times and SCI.25,26 Hollier et al25 studied five patients with paraplegia who had cross-clamp times less than 20 min; conversely, Najafi26 reported no SCI with a mean cross-clamp time of 58 min. The
discrepancy in the results of these studies seems to stem from a failure to delineate the location of the aneurysm and its relationship to the ARM.

Katz and colleagues showed a direct and highly significant correlation between the duration of aortic occlusion and the frequency of neurologic deficit. With up to 25 min of aortic cross-clamping the probability of lower extremity neurologic deficit is virtually nonexistent. After 25 to 30 min of cross-clamping, without other adjuvant techniques, however, the probability of paraplegia or paraparesis rises in a linear fashion such that at 50 min of cross-clamping, virtually all patients exhibit lower extremity neurologic deficits. Obviously, repair of extensive aortic aneurysms requires longer periods of aortic cross-clamping, which would result in unacceptably higher frequency of paraplegia.

**Distal Aortic Perfusion**

Although the “clamp and go” technique has been used successfully in most cases, a number of studies have confirmed the need for an additional protective measure with aortic cross-clamp times greater than 30 min. Katz et al. reported a 71% incidence of SCI in patients with disease of the descending thoracic aorta and cross clamp times greater than 30 min. Jex et al. showed the risk of SCI to decrease from 44 to 8% when distal aortic perfusion was used. In patients undergoing operative repair of dissections of the descending thoracic aorta.

A number of techniques have been advocated for perfusing the distal aorta in a retrograde fashion. The fundamental premise has been that increasing the distal aortic perfusion pressure will result in increased blood flow to the entire spinal cord, and thus decrease SCI during aortic cross-clamping. These methods have included roller pumps, passive shunts, and centrifugal pumps.

From a historical perspective, roller pumps were used for distal aortic perfusion during the 1960s and 1970s. Partial or total cardiopulmonary bypass can be used to increase distal perfusion beyond the aortic clamps. The various bypass techniques can be used to control the patients’ hemodynamics. Unfortunately, the use of a roller pump requires systemic heparinization. In a series of patients undergoing cardiopulmonary bypass for dissection of the aorta from the Massachusetts General Hospital, Stanford, and the Mayo Clinic, 20 to 30% of the patients had complications related to hemorrhage and one third of the deaths were the result of bleeding.

Some of the earliest resections of the thoracic aortic aneurysms were performed with either temporary internal shunts or a temporary external conduit. The Gott shunt, a united polyvinyl chloride catheter with a transparent tridodecyl methylammonium chloride heparin coating was introduced in 1966 and further refined in 1969. The shunt is placed between the proximal aorta and the segment of the aorta distal to the segment isolated by the cross-clamps. In 1988, Verdant et al. reported the use of the Gott shunt in 173 patients undergoing repair of descending thoracic aneurysms. With a mean aortic cross-clamp time of 37 min no paraplegia or other SCI was seen. As a result of the heparin coating, the use of the Gott shunt obviates the need for systemic heparinization. However, in two recently published reports of traumatic tears of the thoracic aorta, the use of the Gott shunt did not decrease the incidence of paraplegia compared with the “clamp and go” technique. It has been emphasized that to minimize SCI the distal aortic perfusion pressure needs to be greater or equal to 60 mm Hg. Although the flow through a Gott shunt can be monitored with a flow probe, by nature of being a passive shunt the flow cannot be regulated. The inability to regulate the flow through the shunt, results in the inability to insure a distal aortic perfusion pressure of greater or equal to 60 mm Hg. This difficulty makes the Gott shunt less desirable than techniques where the flow can be actively maintained. The inability to regulate flow through the shunt, and furthermore, the inability to retrieve spilled blood make the Gott shunt less desirable in the setting of a thoracic aortic aneurysm in danger of rupture.

Centrifugal pumps (Biomedicus pump, Medtronic-Biomedicus Inc; Eden Prairie, Minn) obviate the difficulties associated with active roller pumps as well as passive shunts. These pumps represent the best means of maintaining distal aortic perfusion. Cannulation can be from the left atrium, the pulmonary veins, or the ascending aorta to the descending aorta or the femoral artery. With centrifugal pumps flow can be regulated, damage to the blood components is less than with roller pumps, minimal heparinization is required, and a reservoir can be used in the setting of trauma or a ruptured aneurysm.

In an analysis of 596 patients undergoing traumatic rupture of the aorta reported in the English literature, Svensson and Loop calculated the risk of paraplegia to be 2.2%, 2.3%, and 5.8% with bypass, shunts or “clamp and go” techniques, respectively. In these same groups the patients with bypass had a significantly higher mortality rate, 16.7% vs 11.4%, and 5.8% when compared with shunts, and “clamp and go,” respectively. Furthermore, they reported a higher incidence of neurologic events with the use of bypass or shunts. This is presumably the result of atheroemboli or air emboli resulting from the cannulation of the diseased aorta. On the other hand, Kaplan et al. found active distal bypass techniques to result in maintenance of intracranial pressure, and a significantly greater distal aortic pressure than that achieved with either aortic cross-clamping alone or passive shunting. These au-
thors have reasoned that active distal circulatory support produces the most favorable effect on the two determinants of spinal cord perfusion, intracranial pressure, and distal aortic pressure.

Unfortunately the use of distal perfusion techniques does not protect the spinal cord in all patients. Perfusion techniques simply provide blood flow to the distal aorta. If the arteries supplying the anterior spinal artery arise from the excluded segment of the aorta, the spinal cord will remain ischemic even in the face of excellent distal aortic perfusion.

The distal perfusion techniques reduce cardiac afterload but also decrease the pressure in the proximal aorta. By reducing the proximal aortic pressure, the perfusion pressure of the spinal cord is decreased. Potentially, this can contribute to further spinal cord ischemia. Furthermore, it has been shown that even when the ARM is perfused using distal perfusion techniques, an increase in blood flow is seen only to the segment of the spinal cord below the junction of the ARM with the anterior spinal artery. This is accounted for by the observation that there is a size discrepancy between the anterior spinal artery above and below the junction of the ARM with the anterior spinal artery. The anterior spinal artery is smaller above the junction with the ARM than below; consequently, because of a decreased resistance, the greater part of the flow is directed to the spinal cord below the junction of the ARM with the anterior spinal artery. Thus even with excellent distal perfusion, the thoracic spinal cord that is fed by the anterior spinal artery above its junction with the ARM remains relatively ischemic.3,38

IDENTIFICATION OF THE ARM

It has been reasoned that an effective means of preventing paraplegia after surgical procedures on the thoracic aorta is to incorporate the intercostal arteries into the graft. The results of blindly incorporating a large cluster of back-bleeding intercostal arteries between T9 and T12 have been disappointing.39 The difficulty with this approach has been that the time involved in reimplanting the intercostals increases the ischemia time, and if the surgeon has guessed incorrectly, this approach leads to a higher risk of paraplegia. A logical approach, therefore, would be to identify preoperatively the vessels that provide the blood flow to the anterior spinal artery. This approach, however, has not gained widespread use because of the fear that direct injection of contrast material into the ARM will result in paraplegia.40-42 The risk of paraplegia in this situation has been attributed to the toxic contrast materials injected at high volumes. In fact, no neurologic consequences have been seen with direct injection of less toxic contrast material into the intercostal arteries.41,43-45

Kieffer et al44 reported a series of 45 patients in whom an attempt was made angiographically to identify the ARM. In 85% of the patients, the ARM was identified on the basis of preoperative contrast studies. In these patients the risk of paraplegia was 5% if the ARM was identified in the excluded segment and that segment of the aorta was completely revascularized. On the other hand, the risk of paraplegia increased to 50% if the segment of aorta bearing the ARM was not revascularized. Overall 60% of the patients in whom the origin of the ARM could not be determined by preoperative angiography became paraplegic. In the same group of patients, the risk of paraplegia was higher when the origin of the ARM was occluded and the vessel filled by collaterals, and when the aorta was clamped for more than 45 min. Williams et al46 reported selective intercostal angiography in 47 patients undergoing repair of thoracoabdominal aneurysms without complications. The origin of the ARM was found in 55% of the patients. When the origin of the ARM could be included as part of a long proximal or distal anastomosis, the risk of paraplegia was 8%. However, if the critical intercostal arteries had to be implanted as a mid-graft anastomosis separate from the proximal or distal anastomoses, 78% of the patients either died or were paralyzed. Of the patients in whom the origin of the ARM was not identified, 30% either died or were paralyzed. Based on preoperative angiographic localization of the ARM, Williams et al46 identified four risk categories: groups A, B, C, and D. Group A patients are patients with a large thoracoabdominal aneurysm and a large patent ARM arising from a large intercostal branch in the area of aortic exclusion. These patients are at greatest risk for paraplegia. Group B patients have equally extensive aneurysms, but with a smaller ARM originating from smaller branches of intercostal arteries. The risk of paraplegia in these patients is lower than in group A. Group C patients are those in whom the ARM cannot be identified, and group D patients are those in whom the ARM originates from the normal aorta or in whom the ARM can be included in the proximal or distal anastomosis. In these people, the risk of paraplegia is lower than in groups A and B.

Svensson et al47 described an intraoperative technique for identifying intercostal arteries that supply the spinal cord. They used a platinum electrode on the spinal cord and injected hydrogen ions into the intercostal arteries to delineate the vessels that supplied the spinal cord. Reimplantation of the intraoperatively identified intercostals significantly influenced the development of SCI in an animal model.

CSF DRAINAGE

In the early 1960s, Blaisdell and Cooley31 and Miyamoto et al48 reported that drainage of the CSF before aortic cross-clamping significantly decreased
the incidence of paraplegia in an animal model. They
stressed the concept of a “relative spinal cord perfusion
pressure.” The perfusion pressure of the spinal cord is
determined by the difference between the pressure in
the spinal artery and the pressure of the CSF. It has
been shown that after cross-clamping the thoracic
aorta in dogs, spinal cord perfusion pressure can be
increased with drainage of the CSF resulting in a de-
crease in the incidence of paraplegia.10,49-51 This effect
is presumably because of a relative increase in the
perfusion pressure of the spinal cord. This hypothesis
is supported by Svensson et al52 who measured spinal
cord blood flow during aortic occlusion and found im-
proved cord blood flow with spinal fluid drainage. In
pig and baboon models, however, CSF drainage has
not been shown to be protective.52-53 This discrepancy
is most likely the result of experimental design in the
pig and baboon models.

The encouraging data from the canine experiments
have resulted in the use of CSF drainage in patients
undergoing resection of the thoracic or thoracoabdom-
nal aortic aneurysms. After induction of anesthesia, a
silastic intrathecal catheter is placed in the second
lumbar space. This catheter is used for continuous
monitoring of CSF pressure. Initially, 15 mL of CSF is
removed. The CSF pressure is maintained at or be-
low 10 mm Hg by intermittent drainage of 10 to
15-mL aliquots of CSF.54

Spinal cord perfusion pressure can be increased by
increasing the arterial perfusion pressure. To that end,
after placement of the aortic cross-clamp, the periph-
eral arterial pressure is maintained higher than normal
with judicious use of fluids and nitroprusside. Using
this technique, McCullough et al49 reported no neu-
rologic defects in 24 patients undergoing repair of
thoracoabdominal aneurysms. However, in some pa-
tients, in addition to CSF drainage, intercostal arteries
were reimplanted. Acher et al55 reported a 2% inci-
dence of neurologic deficit with this technique.

However, despite the promising laboratory data, and
anecdotal clinical experience, in a prospective random-
ized series of patients with extensive aneurysms of the
descending thoracic and thoracoabdominal aorta, CSF
drainage was not beneficial in preventing paraplegia.55

The CSF drainage catheter should not be placed in
a heparinized patient. If postoperative paraplegia oc-
curs, a subdural hematoma needs to be ruled out as the
cause of the paraplegia as opposed to spinal cord
ischemia. CSF removal should be avoided if the initial
pressure is high because of the potential for cerebral
herniation.

**Pharmacologic Agents**

A number of pharmacologic agents have been used
experimentally and in the clinical setting in an attempt
to reduce spinal cord ischemic injury. The use of su-
peroxide dismutase (SOD), allopurinol, calcium-chan-
nel blockers, barbiturates, steroids, naloxone, papav-
erine, perfluorocarbons, and hypoglycemia have had
variable success.

There is increasing evidence that oxygen free rad-
cals result from ischemia and contribute to postis-
chemic spinal cord injury.56 Free-radical scavengers
such as superoxide dismutase (SOD) and catalase have
been shown to be important enzymes in the control of
free radicals. Although SOD has been shown to be ef-
eective in preventing paraplegia at 30 min of spinal cord
ischemia in the dog, it has not been shown to be ef-
eective with extended cross-clamp times.57-58 It has
been postulated that reasons for the limited effective-
ness have been the short half-life of SOD and its
inability to pass readily through the neuronal cell
membrane. Polyethylene glycol has been used as a
carrier with other pharmacologic agents and is believed
to have an acceptable safety proli for use in humans.
Conjugation of SOD with polyethylene glycol (SOD-
PES) may facilitate intracellular access and increase
circulatory half-life of SOD. Agee et al59 have shown
in an animal model that treatment with SOD-PES be-
fore and during aortic occlusion for 40 min, de-
creased spinal cord ischemic injury.59 Similar results
were reported by Granke and associates.60 On the
other hand, after 60 min of aortic cross-clamping, Sver-
ssoon et al52 have shown that SOD-PES had no
effect on the incidence of paraplegia. It is possible that
even though oxygen free radicals are mediators of spi-
nal cord injury during reperfusion after a short period
of ischemia, with longer periods of ischemia other less
reversible mechanisms of cell injury such as calcium
ion inlux become important. We can only conclude
that the use of SOD to decrease spinal cord ischemia
is not clear. Xanthine oxidase inhibitor, allopurinol, has
not been shown to be effective in decreasing SCI.52,56
Deferoxamine, which chelates free iron, a catalyst for
hydroxyl radical formation, has been found to be neu-
roprotective; however, a dose dependent toxicity has
been observed.61

Barbiturates have been shown to protect the CNS
from ischemia.62 Thiopental has been the preferred
barbiturate due to its high lipid solubility allowing
easier penetration of the CNS. Barbiturates may exert
their protective effect by reducing neuronal metabo-
lism. Nylander et al63 reported a protective effect
against paraplegia with the administration of barbitu-
rates in a canine model of spinal cord ischemia.
Kirshner et al58 however, found that barbiturates were
not protective when used alone.

Data regarding administration of corticosteroids for
cerebral protection remains controversial. Laschinger
et al64 have shown that in dogs after pretreatment with
steroids there was no neurologic injury compared with
a 67% incidence of spastic paraplegia in the control
animals. Recently there have been reports of impaired neurologic outcome in humans after spinal cord traumatic injury by high-dose steroid therapy. On the other hand, Fowl et al.\(^6\) reported a decrease in the rate of SCI in rabbits after administering 21-amino steroid U74006F. 21-Amino steroids lack any mineralocorticoid or glucocorticoid activity, are potent scavengers of superoxide and peroxyl radicals, and are inhibitors of iron-dependent lipid peroxidation.\(^6\) It is thought that the protective effect of steroids is related to their ability to stabilize membranes, modulate the immune system, and scavenge free radicals.

Endogenous opiates have been implicated in potentiating the CNS injury. Levels of B-endorphin, an endogenous opiate, rise dramatically in the CSF of dogs with spinal cord ischemia induced by aortic clamping.\(^6\) Opiates seem to decrease cerebral blood flow, increase vascular resistance, depress the firing rate of single neurons, and decrease central nervous system acetylcholine turnover.\(^6\) Naloxone, an opiate antagonist, improves neurologic recovery from trauma and spinal cord ischemia. In the setting of trauma, Naloxone has been shown to improve spinal cord blood flow, inhibit proteinolysis, stabilize lysosomal membranes, inhibit neutrophil superoxide release, inhibit lysosomal lipid peroxidation, and reverse derangements in calcium flux across cell membranes.\(^7\) In patients undergoing repair of thoracic and thoracoabdominal aneurysms, Archer and colleagues\(^5\) demonstrated a significant reduction in the incidence of neurologic deficit with the use of naloxone and CSF drainage.

Papaverine, a potent vasodilator, has been introduced directly into the CSF. In baboon experiments Svensson et al.\(^5\) showed that CSF drainage and intrathecal papaverine completely prevented paraplegia with 60 min of aortic cross-clamping.\(^5\) Furthermore, these authors have shown that intrathecal papaverine dilates the anterior spinal artery, increasing the lower thoracic and lumbar spinal cord tissue blood flow by 15 and 10 times, respectively. Initial clinical experience has been consistent with experimental findings. CSF drainage and intrathecal papaverine have been protective for paraplegia in all patients.\(^3\)

Perfusion of ventriculocisternocisternojaceanoid space with oxygenated perfluorocarbon has been shown to maintain electrical activity during brain ischemia. Intrathecal perfusion with fluosol-DA (20%) has been proposed as a means of protecting the spinal cord during aortic cross-clamping. Maughn et al.\(^7\) have proposed the use of the intrathecal space as an alternate vascular tree. In the canine model, the intrathecal infusion of fluosol-DA 20% at a rate of 15 mL/min beginning 15 min before the application of the cross-clamp and continuing through 70 min of normothermic aortic occlusion resulted in uniform prevention of paraplegia.\(^7\)

Clinical and laboratory evidence indicates that an increased blood glucose value before ischemia predisposes patients to a poorer neurologic outcome after cerebral ischemia. In a rabbit model, Drummond and Moore\(^7\) have shown that increased pres ischemic blood glucose levels result in greater incidence of paraplegia after temporary aortic occlusion. It is hypothesized that the increased substrate supply results in greater lactic acid accumulation during the period of ischemia and a less favorable intracellular environment during reperfusion. Based on these observations, in practice, glucose levels are to be monitored closely and IV fluids devoid of glucose are to be used during the procedure.

The role of calcium channel blockers in prevention of SCI has been controversial. While one study\(^4\) showed near complete protection with the use of nimodipine after 30 min of ischemia, Lyden et al.\(^5\) found no protective effect by any of the three calcium-channel blockers, which are selective for the cerebrovascular system.

Giulian et al.\(^7\) have shown in a rabbit model that hypothermic adenosine infusion into the ischemic cord provides complete protection from injury after 40 min of ischemia. Adenosine is thought to exert its protective effect by interacting with both type 1 and type 2 receptors.\(^4\) Activation of type 2 receptors, which are found on smooth muscle and vascular endothelium, inhibits neutrophil activation, platelet aggregation, and free radical production.\(^4\) Activation of type 1 receptors, which are located on neural tissue, decreases neuronal excitation, thereby limiting the influx of calcium into the cell. Without calcium release of aspartate and glutamate is inhibited. Excitatory amino acids aspartate and glutamate act on specific neuronal receptors and have been shown to be neurotoxic.\(^6\) In an experimental model, administration of receptor antagonists MK801 and LY233053 has been shown to provide some protection from SCI\(^5\)\(^,\)\(^6\)

Chloroquine and colchicine inhibit the functions of mononuclear phagocytes and may have a role in attenuating reperfusion injury. The use of these agents has been shown to prevent SCI after 20 min of spinal cord ischemia in a rabbit model.\(^6\)

The glycoprotein CD18 is required for leukocyte adherence to the vascular endothelium. An antibody to glycoprotein CD18 may prevent leukocyte adherence and thereby attenuate reperfusion injury. After 30 min of spinal cord ischemia in a rabbit model, there was a significant reduction in SCI with the use of such an antibody.\(^3\)

**Hypothermia**

It is reasoned that the deleterious effects of inadequate blood flow can be obviated with techniques, which decrease the metabolic demands of the spinal
cord. Hypothermia represents one such technique. Initially hypothermia was used during cardiac surgical procedures for the protection of the brain. The rationale for the use of hypothermia in resection of aneurysms of the thoracic and thoracoabdominal aorta is to increase the tolerable duration of spinal cord ischemia so that the blood flow can be reestablished before the onset of irreversible spinal cord injury. Spinal cord cooling can be accomplished by systemic cooling or by direct intrathecal spinal cord cooling. In experimental studies, direct perfusion cooling of the spinal cord with 5°C lactated Ringer’s solution has been shown to significantly prolong the tolerance of the spinal cord for ischemia. When compared with pharmacologic agents, hypothermia has been found to be superior to naloxone and comparable with barbiturates in protecting the spinal cord. Hypothermia combined with thiopental has been found to be superior to each agent alone. Furthermore, Ueno et al have shown in a rabbit model that a hypothermic solution of lactated Ringer’s solution with methylprednisolone, mannitol, and vitamins E and C achieves better spinal cord protection than each of the components alone. The technique of perfusion cooling of the spinal cord is limited by the rapid rewarming of the spinal cord due to collaterals carrying normothermic blood and the inability to insure spinal cord core cooling.

Slow systemic core cooling on cardiopulmonary bypass (CPB) can obviate these difficulties. Using this technique along with hypothermic circulatory arrest, one study showed a repair of a traumatic distal aortic arch to innominate vein fistula in 1964. Guilmet et al, Mahfood et al, Massimo et al, Crawford et al, Caramutti et al, and Kouchoukos et al have used core cooling on CPB with periods of circulatory arrest for replacement of the aortic arch and the descending thoracic and thoracoabdominal aorta. In animal studies, Kouchoukos et al have found that with occlusion of the aorta distal to the left subclavian artery, low flow CPB combined with hypothermia to rectal temperature of 15°C provided superior protection to cardiopulmonary bypass at 37°C. Based on these data, Kouchoukos et al have used the technique of hypothermic CPB to bladder temperatures of 15 to 19°C with intermittent deep hypothermic circulatory arrest and low flow in patients requiring the replacement of the entire descending and upper abdominal aorta. In these patients, who are at the highest risk for spinal cord ischemia, this technique allowed for reimplantation of all patent intercostal and lumbar arteries. Although there were only seven patients in this group, no paraplegia was observed.

The technique of hypothermia with cardiopulmonary bypass necessitates retrograde aortic perfusion, a requirement that contraindicates the use of this technique in patients with aortic insufficiency. Because of lower coronary perfusion pressures, which are observed with nonpulsatile CPB, coronary artery disease is a relative contraindication for this technique. The most commonly found complication with hypothermic CPB are related to the need for full heparinization. The patients frequently experience hemorrhagic pulmonary contusions or excessive bleeding from the graft. These complications can be reduced by the use of one lung anesthesia, which allows for complete deflation of the ipsilateral lung. The deflated lung does not require vigorous retraction which is commonly the cause of significant pulmonary contusion. The use of newer impervious grafts has virtually eliminated the bleeding from the graft.

Although the results from this approach are preliminary, it represents a possible approach for the reduction or elimination of spinal cord ischemic injury in this very high risk group of patients.

Sensory Evoked Potentials and Motor Evoked Potentials

Short of the excellent results with hypothermic CPB in a small number of patients, the clinical data with regard to the methods for the protection of the spinal cord from ischemia have been contradictory. There is a lack of conclusive evidence from clinical studies that the use of these techniques results in significant protection from paraplegia. The clinical studies to date have been hampered by a number of shortcomings. The majority of studies are retrospective series of patients with historical controls. The patients in these series have had variable diseases and anatomy which has made meaningful comparisons impossible. In many series where distal aortic perfusion has been utilized, the distal aortic perfusion pressure has not been measured. The most important limitation, however, has been the inability to measure spinal cord blood flow. Measurement of spinal cord blood flow would enable the surgeon to take steps in an attempt to restore blood flow to the cord and enable him to predict the occurrence of paraplegia.

The successful use of the electroencephalogram as an indirect measure of cerebral perfusion during procedures on the carotid arteries has compelled surgeons to look for an indirect means of monitoring spinal cord perfusion. Somatosensory evoked potentials (SEPs) were designed to meet this requirement. In clinical and experimental settings, SEP are obtained by stimulation of the posterior tibial nerve with a bipolar input channel. Two hundred consecutive stimuli are delivered and are conducted proximally via the posterior and lateral segments of the spinal cord. The evoked potentials are measured by means of a clinical evoked potential system from electrodes, which are placed in the midline of the scalp nasion and 55% of the distance between the nasion and the inion. The potentials are
amplified 10,000 times and to improve the signal to noise ratio of these small potentials; 200 consecutive responses are averaged for each SEP trace. A baseline tracing is obtained and subsequent recordings are performed every 2 min to monitor the integrity of the lateral and posterior aspects of the spinal cord. Two parameters are monitored: latency of onset and amplitude of the generated response. It has been found that a 10% increase in latency signals the onset of spinal cord ischemia. A decreased amplitude correlates with persistent ischemia. Cunningham et al. attempted to characterize the use of SEP monitoring in patients undergoing resection of the thoracic and thoracoabdominal aorta. They have observed that with the "clamp and go" technique without distal aortic perfusion, the SEP latency increases and the amplitude decreases. Complete loss of conduction is seen in 8 to 9 min after aortic cross-clamping. If the cross-clamp time is greater than 30 min, the rate of paraplegia is 37%. With distal aortic perfusion while maintaining a mean pressure of 60 mm Hg, the SEP tracing remains normal. In this setting, with a normal SEP tracing, these authors surmised that the critical intercostal arteries are not in the excluded segment of the aorta. In these patients, none of the intercostals were implanted and there was no paraplegia. In contrast, if the SEP became abnormal despite distal aortic perfusion with a mean pressure greater than 60 mm Hg, they concluded that the critical intercostal arteries were in the excluded segment of the aorta. In these patients, back bleeding intercostals were implanted into the graft and after reimplantation no paraplegia was seen. However, if the intercostals were not implanted in patients with a persistent mean aortic pressure of less than 60, SEP tracing faded out gradually and the risk of paraplegia increased to 33%. Although these and other clinical and experimental results have been encouraging, there has been a high rate of false positives (abnormal SEP with normal motor function) and false negatives (normal SEP despite abnormal motor function) responses. Undoubtedly, SEP has several limitations. SEP tracings are altered by the use of halogenated anesthetic gases. By definition, SEP only evaluates the function of the posterior and lateral columns of the spinal cord. The posterior and lateral columns are supplied by the paired posterior spinal arteries, which continue to be supplied by multiple collateral sources during aortic occlusion. Since paraplegia results from ischemia of the anterior spinal cord motor tracts which are supplied by the anterior spinal artery, SEP fails to monitor directly the function of the anterior spinal cord. Lastly, SEP monitoring requires intact peripheral nerve and cortical function.

Some of the limitations of SEP monitoring can be avoided with the ability to directly monitor motor tract function by motor evoked potentials (MEPs). In this technique the anterior motor tract is stimulated at T3 and T4 by a bipolar square wave constant current measuring 4.3 Hz, 5 to 10 mA, for 0.02 ms. Anterior spinal cord conduction can be recorded by placing subcutaneous electrodes from T10 to L4. The 20 ms period after each stimulus is analyzed, 25 responses are electrically averaged and a composite MEP is constructed. In a dog model, Laschinger et al. have demonstrated a characteristic time and level-dependent deterioration and loss of MEP. Spinal cord ischemia progressed from the distal to the proximal cord and was reversible if distal spinal cord perfusion was restored within 20 min. With continuous distal aortic perfusion with a mean pressure of 95 mm Hg, normal MEP was maintained throughout the cross-clamp period. The use of MEP allows on-line assessment of the adequacy of spinal cord perfusion. This should allow both experimental and clinical assessment of the factors that contribute to intraoperative spinal cord ischemia and paraplegia. The use of MEP should furthermore allow for the evaluation of the techniques, which are used for the prevention of spinal cord ischemia.

In summary, despite significant advances in the surgical treatment of the diseases affecting the aorta, paraplegia remains a devastating complication of procedures on the thoracic and thoracoabdominal aorta. Based on the present information, our approach for the protection of the spinal cord can be divided into three categories.

**Category 1:** In patients with disease confined to the upper thoracic aorta, we use a centrifugal pump with cannulation of the left inferior pulmonary vein and the left femoral artery. The distal aortic perfusion pressure is maintained at greater than or equal to 60 mm of mercury. This technique requires minimal heparinization and is applicable to patients suffering from traumatic transection of the aorta. Spinal fluid drainage and pharmacologic agents which may provide additive protection are used on an individual basis.

**Category 2:** In patients with short segment disease of the lower thoracic aorta, in addition to the technique that is outlined above, precise identification and preservation or implantation of the critical intercostal and lumbar arteries should be undertaken.

**Category 3:** In patients with involvement of a long segment of the thoracic aorta or the thoracoabdominal aorta, optimal protection of the spinal cord during aortic occlusion is achieved by hypothermic cardiopulmonary bypass and circulatory arrest. This technique can be supplemented further by the use of pharmacologic agents and identification and reimplantation of the critical intercostal arteries.

In all of the above categories, the use of MEPs allows for the evaluation of the efficacy of the technique for the prevention of spinal cord ischemia.
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