Prevention of spinal cord ischaemia during descending thoracic and thoracoabdominal aortic surgery

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Summary

Surgery of the descending and thoracoabdominal aorta has been associated with post-operative paraparesis or paraplegia. Different strategies, which can be operative or non-operative, have been developed to minimise the incidence of neurological complications after aortic surgery. This review serves to summarise the current practice of spinal cord protection during surgery of the descending thoracoabdominal aortic surgery. The pathophysiology of spinal cord ischaemia will also be explained. The incidence of spinal cord ischaemia and subsequent neurological complications was associated with (1) the duration and severity of ischaemia, (2) failure to establish spinal cord supply and (3) reperfusion injury. The blood supply of the spinal cord has been extensively studied and the significance of the artery of Adamkiewicz (ASA) being recognised. This helps us to understand the pathophysiology of spinal cord ischaemia during descending and thoracoabdominal aortic operation. Techniques of monitoring of spinal cord function using evoked potential have been developed. Preoperative identification of ASA facilitates the identification of critical intercostal vessels for reimplantation, resulting in re-establishment of spinal cord blood flow. Different surgical techniques have been developed to reduce the duration of ischaemia and this includes the latest transluminal techniques. Severity of ischaemia can be minimised by the use of CSF drainage, hypothermia, partial bypass and the use of adjunctive pharmacological therapy. Reperfusion injury can be reduced with the use of anti-oxidant therapy. The aetiology of neurological complications after descending and thoracoabdominal aortic surgery has been well described and attempts have been made to minimise this incidence based on our knowledge of the pathophysiology of spinal cord ischaemia. However, our understanding of the development and prevention of these complications require further investigation in the clinical setting before surgery on descending and thoracoabdominal aorta to be performed with negligible occurrence of these disabling neurological problems. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

A major concern associated with re-constructive surgery of descending and thoracoabdominal aorta is the development of post-operative paraplegia or paraparesis [1–4]. With advances in anaesthetic and surgical techniques, the incidence of intractable neurological complications has declined, but the rate of paraplegia or paraparesis still ranges from 5 to 40%. Both clinical and experimental work has now improved our understanding of spinal cord ischaemia and has led to the development of a multi-modality approach to spinal cord protection during extensive aortic surgery. This review will discuss the pathogenesis of spinal cord ischaemia, the monitoring techniques which are available to detect its occurrence and the surgical techniques or additional procedures that can be performed to minimise neurological complications following complex re-constructive aortic surgery.

2. Pathogenesis of spinal cord ischaemia

The development of paraparesis or paraplegia after aortic surgery can be classified as immediate or delayed. Immediate neurological complications are considered a direct result of hypoperfusion of the spinal cord and secondary in hypoxic damage. Delayed complications can develop between 1 and 21 days following surgery [5]. This has been postulated to be the result of reperfusion hyperaemia and free radical generation leading to oedema of the cord with regional hypotension and reduced perfusion of the vascular plexus [6]. Svensson attributed the major cause of spinal cord injury, during and after aortic surgery to the occurrence of one or more of the three following events. (I) the duration and degree of ischaemia; (II) failure to re-estab-
lish blood flow to the spinal cord after repair; (III) a biochemically mediated reperfusion injury [7].

In Svensson’s series of 1509 patients who underwent 1679 thoracoabdominal aortic repairs between 1960 and 1991, different independent predictors of postoperative paraplegia or paraparesis were identified [8]. These included the patients age, aortic cross clamp time, the extent of aneurysm resection, the presence of aortic rupture, concurrent aeurysmal disease of the proximal aorta and preoperative renal dysfunction. However, neurological injury in thoracoabdominal surgery remains one of the greatest unsolved mysteries [9]. It is virtually impossible to predict preoperatively which patient will develop paraplegia or paraparesis and this may be explained by the diverse variations of the blood supply of the spinal cord seen amongst individuals.

2.1. Duration and degree of ischaemia

2.1.1. Blood supply of spinal cord

In order to understand the pathophysiology of spinal cord ischaemia, the complex anatomy of the blood supply of the spinal cord needs to be appreciated. In the human embryo, there are paired radicular arteries which supply the spinal cord [10]. With growth, these radicular arteries involute, and as a result, there are only a few radicular arteries remaining in adults [12]. These radicular arteries are linked together by the longitudinal arteries of the spinal cord, namely the paired posterior spinal artery and the single anterior spinal artery (ASA), which supplies the anterior two third of the spinal cord [11]. In contrast to the previously held belief of segmental distribution of the ASA, it has been demonstrated that the ASA is a continuous structure throughout the length of spinal cord [12]. Among the radicular arteries at different levels, there is one which is exceptionally large called the artery of Adamkiewicz (ARM) [12,13]. It has a characteristic hairpin bend that perfuses the spinal cord distal to its junction with the ASA. An interesting finding is that the ASA above the ARM is considerably smaller in diameter compared with that below the ARM [12]. The level at which the ARM arises from the aorta varies amongst individuals but it arises from T9 to T12 in 75% of individuals [13,14]. Dissection of cadavers shows that 70% of ARMs originate from intercostal or lumbar arteries on the left side frequently at the level of T8–L1 [15], and the origin of the ARM can vary from T7 to L4 [16]. The spinal cord may be thought of as an organ in which 75% of blood supply comes from the ASA which is continuous throughout the spinal cord. The ASA is fed by different inputs. If most of these inflow tracts are disconnected from the aorta, there will be a decrease in the pressure in the ASA and retrograde flow of blood through the opened intercostal and lumbar vessels to the operating field instead of going through the ASA due to a steal mechanism [17]. This explains the clinical observation that the more extensive the aortic involvement and resection, the higher will be the rate of paraplegia [8].

2.1.2. Effect of aortic cross-clamping

Clinical studies have demonstrated that the duration of aortic cross-clamping is a major determinant of postoperative paraplegia [8]. The rate of paraplegia increases from 0% when the cross-clamp time is less than 15 min, to 25–100% when the time exceeds 60 min [18,19]. The application of the aortic cross clamp will lead to hypertension proximal to the clamp which increases the afterload of the heart resulting in heart failure and causes hypotension distal to the clamp [20]. The other effect of aortic cross clamping is an increase in CSF pressure [21]. Both the increase in CSF pressure and hypoperfusion of cord may contribute to significant neurological complications.

Experimental studies demonstrated that the CSF pressure rose significantly after 60 min of cross clamping. If the CSF pressure was uniformly raised to, or exceeded that in the distal aorta, the incidence of paraplegia was 100% [22]. This has led to the concept of ‘relative spinal cord perfusion pressure’ which is equal to the distal mean arterial pressure minus the CSF pressure [23]. Hence, an isolated rise in CSF pressure will lead to decreased perfusion of the cord. However, controversies still exist, since in animal experiments the CSF pressure measured in the cisterna magna may not accurately reflect CSF pressure in the vicinity of the lumbar spinal cord [24] and distal aortic pressure does not reflect the spinal cord arteriole pressure [25]. Based on the results of the above experimental and clinical studies, different modalities of spinal cord protection techniques have been developed.

2.2. Failure to re-establish spinal cord blood flow: monitoring techniques

Techniques have been developed to monitor the function of the spinal cord during surgery so that surgeons can obtain information concerning the adequacy of blood supply to the spinal cord.

2.2.1. Evoked potential monitoring

The primary injury to the spinal cord during surgery and aortic cross clamping is hypoxic damage to the neurones. The conduction of nerve impulse along the neurones is highly sensitive to hypoxia. The nerve impulse is elicited by electrical stimulation peripherally. The signal amplitude and conduction time along the spinal cord are recorded at the cortical projection on the contralateral postcentral gyrus. This is the evoked potential and the amplitude and latency of this is affected by disruption of spinal cord blood supply. This concept has led to the development of somatosensory evoked potential (SSEP) [26]. SSEP amplitude decreased by 40% after cross clamping with hypotension for 3–4 min. If this was allowed to persist, a flat-line SSEP response would be observed indicating the absence of conduction [26,27].
Practically, SSEP is obtained by stimulation of the posterior tibial nerve at the medial malleolus by a bipolar input channel. The SSEP waveforms can be recorded by electrodes placed on the scalp. Measurements are made before aortic cross clamping which serve as baseline. Tracings are recorded at 2-min intervals during the rest of the operation [28]. The potentials are amplified by 10 000 times and each SSEP trace is the average response of 200 consecutive stimulations of the posterior tibial nerve. This serves to improve the signal to noise ratio of small evoked potentials as the background noise generated from normal EEG activity is relatively large. The amplitude and latency of the generated potentials are monitored and a comparison with the baseline value is made. A 10% increase in signal latency usually precedes a decrease in the amplitude. This shift in latency is directly related to the decrease in perfusion pressure of the spinal cord. The duration of ischaemia required to shift the latency 10% from its baseline is defined as the L10 time, indicating the need to re-establish spinal cord perfusion in 4–6 min [28].

There are four classical types of SSEP response [29]. Type I responses are characterised by a decreased amplitude and increased latency 3–5 min after aortic cross-clamping. This indicates failure to provide adequate perfusion pressure of up to 60 mmHg distal to the clamp. For Type II responses, SSEP is maintained throughout the period of aortic cross clamping indicating adequate distal perfusion pressure. This indicates that the critical segmental arteries are not located within the segment of aorta between the cross-clamps. Type III responses are represented by the sudden loss of sensory conduction after application of the proximal cross clamp indicating that the critical arteries are located within the excluded segment of the aorta. This is an indication for reimplantation and reperfusion of the excluded intercostal segments. Type IV responses are characterised by gradual ‘fade out’ of normal SSEP tracings in 30–50 min. This indicates marginal or deficient distal perfusion even in the presence of proximal to distal bypass with acceptable distal perfusion pressure. This occurs in the presence of profound vasodilatation, extensive aneurysmal disease and failure of retrograde perfusion distal to aortic clamp. The surgeon must react quickly to further re-establish distal perfusion at a higher perfusion pressure usually greater than 70 mmHg. Clinical studies [30–34] have shown that SSEP is sensitive and offered an improvement in surgical strategy during thoracoabdominal aortic surgery. It allows efficient identification of the critical vessels to be implanted in an attempt to avoid immediate paraplegia [35,36]. However, SSEP only records the activity of the posterior and lateral columns of the spinal cord. It fails to represent the function of the anterior spinal cord which is supplied by the single ASA. The anterior corticospinal tract is the critical area which when affected by an ischaemic insult may lead to paraplegia. Thus SSEP does not reflect motor function and motor tract supply. The specificity of SSEP measurement is low with a false positive rate of 67% [37].

In view of the above disadvantages, the use of motor evoked potentials (MEP) has been proposed. MEPs are elicited either transcranially or by stimulation of the cord directly. Motor responses can be recorded at the level of the cord (spinal MEP), the nerve (neurogenic MEP) or the muscle (myogenic MEP). Experimental studies suggest myogenic MEP may be sensitive in predicting paraplegia [38]. Transcranially elicited MEP has been used clinically with detection of cord ischaemia within minutes, and no false positive or false negative results were observed [39]. However, preoperative anaesthetic planning is necessary as most volatile anaesthetic agents will depress myogenic responses [40]. Neurumuscular blocking agents can affect the amplitude of the MEP and the level of the drugs have to be maintained precisely. The other shortcoming of MEP is that axonal conduction is resistant to ischaemia and the disappearance of MEP is slow after spinal blood flow has been interrupted [39,41,42]. Conflicting results have been described in animal experiments [43,44] and the use of MEP monitoring is limited to only a few clinical centres.

2.2.2. Identification of critical segmental arteries

2.2.2.1. Preoperative angiography. Because of the anatomical diversity of the spinal cord blood supply, reattachment of back bleeding intercostal arteries blindly will not necessarily prevent postoperative paraplegia [45]. The extra time needed to reimplant the vessels will increase the cross-clamping time resulting in an increased risk of paraplegia. This has stimulated interest in preoperative angiography aimed at identifying the segmental arteries which give rise to the critical radicular arteries supplying the cord. The major problem of this method is the direct injection of toxic contrast agents via the ARM which may itself result in paraplegia [46]. The use of smaller volume of less toxic contrast medium can reduce the incidence of neurological complication [46–49]. Preoperative angiography may identify the ARM in 85% of cases. With the ARM identified and that particular segment of aorta revascularized, the risk of paraplegia was 5%. If reimplantation was not carried out within the excluded segment bearing the ARM, the risk of paraplegia was 50% [50]. Clinical studies using highly selective angiography and concluded that patients with extensive thoracoabdominal aneurysms, and a large patent ARM arising from intercostal branch in the excluded aortic segment are at greatest risk of paraplegia. If the ARM is small and originates from normal aorta or is included in the anastomosis either proximally or distally, the risk of paraplegia is lower [51].

Recently, magnetic resonance angiography has been proposed as an alternative non-invasive method for studying of the ARM preoperatively [139]. It has been shown that the ARM could be demonstrated in 69% of the patients, however, the number of patients in this study is relatively small [140].
2.2.2.2. Intraoperative localisation of critical segmental arteries. A technique which allows intraoperative identification of which segmental arteries can be oversewn and which arteries that ought to be reimplanted has been described [52]. The basis of this technique is that hydrogen is dissolved in solution with the production of a weak current when in contact with platinum. If hydrogen is injected into a radicular artery that supplies the spinal cord, it is carried to the ASA. The hydrogen will pass through the membrane and the wall of the artery. This is then detected by a platinum electrode placed alongside the spinal cord [52]. In animal models, the re-attachment of intraoperatively identified intercostal vessels by this method reduces the rate of development of cord ischaemia [38,52]. In clinical experiments, highly selectively angiography was used postoperatively to validate the accuracy of this technique. These showed that the hydrogen mapping method was accurate and there was a trend towards a shorter cross-clamping time in patients in whom it showed that there were no vessels supplying the spinal cord. They also noted that not all patent intercostal arteries need to be attached. The same group of investigators also described the use of polarographic techniques [136] which study spinal cord oxygenation. Monitoring of oxygen content is a sensitive method of determining whether the cord is ischaemic but its main application currently, is still limited to the field of research.

2.3. Reperfusion injury: mechanism

Reperfusion injury has been postulated as one of the aetiologies of delayed spinal cord injury [7]. Reperfusion is the restoration of blood flow to the organ after a period of ischaemia. Reperfusion of ischaemic neuronal tissues leads to release production of oxygen derived free radicals, produced as a result of incomplete oxygenation during the period of ischaemia. The presence of ischaemia leads to accumulation of breakdown products of ATP i.e. xanthine and hypoxanthine. During reperfusion, xanthine dehydrogenase will be converted to xanthine oxidase. Metabolism of xanthine and hypoxanthine by xanthine oxidase will lead to production of superoxide free radicals. Chain reactions occur when free radicals form bonds with non-radicals and results in the peroxidation of unsaturated free fatty acids by oxygen [137]. The cell membrane is made up of fatty acids and lipids and peroxidation will lead to damage of cell membrane. The synthesis of prostacyclin (PGI2) is inhibited by lipid peroxidation resulting in vasoconstriction with platelet aggregation. This will lead to reduced blood flow and ischaemia. Superoxide on its own is not highly reactive [138], however, when it reacts with transition metal such as iron, superoxide and its metabolite, hydrogen peroxide, can be converted into iron oxygen complexes and hydroxyl radicals. These are extremely reactive and can cause considerable cellular damage. Neural tissue is very vulnerable to iron related free radical injury. Efforts have been made to discover free radical scavengers so as to reduce ischaemic cellular damage.

3. Strategies to prevent spinal cord ischaemia

In view of the multifactorial nature, different surgical strategies and adjunctive measures have been developed to reduce the incidence of spinal cord ischaemia. However, there is no single ideal method that can prevent it. As previously noted, there are three major contributing factors that govern the development of postoperative paraplegia [53]. They are the degree and duration of ischaemia during aortic cross-clamping, failure to re-establish adequate blood flow to the spinal cord after repair, and delayed injury due to biochemically mediated reperfusion, episodes of hypotension and programmed cell death. Based on the above concepts, the following methods of spinal cord protection have been described.

3.1. Reduction of the duration of ischaemia

The duration of spinal cord ischaemia during aortic cross-clamping is of utmost importance as the rate of postoperative paraplegia increased with cross-clamping time, which we have described earlier. Different surgical approaches have been developed to shorten the duration of aortic cross-clamping.

3.1.1. Crawford aortic inlay technique

In the early 1950s, aortic aneurysms were primarily treated by resection of the diseased segment, followed by interposition of prosthetic graft in order to restore aortic continuity. In 1965, Crawford described the replacement of thoracoabdominal aorta using the inlay inclusion technique which has now become standard [54,55].

3.1.2. Single-clamp repair technique

As time is the most critical factor in governing spinal cord ischaemia, the use of a single-clamp technique with limited dissection around the distal aorta which can be accomplished within a short cross-clamping period has been described [56–58]. The aorta is dissected proximally at the proposed site of cross-clamping. The aorta is then opened with only the proximal cross-clamp in place and intraluminal thrombus rapidly removed. Back bleeding was allowed to occur freely from the opened distal aorta and segmental arteries. Blood is aspirated by cell-saver autotransfusion device and returned to the patient. This was described by Cooley as partial exsanguination. Aortic continuity was restored using a prosthetic graft with the distal anastomosis first created as a oblique suture line that incorporates segmental vessels into the new lumen. It was postulated that by partial exsanguination, the circulatory volume would be reduced as would be the central venous and CSF pressure [23,58]. In Cooley’s series of 112 patients, only seven patients developed neurological complications.
3.1.3. Sequential aortic clamping technique

This technique is particularly useful for extensive disease of thoracoabdominal aorta. After the patient was put on atriofemoral bypass, the proximal descending aorta is cross-clamped for a short segment. The proximal anastomosis can be performed first and distal perfusion is being maintained. The proximal can then be placed below the proximal anastomosis to allow reperfusion of left subclavian artery. The distal clamp can be placed just above the coeliac axis and the intercostal arteries can be reattached to the graft. The clamps can then be moved further distally to facilitate the reimplantation of visceral and renal arteries [74]. The sequential aortic cross-clamping helps to maintain both the proximal and distal perfusion.

3.1.4. Techniques of unproven value

The total cross-clamping can be reduced by dividing the operation into two stages. The first stage is the elephant trunk procedure which consists of placing tubular aortic graft prothesis into the distal aorta while repair of ascending or arch of aorta is undertaken [59,60]. This can be followed by second stage repair of descending thoraco-abdominal aorta later.

With the recent advancement of endovascular techniques, transluminal endovascular stent graft placement has been employed in the treatment of thoracic aortic disease. It has been postulated that disruption of intercostal arteries may be minimised with the endoluminal approach and this may be translated into a lower risk of paraplegia [65]. The first generation of stents were custom-designed for individual patients. It was composed of a self-expanding stainless-steel endoskeleton with ‘Z’ stents being covered by woven Dacron [65]. Preoperative planning is important so that the appropriate size and length of stent can be chosen. This can be accomplished by CXR, CT scan and angiography, and anatomical relationships with critical segmental branches from aorta can also be defined. Guidewire and sheath placement is performed under fluoroscopic and transoesophageal echo guidance [66,67]. The stent is then deployed with its position being checked. The first generation stents were used in 103 patients with only three of them developed postoperative paraplegia. Paraplegia occurred more commonly when access was gained through the abdominal aorta. There was no change in the evoked potentials before or during stent placement [68]. The use of transluminal stenting provides an alternative approach in the treatment of thoracic aortic disease especially for patients who are not fit enough to undergo open surgery. However, the indications for the routine use of this technique still need to be defined.

3.2. Reduction of the severity of ischaemia

When prolonged duration of spinal cord ischaemia is anticipated, it is important to minimise the severity of ischaemia. Different methods have been proposed which may increase the tolerance of the cord to ischaemic insults.

3.2.1. Distal aortic perfusion techniques

These techniques serve to augment the drop in blood pressure in the aorta distal to the aortic cross-clamp and also help in unloading the proximal aorta. It is important to maintain distal aortic perfusion pressures between 60 and 70 mmHg. As perfusion falls below 60 mmHg, the spinal cord blood flow falls in proportion to perfusion pressure [122]. With the use of distal perfusion techniques, a significant reduction in the risk of spinal cord ischaemia has been reported [123]. Different techniques have been described to maintain distal aortic perfusion. These can be divided into passive shunts and left atrial femoral artery bypass.

3.2.1.1. Passive shunts. In the 1960s, temporary external conduits were used as shunts in thoracic aortic surgery. The most popular shunt was the one developed by Gott [124]. It was made of polyurethane polyvinyl plastic with internal diameter of 5–6 mm and the lumen was coated with a heparin-bonded nonthrombogenic material (benzalkonium or methylamonium). The shunt was used to bypass the cross-clamped aorta. As the shunt has got relatively small diameter, the resistance to the blood flow is quite significant which may compromise distal aortic perfusion, and the proximal aorta may not be adequately decompressed. The maximum flow through the shunt at a pressure gradient of 60 mmHg represents only 50% of the cardiac output [125]. A review of the use of the Gott shunt in 173 patients showing no postoperative paraplegia after descending aortic surgery [126]. However, the use of passive shunts in the setting of repair of traumatic aortic injury did not result in a decrease in the rate of postoperative paraplegia [127]. The use of a passive shunt in pig models showed a mean flow that corresponded to 43.5% of baseline cardiac output which lowered the proximal aortic pressure to approximately 30% of pre-clamped figures and produced a mean distal pressure below 40 mmHg [40]. However, the monitoring and control of distal perfusion with the use of passive shunt is difficult [128], and these problems led to the development of left atrial-femoral bypass with the use of the centrifugal pump.

3.2.1.2. Left atrial to femoral artery bypass (LAFA). With the use of LAFA bypass, the flow to distal aorta can be regulated by a roller or centrifugal pump. The centrifugal pump causes less haemolysis and it is relatively free of the complications of air embolism as any air being trapped in the pump will cause cessation of its function [129]. The LAFA bypass is set up with cannulation of the left atrium or left pulmonary vein. Blood is returned to one of the femoral arteries for distal perfusion. Minimal heparinisation is needed but it is recommended for patients with distal aortic perfusion or femoral occlusive
3.2.2. Drainage of cerebrospinal fluid.

3.2.2.1. Drainage of cerebrospinal fluid. As we have discussed in the section on pathophysiology of spinal cord ischaemia, the animal experiments [23] showed that by lowering the spinal fluid pressure, the incidence of paraplegia after descending aortic occlusion was reduced. When CSF pressure equalled or exceeded distal aortic pressure, paraplegia uniformly occurred [23]. The combined effects of decreased arterial pressure and an increase in CSF pressure during aortic cross-clamping resulted in decreased spinal cord perfusion pressure. The perfusion pressure can be maintained by decreasing the CSF pressure, i.e. by CSF drainage. The use of CSF drainage before aortic cross-clamping in experimental studies has shown that the incidence of paraplegia was lower when compared with a control group [69]. Based on the results of these experiments, the concept of CSF drainage has been applied clinically. In high risk patients, the use of CSF drainage and naloxone reduced the incidence of paraplegia [70]. The beneficial effects of CSF drainage and distal aortic perfusion has also been described, especially in high risk patients with type II thoracoabdominal aortic aneurysms [71]. However, a prospective randomised study failed to show any significant benefit of CSF drainage alone in reducing the incidence of paraplegia [72]. There has been criticism of this study because the volume of CSF drainage was only 50 ml during the period of cross-clamping. CSF was not allowed to drain freely by gravity and drainage was not continued during the postoperative period [73]. A more recent prospective randomised study in which CSF drainage was used in combination with intrathecal papaverine has been performed [74]. In this study, 20 ml of CSF was drained 20 min before cross-clamping and 3 ml of warmed preservative free papaverine solution was introduced. CSF was allowed to drain freely by gravity but stopped after unclamping the aorta. CSF was then allowed to drain freely during postoperative period if the CSF pressure exceeded 7–10 cmH2O. On multivariate analysis, CSF drainage and intrathecal papaverine was shown to be protective. In view of these encouraging clinical results, CSF drainage has been incorporated as one of the most important components in the modern multimodal approach to spinal cord protection.

3.2.2.2. Pharmacological agents. Several pharmacological agents have been suggested as being effective in protection of the spinal cord during the period of hypoperfusion.

The use of intrathecal papaverine and CSF drainage has been described [74]. Experiments in baboons showed that even with 60 min of cross-clamping, the use of CSF drainage and intrathecal papaverine prevented the development of paraplegia [75]. The role of papaverine is as an arterial dilator which helps to increase regional spinal cord perfusion. The results of the animal experiments provided the foundation for the randomised prospective study we described previously which showed that CSF drainage with intrathecal papaverine reduced the incidence and severity of neurological injury [74].

During aortic cross-clamping in dogs, the level of β-endorphin in the CSF was increased [76]. The opiate antagonist naloxone, has been shown to improve neurological outcome following ischaemic insults to neural tissue [77,78]. The combination of CSF drainage and naloxone has been studied in 61 patients compared with 49 patients as a control group, and significant protection from neurological deficits demonstrated [71].

Free radicals have been implicated as major factors in ischaemia-reperfusion injury and later neurological problems following aortic surgery [79,80]. Pharmacological agents with antioxidation property can block the generation of free radicals and inactivate them. Allopurinol has been tested for its efficacy in the prevention of paraplegia after aortic cross-clamping butely was ineffective [75]. Superoxide dismutase (SOD), which catalyzes the dismutation of superoxide radicals to hydrogen peroxide, has been tested but experimental studies have been disappointing [75]. SOD is limited in its effectiveness because of its short half-life and its inability to pass through the cell membrane [81]. CSF was conjugated to polyethylene glycol (PEG) which may facilitate its access through membranes and prolong its half-life [82]. Experiments with rabbits showed that treatment with PEG-SOD before and during occlusion increased the rabbit spinal cord tolerance to ischaemia [83]. However, the beneficial effect of PEG-SOD in the prevention of para-
able for calcium antagonists in the prevention of postoperative paraplegia is still unknown. In animal experiments, no beneficial effect has been shown for calcium antagonists in the prevention of spinal cord ischaemia [85]. In cerebral ischaemic models, neuronal voltage-dependent sodium channel antagonists have been shown to be neuroprotective. In a rabbit model, phenytoin which is a neuronal voltage-dependent sodium channel antagonist, was investigated. Retrograde venous perfusion of the spinal cord in rabbit was shown to provide significant neuroprotection during prolonged spinal cord ischaemia [61].

As exitotoxic mechanisms have been implicated in the pathophysiology of spinal cord ischaemia [62], anti-excitotoxic agent has been investigated. Riluzole which is an anti-glutamate drug was shown to prevent neuronal necrosis and apoptosis in rat during spinal cord ischaemia [63]. Another noncompetitive N-methyl-D-aspartate receptor antagonist, memantine, was also shown to have significant neuroprotective effect after ischaemic reperfusion of the spinal cord in rabbits [64].

Other agents that have been shown to be effective in protection of the spinal cord during ischaemia include phenobarbital which reduces the free fatty acid and arachidonic acid levels [85], adenosine antagonists and A1 selective adenosine derivatives of the A1 adenosine receptor [86,87]. The adenosine pathways can be affected at the receptor level by synthetic agonists and at the level of adenosine production by inhibition of adenosine transport [86]. The activation of A1 receptor on neural tissues will decrease the excitation of neurones which results in reduction of the influx of calcium which in turn inhibits the release of aspartate and glutamate [84]. No clinical studies so far have shown efficacy of these agents.

3.2.3. Hypothermia

The use of systemic hypothermia and cardiopulmonary bypass with periods of circulatory arrest have been described by different authors [88–93]. Hypothermia is one of the most effective methods in the protection of neural tissues during ischaemia. Experimental work has shown that during the periods of aortic cross-clamping, hypothermia conferred a protective effect on spinal cord function [94–99]. Hypothermia increases the tolerance of neural tissue to ischaemia [100–102] by decreasing oxygen demand and the metabolic rate, and mild hypothermia can confer a marked protective effect on the spinal cord [103]. Other mechanisms may also account for the protective effect of hypothermia. The release of neurotransmitter has been implicated in the pathogenesis of ischaemic injury of the spinal cord [104–106]. The inhibition of the synthesis and release of these neurotransmitters by hypothermia has been proposed as an additional factor that results in the protection of the spinal cord [107,108]. In a model of spinal cord ischaemia, deep hypothermia prevented the release of amino acids in the extracellular space and glutamate levels remained depressed even after rewarming to normothermia [109]. In the past, delayed paraplegia was believed to be the result of postoperative factors leading to regional hypoperfusion. Recent studies suggest that delayed paraplegia represented delayed cell death by apoptosis [110,111]. Apoptosis is produced by initial sublethal injury. Intraoperative hypothermia can prevent delayed ischaemic spinal cord injury by conferring adequate protection to neurones possibly by inhibiting the release of neurotransmitters such as glutamate [112].

Cardiopulmonary bypass is usually established with femoral arterial and venous cannulation [113]. The descending aorta is exposed through a left posterolateral thoracotomy. Body temperature is cooled until nasopharyngeal temperatures of 12–14°C are achieved. Methyprednisolone and thiopental are given during cooling. Circulatory arrest can be established with 1000–1500 ml of blood drained into the venous reservoir. For procedures confined to the distal arch and proximal descending aorta, resection and graft placement may be performed within a single period of circulatory arrest without placement of proximal cross-clamp. For procedures on the descending or thoraco-abdominal aorta, the proximal aorta is transected after circulatory arrest is established, and the proximal anastomosis completed first. The graft is then cannulated and clamped so that flow to the upper aorta is re-established. Re-implantation of lower intercostal lumbar, visceral and renal arteries may be performed, and the clamp repositioned on the graft below the level of the intercostal artery re-implantation to allow perfusion of implanted vessels whilst the distal anastomosis is performed. Kouchoukos et al. reported a 8% 30-day mortality with a paraplegia or paraparesis rate of 2.8%. He concluded that the use of hypothermic cardiopulmonary bypass and circulatory arrest provided substantial protection against paraplegia and allows complex operations on the descending thoracic and thoracoabdominal aorta to be performed safely [112]. However, the use of cardiopulmonary bypass necessitates full heparinisation of the patient making CSF drainage and intrathecal manoeuvres hazardous due to potential bleeding.

Apart from systemic hypothermia, regional hypothermia has been used for spinal cord protection. Experiments showed that regional hypothermic perfusion applied to the epidural or intrathecal space may protect the spinal cord during cross-clamping of the aorta [114–117]. However, open laminectomy has to be performed if such a degree of hypothermia (15–18°C) is to be achieved. A clinically applicable closed epidural infusion system to achieve moderate spinal cord hypothermia (26–28°C) has been described in dogs [118], and other similar systems has been reported [119]. The principal component of the system is an epidural catheter placed at T10–T12 level with infu-
sion of ice (4°C) normal saline [120]. With the above technique, over 100 patients with Type I–III thoracoabdominal aneurysms have been operated on with a lower limb neurological complication rate of 3.5% [121].

3.3. Reestablishment of spinal cord blood flow

Controversies exist among different surgeons concerning the reattachment of segmental arteries after reconstructive surgery of the aorta. Griepp et al. [134] proposed stepwise sacrifice of intersegmental arteries the start of the procedure before the aneurysm was opened. At the same time, somatosensory evoked potentials were used to monitor spinal cord function with temporary occlusion before the segmental arteries were tied off permanently [134]. The concept of oversewing segmental vessels with appropriate monitoring of the spinal cord is based on the fact that many clinical studies showed that the rate of postoperative paraplegia increases with cross-clamping time. Time might be saved by not reattaching the non-critical segmental arteries. However, a large number of intercostal and lumbar arteries are oversewn, the risk of neurological complications may be increased. Preischaemic conditioning by temporary occlusion before cross-clamping may provide a certain degree of protection for the spinal cord [135], and the reattachment of segmental arteries especially from below T6 to L2, may be important even if the cross-clamping time is prolonged [135]. Svensson and colleagues studied 99 patients and found that if patent intercostals were oversewn, the incidence of paraplegia was 37% whilst if all patent intercostals and lumbar arteries were reattached, this incidence dropped to 6% [132]. However, there is still no prospective randomised study showing significant reduction in the risk of postoperative paraplegia by reattachment of segmental arteries. Different methods of intraoperative monitoring have been discussed in our previous section which may enable identification the critical segmental vessels. With the refinement of hydrogen mapping techniques, together with monitoring of evoked potentials, the goal of shorter cross-clamping time and selectively reattaching the critical segmental arteries may be achieved [135].

4. Conclusions

Reconstructive surgery of the descending and thoracoabdominal aorta remains a challenging surgical procedure with a recognised incidence of postoperative neurological complications. The aetiology of these post-operative neurological problems has now been well described and attempts have been made to reduce this incidence based on our knowledge of the pathophysiology of spinal cord ischaemia. However, our understanding of the development and prevention of these complications require further investigation in the clinical setting before surgery on the thoracic and thoracoabdominal aorta can be performed with negligible occurrence of these disabling neurological problems.

References


[106] Simpson R, Robertson CS, Goodman JL. Spinal cord ischaemia


