Part IX

Alternative treatments

Lumbar Sympathectomy in Critical Limb Ischemia

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Lumbar sympathectomy for the treatment of peripheral arterial diseases is already carried out since one century. Today this procedure is nearly as controversial and confusing concerning the indications and results as when it was first performed. Several vascular surgeons lay great store by it claiming excellent results, while others rarely perform it contending low success rate. The increased use of distal arterial reconstruction and more recently the introduction of thrombolytic and endovascular treatments caused a downfall of lumbar sympathectomy. However it enjoyed a new period of popularity during the last years since the use of laparoscopic techniques to perform a standard sympathectomy.

In this chapter, the history, the physiologic effects, the potential role and benefits, and the different techniques of interruption of the sympathetic chain in the treatment of critical lower ischemia are presented.

History

Sympathectomy as a mode of therapy for vasospasm has its origin in the works of Jaboulay (1) in 1900 and Leriche (2) in 1913. These two distinguished surgeons of Lyon performed periarterial sympathectomy by stripping the adventitia from the femoral artery/ to treat ulcers of the legs. This operation seemed very popular at that time but it quickly became clear that the benefits of this procedure were poor with reinnervation and recurred vasospasm and ulcers after a few weeks.

It were Royle (3), orthopedic surgeon in the Lewisham Hospital in Sydney, and Hunter (4), Professor of Anatomy at the University of Sydney, that worked out the steps of the true operation for sympathetic denervation by preganglionic lumbar sympathectomy in 1923 (Most of the historical data were found in the excellent paper of Ewing (4)). This operation was carried out for an experimental but nevertheless succesfull treatment of spastic paralysis of the leg of a military victim of World War I. In his first paper, Royle (3) has drew attention to the quite interesting skin changes of the leg on the side of the lumbar sympathectomy, which were observed six hours after the operation. The skin felt warmer and became deeply pink coloured. However at that time Royle did not recognize the potential importance of this observed vascular result of sympathectomy.

Diez, a surgeon at the University of Buenos Aires, followed with interest the vascular consequences of sympathetic chain interruption. He noticed by chance, that in patients in whom he removed the left stellate ganglion to relieve angina pectoris, showed an improvement in the circulation of the left arm. Based on these findings, in 1924 he removed the sympathetic chain of a patient with thromboangiitis, with excellent clinical results (5).

At the same time as Diez, Adson and Brown (6), neurosurgeons at the Mayo Clinic in Rochester, became also deeply interested in the potential of the operation in the treatment of vasospastic disorders of the lower limb. In 1925, they succesfully treated a sixteen-years-old girl with cold feet and skin ulcers by bilateral excision of the lumbar sympathetic trunk and stripping of the outer sheath of both common iliac vessels.

These historical reports appealed in a period of 30 years in which lumbar sympathectomy became the possible alternative treatment to amputation in patients with severe peripheral arterial occlusive diseases. Its efficacy was almost not criticized because other methods for improving distal limb perfusion did not exist at that time. With the advent of reconstructive arterial surgery in the sixties, the value of lumbar sympathectomy became more and more controversial.

Another method for sympathetic interruption is chemical sympatholysis produced by injection of phenol. This technique finds its origin in 1924 in the work of Brunn and Mandl (7) treating visceral pain by the paravertebral injection of 85 per cent alcohol. Chemical sympathectomy with phenol, as a treatment of peripheral vascular disease, was first described by Haxton (8) in 1949. More recently in 1970, Reid popularized this technique in his paper with a discription of the technique and its results (9).

The clinical application of videolaparoscopy in the resection of the sympathetic chain started in the beginning of the nineties. The retroperitoneal endoscopic approach was first reported by Wittmoser (10). Since then, various urologic procedures performed with retroperitoneoscopic techniques have been introduced (11,12). Bannenberg (13) was the first to describe their laboratory and clinical experience with retroperitoneal endoscopic lumbar sympathectomy. In his footsteps other surgeons (14,15) reported their endoscopic techniques and clinical experiences.

The physiologic effects

The autonomic nervous system contains the adrenergic sympathetic and the cholinergic parasympathetic division. A distinctive feature of the sympathetic efferent pathways that run from the central nervous system to the effector organs is that they are made up of fibers of two sorts of nerve cells, the preganglionic fibers lying in the central nervous system and the postganglionic fibers in the peripheral ganglia. The principal structures innervated by these postganglionic fibers are the smooth muscles of vessels and viscera, cardiac muscle, exocrine glands, erector pili muscles and the adrenal medulla. Beside these efferent functions, the sympathetic system also contains afferent pain fibers to the heart, abdominal and pelvic viscera and the limbs (16). The sympathetic activities which may be affected by an interruption of the lumbar sympathetic chain are theoretically the control of vasomotor tone of the arteries and the control of sweat gland secretion. And indeed, the most significant clinical observation after lumbar sympathectomy is a warmer and drier skin with a noticeably deeper pink colour. Whether these changes have potential clinical benefits, especially in an extremity afflicted with arterial occlusive disease is controversial. Critical understanding of these effects requires analysis of experimental and clinical trials. Conventional blood flow studies such as electromagnetic flowmetry (17) and plethysmography (18) have shown that sympathectomy increases total limb blood flow in patients with critical limb ischemia. However, these studies cannot define the distribution to individual tissues such as skin and muscle, nor can it define the relative distribution between capillary (nutritional) blood flow and blood flow through arteriovenous (non-nutritional) shunts. Isotope clearance techniques demonstrated skin blood flow increases of 51 per cent to 83 per cent (19,20), with the degree of change correlating with the clinical respons. On the other hand blood flow measurements by radioactive labeled microsphere in a canine arterial occlusion model (21,22) have failed to show improved muscle perfusion after sympathectomy.

To evaluate the nutritive value of the skin perfusion, investigation of the microcirculatory subsystems, i.e. the thermoregulatory (arteriovenous anastomoses) and the nutritive (capillaries), is needed. Carr (23), measuring skin bloodflow by isotope clearance before and after sympathectomy, did not find effects on the nutritive skinflow. Similar findings were described by other authors. Welch (24), with the isotope clearance technique, noted no improvement of the cutaneus capillary perfusion of ischaemic human legs after denervation. Van Dielen (25) measured the effects of surgical sympathectomy in a rat model of chronic limb ischemia by laser doppler flowmetry, intravital video-microscopy and transcutaneous oximetry. He observed an increase of thermoregulatory skin blood flow but the nutritive skin blood flow and the skin oxygenation were not improved. On the other hand Moore (19) demonstrated in his human study an increase in capillary skin blood flow as documented by an increase in xenon clearance in the sympathectomized leg. In addition, in a study of transcutaneous oxygen tension in normal and ischaemic lower extremities, Rooke (26) demonstrated that changes in sympathetic activity caused changes in nutritional blood flow.

In summary, sympathectomy increases the skin blood flow, but it does not result in direct improvement of muscle blood flow. The increase of skin temperature is caused by an increase of the non nutritive thermoregulatory blood flow through the arteriovenous anastomoses. The contribution in the improvement of the nutritional capillary skin blood flow remains controversial because sometimes opposite results were found in animal and human research.

Further the increased skin blood flow is only temporary with returning to the normal resting value after two weeks to six months (27). Possible explanations are incomplete division of the sympathetic chain, the presence of crossover fibers and intermediate ganglia or hypersensitivity for circulating catecholamines (16).

Alteration of pain transmission

Clinical observations suggest that interruption of the sympathetic outflow to an affected region alleviates the pain. It is known that stellate and celiac ganglion destruction may cause a relief of angina pectoris and pancreatic pain (16,28). In addition, many patients with causalgia obtain pain relief after lumbar sympathectomy (29,30). The afferent fibers running with the sympathetic supply to the targets are painfibers but the exact mechanism of pain relief is not clear and remains speculative (16). Loh (31) noted a striking relation between the presence of hyperpathia and the relief of pain after sympathicolysis. He concluded further that a sympathetic block relieves this abnormal painful status whether the lesion causing them is peripheral or central. This findings suggest that there is a relationship between sympathetic inactivity and a decreased pain threshold caused by a decreased noradrenaline tissue level and a reduced painful stimulus transmission to cerebral centers (32). This pain threshold change is probably the reason why ischaemic restpain has a higher response to lumbar sympathectomy than ischaemic ulceration.

Potential role and benefits in critical limb ischemia

There are no large controlled trials available comparing the results of lumbar sympathectomy with the natural history of critical limb ischemia. Many uncontrolled retrospective clinical studies report a benificial effect of lumbar sympathectomy. In unreconstructable critical limb ischemia, it seems that restpain has a higher response to lumbar sympathectomy than superficial ischaemic ulceration. Several uncontrolled series (33,34,35) report an improvement of rest pain in about 50-70 per cent of the patients after surgical lumbar sympathectomy. Cross (36) published a randomized, controlled, prospective double-blind trial of phenol chemical sympathectomy against placebo bupivacaine injection in 41 limbs. Rest pain was relieved in 83.5 percent of patients at 1 week with a placebo response of 23.5 percent.

The clinical response to lumbar sympathectomy in the treatment of ischaemic ulceration or focal gangrene is less avowedly and depends on the extensiveness of the lesions. Lee (37), reporting a large serie of gangrene of the lower extremity, concluded that lumbar sympathectomy appears to be most beneficial in the management of gangrene of the toe with a limb salvage rate of 75 per cent. The best results were seen when only one toe, not the big toe, was involved. Limb salvage dropped to (38) per cent for gangrene of the foot, and with gangrene of the leg, lumbar sympathectomy had no effect. Repelaer van Driel (38) noted a postsympathectomy healing rate of 36 per cent of patients afflicted with ischaemic ulcers of the toes.

Predictive tests

The high variability of clinical response to lumbar sympathectomy in the treatment of critical limb ischemia prompts to evaluate available parameters for predicting this response. One of this parameters that has a prognostic value in postoperative outcome is the preoperative ankle/brachial Doppler index (ABI). In general a threshold ABI of 0.3 is accepted as a minimum amount of arterial bloodflow in order to determine the patients who could benefit from this operation (34,38,39,40). Prudence is called for diabetic patients where ABI measurements can be falsly high due to arterial wall calcifications. Some authors (41,42) used a Doppler systolic above-knee/brachial Doppler index of 0.6 or higher as a criteria for patient selection.

The diabetic patient requires special attention in the planning of lumbar sympathectomy. The concept of "autosympathectomy" due to progressive diabetic neuropathy is generally accepted and was demonstrated by Imparato (43). On the other hand many clinical series (34,38,44,45) seem to demonstrate that the presence of diabetes does not affect the clinical results of lumbar sympathectomy. It should be mentioned that in these reports the grade of diabetes and neuropathy is not specified. In contrast with this assessment the relation between the severity of the diabetic neuropathy and the unresponsiveness to lumbar sympathectomy in the majority of the patients is clearly reported in some clinical studies (19,43,46). It seems that the diabetic patient with severe neuropathy is not the ideal candidate for lumbar sympathectomy.

Many tests have been proposed to predict the clinical outcome of lumbar sympathectomy. The sympathetic activity can be suppressed by injecting local anaesthetic agents around the lumbar sympathetic chain, the sciatic nerve or the posterior tibial nerve. An other method to simulate a sympathectomy is the pharmacological way by inhibitors of the adrenergic transmitter mechanism (16). The potential effects of this procedure can be clinically evaluated (warmer and drier skin) or objectified by skin temperature measurement (17), electromagnetic flowmetry (17), plethysmography (18), isotope clearance technique (24), laser doppler flowmetry (25), intravital video-microscopy (25), transcutaneous oximetry (25) or skin 9 potential response measurement (36). The acetylcholine sweatspot test is another way to select patients and to verify the completeness of sympathectomy (47).

Different techniques

Anatomy

The sympathetic nervous system consists of a pair of ganglionated nerve trunks which extend from the first cervical level to the coccyx. Rami communicantes connect the paired paravertebral trunks with the spinal cord through the spinal nerves. The trunks bear a variable number of ganglia which communicate with the central nervous system and with the peripheral nerves through rami entering the ventral roots of the spinal nerves. Characteristically, the ganglia generally communicate with more than one spinal nerve root (16,48). The lumbar sympathetic chain is located medial to the psoas muscle and lies over the transverse processes of the lumbar vertebra, laterally from the inferior vena cava at the right side and the abdominal aorta at the left side. The number and the location of the lumbar ganglia is very variable. Perlow (49) found a variation from a single large lumbar ganglion to as many as six small ganglia. Most commonly, three lumbar ganglia are found with a fusion of the first and second ganglia.

From the surgical point of view it is important to be well informed about the possible anatomical anomalies which can lead to unsuccessful denervation. These include the presence of intermediate ganglia and crossover fibers. Intermediate or "ectopic" ganglia contain autonomic ganglionic cells which did not reach the paravertebral ganglia during the embryogenic migration from the primitive neural crest. Most of these collections of abberant neurones and their connections were found on or within the rami communicantes or less frequently in the ventral roots of the spinal nerve. They may be quite large and indistinguishable from the paravertebral ganglion (50,51). Another possible pit-fall is the presence of nerve fibers passing medially behind the aortic bifurcation and hypogastric vessels to join the sympathetic trunk on the contralateral side. These crossover fibers occur in 15 per cent to 28 of the patients (52,53), but in only 4 per cent of the cases there is evidence of functional activity (49).

The lower limb receives its preganglionic innervation of the 10th thoracic to the third lumbar segments of the spinal cord and these arise in all paravertebral ganglia below the first lumbar (16,27). Division of the sympathetic trunk above this level is not advised because the risk of damaging the innervation of the sfhincter mechanism of ejaculation. It is recommended to resect the second and third lumbar ganglia, responsible for the sympathetic outflow of the feet and toes. If possible the fourth lumbar ganglia with potential cross over fibers can be removed.

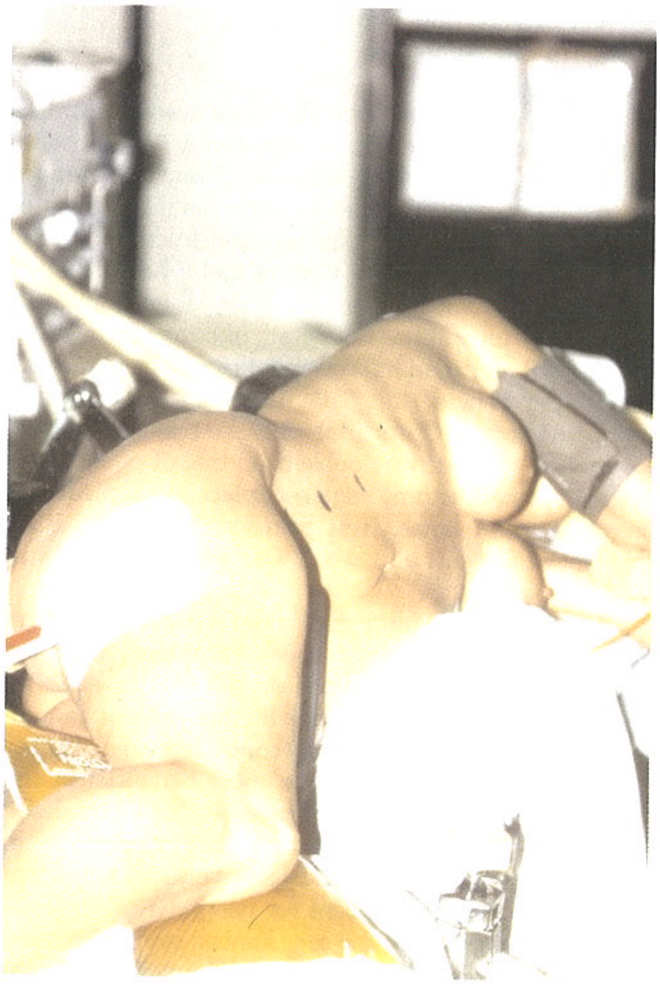

FIGURE 1
Patient in (right) lumbotomy position for open or laparoscopic sympathectomy

Open procedure

The paravertebral area can be exposed by a posterior (4)or an anterior transperitoneal (6) incision but the most popular way is the anterolateral approach of Flowthow with retroperitoneal dissection (55). Lumbar sympathectomy is done under general anesthesia with the patient positioned 30° to 45° laterally with the operating table broken at the level of the third lumbar vertebra (Fig.1). An oblique incision is made beginning at the edge of the rectus muscle, crossing the space between the 12th rib and the iliac crest and ending anteriorly of the quadratus lumborum muscle. The external and internal oblique and transverse abdominalis muscles are divided or separated in line with the incision. The transverse fascia is then divided and a plane between this fascia and the peritoneum is created by blunt finger dissection beginning laterally. The retroperitoneal space is further bluntly developed and the peritoneal sac is retracted medially and upward. The next crucial step is to identify the psoas muscle, the most important landmark. Care must be taken to avoid being trapped into a plane dorsal to the psoas muscle or into the posterolateral flank muscles. The genitofemoral nerve which lies over the ventral surface of the psoas muscle is identified and should not be confused with the sympathetic trunk. The ureter and the gonadal vessels are retracted together with the peritoneal sac. The lumbar sympathetic chain lies in a groove medially from psoas muscle, over the transverse process of the lumbar spine and laterally from the great vessels. Once the lateral aspect of the spinal column has been exposed, the chain can be identified by palpating a cord- or guitarstring-like structure. A structure which can be easy elevated off the vertebrae, without pulling and without needing to divide its fibrous attachments, is not the sympathetic trunk but is probably a paravertebral lymph node. Once the sympathetic chain is identified with certainty it is dissected from the surrounding tissues and at least two ganglia with their rami communicantes are resected. The chain can be divided with coagulation or secured with metal clips. Occasional anteriorly crossing lumbar vessels are

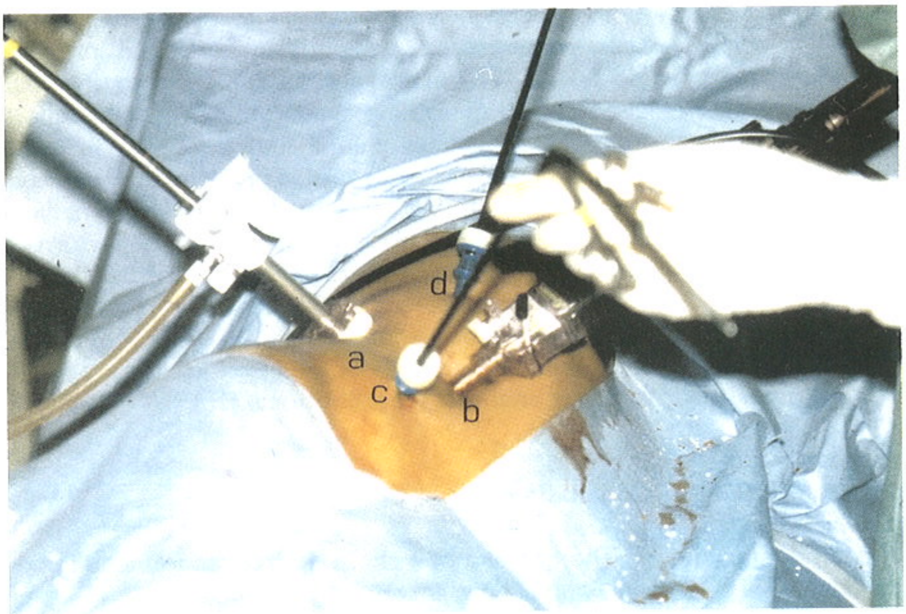

FIGURE 2
Overview of port placement.
a= muscle-splitting incision anterior to quadratus lumborum muscle;
b= 10 mm port; c and d= 5 mm ports.

divided with clips. After the hemostasis a drain is placed into the retroperitoneal space. The operating table is positioned in the normal position and the incision is closed in layers.

Laparoscopic procedure

This new minimal access surgical technique can be performed by transperitoneal approach (56) but the most popular way is the retroperitoneoscopic lumbar sympathectomy (13,14,15). In this chapter we describe our own technique (15). The procedure is done under general anesthesia with the patient positioned 45° laterally with the operating table broken at the level of the third lumbar vertebra (Fig.1). The two surgeons stand in front of the patient and the assistant nurse on the opposite side. The retroperitoneum is entered by blunt dissection through a 12-mm horizontal muscle-splitting incision midway between the 12th rib and the iliac crest anteriorly to the quadratus lumborum muscle. A transparent distension balloon (PD Balloon 1000; Origin Medsystems, Inc., Menio Park, CA, USA) is inserted into the retroperitoneum through this incision. A 10-mm, 0° endoscope 12 (Karl Storz, Tuttlingen, Germany) is introduced into the balloon, and the retroperitoneal dissection is done by inflating the balloon under camera control.

Then the balloon is replaced by a 10-mm balloon-tipped trocar, and C02 insufflation is begun to maintain the retroperitoneal space. The CC>2 flow may vary from 4 to 10 L/min, and the maximum pressure is set at 14 mm Hg. A second 10-mm port is inserted under visual control at the edge of the rectus sheath and at the level of the umbilicus. The endoscope is introduced into this second trocar. Then two 5mm trocars are placed inferiorly and superiorly to this last one (Fig. 2). If the peritoneum is damaged and a pneumoperitoneum is accidently created, a Veress needle is introduced into the peritoneal cavity. The retroperitoneal anatomic landmarks such as the psoas muscle, the genitofemoral nerve, the lumbar spine, the great vessels and the sympathetic trunk are identified. The sympathetic chain is resected between the second and the fourth lumbar vertebrae, including at least two ganglia and two rami communicantes, using a retractor for the psoas muscle, an atraumatic grasper, and a shear with monopolar coagulation or a suction device. The trunk is divided with coagulation, and the occasional anteriorly crossing lumbar vessels are divided between clips or cut with diathermy. No drains are used at the end of the procedure.

Chemical procedure

The technique described by Reid (9) can be done under local anesthesia. The patient lies on an X-ray translucent table in lateral position with the side to be treated uppermost. An image intensifier must be used to obtain lateral and anteroposterior views of the vertebral column. After local anesthesia two 12.5 or 15 cm 22 gauge needles are inserted through the fascial layer on the anteromedial aspect of the psoas muscle, so that the tips rest near the anterolateral surface of the third and fourth lumbar vertebrae just in front of the anterior longitudinal ligament. The position of the needles is verified with fluoroscopy and after repeated aspiration a last control is done by injection of 0.5 13 or 1 ml contrast medium to confirm proper spread. Then 4 to 5 ml of 6 per cent phenol in water are injected in each needle. Bed rest is recommended for a few hours. As an alternative for fluoroscopy a chemical interruption of the lumbar chain can also be performed with computed tomography guiding (59,60). There also exist reports of percutaneous radiofrequency destruction where the sympathetic trunk is coagulated at 70°C using a Radionics lesion generator (61,62).

Complications

There are no prospective randomized trials available comparing the perioperative morbity and mortality of open, laparoscopic and chemical lumbar sympathectomy. Large series of 2038, 275 and 100 open procedures have a perioperative mortality from respectively 1.9 per cent, 3 per cent and 4 per cent (63,64,33). The one month mortality of the laparoscopic and chemical technique is difficult to assess because of the lack of large series. Debing (15) reported zero per cent mortality in 23 retroperitoneoscopic sympathectomies and Keane (64) noted a 5.5 percent mortality in 126 chemical procedures.

Severe complications after open, laparoscopic and chemical lumbar sympathectomy are rarely seen. One of the most common complications is the so-called post-sympathectomy neuralgia, characterised by a temporary pain in the groin radiating down to the thigh. This appears in approximately 25 to 50 per cent of the patients beginning a few days to several weeks after the sympathectomy and disappearing gradually during the next four to eight weeks (48,66,67). The cause of this pain is speculative and not related to technical problems during the operation. Probably it is the postoperative oedema causing irritation of the neighbouring somatic sensory nerves (68). The pain is relieved with mild analgesics.

Retrograde ejaculation and impotence can be expected in about 50 percent of the male patients undergoing extensive bilateral lumbar sympathetomy with removal of both first lumbar ganglia. This sexual dysfunction is extremely rare after unilateral second and third lumbar ganglionectomy (68,69).

In the sixties there was some talk of paradoxe gangrene" after lumbar sympathectomy. This complication is not a physiologic consequence but either a problem of extensive thrombosis due to perioperative hypotension or mechanical injury of the arteriosclerotic arteries (70).

Other surgical related complications are injury of the genitofemoral nerve or the ureter, paralytic intestinal ileus, psoas abscess, wound haematoma and infection (48,64,71). The open lumbar sympathectomy has the disadvantage of causing significant patient discomfort from the sometimes painful muscle-splitting incision. More chemical technique related problems are renal and vascular trauma, phenol injury of the ureter and nerves, limb paralysis, incomplete sympathectomy and return of sympathetic tone (72,73,74). It seems that the laparoscopic technique offers the patient the benefits of a minimally invasive approach, i.e. less discomfort and short hospital stay, without the inconsistent therapeutic results of chemical sympathectomy (15).

Conclusion

The first and best choice to treat critical limb ischemia when possible are the endovascular and open reconstructive surgical techniques. However, lumbar sympathectomy maintains its place in the treatment of inoperable arterial occlusive diseases with limb-threatening ischemia. Restpain has a higher response to the postsympathectomy increase of skin blood flow than superficial ischemic ulceration. The high variability of clinical results can be decreased by careful selection of the patients. Available predicting factors are a threshold ankle/brachial Doppler index of 0.3, absence of severe diabetic neuropathy and the presence of non-extensive superficial ulceration.

Traditionally, the lumbar sympathectomy is performed by an anterolateral approach with retroperitoneal dissection. This allows safe and complete ganglionectomy but has the disadvantage of significant patient discomfort from the sometimes painful muscle-splitting incision. The alternative of chemical sympathectomy is minimally invasive but sympathectomy may be incomplete with rapid return of sympathetic activity. It seems that the use of the laparoscopic technique brings together the advantages of minimally invasive surgery and the reliability of the established open procedure.

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Spinal Cord Stimulation in Critical Limb Ischemia

Luciano Pedrini

The first application of spinal cord stimulation (SCS) was the treatment of pain. The rationale of this kind of treatment was based on the gate-control theory for segmental pain suppression (1).

Reports of the last decade have shown that SCS may alleviate pain in intractable angina pectoris (2,3) with significant pain relief often above 80% with beneficial effects on the ischaemic condition *per se* (4). Recent studies have shown an alteration of myocyte oxygen demand (4).

Experimental studies during the last decade suggested that SCS may suppress efferent sympathetic activity with secondary vasodilatation and pain relief (4,5). More recently, experimental studies suggested that SCS (even at intensities far below the motor threshold), may activate antidromic mechanisms with an associated CGRP release in peripheral and consequent vasodilatation (5). Very probably several mechanisms are simultaneously involved. These data should confirm other mechanisms of action and not only a pain control.

Some observations of pioneer showed the possible relief of pain associated with peripheral circulation (7) due to arteriosclerosis or to diabetic vasculopathy. Surprisingly, in some patients, pain reduction was followed by improving of ischaemic ulcers. A not controlled study reported pain resolution in 94% out of 38 patients; in about half of patients it was observed the healing of ulcers (8).

Successively it was demonstrated that ischaemic pain in patients suffering with Raynaud's disease responded positively to SCS.

For many years spinal cord stimulation for pain treatment in patients with critical limb ischemia (CLI) has been proposed prevalently by some European centres in cases that could not be submitted to surgical revascularization (9).

Results were positive in many reports; nevertheless, the data available were not convincible for angiologist and vascular surgeons who wrote the European Consensus on CLI (10), the TASC (11) and some national guidelines (12). The major problem is whether spinal cord stimulation is effective only for control pain or if microcirculatory modification can reduce the amputation rate or the amount of tissue lost.

Blood perfusion, in the first years of implantation, was studied only in small groups, in which an increase of microcirculation was observed. A non controlled study reported ulcers healing and a microcirculatory improvement using capillaroscopy in 12 out of 18 patients (13). An increase of $TcPO_2$ has been shown even in diabetic patients with ulcers greater than 3 cm (14).

A $TcPO_2$ increase greater than 50% within 3 months after SCS implantation was predictive of success in a sample of 177 patients with untreatable CLI, with a 66% cumulative limb salvage at 4 year follow-up (15). A significant $TcPO_2$ increase within 2 weeks of temporary implantation resulted associated with clinical improvement and SCS success (16).

More recently, about all the studies report the modifications induced by SCS on microcirculation, so that the evaluation of almost one of microcirculatory parameters is now used by almost all the researchers to predict the efficacy and the results of SCS implantation.

Indications to spinal cord stimulation

Lower limbs revascularization using the in situ technique, allowed vascular surgeons to extend the distal anastomosis to the ankle and the foot; some technical tricks such as the Miller cuff (17) or the Taylor patch (18) have improved the results of prosthetic graft anastomized to the tibial arteries.

Balloon angioplasty using cardiac material has been proposed in femoropopliteal and in tibial vessels. Tibial PTA has generally been reserved for limb salvage patients (11). The subintimal angioplasty proposed by Bolia (19) reduces the number of untreatable patients further; nevertheless, a group of patients not suitable for vascular reconstruction remains.

The chapter about non-surgical treatment of critical ischemia in "The evidence for vascular surgery" states that: "The results of non-surgical treatment of CLI are largely disappointing, although administration of prostanoids or spinal cord stimulation may have a palliative role, particularly for the treatment of pain or small ulcers in patients with inoperable disease" (20).

The Italian Society for Angiology and Vascular Medicine (SIAPAV), in patients with CLI with rest pain and/or small skin lesions, unsuitable for revasculariza-

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tion due angiography or to operative risk, and not improved after a pharmacological treatment, contemplates the implantation of a SCS after a 10-30 days trial period of temporary stimulation (recommendation 28) (21).

As till now a few studies have demonstrated a greater limb salvage rate following SCS implantation, when compared with conservative treatment (standard medical treatment or treatment with prostaglandins), TASC (11) recommendation 100 reports: "On current evidence, spinal cord stimulation cannot be recommended in the treatment of critical limb ischemia". The guidelines of the Italian Society for Vascular and Endovascular Surgery (12) report the same statement reported by the TASC guidelines.

However, even in lack of evidence, there are many clinical reasons to treat with SCS patients with CLI on the basis of the experiences reported in medical literature.

- Pain relief is significantly better in the SCS groups, in almost all the reports, even if Smith highlighted the 26% increase in the overall cost of spinal cord stimulation over best medical treatment (20). Recent experiences propose repeated treatment with prostanoids (3-4 times a year) in CLI patients, with increasing costs for medical treatment, while SCS implantation works for about 3 years without any further cost.
- The differences of the outcomes reported in 3 prospective randomized controlled trials are impressive. Jivegård et al. treated 25 patients with oral analgesic and 25 with SCS in a prospective study with an 18 months follow-up; limb salvage was 62% in SCS group versus 45% controls (not significant), meanwhile long term pain relief occurred significantly in SCS group, but not in the control group (22). Claeys et al. treated 45 patients with Fontaine stage IV with SCS plus PGE_1 and 41 with PGE_1 alone. At 12 months total healing of foot ulcers occurred in 69% of SCS group versus 17% of controls ($p<0.0001$), however the amputation rate between the two groups was not significantly different (23). The Dutch Multicentre Study Group, on the contrary, failed to demonstrate a significant reduction of major amputation, or differences in ulcers healing in a sample of 122 patients with CLI (24). Another randomized controlled study in patients with inoperable severe CLI, compared SCS plus best medical treatment to the best medical treatment only. There was no difference in mortality between the 2 groups; the major amputation rate was lower in the combined treatment group (42% versus 48%), but the difference was not statistically significant (25).

Even if the main accepted indication of SCS implantation is CLI unsuitable for vascular reconstruction, there are other patients who can improve their quality of life with this therapy: they are the patients in which the revascularization is incomplete due to anatomical reason (profundaplasty, femoro-distal bypass attached on a blind popliteal artery), and patients submitted to a functioning femoro-distal bypass, whose ulcers do not heal, with persistent rest-pain.

Selection criteria

One of the must important problem is how to identify patients that very probably will have good results and those whose treatment either with SCS and/or prostacyclin will be followed by an amputation.
Microcirculation can be studied using laser-Doppler, capillaroscopy and $TCPO_2$, however this last is the microcirculatory parameter most utilized in the evaluation of patients with CLI, so the criteria for predicting the clinical outcome are prevalently based on this technique.

The Dutch study (26), using these criteria, found a marked separation of the Kaplan-Meier limb-salvage curves only in the intermediate group of patients with a pre-treatment $TcPO_2$ between 10-30 mmHg, even if it did not reach statistic significance ($p=0.08$).

The supine and sitting position determination of $TcPO_2$ proposed by Gersbach et al (27). enabled to predict a positive treatment outcome in 88% of the cases. This good prediction is associated to an increase of $TcPO_2$ from supine to sitting position of at least 15 Torr. Even a pre-treatment supine value greater than 15 Torr was associated to a high limb-salvage rate, while a sitting $TcPO_2$ value < 20 Torr accurately predicted an unfavourable outcome, but with a lower specificity (56%).

The greatest number of centres utilize even a trial period of 1-2 weeks to predict the outcome. Some authors like Horsch don't use it because some cases need a very long period of stimulation to show a microcirculatory modification that is associated with a good outcome. A 3-4 weeks trial period of stimulation should be more predictive but it can be associated to a higher risk of infection, so it cannot be recommended.

At present, only the association between a supine 10-30 mmHg $TcPO_2$ value and supine-sitting changes greater than 15 mmHg (28) predict good results. However, these limits exclude a relevant number of patients that could have a good outcome after a SCS implantation; in particular patients with a basal value lower than 10 mmHg, that in some experiences had a good outcome, with pain relief and ulcer healing. Even patients with a $TcPO_2$ greater than 30 mmHg often don't improve their ulcers and/or need months or years for healing. This condition is associated with pain, poor life quality and the need of drugs and continuous ulcer medication, that probably could be improved by a SCS.

Practical applications

Preoperative treatment must include an accurate angiography, to exclude the possibility of a surgical or endovascular treatment, completed by Colour-Doppler evaluation, and by an evaluation of microcirculation using $TcPO_2$, laser-Doppler or capillaroscopy. The assessment should be performed by qualified vascular surgeon and interventional radiologist.

After these evaluation there is the phase of electrode implantation, that must be positioned in the epidural space at T10-L1 level under fluoroscopic control. The electrode is positioned centrally for bilateral ischemia or in paramedian position for unilateral disease. The localisation of paresthesias in the entire painful zone will indicate a correct positioning of the electrode.

Trial stimulation phase can be continuous or intermittent (only by day in particular during temporary implantation). Due to the experimental demonstration of CGRP release in peripheral and consequent vasodilatation even at intensities far below the motor threshold, nowadays it seems more indicated a continuous stimulation in the temporary period, so regulated: pulse length 180-270 μs, intensity 0.2-4 V, frequency 80-180 Hz (prevalently near 80). After the definitive implantation, we use a programme of cyclic stimulation 1' on and 2' off. Paresthesias must be pleasant and must not trouble. Their intensity does not seem to be related with the outcome. We need further information about relationships between stimulation and results; a dose-effect ratio, such as those observed with drugs, cannot be excluded.

The removal of the temporary SCS or the implantation of a definitive device can be supported by the clinical efficacy of the temporary stimulation: pain reduction or complete pain relief, increase of $TcPO_2$, positive changes of ulcers and skin perfusion are predictive of good outcome and are at the basis for the implantation of the stimulator. Following implantation, patients must be periodically evaluated to control the stimulation parameters and the battery level. Being these patients many old, very few of them are able to modify the stimulation parameters by themselves.

The more frequent complications are: skin lesions in the implantation site, changes of position of the electrode, infections and allergy to metal.

In our department, from 1989 to 2000, the implantation of a SCS has been proposed in 78 patients; many of them had already submitted to failed revascularization and/or to prostanoid. The permanent device has been implanted only in 66 (intention to treat efficacy 84.6%); of the 12 patients not implanted, 5 underwent an early major amputation (41.7%), 1 underwent amputation and died (8.3%), 3 (25%) died within 3 months without amputation and 3 (25%) were lost at follow-up. At 1 year follow-up the 66 implanted patients had a limb salvage-rate of 68.9% and a survival-rate of 85.5%, using the life-table analysis. To reach more detailed information, since July 1996, patients submitted to SCS implantation have been studied prospectively; in this period 32 patients received a definitive SCS implantation, while 7 had only a trial stimulation. All of these patients was unsuitable for vascular reconstruction; 78% had ulcers or gangrene. Sixty-nine percent of implanted patients were alive with saved limb at 1 year, using the life-table analysis. Three of these patients with healed lesions, needed the removal of SCS 6-11 months after implantation for local complications; all complained again CLI and 2 needed a major amputation (unpublished data).

Discussion and conclusions

The treatment of patients with CLI is primarily endovascular or surgical, but often these patients need further treatment when their revascularization fails, moreover, some of them are not suitable for a vascular reconstruction.

In clinical practice, patients with CLI not suitable for revascularization can subdivided in two subgroups:

- Cases in which a revascularization is absolutely impossible due to the lack of tibial or pedal vessels;
- cases with ankle or pedal vessels without veins, or with failed bypass graft, in which a prosthetic revascularization has a high probability of early failure. In this group can be included even patients with very high operative risk.

At present is not possible to identify differences in the outcome of the two subgroups.

Moreover, all the classification till now available cannot perfectly identify the patients at the Fontaine stage fourth. The extension of the ulcers is not discriminant: patients with large ulcers can heal quickly, on the contrary, patients with small lesions or gangrene can need many months to improve their lesions; some of these will never heal.

Even microcirculatory parameters, that indicates patients with the greatest probability of success, cannot exclude good results in a limited number of those out of the ranges.

The possible treatments, waiting for the results of angiogenic revascularisation and gene therapy, are: prostanoids and SCS. Although many papers report good outcomes in selected patients suffering from CLI, with a limb salvage-rate ranging between 42% and 88% and a pain relief up to 80% or pain reduction up to 94%, the randomised data available failed to show evidence of spinal cord stimulation in the treatment of critical limb ischemia.

The general impression, reading many of the papers reported in literature, is that patients unsuitable for vascular reconstruction are proposed for SCS implantation when their microcirculation is particularly compromised, in other words "too late", when repeated surgical and medical treatment have failed, with consequent poor outcomes. To improve results the identification of predictive parameters is mandatory.

However, almost all the data reported in literature showed a higher pain control with SCS than with medical treatment and significantly less tissue lost. For this reason, further studies have been designed, to improve selection of patients who can obtain good results with a SCS implantation, with a good cost-benefit ratio.

Waiting for the results of ongoing trials, the criteria emerged by the review analysis reported by Spincemaille et al. (28) could be considered as guidelines for SCS implantation. In patients with a supine $TcPO_2 < 10$ mmHg, with an increase of 15 mmHg with pending position, a 1-2 weeks trial of temporary spinal cord stimulation can be proposed before limb amputation; if a pain reduction of almost 50% within 2 weeks trial period and an increase of supine $TcPO_2$ after spinal cord stimulation is reached, the implantation of a definitive SCS can be considered.

In patients unsuitable for vascular reconstruction with a $TcPO_2$ greater than 30 mmHg, with ulcers that don't heal for months with the best medical treatment, and with rest pain that need medication, or in patients already revascularized but with persistent ulcers and pain, the implantation of a SCS could be considered prevalently for pain control, after a trial period of temporary stimulation.

In a selected number of patients, SCS can be a true alternative to limb amputation; the possibility of trying its efficacy at low risk and low costs must be considered for ethical and humanitarian reasons.

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