Pathology of the Peripheral Nervous System

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Abstract

In this review, we analyze four papers dealing with important clinical and experimental issues on peripheral nerve surgery. The first paper is a retrospective study of 180 patients operated on for radial nerve injuries. Surgical outcome is presented for any level of the radial nerve, considering the mechanism of injury and modality of surgical procedure. In radial nerve lesions in continuity, nerve action potentials (NAPs) are used to decide for either only neurolysis or resection of the injured segment followed by nerve reconstruction. Painful paresthesias due to superficial sensory radial nerve (SSRN) injuries are treated by nerve resection with amelioration in 70% of the patients.
The second paper deals with peripheral nerve injuries of iatrogenic origin: mechanisms, types of injuries and treatment are presented. This study shows how even "minor" surgical operations can be responsible of nerve injuries. The importance of early diagnosis and surgical treatment is stressed. The third paper is related to experimental studies in rats. After sciatic nerve repair with laser, or fibrin glue or sutures, the results were compared by means of functional, histological and morphometric studies. No significant differences were detected between the three methods. The fourth paper is another experimental study in rats. Longitudinal sutures, with or without interposed nerve segments, were used as bridges to cover 7 and 15 mm long sciatic nerve gaps. Nerve regeneration was evaluated in the different groups of rats and compared also to nerve regeneration after sciatic nerve repair with autologous nerve grafts. The results are of some interest and might be the start for other studies using polyglactin sutures associated to growth-promoting factors.

Key words: *Radial nerve - Nerve injury - Iatrogenic lesion - Nerve repair - Nerve suture - Neural regeneration - Nerve graft.*

Introduction

In the first paper, the surgical results obtained in 180 patients with radial nerve injuries are presented. Injuries to the radial nerve are relatively frequent and greatly affect the motor function of the superior extremity. Radial nerve palsy is characterized by loss of extension of the forearm, wrist and fingers. The ability to grasp is reduced by loss of wrist extension. Injuries to the superficial sensory radial nerve (SSRN) result in painful hypesthesia over the radial aspect of the dorsum of the hand that may be difficult to treat. The second paper deals with a very important chapter of the pathology of the peripheral nervous system i.e. the injuries of iatrogenic origin. This mechanism of nerve injury is relevant and its early recognition is important for an effective timely surgical repair . In the third paper, either fibrin glue or laser-assisted rat sciatic nerve repair were investigated as alternatives to miscrosutures. The aim of similar studies is to

search for a method able to diminish fibrous scar tissue formation at the nerve endings favoring regeneration. Any alternative method of nerve repair has to be compared with the traditional one that is still based on the use of microsutures. The use of autologous nerve grafts, is still the gold standard for repairing nerves with long gaps between the nerve stumps. Alternatives to the limited availability of autologous nerve grafts are searched and various artificial graftings and different tubing systems have been used. It seems that modifications of these conducts, like introduction of Schwann cells, interposition of nerve segments or permeabilization of the conduct itself, are necessary to allow nerve regeneration when long gaps exist. In the fourth paper, long gaps between the rat sciatic nerve stumps were bridged by a framework of longitudinal polyglactin sutures, with or without the interposition of nerve segments.

[1] SURGICAL MANAGEMENT AND OUTCOME IN PATIENTS WITH RADIAL NERVE LESIONS
J NEUROSURGERY (2001) 95: 573-583

Information

At Louisiana State University Health Sciences (LSUHS), between 1967 and 1997, 180 patients with lesions of the radial nerve and its branches underwent surgical treatment. The mean age of patients was 42 years. The level of injury was the arm in 83 patients, the elbow-forearm in 30, the posterior interosseous nerve in 37, the dorsal forearm in 9, and the distal forearm-wrist involving the superficial radial nerve in 21 patients. The nerve was injured by bone fracture, laceration, blunt trauma, nerve entrapment, gunshot wound, and iatrogenic causes. External neurolysis was performed in all surgical cases, both proximally and distally to the site of injury, and then Nerve Action Potentials (NAPs) were measured. If the NAPs were absent across a lesion in continuity, resection and repair of the injured nerve was undertaken. If the NAPs were transmitted across the lesion, internal neurolysis was made. The minimum follow-up period was 12 months and the results were considered favorable functional recovery if the muscle strength after surgery was at least moderate or Grade 3 according to the LSUHS grading system (Grade 0 - absent motor function; Grade 5 - full functional recovery). The results were analyzed considering the level at which the nerve had been injured and the mechanism of injury. Arm level. Eighty-three patients were operated on at this level. The mechanism of lesion was a fracture-related contusion in 36 patients and 32 of them achieved Grade 3 or better functional recovery after surgery. In 13 cases there was contusion without fractures: all had favorable functional recovery, except 2 patients who needed graft repair (longer than 7 cm). Nerve injuries due to laceration, gunshot wounds, and iatrogenic injections recovered well after surgery in more than 90% of cases. Elbow and Forearm level. Thirty-five patients needed surgery for lesions of the nerve at this level. Fracture-related contusions or lacerations were the main mechanisms of injury. Overall, satisfying post surgery results were obtained in 86% of cases. Posterior interosseus nerve (PIN). At this level, 37 patients underwent surgery. Almost half of the patients were suffering from PIN entrapment at either the arcade of Frohse or the distal margin of the supinator muscle. After complete division of the volar head of this muscle 18 on 19 patients obtained satisfactory results. Excellent results were obtained following repair of lacerations and fracture

related contusions of this nerve. Dorsal forearm level (branches of the PIN). At this level 9 patients underwent surgery and 6 had satisfying results. Second graft repair had satisfactory results in 2 patients out of 4. Superficial sensory radial nerve (SSRD). Twenty-one patients underwent surgery for injuries to the SSRN causing painful hypaesthesia over the dorsum of the hand. The main mechanisms of injury were lacerations and contusions. In 16 out of 19 patients who underwent resection of a segment of the SSRN significant relief of pain was seen. Two patients underwent neurolysis and experienced poor amelioration of pain postoperatively. Analysis: Favorable motor functional recovery was obtained in 88% of patients operated on the four levels of the radial nerve without considered those with SSRN injuries. Favorable motor functional recovery was obtained in 98% of the neurolysis, in 83% of the direct sutures, and in 80% of the grafting repairs. Eighty-seven percent of patients with injuries at the level of the arm and elbow, 95% of those with PIN injuries and 67% of those with injuries at the level of the dorsal forearm reached satisfying results. Then, prognosis was better for the proximal radial nerve injuries than for the most distal ones. Favorable motor functional recovery was obtained after grafting repair in 50% of injuries at the elbow level and 60% of injuries at the dorsal forearm level. For injuries treated by direct suture of the nerve stumps at the PIN and at the dorsal forearm level, favorable motor functional recovery was obtained in 67% of cases. In this study the importance of intraoperative NAPs was underlined: they were necessary for the surgical decision between simple neurolysis and nerve repair. SSRD lesions are considered difficult to treat and often pain recurrence follows a post operative significant relief of pain. In the present paper, significant relief of pain was obtained in 76% of cases. Contrary to what happens at the level of the motor component of the radial nerve, neurolysis was ineffective in injuries of the sensitive branch, whereas excision of a nerve segment was followed by significant relief of pain in 84% of cases.

[2] EVALUATION OF IATROGENIC LESIONS IN 722 SURGICALLY TREATED CASES OF PERIPHERAL NERVE TRAUMA J NEUROSURGERY (2001) 94: 905-912

Information

In this study, a retrospective evaluation of the number and types of iatrogenic nerve injuries surgically treated during a 9-year period is presented. Of 722 consecutive cases of traumatic nerve lesions operated on between January 1990 and December 1998, 126 (17.4%) were iatrogenic. During that time interval, 4.5 % of all the peripheral nerve operations were related to iatrogenic injuries. The lower extremity was involved in 41.3%, the upper extremity, including the spinal accessory nerve, in 40.5%, and the groin region in 14.3%. Less than 4 % were injuries at rare locations. The most commonly involved nerves were: accessory 11%; peroneal 9%; genito-femoral branches 8%; superficial sensory radial 8%; median 7%; ilioinguinal 7%; superficial peroneal 7%. The main categories of procedures that caused iatrogenic injury were: orthopedic procedures: 42 (osteosynthetic procedures, osteotomies, ligament repairs, and removal of plates); minor surgery: 27 (lymph-node biopsy in 15 cases; ganglion cyst removal in 5 cases); inguinal hernia repair: 13 (herniorrhaphy was the main cause of groin-level injuries); hand surgery: 11; other surgical procedures: 10 (5 cases were secondary to operations for varicose veins); non operative treatment:

12 (5 cases were due to cast application). Follow-up data were available in 97 of the 126 cases. Forty-five cases achieved a good outcome, 23 a very good result, 25 were unchanged, and 4 patients complained of worsened pain. Then, 70% of the patients improved. Very favorable results were obtained with spinal accessory nerve repair: all the 11 cases had improved and 3 had a very good result. Five of 11 groin-region injuries improved as did seven of 10 injured superficial radial nerves. Autologus nerve grafts for loss of motor function worked well especially for spinal accessory nerve repair, but also for posterior interosseus, femoral, and common peroneal nerve repairs. The three patients with sciatic nerve lesions who underwent internal and external neurolysis showed improvement. Neuromas due to sectioned digital or dorsal foot cutaneous nerves were resected rather than repaired and all patients' conditions improved, with only one exception. The latency between nerve injury and repair could be evaluated retrospectively in 124 cases: 43 (35%) were treated within the first 6 months after trauma; 40 (32%) 6 to 12 months after trauma; 41 (33%) 1 year or more after the iatrogenic injury. Thus, 65% of the cases weren't treated within the time interval deemed appropriate for elective secondary repair (< 6 months), usually because of delayed referral. Analysis. In this paper, the importance of iatrogenic nerve lesions is well underlined. The surgical results are rather good, especially for spinal accessory and superficial radial nerve injuries. Nonetheless, it appears surprising that almost 7 out of every 10 iatrogenic cases in an advanced country are still referred tardily to the neurosurgeon. Therefore, it is advisable to provide more information about prevention and diagnosis of nerve iatrogenic injuries to general, vascular, orthopedic surgeons, and family doctors. Early treatment of such nerve injuries should provide a higher rate of motor, sensory and pain improvement than that reported in this paper.

[3] LASER, FIBRIN GLUE, OR SUTURE REPAIR OF PERIPHERAL NERVES: A COMPARATIVE FUNCTIONAL, HISTOLOGICAL, AND MORPHOMETRIC STUDY IN THE RAT SCIATIC NERVE J NEUROSURGERY (2001) 95: 694-699

Information

Peripheral nerve repair with micro sutures is the gold standard against which any alternative technique must be compared before being accepted as worthwhile. In this study laser and fibrin glue nerve repair were compared to the gold standard in an experimental model of nerve injury. Method. In 24 male rats of an inbred Wistar strain, the right sciatic nerve was isolated, transected and the ends were trimmed with a razor blade. All the injured nerves were initially approximated using two monofilament 10-0 polyglycolic acid stay suture, placed at 0° and 180° in the epineurium and perineurium. This was done to obtain adequate tensile strength and to facilitate manipulation of the nerve during the subsequent repair, made in different ways, in three groups of 8 rats each: in the laser repair Group, the external epineurium was coated with a small amount of bovine albumin dissolved in saline. Repeated pulses of CO2 laser energy produced fixation of the albumin that acted as a protein solder; in the fibrin glue repair Group, the area of repair was covered by a biological fibrin glue, composed of a fibrinogen solution and thrombin forming a white elastic mass that mimics a natural blood clot; in the suture repair Group, the nerves were repaired with the placement of more sutures for a total of four to six. The results of the nerve repair were

examined in different ways: the rats were examined at 8 and 16 weeks post surgery by using a modified version of the toe-spreading test, that measures the motor function loss due to the sciatic nerve injury; the rats were killed 16 weeks after surgery, the nerves exposed, inspected and removed for europathological examination. Transverse sections were obtained from the proximal and distal segment of the nerve, whereas longitudinal sections were cut from the repair zones. This sections were examined with light microscopy (after staining with 1% toluidine blue) and semi quantitatively scored for: epineurial fasciculation; neuroma formation; extraneural nerve fibers at the repair site; intraneural scarring; axonal alignment; extraneural nerve fibers in the distal nerve segment. Light micrographs were used to perform a morphometric analysis of the nerves. Nerve tissue area, axon count, diameter of myelinated nerve fibers, and nerve fiber density were determined for the proximal and distal nerve segments. Results. There was no difference in recovery of motor function among the three repair groups. All had a progressive increase in motor function to approximately 60% of normal at 16 weeks. Dehiscence of the nerves was not found in any of the three groups. Slight adhesions were found in four rats in the laser and fibrin glue repair groups, whereas moderate adhesions were found in six rats in the suture repair group. Some thickening at the repair site was observed in three, three and five rats from the laser, fibrin glue, and nerve suture repair groups, respectively; in this last group the thickening was more pronounced. At the light microscopic examination the differences were mainly quantitative among the three different repair groups. Neuroma formation was only present in two nerves: one in the laser repair and one in the suture repair group. Intraneural scar tissue was present in all nerves, but fibrosis was more abundant in the sutured nerves. Axonal alignment was good to moderate in laser and fibrin glue repair groups, good to poor in the suture one. Extraneural fibers at repair site and in distal nerve were present regardless of the repair method. The mean myelinated axonal diameter, axon count, and density was not significantly different among the three repair groups, although there was a trend toward more and thicker fibers in the laser repair group.

[4] NEURAL REGENERATION ALONG POLYGLACTIN SUTURES ACROSS SHORT AND EXTENDED DEFECTS IN THE RAT SCIATIC NERVE J NEUROSURGERY (2001) 95: 316-323

Information

A method of nerve repair in which an intrinsic framework of longitudinal sutures is used to bridge a 7-mm gap has been described recently (Scherman et al, 2000). In this work this method was compared to that using autologous nerve grafts across short defects (7mm); it was also used in the attempt to support regeneration across an extended gap (15 mm) with or without the interposition of a nerve piece along the sutures. Methods. In 40 female Wistar rats, the sciatic nerve was exposed on both sides. Three different groups were made: in Groups I and II, a 10-mm long nerve segment was resected bilaterally; in Group III a 17-mm long segment was resected bilaterally. The nerves were then managed in different ways: In Group I (4 rats), the nerve endings were merely fixed by a 9-0 single epineurial suture to the adjacent muscle, leaving a 7-mm gap between the

nerve endings and keeping the nerve endings facing each other; In Group II (8 rats), on one side, 8-0 polyglactin sutures were used in a continuous longitudinal fashion to bridge a 7-mm gap; the sutures were placed through the perineurium and three laps, creating six traversing lengths, were completed. On the other side, the sciatic nerve was repaired by using a 7-mm long nerve graft, incorporated orthodromicall, fixed with standard 9-0 epineurial sutures; In Group III (24 animals) 8-0 polyglactin sutures were used to bridge the 15 mm-long gap of the sciatic nerve bilaterally; in addition, only on one side a 2 mm long nerve segment was centered in the gap and maintained by the sutures; four rats were left intact to serve as healthy control. The animals were killed at 2, 4, and 12 weeks. Schwann cell distribution was analyzed at 2 weeks by using fluorescence microscopy. Macrophage populations at 2 and 4 weeks, and axonal growth at 4 and 12 weeks were evaluated by using light microscopy. At 12 weeks tetanic force measurements were performed bilaterally in rats of Group II, III, and in control rats. Results. In the non-repaired Group I, there was no nerve continuity after 12 weeks. In all sutured cases of Group II and III, a distinct structure without branching had formed between the nerve endings. At 2 weeks, in Group III the sutures were still visible and the interposed nerve segment was easily recognized as a spindle-shaped structure incorporated in the middle of the regenerated structure. At 4 weeks the sutures were difficult to see and at 12 weeks they had vanished. In Group III rats, the regenerated structure on the side without interposed nerve segment was thin compared with that of the side with the interposed nerve segment. In Group III, Schwann cells were present throughout the regenerated structure only in the nerve sutured with an interposed nerve segment; in the others there was a space with no S-100-positive cells in the center of the regenerated segment. The sections with the interposed nerve segment generally had a greater cross-sectional area and contained more minifascicles than those without interposed nerve segments, but no other major differences were seen. No significant difference in the number of myelinated fibers in the distal tibial trunk was seen between the sutured and nerve grafted sides in Group II. In Group III, the number of fibers was significantly greater on the side with the interposed nerve segment. The same difference was seen considering the return of muscle force and functional recovery. There was a positive correlation between the results of the tetanic force measurements and the results of the axonal counts in both Groups II and III. Analysis: The last two papers deal with methods of nerve repair and we will therefore discuss them together. In the first one, a comparison between three different nerve repair methods was done: the result was that there's no difference between the suture, laser-assisted and fibrin glue repair methods. We think that this study is rather criticizable and that similar efforts should be better directed. For repairing a rat sciatic nerve is sufficient one or maximum two 10-0 nylon sutures. Therefore: a) 4 to 6 10-0 sutures are unnecessary and put the basis for greater local fibrous scar tissue reaction hindering axonal regeneration; b) to add laser action or fibrin glue to two preventive sutures means to add something that is not necessary because the two preventive sutures are already sufficient. This study could be useful to understand that searching for less traumatic and more effective alternative methods to nerve suture might be commendable if the alternative methods are really alternative and not based on the use of preventive sutures. The second paper is related to a search of alternatives to nerve grafts for nerve repairing. It was studied a new way of bridging long nerve gaps. Absorbable longitudinal sutures between the nerve endings cover 15 mm long gaps and served as a support for some axonal

regeneration especially when a short nerve segment was intercalated. It is underlined the importance that can have a communication between the nerve milieu and the environment around it. It was demonstrated that the matrix formation around a simple framework of sutures does allow some axonal growth as well as some limited functional recovery. It is remembered the possibility to enhance the power of these sutures as a vehicle of axonal regeneration by adding growth factors. As a criticism to this study, we remember that sciatic nerve regeneration in rats is extremely valid. In our experience, empty gaps of 15 mm in length may be compatible with some grade of axonal regeneration reaching the distal nerve stump spontaneously. Another fact is that Schwann cells were not detected along the bridge of pure sutures and these cells are essential for axonal regeneration and should be provided as a continuous bridge like is when nerve grafts are used. At the moment, this study represents a commendable initial attempt to find valid options to the use of nerve graftings for nerve repair.

Synthesis

It is well known that the radial nerve is one of the best peripheral nerves for what concerns surgical prognosis. This fact was confirmed by the rich experience of the LSUHS. After reconstructive procedures at the dorsal level of the forearm, favorable functional recovery was obtained in a percentage of patients lower than after reconstruction of the radial nerve at more proximal levels. This contradictory fact may be explained by the more complex anatomy at the radial distal level where the nerve gives origin to branches for the extensor muscles. Peripheral nerve injuries of iatrogenic origin are frequent and must be repaired like any other traumatic lesion. The possibility to cause nerve injuries during some operations should be taken in mind by surgeons to avoid or early diagnose them, as well as, family doctor should be informed on iatrogenic lesions to early address patients to neurosurgeons. Attempts to find alternatives to sutures and to nerve grafting for nerve repair are very difficult as demonstrated by the last two reviewed papers. A higher effort should be made to address energies towards construction of better experimental designs.

Papers reviewed

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