Conventional Strategies for Nerve Repair

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Mario G. Siqueira and Roberto S. Martins

Contents

> The central objective of nerve repair is to assist regenerating axons to re-establish useful functional connections with the periphery. Sir Sydney Sunderland

During the last decades, significant changes in the surgical management of nerve injuries have occurred, based on an improved knowledge of basic nerve biology and on the advance of surgical technologies like the use of magnification, bipolar coagulator, microinstruments, and fine suture material and the introduction of electrophysiologic methods for intraoperative assessment of nerve injuries. These advances led to improved functional results, increasing the number of surgical explorations and the attempts to repair lesions that previously were considered irrepairable.

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In this chapter we describe the common surgical techniques in current use for nerve repair, external and internal neurolysis, end-to-end suture, and nerve grafting and two less used techniques, end-to-side suture and muscular neurotization.

4.1 Neurolysis

Neurolysis has been defined by Seddon [26] as an operation in which an injured nerve is freed from scar tissue or other neighboring tissue to facilitate regeneration. In this procedure whenever possible the tissue dissection should occur along anatomical planes. Attention should be devoted to hemostasis and minimal tissue damage, since bleeding and tissue debris will promote excessive scarring, which will attenuate the results of the surgical procedure.

There are two types of neurolysis, external and internal.

4.1.1 External Neurolysis

The external neurolysis consists of freeing the nerve from a constricting or distorting agent by dissection outside the epineurium, usually including the mesoneurium, an adventitious tissue that contains collateral blood vessels, and sometimes including the most external epineurium as well. The inner layers of the nerve remain intact. Nerve segments are freed circumferentially using a number 15 scalpel or Metzenbaum scissors. Seldom used as the treatment itself, the external neurolysis should be performed in all lesioned nerve segments before surgical reconstruction. It is usually begun by working from normal to abnormal nerve sections beginning well distal as well as proximal to the lesion site. Thickened or scarred portion of the external epineurium will then be resected. If carefully done, long lengths of nerves can be mobilized without serious interference with their blood supply. However, extensive manipulation may, in rare cases, promote neurological deterioration. A good deal of argument about the value of external neurolysis for the improvement of function in a direct fashion still exists. Apparently this technique could be valuable when the nerve is intact but tethered or immobilized by scar tissue and the patient complains of severe neuritic pain. In spite of this limited indication, external neurolysis is performed as the first step of almost all types of nerve repair. Figure 4.1 demonstrates the situation of a scarred sciatic nerve (Fig. 4.1a) and its appearance after external neurolysis (Fig. 4.1b).

4.1.2 Internal Neurolysis

Internal neurolysis is the exposure of nerve fascicles after epineurotomy and their separation by interfascicular dissection or by removal of interfascicular scar tissue. It is an essential part of some procedures [2] as follows: (1) separation of intact from damaged fascicles in partially damaged nerves, (2) separation of a fascicle during a

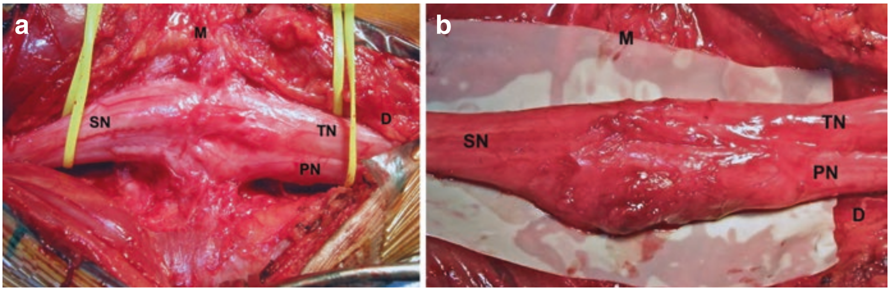

Fig. 4.1 Intraoperative view of a gunshot injury to the sciatic nerve. (**a**) Scar tissue involving the nerve. (**b**) After external neurolysis the main trunk of the nerve as well as its peroneal and tibial divisions can be identified. *D* distal, *M* medial, *PN* peroneal nerve, *SN* sciatic nerve, *TN* tibial nerve

nerve transfer, and (3) separation of intact fascicles during removal of a benign nerve tumor. Another indication for this procedure is given when there is an incomplete nerve tissue loss distal to the lesion, but the patient has pain of neuritic nature which does not respond to conservative management. When performing this technique, the surgeon should keep in mind that the removal of abundant fibrous tissue between the fascicles may impair the blood supply to this structure [18] with the potential risk of some loss of function.

4.2 End-to-End Neurorrhaphy

Since Hueter in 1873 [6] described an end-to-end coaptation of nerve ends by placing sutures in the epineurium, the end-to-end suture became the procedure of choice for nerve lesions where opposition of stumps can be gained without excessive tension. Excessive tension across a nerve repair site is known to impair the local blood circulation, to increase the scarring at the coaptation site, and finally to impair regeneration. The opposition of the nerve ends is facilitated by mobilization of the stumps, transposition of the nerve, and, in selected cases, mild flexion of the extremity. Every nerve repair should be performed with optical magnification (surgical loupes or microscope) and adequate lighting. The end-to-end neurorrhaphy should be done only when the nerve gap is small (usually less than 2 cm). A test to evaluate the possibility of direct suture without prohibitive tension involves passing an epineurial suture of 7-0 nylon. If the suture keep the stumps together without tearing the epineurium, the end-to-end neurorrhaphy is possible.

There are three types of end-to-end neurorrhaphy: epineurial, perineurial, and group fascicular. All three procedures always initiate with the preparation of the nerve ends. Transverse cuts, distant 1 mm from each other, are progressively made with a sharp instrument (micro scissors or surgical blade) until an area of healthy appearing fascicles without fibrotic tissue is reached. Following resection of the devitalized tissue hemostasis is imperative because bleeding could lead to excessive fibrosis and distortion of the nerve architecture. A small tipped bipolar coagulator or sponges dipped in a solution of 1:100,000 epinephrine in 10 ml of saline should be used for this purpose. The prepared nerve ends are then gently mobilized and approximated to be coapted, without excessive tension. In the *epineurial technique* the entire nerve trunk is sutured as a unit. Finely spaced interrupted nylon sutures inserted into the epineurium are used to approximate the stumps, first laterally and then along volar and dorsal epineurial surfaces. Suture material should be passed through the epineurium only, as the incorporation of neural elements results in scar tissue formation. The sutures should be placed approximately 0.5–1.0 mm from the incised edge, with the needle piercing the surface of the nerve and emerging just subepineurially. In the opposing nerve stump, the second passage of the needle begins subepineurially and emerges on the surface. The size, the depth, and the number of sutures should be minimized to decrease iatrogenic trauma and the formation of foreign body granuloma. The number of sutures required for adequate alignment of the stumps varies depending upon the nerve diameter. Having in mind that an adequate alignment is paramount for the success of the surgical procedure, it is desirable to perform the smallest number of sutures possible because all suture materials evoke an inflammatory reaction, which can result in production of excess granulation tissue. To maintain alignment of the nerve stumps, the first two sutures are placed in the nerve trunk 180° apart. Additional sutures are then placed in the upper portion of the nerve. Grasping carefully the ends of the two first sutures, the nerve trunk is rotated to expose the underside of the nerve where additional sutures are placed, completing the apposition of the nerve stumps. All sutures should be tied with equal tension. The tension applied should be just enough for alignment and contact of the neural bundles. Excessive tension may result in crushing and malalignment of the nerve bundles. Identification of the longitudinal epineurial blood vessels, which are not always present, helps to avoid rotation of the nerve ends and consequent malalignment of the fascicles. The visualization of fascicular patterns on the cut nerve surfaces can also be effective to help the correct realignment of peripheral nerve stumps in areas of consistent topography (e.g., distal ulnar and median nerves). The fascicular topography changes after 1–2 cm of neural trimming, but groups of fascicles can usually be opposed as closely as possible even though the repair is done at epineurial level. The epineurial technique is the most performed end-to-end neurorrhaphy in clinical practice and illustrated in Fig. 4.2.

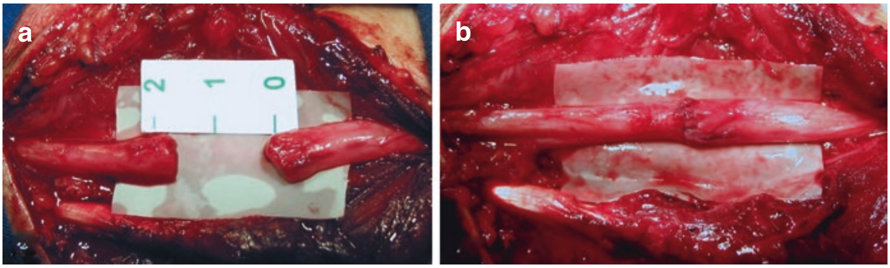

Fig. 4.2 Intraoperative view after resection of a neuroma in continuity of the ulnar nerve at the elbow. (**a**) Distance between the two stumps of the nerve after resection of the lesioned tissue and normal retraction (*nerve gap*). (**b**) End-to-end epineurial repair

As expertise and technical development in microsurgery have progressed, suture repair of peripheral nerve subunits, like the *perineurial or fascicular repair*, has increased in popularity. The technique involves resection of the outer epineurium, followed by intraneural dissection of fascicles in both nerve stumps and perineurial suturing of individual fascicles with one or two sutures of 10-0 suture material. The perineurial repair represents the best possibility of nerve alignment by the surgeon. However, this advantage may be offset by the amount of neural trauma the technique demands. In clinical practice this procedure is seldom performed. *Grouped fascicular repair* is a less aggressive method of nerve alignment done by the identification of grouped fascicular patterns in both nerve ends and suturing through the thickened inner epineurium. This technique is used mainly in areas of well-defined nerve topography such as the distal median and ulnar nerves and the radial nerve around the elbow.

Superiority of one end-to-end neurorrhaphy over another has never been clearly demonstrated [8]. In practice, the accurate alignment of the fascicles or grouping of fascicles is often difficult because of trauma, edema, and scarring that can distort the normal topography.

4.3 End-to-Side Neurorrhaphy

End-to-side neurorrhaphy was first described by Letievant in 1873 [30], but the idea was abandoned due to poor results. More than a century later, Viterbo et al. [32] reintroduced the technique with apparently promising results. The end-to-side neurorrhaphy involves coaptation of the distal stump of a transected nerve to the trunk of an adjacent healthy donor nerve. It has been proposed as an alternative technique when the proximal stump of an injured nerve is unavailable or when the nerve gap is too long to be bridged by a nerve graft. Collateral sprouting is the accepted mechanism of nerve regeneration following end-to-side neurorrhaphy, where regenerating axons originated from the most proximal Ranvier's node of the donor nerve grow toward the coaptation site [29, 37]. Whether the receptor nerve should be coapted to the donor nerve through an epineurotomy or a perineurotomy is still controversial. Although some experimental papers revealed no difference if a nerve window at the coaptation site was made or not [32, 33], other investigators claim that the greater degree of axonal damage to the donor nerve after a perineurotomy enhances axonal regeneration with better histological results [35, 36]. The clinical experience with this technique has been published in the form of case reports and small clinical series, and no randomized clinical trials have been performed in order to compare end-to-side coaptation to other reconstructive techniques. The clinical outcomes of end-to-side repair are often disappointing. In a recent published review of the clinical applications of the technique, Tos et al. [30] demonstrated that a discrepancy between experimental and clinical results still exists, and the authors concluded that at present the end-to-side repair could not substitute standard techniques in most situations. In the majority of cases, it will provide only limited sensory recovery [23, 28, 34]. It can be considered a valid therapeutic option only in cases of failure of other attempts of nerve repair or whenever other approaches are not feasible, especially when protective sensibility is a reasonable goal.

4.4 Graft Repair

Nerve grafting dates back to Philippeaux and Vulpian in 1817 [9]. In extensive injuries, especially those due to blunt mechanisms, loss of nerve tissue may produce lengthy lesions which, when resected, result in a large nerve gap. A nerve gap is defined as the distance between two ends of a severed nerve and consists not only of an amount of nerve tissue lost in the injury or debridement but also of the distance that the nerve has retracted due to its elastic properties [15]. Small nerve gaps (<2 cm) can be overcome by stretching the nerve stumps to a limited extent to attain apposition, making possible a primary repair. But when a significant amount of stretching and mobilization is necessary, the consequent increase in the suture line tension endangers the extrinsic vascular supply to the nerve leading to connective tissue proliferation and formation of scar tissue [13]. In this situation of an irreducible nerve gap, the gold standard management continues to be autologous nerve grafting. The nerve grafts serve as a guide for the axons of the proximal stump as it regrows toward the distal stump.

Small-caliber grafts seem to serve better than longer whole nerve grafts [14]. For a nerve graft to survive, it must be revascularized, and when the nerve is too thick, the central part of the nerve graft will not become revascularized, and the outcome of the repair will be poor. The sural nerve, by far the most commonly used donor nerve, is harvested from the ankle until near the knee, and 30–40 cm of the nerve is usually obtained in adults from each leg for grafting. Other sensory nerves like the medial antebrachial cutaneous or the sensory branch of the radial nerve are used as well. The grafts should be harvested after the injured nerves have been exposed, the extent of lesion defined, and the gap between the prepared nerve stumps measured. Then the number of grafts required is calculated. To release tension on suture lines, the length of the grafts should be about 15–20% greater than the measured gap because they always present some shrinkage owing to a relative initial hypovascularization. The nerve grafts are initially similar to other devascularized tissue implants. The regeneration of the blood supply must be provided by the nerve stumps and surrounding tissues and takes some time. In the beginning the graft relies on the imbibition from the surrounding for nutrition. Consequently, long grafts and a poorly vascularized tissue bed could be responsible for ischemic necrosis of the central graft core, with destruction of Schwann cell tubules and failure of axonal regeneration through the graft.

The most popular as a graft technique is an interfascicular grouped fascicular approach described by Millesi in the early 1970s [16, 17]. The principles and surgical technique of nerve grafting are similar to direct repair. The proximal and distal ends of the nerve are transversely sectioned until viable fascicles are visualized, and groups of fascicles are then isolated both proximally and distally. Usually oriented in a reverse fashion to minimize the diversion of regenerating fibers from the distal neurorrhaphy, a number of small-caliber nerve grafts are attached between the nerve ends, connecting corresponding groups of fascicles. The coaptation is maintained by one or two fine sutures often supplemented by fibrin glue. As much of the

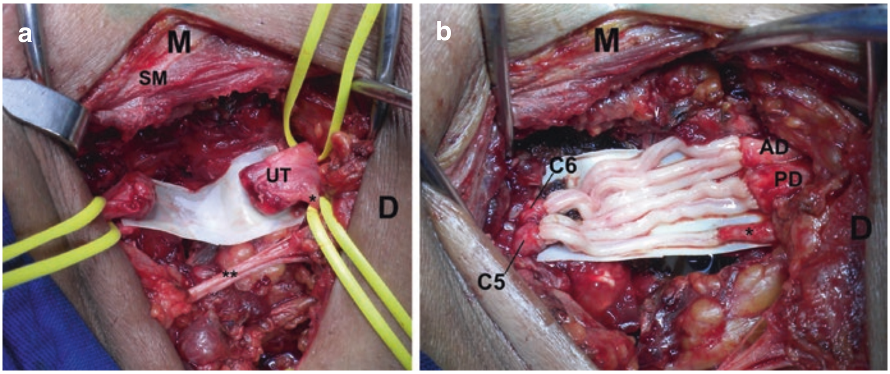

Fig. 4.3 Intraoperative view of a penetrating stab wound to the right supraclavicular region. (**a**) An injury of the upper trunk of the brachial plexus was identified. (**b**) Reconstruction was performed with nerve grafts. *AD* anterior division of the upper trunk, *C5* fifth spinal nerve, *C6* sixth spinal nerve, *D* distal, *M* medial, *PD* posterior division of the upper trunk, *SM* sternocleidomastoid muscle, *UT* upper trunk, * suprascapular nerve, ** supraclavicular nerves

fascicular structure of each stump as possible is covered in this fashion. Individual grafts should be positioned loosely, not too close to each other, to permit maximal contact with a viable recipient bed. Figure 4.3 illustrates a brachial plexus injury that has been repaired by an interfascicular grouped fascicular approach.

Graft length might influence regeneration as longer grafts may be harder to revascularize, but in clinical practice no agreement exists on the maximal length that may be bridged by a nerve graft. Although good results are eventually reported with longer grafts, most nerve surgeons agree that the outcome is worse with grafts greater than 10 cm.

4.5 Direct Muscular Neurotization

Described in the beginning of the twentieth century, the surgical insertion of peripheral nerves directly into denervated muscles is called direct muscular neurotization. This procedure is indicated when no distal nerve stump is available for neural coaptation or when the lesion involves the neuromuscular junction [24]. Experimentally it was observed that the implantation of a normal nerve near denervated motor end plates reinnervates this site and that axons that do not have contact with those persistent motor end plates will induce new ones in previously denervated areas [22]. However, clinically the neurotization restores significantly less function, when compared with direct repair or grafting, leaving areas of the target muscle denervated [12]. In most published reports, an entire nerve was implanted into the target muscle, probably leaving denervated areas outside the reach of the regenerating axons. To overcome this problem, Brunelli [4] suggested that the donor nerve should be splitted into multiple fascicles and distributed widely across the muscle. Direct muscular neurotization is a potentially effective technique when the normal nerve-muscle interface has been destroyed [1], but until now there are only a few reports of clinically successful reinnervation in the literature, and this technique has no stablished role in reconstructive nerve surgery.

4.6 Fibrin Glue Versus Suture

Epineurial suture repair is generally considered as the gold standard for peripheral nerve repair, but when nerve trauma is extensive, the suture method can be difficult and time-consuming. Specific training is necessary for nerve repair by suture which requires the placement of stitches that persist as foreign bodies producing inflammation and different degrees of scarring. The number of stitches (the less the better [11]) and the surgical skill certainly play a role in the improvement of outcomes.

Fibrin glue is one of the alternatives to suture [10]. Concentrated fibrinogen and thrombin are common ingredients in the mostly used fibrin glues, which are differing in the antifibrinolytic agent contained or the application procedure. Currently, the use of fibrin sealants as nerve glue still has not been approved and their use on nerve surgery is considered off-label.

The fibrin sealants simulate the last stages of the clotting cascade forming a substance resembling a physiologic blood clot that holds the nerve ends together [7]. The artificial “clot” protects the repair from scar tissue and allows healing to occur. Its structural integrity is preserved for about 3 weeks by the antifibrinolytic component of the sealant [5].

The potential advantages of fibrin glue for nerve repair include ease of use, reduced operative time, less tissue manipulation/trauma with consequent less inflammation/fibrosis, and maintenance of nerve architecture with better fascicular alignment [3, 19, 20, 27].

The amount of publications concerning the use of fibrin sealants as nerve glue is small. A recently published systematic review [25] found 14 animal studies, one cadaver study, and only one clinical study that fit the study criteria. Although some of the results were conflicting, most found fibrin glue repair to be efficient (and sometimes even superior) to suture repair.

The following are some practical remarks: (1) Nerve repair with fibrin glue has an initial low tensile strength, and its use should be limited to situations without tension in the coaptation (grafts and nerve transfers) and in cases with difficult exposures or exceptionally small-caliber nerves; (2) Before the use of the glue, a meticulous hemostasis should be done, and the nerve surfaces should be dry of excess fluids to ensure optimal adherence [31]; (3) After nerve repair, the nerve glue should be left to polymerize and cross-link for several minutes before irrigation; (4)The inevitable small amount of glue that stays between the nerve ends should not be a concern as fibrin glue is nontoxic and does not block axon regeneration [21]; (5) Like in the repair by suture, at the end of the surgery, the upper extremity should be immobilized for 3 weeks to ensure an ideal environment for axon regeneration.

Despite the apparent advantages of fibrin glue, its low tensile strength should always be kept in mind. To overcome this potential disadvantage, two combined strategies were created: to add fibrin glue to a standard suture repair and to reduce the number of stitches by using fibrin glue to reinforce the repair. There is no advantage with the first strategy, but the reduced number of stitches may ultimately lead to better outcomes. In practice the use of a few stitches complemented by the fibrin glue to enhance the coaptation has been adopted by many nerve surgeons.

4.7 Factors Influencing the Results of Surgical Repair

Besides the surgical techniques, the results of repair of peripheral nerves are certainly influenced by some biological aspects:

1. Younger patients recover more completely and in a shorter period of time. This is probably related to shorter limb length, faster rate of regeneration, and greater adaptability and compensatory sensory and motor reeducation.
2. The level of the injury. Too proximal injuries require greater metabolic biosynthesis for functional return, and this may exceed the capabilities of the nerve cell body and result in cell death.
3. The result of the repair of pure motor or pure sensory nerves is usually better. In mixed-function nerves, the potential for transposition of axons during regeneration with improper end-organ reinnervation exists.
4. The extent of the injury. Lesions in continuity or those with focal neuroma formation or small gaps will present better results than injuries with irreducible gaps or long length of defect owing to segmental vascular supply, suture line tension, and biologic considerations in nerve grafting.
5. Associated injury may add further difficulty to nerve regeneration. Polysystemic trauma, massive deep wounds, sepsis, scar formation, and contraction wound healing may interfere with the management of the patient.
6. The merits and indications for immediate versus early secondary repair have been discussed in Chap. 3. However, it is important to emphasize that as the interval between the time of injury and surgical intervention increases, irreversible changes occur in the nerve trunk, particularly in the distal segment. In addition, neurogenic atrophy and fibrosis of denervated muscle segments complicate the potential for functional recovery. Therefore, early repair is advocated, whenever possible.

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