Nerve transfers for severe brachial plexus injuries: a review

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Nerve transfer procedures are increasingly performed for repair of severe brachial plexus injury (BPI), in which the proximal spinal nerve roots have been avulsed from the spinal cord. The procedure essentially involves the coaptation of a proximal foreign nerve to the distal denervated nerve to reinnervate the latter by the donated axons. Cortical plasticity appears to play an important physiological role in the functional recovery of the reinnervated muscles. The author describes the general principles governing the successful use of nerve transfers. One major goal of this literature review is to provide a comprehensive survey on the numerous intra- and extraplexal nerves that have been used in transfer procedures to repair the brachial plexus. Thus, an emphasis on clinical outcomes is provided throughout. The second major goal is to discuss the role of candidate nerves for transfers in the surgical management of the common severe brachial plexus problems encountered clinically. It is hoped that this review will provide the treating surgeon with an updated list, indications, and expected outcomes involving nerve transfer operations for severe BPIs.

KEY WORDS • brachial plexus injury • nerve transfer • neurotization • accessory nerve • C-7 spinal nerve • intercostal nerve • medial pectoral nerve

Nerve transfers (so-called neurotization) involve the repair of a distal denervated nerve element by using a proximal foreign nerve as the donor of neurons and their axons to reinnervate the recipient nerve and muscle that will undergo reinnervation.71 The first report of neurotization in an attempt to restore injured plexus function was published by Tuttle100 in 1913. A review of the historical precedents as well as the anatomical basis and rationale for nerve transfers in brachial plexus surgery was most clearly presented 20 years ago by Narakas.70 Since then, nerve transfers have become increasingly popular and used for the repair of BPIs, especially in cases in which the proximal motor source of the denervated element is absent due to avulsion from the spinal cord.88 Increasingly advocated as well is the use of nerve transfers in cases in which the proximal motor source is available but the distance between removal and reimplantation is so long that the outcome would be poor;30,31 a nerve transfer into the denervated distal nerve stump close to the motor end organ would then restore function, which otherwise would not be possible.72 The use of nerve transfers has been a major advance in the field of brachial plexus nerve reconstructive surgery, with many different ingenious transfers associated with improving results, as reported and reviewed recently.11,43, 64,88,98

The anatomical and physiological principles that underlie nerve transfers are relatively straightforward. Because motor recovery has been the main goal, the choice of a donor nerve element with a reasonable amount of motor fibers is required.71 The loss of the muscle due to denervation when transferring the donor nerve must not represent loss of important or critical function.55 Obviously, the value of the neuromuscular element to be reinnervated must greatly exceed the utility of the sacrificed one. An excellent compromise is achieved if some function of the donor muscle can be retained, by using only a portion of the nerve as the donor, which has been exemplified by the use of half of the hypoglossal nerve (thus, not completely denervating ipsilateral tongue) for transfer to the facial nerve for reanimation of the face.6,22,28,83

There are several important principles to adopt to maximize outcome in nerve transfers, the first of which is to reinnervate the recipient nerve as close to the target muscle as possible.72 An outstanding example of the latter is the transfer of an ulnar nerve fascicle directly to the biceps branch of the musculocutaneous structure in close proximity to its entry into the muscle.74 The second principle involves performing a direct repair, without intervening grafts; this tactic seems to be associated with improved outcomes, as reported convincingly after intercostal–musculocutaneous transfers.45,58,69,76,103 The third principle is to use combinations of similarly behaving neuromuscular units, maximized when agonistic donor and recipient are chosen, as cortical readaptation is the physiological basis for functional recovery.36,59 This may also be the physio-

Abbreviations used in this paper: BPI = brachial plexus injury; MRC = Medical Research Council.
NERVE TRANSFER TECHNIQUES

Surgical Approach

The surgical management of patients with a severe BPI is first to determine preoperatively whether most or all the nerve roots are truly avulsed.64 The second aspect of surgery is to perform nerve repair, which, in the severe cases with avulsion, incorporates appropriate nerve transfers to reanimate the extremity.65 Surgical exploration therefore warrants exposure of the entire supra- and infraclavicular plexus, with an appropriately made incision, as well as marking of incisions that will allow exposure of donor nerves that may need to be transferred (Fig. 1). The upper extremity, extending to the anterior and lateral chest wall, and both legs being targeted for donor sural grafts, should be appropriately prepared.

After complete and thorough exposure of the plexus, including intraforaminal dissection and external neurolysis of the nerve-in-continuity, intraoperative electodiagnostic studies should be conducted.66 First, motor evoked stimulation is used to determine which roots are conducting by observing the distal muscles contraction, occasionally augmented by needle-based electromyography. Nerve action potentials are measured across the neuroma or in clinically nonfunctioning roots, with large fast-conducting (preganglionic) nerve action potentials seen when the nerve root is avulsed.49,51,66,67 Somatosensory evoked potentials produced in the contralateral cortex help gauge the integrity of sensory roots but do not reflect the status of the motor (ventral) roots, which can be measured using motor evoked potential and/or neck muscle potential monitoring.53,72 The intraoperative electrical tests and operative findings are used in concert with the preoperative clinical, electromyography,6 and imaging findings to determine the extent of injury and presence of nerve root avulsion and to guide operative decisions concerning the suitable nerve reconstructive procedure.

The goal in the management of upper (C-5 and C-6) nerve root paralysis is complete repair. When the upper two roots are avulsed from the spinal cord, the only repair option is neurotization by a nerve transfer. The nature of the reparative strategy is then dictated by the number of root avulsions, including the consideration of whether C-7 is also avulsed. On the other hand, even in complete severe palsies, the C-5 spinal nerve may be singularly spared, thus allowing it to be used as the source of axons for a plexus–plexus repair to distal elements.34,47 There are some cases in which the proximal root stump may not be suitable for grafting. A very proximal intraforaminal dissection of the nerve roots is invaluable for assessing the nerve anatomically,66 and combined with the examination of frozen section of the very proximal stump to assess the fascicular pattern and absence of ganglion cells, has been useful in decision making. Other authors have assessed the degree of myelin staining to predict the quality of the stump;61 however, in uncertain circumstances, a nerve transfer is preferred to using a proximal stump of questionable integrity. The combinations for repair therefore include intraplexal grafts alone obtained from a single functioning root, intraplexal grafts, and selective transfers (the usual scenario) or transfers alone for the devastating cases in which all nerve roots are avulsed (Fig. 1). The nerve transfer options available will be discussed further.

Accessory Nerve Transfer

In the earliest report of a nerve transfer by Tuttle90 in 1913, the author mentioned using the accessory nerve (as well as elements of the cervical plexus) as the donor. Accessory (11th cranial) nerve transfers for otherwise irreparable BPIs, however, were popularized independently in the early 1980s by Allevi, et al.,54 and others.55 In the early series, a diverse number of recipient targets were chosen, and, depending on the distal nerve element, interposed grafts were often needed. Based on cadaveric studies,46 an improved appreciation of the extracranial accessory nerve’s anatomy has led to the use of more distal dissection of the nerve close to trapezius muscle insertional points, where the very distal nerve is divided prior to its transfer.41 This preserves some trapezius innervation and allows a direct transfer to the adjacent suprascapular nerve, without the need for an interpositional graft (Fig. 2).

For restoration of dynamic shoulder function, both the supraspapular and axillary nerves have been chosen as targets. Whereas the former can be repaired directly by end-to-end suture with the distal accessory nerve, the latter requires planning an interposed nerve graft. The authors of recent series have confirmed Alnot’s bias that the supraspapular, compared with axillary, nerve is a superior target for accessory nerve transfer, with generally good

Fig. 1. Photograph showing incisions to expose various plexal and extraplexal donor and recipient nerve elements. This patient suffered clinically complete Erb palsy and avulsion of C-5 and C-6 spinal nerves; he underwent surgery after a delayed referral (the same patient is represented in Figs. 6 and 7).
Nerve transfers for brachial plexus injuries

results reported in the majority of patients (Fig. 3).19,40,77 A detailed analysis of glenohumeral function in patients with long-term follow up who underwent accessory nerve–suprascapular nerve transfer, however, has demonstrated rather poor true abduction (Malessy, personal communication), supporting the observation that shoulder function will be optimized if both suprascapular and axillary nerves and their muscles are reinnervated.79 In a recent metaanalysis of the literature related to nerve transfers, Merrell, et al.,64 concluded that best results for shoulder abduction were achieved by conducting accessory nerve–suprascapular nerve transfers.

The other major target for accessory nerve transfer has been the musculocutaneous nerve. In recent series the results for elbow flexion were shown to be very good, with an MRC Grade 3 or better outcome in 65%,79 72%,80 72.5%,89 and 83%103 of patients in respective studies. In the analysis of factors predicting outcome, the most important negative predictor was increased duration between injury and surgery, whereas the need for a lengthier graft also negatively influenced results.80,103 Although a metaanalysis of the literature has indicated that intercostal nerve donors are best for musculocutaneous nerve as the recipient nerve,64 only Waikakul, et al.,103 directly compared two extraplexal donors, reporting that the accessory nerve achieved superior outcomes for elbow flexion compared with intercostal nerves.

Intercostal Nerve Transfers

The concept for intercostal nerve transfers to repair BPIs can be credited according to Narakas,70 to Yeoman, working with Seddon, and Seddon;84 this early experience is reviewed in the latter’s classic textbook. Although Seddon reported the use of the second–fourth intercostal nerve transfer to the distal musculocutaneous nerve, Dolenc24 performed multiple intercostal transfers to several additional distal elements of the plexus, including axillary, median, and radial nerves. He used sural and ulnar nerves as interposed grafts and reported considerable success, although few details were provided.23 Subsequently, several other surgeons independently adopted this technique for reinnervation of the musculocutaneous nerve but with variable success.45,67,68,71,85–87

Friedman and colleagues29 used standardized techniques involving transfer of three intercostal nerves (third–fifth) to the distal musculocutaneous nerve, without interposed grafts, which led to more consistent results, approaching MRC Grade 3 or better function in approximately 50% of the patients. These authors provided the first detailed evidence of independent (that is, without synkinesis) biceps function over time, hinting at cortical plasticity, a concept that has subsequently been validated by electrophysiological and functional brain mapping/imaging studies.56,59,60,62 Indeed, it has been suggested that functional return depends on cortical readaptation and that failures have been construed as lack of such adaptation;56 this hypothesis, however, requires validation.

More recently investigators studying intercostal–musculocutaneous nerve transfer have demonstrated significantly improved results, (MRC grade ≥ 3 elbow flexion in 64–88% of reported cases).26,45,58,69,76,88,103 Intercostal nerve transfers to musculocutaneous nerves in infants with obstetrical brachial plexus palsy produced reliably good outcomes (MRC grade ≥ 4 elbow flexion in nearly 85% of patients).44 The authors of these recent series have stressed the importance of dissecting the intercostal nerves well distally along the rib to allow their transfer easily to the axilla and direct repair without graft placement, as has been demonstrated in anatomical studies (Fig. 4).7

The group from Duke University has also reported, in
selected cases, intercostal neurorization of nerve to a free muscle graft that successfully achieved elbow flexion.29 Although Waikakul, et al.,103 have reported superior results when using accessory nerve, compared with intercostal transfers for elbow flexion, the authors of a large series of 37 adolescents and adults who underwent placement of gracilis muscle grafts for elbow flexion found that intercostal neurorization of nerve to free muscle was a better choice than using the accessory nerve.21 In severe obstetrical brachial plexus palsy, a gracilis free muscle transfer (innervated by the accessory nerve) has been shown to restore elbow flexion.10 Doi and colleagues23 have reported a two-stage (“double”) free muscle transfer procedure that successfully restored prehensile function in a few very severe cases.

Unilateral intercostal nerve transfers do not disturb respiratory function,32 but they should not be performed if the phrenic nerve is dysfunctional or used on the ipsilateral side as a donor for transfer.55

Ipsilateral and Contralateral C-7 Spinal Nerve Transfer

In some cases of Erb palsy,27 in which both C-5 and C-6 nerves are avulsed, the C-7 spinal nerve is intact and available as an intraplexal donor for reinnervating the distal upper truncal or its divisional outflow.47,50,57 Such a transfer can be associated with very good outcomes in terms of recipient elements,47,95,56 with little risk of functional loss secondary to harvesting the C-7 spinal nerve.36 Considerable caution, however, is required if significant lower plexus lesions coexist36 because the muscles innervated by C-7, which would be normally redundantly supplied by C-8 (and T-1) spinal nerves, will not be present.50

The use of the contralateral C-7 spinal nerve as donor for transfer has corroborated the redundancy of the C-7 nerve, confirming the safety of sacrificing this structure.3,35 Other than mild loss of triceps function and clinically inconsequential loss of the triceps reflex, the procedure appears to be safe as far as motor loss is concerned.18,55 Sensory abnormalities, however, are common after C-7 sacrifice and may be permanent in 5% of cases.52 Moreover, neuropathic pain may be evoked temporarily in a minority of patients,2 and in rare cases permanent motor deficits in wrist extension may develop.90 Selective use of anterior or posterior portions of the contralateral C-7 nerve, aided by intraoperative electrophysiological testing,24 may make the procedure safer, furthering the specificity of the reinnervated element to which it is transferred.35

Chuang and colleagues30 first reported the use of the contralateral C-7 spinal nerve obtained from the normal, noninjured side, where the first stage involved the repair to the C-7 nerve and placement of long sural nerve grafts across the chest. In their initial series of 15 patients, eight were candidates for the second stage (~1 year later) consisting of innervation of free muscle grafts placed in the affected paralyzed limbs. They reported modest results of nonindependent movement in the paralyzed limb in this pioneering effort, attesting to both the possibility but also limitations of the technique. Authors of subsequent series in adolescents and adults reported the results of contralateral C-7 transfer by grafting across chest sural or vascularized ulnar nerve directly to recipient infraclavicular plexal nerve elements.18,35,37,95,96,102,107 In the largest reported series, the long-term functional outcome was very good, but the authors only reported data obtained in 20 of 82 patients in their initial study and 30 of 224 patients who underwent the procedure.35,37 Additionally, synchronous movement of the unaffected arm during attempts to move the reinnervated limb have been a repeated concern.35 The best results associated with using the contralateral C-7 nerve in 98 adolescents and adults with complete avulsion injuries were published by Waikakul and colleagues;102 they noted that when the median nerve was the recipient, good sensory function was achieved in approximately half the adolescents, and some also exhibited forearm muscle recovery. In a carefully reported 3-year follow-up study, Songcharoen and associates90 reported median nerve motor recovery (MRC Grade 3 or 4) in approximately 20% of their patients, whereas in another 20% MRC Grade 2 outcome in wrist flexion was observed. Sensory domain outcome was somewhat better, especially in adolescents, with 50% exhibiting useful sensory restoration in the median nerve distribution. In study of adults with BPIs, Terzis and coworkers55 reported that the mean MRC grade was 3 (antigravity) in their series. One group transferred C-7 spinal nerves via vascularized ulnar nerve graft, to the
Nerve transfers for brachial plexus injuries

lateral cord contribution to median nerve; they reported a 100% success rate with good sensory recovery.26

One of the main criticisms of this transfer technique remains the long graft (and hence regeneration) distance. The possibility of a prespinal retropharyngeal route for graft placement has been proposed.89 Nevertheless, the technique remains limited because of the rather modest motor recovery, the fact that synchronous movement of the unaffected side is required, and the small but real risk that the donor site may be injured and a functional deficit results.90,92 Perhaps a targeted approach to obtaining median nerve distribution sensory recovery is warranted,26 although similar outcomes may be possible with a less cumbersome transfer from the lower intercostal nerves to the sensory (lateral cord) head of the median nerve.24

Cervical Plexus

The use of the anterior branches of the cervical plexus (C-3 and C-4) for transfer to the distal elements usually supplied by (the avulsed) upper spinal nerves was first advocated by Brunelli and Monini.14 Based on cadaveric studies in which they observed present (but variable-sized) discernible sensory and motor branches, the authors reported modest results after selective transfer of motor branches to musculocutaneous, suprascapular, and axillary nerves and sensory branches to the median nerve. Earlier efforts to transfer the entire cervical plexus elements to the avulsed C-5 and C-6 roots failed, likely because of the great disparity between the number of axons in the donor cervical plexus elements and the recipient elements.14 Recently, however, Yamada and colleagues106 performed surgery in three cases in which they transferred the anterior primary rami of C-3 and C-4, just distal to phrenic nerve, via sural nerve grafts directly to the upper trunk; the patients had suffered C-5 and C-6 avulsion injuries, and the authors reported good results postoperatively in shoulder girdle and biceps muscles, as well as improved sensation. In a larger series, they obtained even better results in cases involving upper plexus palsy and, surprisingly, in cases involving complete flail arm.107 Other investigators have been unable to validate these remarkable results, demonstrating more modest success when using the motor components (which are unfortunately quite limited after phrenic nerve supply)14 to branches of the upper trunk when both C-5 and C-6 nerves are avulsed.24-27,30

Phrenic Nerve

Unlike the cervical plexus, which contains a variable number of motor fibers,14 the phrenic nerve contains a large number of pure motor axons that allow the possibility of entire or partial transfer with success.101 In the early use of the phrenic nerve for transfer, investigators noted good outcomes.17,101 Subsequently, transfers involving the phrenic nerve as the neurotizer have been performed with considerable success.17,39,43,101,107 In one study of 12 patients, phrenic nerve transfer to musculocutaneous, suprascapular, or axillary nerves was successful in 75% of cases.89 Particularly, the transfer to the musculocutaneous nerve has been an excellent tactic, with 11 of 12 patients exhibiting better than antigravity function (MRC Grade 3) and 58% exhibited MRC Grade 4 function.55 One group, however, noted that in their hands, a portion of the median nerve was a more reliable donor for achieving elbow flexion recovery than the phrenic nerve.43 When the phrenic nerve is sacrificed, one important issue is the resulting respiratory compromise, in which decrease in vital capacity has been measured to be a mean of approximately 10%.35 Although not clinically important in the majority of situations, this degree of respiratory loss will produce symptoms in higher-demand situations and may be severely detrimental to infants and children who develop respiratory infections. This factor essentially precludes the use of the phrenic nerve as a donor in infants undergoing nerve reconstruction for obstetric palsy. Moreover, it also implies that the intercostal nerves should not be used as donors for transfer when phrenic nerve function is absent preoperatively or when the phrenic nerve is transferred.

Medial Pectoral Nerve

The pectoralis major muscle has dual input from the medial and lateral pectoral nerves, arising from the medial and lateral cords, respectively. Because C-5 and C-6 avulsion interrupts the lateral cord supply, the muscle remains innervated (and strong) as long as a significant injury is not incurred to the C-7 and C-8 elements. Although popularized recently for upper plexus injuries,13 using the medial pectoral nerve as a donor for transfer was previously considered and infrequently used, as indicated by Narakas70 for adults and Gilbert33 for obstetric palsy. Brandt and Mackinnon14 directed the medial pectoral to the musculocutaneous nerve, with the additional innovation of turning the lateral antebrachial cutaneous nerve (the cutaneous derivative of the musculocutaneous nerve) into the biceps muscle to avoid loss of motor axons into the cutaneous distribution. A resurgence of interest in this transfer has been associated with reports of useful outcomes (defined as MRC grade ≥ 3) in elbow flexion in approximately 84% of patients.94 Excellent results in obstetric palsy too have been published, with success in 68% of cases.12 Others have criticized the use of this transfer strategy in obstetric palsy because of loss of arm adduction, which can be useful for the infant, toddler, and child to hold objects against the trunk.59 especially because the intercostal transfer yields such favorable results in this setting.44 The results of various series vary, however, and Samardzic, et al.79 have noted that medial pectoral nerve transfers were associated with significantly improved outcomes in elbow flexion compared with intercostal and accessory nerve transfers. These authors have also been one of the few groups to demonstrate remarkably good results after axillary nerve transfer; they observed useful results in greater than 80% of patients.78

With the increasing interest in the medial pectoral nerve as a donor, the anatomy of the pectoral nerve complex has been more clearly defined.8,39 The traditional concept of separate lateral and medial pectoral nerves innervating the pectoralis minor and major muscles as discrete nerves has been replaced; in fact, these nerves run toward the pectoralis minor and major muscles, exhibiting considerable branching and intermingling. Not infrequently, a plexus forms where branches from the medial and lateral pectoral nerves, destined for the pectoralis major, merge and then final branches move toward the muscle (Fig. 5A).8,39 Be-
cause only one or, at times, two of these terminal branches to the pectoralis are required (and quite distally) for the transfer, the practical implication is that some pectoralis major muscle supply can be preserved and a direct repair without intervening graft can be performed to the musculocutaneous nerve in the distal axilla (Fig. 5B). Caution needs to be exercised if C-7 and C8 nerves are significantly injured; in this case, the pectoralis major muscle will be quite weak preoperatively, and this finding is a contraindication to medial pectoral transfer. A similar sophisticated appreciation of the innervated anatomy to the biceps and brachialis muscles has prompted evolution in transfer techniques so that both the biceps and brachialis muscles discretely become reinnervated.

**Distal Interplexal Transfer**

An exciting development in neurotization has been the transfer of portions of functioning distal plexal elements for the direct reinnervation of nerve branches going to critical muscles that are paralyzed. This era really began recently with anatomical studies of the fascicular patterns and their application in several patients in whom a single redundant ulnar nerve fascicle was transferred to biceps branches in the medial arm to restore elbow flexion (Fig. 6). These initial excellent results were validated by several authors. Most impressive have been the results reported by Sungpet and associates who used a single ulnar nerve fascicle directed to the biceps muscle; they observed MRC Grade 3 or better outcome in 34 of 36 patients. They also noted that time to reinnervation began as early as 3.3 months postoperatively and that hand and ulnar function, assessed using a series of tests and functional tools, was not compromised during a long-term follow-up period. The key aspect of the procedure is to reinnervate the biceps branch close to its motor entry into the muscle.

The authors of a recent report indicated that elbow flexion function will be further augmented (especially in cases of delayed surgery) by also concomitantly reinnervating brachialis muscle by using a graft from the medial pectoral nerve. Another alternative to the ulnar fascicle is a fascicle of the adjacent median nerve to transfer to biceps muscle nerve; good results have been reported in 64% to 80% of patients.

An emerging transfer technique is the direct repair of the anterior branch of the axillary nerve; in this procedure, the nerve to the long head of triceps in the posterior arm is used (Fig. 7). The anatomy involved in this transfer operation as well as good-to-excellent results achieved in seven cases, especially when combined with accessory–suprascapular nerve transfer, may herald improved dynamic shoulder function than previously possible with the flail shoulder after C-5 and C-6 avulsions. Indeed, authors of the most recent series have demonstrated the benefit of several targeted transfers in patients with plexus avulsions.

**Other Transfers**

Although the hypoglossal nerve has been an excellent donor for transfer to the facial nerve, it has an extremely limited value for neurotization of brachial plexus elements.
Nerve transfers for brachial plexus injuries

Fig. 7. A posterior arm incision (A) between the posterior border of the (denervated) deltoid (D) and the triceps (T) muscles allows exposure of the axillary nerve (B) in the quadrilateral space (vessel loop), as well as the radial nerve and the nerve to the long head of the triceps muscle (forceps) in the triangular space. Transfer of the latter to the anterior branch of the distal axillary nerve is easily accomplished for direct repair, without tension.

Choosing a Nerve Transfer Technique

Much of the literature related to brachial plexus surgery comprises retrospective case reviews, anecdotal experience, a small number of prospective studies, and no randomized studies involving different surgical techniques. Moreover, the field has been in flux, with traditional plexus-plexus repairs, gradually being replaced by a much more liberal use of nerve transfers. Thus, evidence concerning the best technique for a particular lesion is limited; however, based on recent review findings, in uncertain cases, the repair from C-5 to distal elements can be augmented by the transfer of accessory and intercostal nerves.

Although the aforementioned strategy is appropriate for the pan-plexus injury, treatment of isolated Erb palsy is different. If C-5 and C-6 are avulsed while C-7 is clearly intact, intraplexal graft repairs from C-7 may be considered to reinnervate the shoulder abductors and elbow flexors. Alternatively, directed discrete transfers should be performed; based on the most recent literature, this seems to be a favored approach. A combination of the following should be performed: distal accessory to suprascapular; ulnar nerve fascicle to biceps nerve (perhaps augmented by a portion of medial pectoral nerve via graft to brachial nerve); and long head of triceps nerve to the anterior portion of the axillary nerve.

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Nerve transfers for brachial plexus injuries


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