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Targeted Muscle Reinnervation and Nerve Transfers for Brachial Plexus Injuries: optimising upper limb functional recovery and minimising donor site morbidity

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Abstract:

This comprehensive review examines targeted muscle reinnervation (TMR) and nerve transfer strategies in the management of brachial plexus injuries (BPI), aiming to restore upper limb function while minimizing donor site morbidity. A focused literature search was conducted on PubMed, restricted to the last 10 years. Commonly utilized transfers, such as the ulnar fascicle and double fascicular transfers for elbow flexion, and spinal accessory or intercostal nerve transfers for shoulder and hand reanimation were evaluated in terms of indications, outcomes, and donor site risks. Among these, the double fascicular transfer demonstrated superior recovery of elbow flexion, especially when performed early. Shoulder reanimation was most effective when both the suprascapular and axillary nerves were targeted, improving abduction and external rotation. Distal nerve transfers yielded better fine motor recovery and faster reinnervation than tendon transfers. Adjunctive strategies, including photobiomodulation and preoperative electrodiagnostic tools, were noted to enhance reinnervation outcomes. TMR, particularly in combination with free functional muscle transfer (FFMT), showed promise in delayed presentations by bringing the site of neurotization closer to the target muscle and reducing axonal regeneration distance. Success depended heavily on appropriate donor nerve selection, timing of intervention, and individualized surgical planning. However, the heterogeneity in reported outcomes and lack of standardized assessment tools remain significant barriers to optimal technique comparison. Future research should emphasize long-term, prospective studies using unified evaluation metrics to strengthen clinical decision-making and guide technique refinement.

Keywords: Brachial Plexus Injury, Targeted Muscle Reinnervation, Nerve Transfers, Functional Recovery, Donor Site Morbidity, Free Functional Muscle Transfer, Photobiomodulation

Abbreviations:

Targeted muscle reinnervation - TMR

Brachial plexus injuries - BPI

Free functional muscle transfer - FFMT

Photobiomodulation - PBM

Introduction:

Brachial Plexus injuries (BPI) severely compromise the function of the upper limb, truly being one of the more challenging conditions in reconstructive neurosurgery. Left untreated, they usually result in complete sensorimotor degeneration in the upper limb [1,2].

Management is further complicated as achievement of functional recovery is opposed by multiple factors such as procedural complexity and time sensitivity. These factors ultimately lead to muscle atrophy and fibrosis. Patients will have functional impairments associated with specific nerve dermatomes. Time sensitivity becomes more apparent when the distance between axons and their respective hand muscles is larger [3]. Traditional treatment modalities such as nerve grafts have proven to be ineffective for severe cases of BPIs; its complexity requires a more effective surgical technique to accommodate for lost nerve function [4,11]. Among some of the most promising treatments is Targeted muscle reinnervation (TMR), a process by which healthy nerves are redirected to denervated targets in an attempt to bring function to paralyzed muscles [6,7].

This precise redirecting of healthy nerves provides significant advantages to accommodate the drawbacks of traditional approaches, circumventing their shortcomings [4]. This systematic review aims to compare and report extensively on TMR procedures in the upper limb, such as the Oberlin, Double fascicular transfers, and the use of adjunctive therapies such as photobiomodulation.

Methodology:

This literature review collected, reviewed and summarized current evidence on targeted muscle transfers and nerve transfer for brachial plexus injuries.

Database and Search Strategy

We searched the pubmed database using the keywords, “Targeted Muscle Reinnervation”, “Brachial plexus injury”, and “nerve transfer” using boolean operators. We applied filters to include only articles published in the last 10 years and excluded books and documents from our search.

Screening and Selection

We screened the titles and abstracts of all the articles on the basis of their relevance to the topic and then included studies which had promising evidence on the subject of interest, and were in English. Conflicts were resolved by consensus or a third researcher.

The ulnar and Double fascicular transfer for elbow flexion:

The loss of elbow flexion is common and is caused due to the BPIs affecting cranial nerves C5-C7; whose functions are commonly restored by nerve transfers. The ulnar fascicular transfer uses a dispensable fascicle which is then diverted to the dermatome of the musculocutaneous nerve [6,3,7]. This method has proven to be an effective and stable way to regain elbow flexion caused by upper trunk BPIs [3].

The Double Fascicular transfer is a comparatively newer technique in which the biceps and brachialis muscles are reinnervated with the ulnar and fascicular nerves respectively. A systematic review of 6 patients observed a very high success rate when done prior to 6 months post-injury [6].

Nerve transfers for Shoulder reanimation:

Restoration of shoulder movement, particularly abduction and external rotation, is of particular importance in recovery after BPIs. These movements are key to the functionality of the upper limb . Reactivation of two primary nerves, the Suprascapular and the Axillary, are involved in the functional restoration of movement.

The two primary shoulder muscles, supraspinatus (initiator of shoulder abduction) and infraspinatus (external rotation) are supplied by Suprascapular nerve [7]. The suprascapular nerve is most often replaced and the dermatome is reinnervated using spinal accessory nerve [7].This approach is common for both partial and complete brachial plexus injuries and can often be done without requiring a nerve graft [7].

Despite it’s popularity, the posterior surgical approach may provide some benefits, such as better access to the distal portion of the external branch of Accessory Nerve, better coaptation or connection to the nerve and better maintenance of the upper trapezius muscle, needed for maintaining stability of the shoulder blade [7]. Concern about this technique impairing function of the scapulothoracic joint by weakening the trapezius, is currently being explored but lack enough evidence to consider a drawback [7]

The axillary nerve , which mainly facilitates deltoid function, can be reinnervated through a number of nerve transfer techniques. Reassignment of multiple nerve branches, such as that of the long head of triceps and its motor branch, to regain deltoid function, are becoming more prevalent. The transfer of the Intercostal Nerve to the axillary nerve, however, requires tunneling subcutaneously around the axilla, further complicating the procedure. In Phrenic nerve transfers, an intercalated nerve graft to span the distance to the Axillary nerve, giving overall results to Intercostal Nerve transfers. Intercostal and Phrenic nerve transfers are employed especially in complete BPIs where intraplexal donor options are limited. These techniques are kept as alternate options due to the potential risk of donor morbidity (such as treatment-induced pleural damage) and the phrenic nerve's involvement in breathing potentially affecting respiratory function [7].

Hand Function:

Anterior interosseous nerve transfer to the motor branch of the Ulnar nerve is the most accepted and implemented technique, done at about 8-10 cm above the wrist crease [1,2]. The Anterior Interosseous nerve is situated at the superior border of the Pronator Quadratus muscles and its motor branch is sited from the middle of the muscle [1]. In this technique, the motor branch of the anterior interosseous nerve is connected to the deep motor branch of the Ulnar nerve [1]. This technique improves holding strength and helps recover vital fine motor skills and hand functions lost due to trauma. The possible drawbacks of this method are hand deformities (Wartenberg's deformity) and improper finger alignment (claw hand), which can be accounted for using concomitant additional procedures such as the Metacarpellopharyngeal joint capsulodesis and Wartenberg's deformity correction [3].

Distal nerve transfer for the hand and forearm is a recent development for BPIs. In comparison to tendon transfer, which is restricted to single and straight action, distal nerve transfer can bring back the natural functions of the muscle, allowing coordinated movements [1]. One of the most important benefits of this procedure is that this transfer is performed in proximity to the nerve that is reinnervated, allowing the nerve to grow again and revive function quickly, which is helpful when the nerve injury is away from the selected area (close to the neck, shoulder or other proximal nerve injuries). Ideally, this technique is employed within 12-18 months of the trauma [1,5].

Targeted muscle reinnervation: Indications and Benefits

TMR is an advanced nerve transfer technique whereby healthy donor motor nerve fascicles are redirected to denervated muscles and nerve endings, with the dual objective of recovering motor function and minimising the risk of neuroma formation. In contrast to traditional nerve repair, which only reconnects damaged nerve ends where physical approximation is viable, TMR allows the utilisation of distal nerve lesions by rerouting donor nerves, to reduce the time and distance necessary to be covered by the regenerating nerve, thereby enhancing functional recovery. Though originally designed for root avulsions, this approach now serves as a viable option for post-ganglionic brachial plexus lesions, severe proximal nerve injuries with long regeneration distances, tiered lesions, and neuromas-in-continuity [11].

A successful TMR requires selection of a donor nerve with sufficient axonal load (70% or more) of the recipient's axon count, accurate matching of nerve diameters, minimizing grafts where possible, and suturing as close as possible to the muscle to achieve a more reliable reinnervation [11].

In severe cases of BPI involving significant muscle loss, a combined approach of TMR principles with free functional muscle transfer (FFMT) has been found to be an effective reconstruction strategy. FFMT technique involves transplantation of a functional donor muscle, more commonly a gracilis muscle flap from the thigh, to upper extremities, while TMR ensures that the donor motor nerves such as the intercostal nerves, spinal accessory nerve, contralateral C7 root, or pectoral nerves, provide a strong axonal supply to the transplanted muscle flap, enhancing the probability of successful muscle reinnervation and functional recovery. This combined approach aligns with the principle of "One muscle-One function", simplifying postoperative motor retraining and maximizing the chance of functional recovery in complex upper extremity injuries, notably elbow flexion and shoulder stabilization. In addition, TMR serves a neuroprotective role by connecting these nerves to non-essential muscle targets, thereby avoiding disorganized nerve sprouting that can lead to chronic pain and neuroma formation [11,12].

Donor Nerve Selection and Donor site risks: Single vs Double transfer

The outcome of nerve transfer procedures greatly depends on the choice of donor nerves. The potential for effective reinnervation and subsequent functional recovery depend on the quantity of axons and the clinical value of the donor nerve [8,14]. Since no extensive overview summarizes all brachial plexus nerve axon counts, systematic reviews are working on defining a standard from existing data of clinical and surgical practice [14]. The clinical value of the donor nerve should also be considered versus the iatrogenic potential of deficits at the site of harvest. The ideal donor nerve has enough axons to innervate the target muscle, is expendable, and leads to minimal functional loss in the donor territory following harvest [8]. Common donor nerves in the upper limb on which to base reinnervation, include fascicles from the ulnar, median, and intercostal nerves such as the transfer of the ulnar fascicles onto the nerve to the biceps is a proven technique of restoring elbow flexion [6,9].

While nerve transfers have many functional advantages, the morbidity of the donor site remains a serious concern. Harvesting a nerve graft or performing a nerve transfer is associated with the risk of denervating the territory of an area previously supplied by the donor nerve. This risk can manifest itself as sensory deficit, weakness, or potentially pain. For instance, if fascicles are harvested off of the ulnar nerve, there is a risk of causing motor and sensory deficits in the hand, but these are potentially minimized through expendable fascicles [6,8]. One such instance is the use of intercostal nerves for latissimus dorsi or serratus anterior transfers which have shown decreased motor asymmetry during movements, though trivial complications such as localized pain or sensory changes may occur [9]. Understanding anatomical distribution and functional contributions of possible donor nerves is vital to identify deficits of donor nerves and to mitigate any further complications. Preoperative counseling on donor site deficits plays a crucial role in making an informed consent [8].

The discussions about Single vs Double nerve transfers for elbow flexion highlights the difficulty in choosing donor nerves. This choice significantly affects donor site morbidity and resultant functional recovery. A Double nerve transfer, though producing greater recovery, inherently damages two donor nerves and predisposes their sites to deficits. It has produced better elbow flexion compared to single nerve transfer, when both the Ulnar and Median nerve fascicles are used together. Yet, there is debate on whether the enhanced functional recovery justify additional toll on the donor sites. Hence, the best approach varies based on the injury pattern, the amount of healthy donor nerves available, and each patient's own acceptable limit of donor site morbidity [6].

Functional Outcomes: Strength Recovery and Success Rates

The functional outcomes of nerve transfers are evaluated using the The Medical Research Council (MRC) grading system, as the Gold-standard. MRC grade 3 or higher is widely recognised as the indicative of successful functional recovery [7].

Elbow Function

In the case of elbow function, the Double fascicular transfer, wherein both biceps and brachialis muscles are reinnervated, has demonstrated significantly superior strength recovery, in contrast to the conventional Ulnar fascicular transfer, which solely reinnervates the biceps. An analysis of 18 studies with a total of 176 patients demonstrated that 83.0% of patients treated with the double fascicular transfer achieved an MRC score of ≥4, compared to 63.3% of the patients who underwent the ulnar fascicular transfer. Furthermore, the double fascicular transfer was found to be the only factor that helped achieve the MRC score of ≥4 [6].

A univariate regression analysis revealed that the double fascicular transfer implementation was directly linked as a factor, for improved strength outcomes, along with reduced time interval to surgery and extensive BPI. Early surgical intervention (≤6 months post-injury) exhibited significantly higher strength recovery rates with MRC score of 4 in more than 50% of the patients and MRC score of 5 in no less than 4.8% of the patients [6]. Overall, the double fascicular transfer has outperformed the ulnar fascicular transfer in regaining elbow flexion strength of MRC ≥4 in C5-C6 or C5-C7 injuries [6]. Supporting this, Ray et al. documented that 97% of patients treated with the double fascicular transfer regained elbow flexion of MRC ≥3 [6], while Liverneaux et al. reported that 100% of patients regained MRC grade 4 elbow flexion with the double fascicular transfer [6].

In lateral cord injuries with no elbow flexion, transferring the Ulnar nerve fascicle to the Biceps branch continues to be the standard technique, whereas for restoration of elbow extension in C5-C7 injuries, the transfer of the flexor carpi ulnaris motor branch to the medial head of the triceps has proven to be more effective [1].

Shoulder Function

Nerve transfers and nerve grafts, both have demonstrated equivalent success in shoulder reanimation, with MRC ≥3 considered as successful functional recovery. Nerve transfers demonstrated a marginally higher recovery rate (72%, 114/158), in contrast to nerve grafts (67%, 36/54); this difference, however, was not statistically significant. In relation to nerve grafts (61%) or isolated transfers (70%), Double nerve transfers involving both the Suprascapular and the Axillary nerves have yielded significantly higher outcomes with 100% of patients (54/54) attaining MRC ≥3 shoulder abduction strength, Moreover, significant gains in abduction range of motion and external rotation were also reported. It was also observed that nerve transfers alone were able to attain a significantly higher functional recovery score compared to combined modalities or nerve grafting alone [7].

Hand and Forearm Function

Early distal nerve transfers in hand and forearm have exhibited excellent results, frequently outperforming tendon transfers, which are conventionally limited to restoring a single function per tendon. Distal nerve transfers intervene in close proximity to the target muscles and sensory end organs, thus promoting accelerated reinnervation and reestablishment of innate muscle function, thereby enabling synchronous movements. Numerous studies have confirmed effective outcomes using various motor nerves in the forearm for the management of peripheral nerve injuries and BPI [1].

Transposition of expendable motor nerves to target end plates have dependably led to rapid restoration of motor function, more often attaining the MRC grades of M3 or M4 within 3.5 to 4.5 months postoperatively. However, the donor nerves are required to have a minimum strength of MRC grade 4 to be considered suitable for transfer. Particularly, the transfer of the Extensor carpi radialis brevis to Anterior interosseous nerve has proven to be successful in restoring M3-M4 muscle strength for thumb flexion, abduction, and opposition, as well as index finger flexion in lateral cord BPI and high median nerve palsy cases. This procedure is also associated with enhanced object grasping and releasing ability [1].

Among distal transfers, the transfer of Anterior interosseous nerve to the deep motor branch of the ulnar nerve is predominantly performed for the restoration of intrinsic hand function, effective enhancement of pinch strength, and prevention of claw deformities without necessitating additional tendon transfers. The majority of patients attain M4-grade motor function recovery and indicate significant enhancements in grip and pinch strength at a mean postoperative follow-up of 18 months, with no notable donor site morbidity [1].

A similar comparison for proximal ulnar nerve injuries, 31% (5 out of 16) patients attained MRC grade 4 or above, while 81% (13 out of 16) attained MRC grade 3 or above [3]. With most procedures conducted approximately within 3 months post-injury, the mean follow-up period was 17 months post-operative. At 18-month follow-up, mild residual claw deformity was noted in 18.8% cases; however, no claw abnormalities were exhibited in 75% of the patients. Upon reviewing 12 studies involving a total of 102 patients, positive outcomes (MRC ≥3) were reported in 86% of cases with a mean time to surgery of 5.17 months and an average follow-up period of 20.72 months [3].

Other successful distal nerve transfers include the transfer of the transverse head of the adductor pollicis to the thenar branch, which is effective in the restoration of grasp, pinch, and thumb opposition while shielding the integrity of the interosseous muscle. Analogously, the transposition of the opponens pollicis brevis to the terminal deep division branch of the ulnar nerve has been noted to be effective in enhancing pinch and grasp strength, and resolving Froment's sign, with the pinch strength regaining 90% of the contralateral hand. Transfers which involve the posterior interosseous nerve and the ECRB branch have been reported to have successful reestablishment of radial nerve function in distal radial nerve injuries, resulting in MRC grade 3 or grade 5 extension of the triceps and thumb [1].

In reference to sensory recovery outcomes, Battiston et al. demonstrated that digital nerve transfers led to S4-level sensory recovery in the majority of patients and S3+ in the remainder, with proximal ulnar nerve injuries. Moreover, the transfer of distal radial sensory branches to palmar nerves successfully reestablished protective sensation in most recipients [1].

Adjunct Strategies and Emerging Techniques

Photobiomodulation after nerve transfer

Photobiomodulation (PBM) is a non-invasive method for activating peripheral nerve regeneration. In PBM, near-infrared bands of 780-830 nanometres are used to stimulate axonal growth, myelination, and stimulates axonal growth while preventing inflammation [5].

The effects of PBM were reported by Foo et al. as an adjunct to the Oberlin Procedure. A wavelength of 808 nm was chosen for its improved tissue penetration and efficient energy delivery to the site of neurotisation. The patients in the PBM group demonstrated reinnervation with significantly higher elbow flexion strength than controls with no side-effects at three months follow-up [5]. Similar findings were observed in a study on animals. PBM has shown to accelerate nerve repair by enlarging axons, thickening myelin sheaths, and promoting better nerve conduction. It also enhances the levels of neurotrophic factors such as the Brain Derived Neurotrophic Factor and Nerve Growth Factor, promoting axogenesis. Paired with reduced release of pro-inflammatory markers, adjunctive therapy using PBM results in both better growth and a better environment to promote healing [5].

Early gains in function and absence of complications are in favor of the addition of PBM to upcoming protocols for enhancing nerve regeneration after microsurgical procedures like the Oberlin transfer [5]. On the other hand, lack of sample size makes it challenging for future clinical implementation.

Electrodiagnostic Guidance using electromyography nerve conduction studies

Electrodiagnostic studies, such as electromyography and nerve conduction studies, are a crucial component of the diagnosis and operative planning for nerve transfer surgery. The studies are helpful in differentiating between neurapraxia, axon injury, and the process of reinnervation, allowing proper timing for surgical intervention. These mechanisms display distinct electromyography signatures such as normal sized motor unit action potentials in the case of neurapraxic recovery. Similarly, axonal injury produces motor unit action potentials that increase in duration and amplitude over time. Electromyography is also crucial in the identification of donor and recipient muscles. It can assess fibrotic, atrophic, or non-viable muscle tissue or abnormalities such as the anastomoses, which are poor factors when considering tissue for nerve transfer. Conversely, the presence of spontaneous activity (fibrillations) and active motor unit action potentials suggests retained muscle integrity and potential for functional restoration [4].

Free Functional Muscle Transfer for Salvage or Late-Stage Cases

In BPI that is severe or delayed, when local transfer of muscle, tendon, or nerve is not feasible , FFMT is a procedure of choice for motor restoration. The gold standard is the gracilis muscle due to its anatomical reliability, adaptability, and negligible donor-site morbidity. Most important in FFMT is donor nerve selection, with the intercostal and spinal accessory nerves being the most frequently used in total BPI [12]. Additionally, the 'banking' method, coapting donor nerves at an early stage prior to muscle transfer, has shown improved reinnervation efficiency and results. Hence, donor selection, tensioning of the muscle, and careful microsurgical technique all play key roles in maximizing outcome. Rehabilitation postoperatively through neuromuscular reeducation is also crucial. Overall, FFMT remains a valuable procedure in otherwise poorer prognosis cases [12].

Considerations in pediatric patients:

Pediatric nerve injuries pose distinct diagnostic and management challenges, because of the children's inability to articulate their sensorimotor deficit, while still being in the process of neurological development. Early diagnosis is crucial, as motor palsy may be interpreted as poor effort, and immobilization can mask the symptoms. It is important to refer to a multidisciplinary team within 3 months for optimal results. Children benefit from shorter nerve regeneration distances and greater neuroplasticity, but motor-end-plate degeneration narrows the window for intervention. Tailored splinting can decrease the risk of contractures [13].

Challenges: Standardisation of Metrics and Reporting

Two major inconsistencies exist in current literature on BPI interventions because of quantitative axon count reporting and non-standardized outcome measures. Understanding nerve regeneration and evaluating TMR and nerve transfer effectiveness is challenging because of different measurement approaches and sample size variations. The different measurement approaches complicate establishing direct comparisons between various studies [14].

The evaluation of functional recovery also remains challenging because of the lack of standardized measures between studies. Multiple research papers show enhanced elbow flexion and shoulder abduction following nerve transfer procedures; however, the variable reporting methods used across different studies create difficulties in measuring these improvements. Different reporting approaches create major obstacles for researchers who want to perform meta-analyses and generate dependable comparative findings [6, 7]. The variations between measurement approaches create problems when researchers want to compare different reconstructive approaches between nerve transfer and nerve grafting for identical functional targets. The inconsistent outcomes demonstrate a rising demand for establishing standardized methods for collecting and reporting data [12].

Conclusion:

TMR is emerging as the most promising surgical modality to provide early reinnervation and better functional recovery for peripheral nerve injuries and BPI [1,3,4,8,11]. It is a more effective alternative to some of the traditional approaches, such as nerve grafting, for restoration of lost function in a wide range of upper extremity nerve injuries [4,11]. Procedures like the Oberlin method and the double fascicular transfers have yielded consistent restoration of elbow function, whereas focused muscle reintervention of the spinal accessory nerve has been found useful for shoulder abduction improvement [1,6,7,8,9].

In spite of these novel developments, the lack of a standardized form of reporting quantitative measures across various studies, still remain the main obstacle. The absence of a unified metric makes it difficult to accurately compare effectiveness of different reconstructive approaches and their functional recovery [6,7,14]. Future studies should therefore prioritize using standardized reporting criteria and outcome measures to improve comparability between studies.

Furthermore, there has been a growing interest in exploring the use of adjunct therapies like photobiomodulation in addition to electrodiagnostic monitoring, such as electromyography and nerve conduction studies, which allows for accurate selection of donors and recipients, and better monitoring of recovery following treatment [4,5]. Thus, though TMR is consistently proving to be a better replacement for traditional methods, its adoption is limited by the lack of standardised measuring modalities and long-term comparative analyses with alternate techniques.

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