



REVIEW

Modern surgical management of peripheral nerve gap

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KEYWORDS

Nerve injury; Nerve regeneration; Nerve conduits; Tissue engineering; Autologous nerve grafts; Nanotechnology Summary The management of peripheral nerve injury requires a thorough understanding of the complex physiology of nerve regeneration. The ability to perform surgery under magnification has improved our understanding of the anatomy of the peripheral nerves. However, the level of functional improvement that can be expected following peripheral nerve injury has plateaued. Advancements in the field of tissue engineering have led to an exciting complement of commercially available products that can be used to bridge peripheral nerve gaps. However, the quest for enhanced options is ongoing. This article provides a review of the current treatment options available following peripheral nerve injury, a summary of the published studies using commercially available nerve conduits and nerve allografts in humans and the emerging hopes for the next generation of nerve conduits with the advancement of nanotechnology.

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The peripheral nervous system is divided into the somatic nervous system and the autonomic nervous system. Peripheral nerve injuries result in a complete or partial loss of motor, sensory or autonomic function of the areas supplied by the lesioned nerve. Following a nerve injury, the axons undergo degenerative processes, followed by an attempt at regeneration. Despite advancements in the precision of microsurgical techniques, full functional

Primary tensionless end-to-end repair should be carried out whenever possible. For longer nerve gaps, the use of autologous nerve grafts is the current 'gold standard'. Over the past few years, the use of the commercially available nerve conduits for bridging short nerve gaps has increased. Silicone was the first synthetic material to be used as a nerve conduit. Due to its resistance to degradation and expansion, silicone can lead to long-term complications such as nerve compression or fibrosis warranting surgical removal; hence, it is no longer used clinically. With the

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recovery following peripheral nerve repair is seldom achieved. 1,2

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evolution of tissue engineering, the use of biodegradable conduits for reconstruction of nerve gaps has shown promising results. In this review, we aim to provide an overview of the basic science underlying nerve regeneration, results of the clinical studies that have used the current Food and Drug Administration (FDA)-approved nerve conduits and data regarding the use of nerve allografts for bridging peripheral nerve gaps.

Anatomy and pathophysiology of the peripheral nervous system

The epineurium, perineurium and endoneurium are the connective tissue structures that protect and provide a framework for the nerve fibres. This framework varies along the distribution of the nerve in that the proximal part of the nerve tends to be monofascicular containing both motor and sensory nerve fibres, while the distal segment tends to be polyfascicular branching into individual specialised motor and sensory subunits. Blood supply to the peripheral nerves stems from the segmental extrinsic and longitudinal intrinsic blood vessels that originate from local and regional arteries. Although there are extensive connections between the extrinsic and intrinsic blood vessels, the peripheral nerves are primarily dependent on the intrinsic blood supply following extensive mobilisation during surgery. In addition, excessive tension along the nerve can significantly compromise the intrinsic blood supply.⁴

At the site of the injury, Wallerian degeneration begins almost immediately, with sealing of the severed axon ends and initiation of the regenerative phase.⁵ Retrograde signalling from the site of axonal injury leads to altered protein metabolism. This results in decreased production of neurotransmitters and increased production of materials necessary for regeneration.⁶ Over the first few days following peripheral nerve injury, the axons in the distal nerve stump will degenerate. However, the myelin sheath and the basal lamina provided by the Schwann cells remain intact. Recruitment of macrophages at the site of injury stimulates the proliferation of Schwann cells in the distal stump. 8,9 Survival of these Schwann cells, in the absence of viable axons, is crucial for the regeneration of injured peripheral nerves. 10 The proliferation of Schwann cells within their basal lamina leads to the formation of tube-like structures called the Bands of Büngner, which provide an important guide so that axons regenerating from the proximal stump can reach their original targets. Multiple axonal sprouts arise from the proximal stump, thus maximising the chance of survival. 11 Proliferating Schwann cells from the distal nerve stump provide the substrate for the growth cones and guide the regenerating axons to their target organs. Spontaneous functional recovery is dependent on the number of correctly matched motor and sensory neurons.

Management of peripheral nerve injuries

The age of the patient, the mechanism of the injury and the associated vascular and soft-tissue injuries will indicate the extent of recovery of the injured nerve. In a first-degree

Sunderland injury (Table 1), the history typically includes a blunt injury, such as stretch or compression, such as with tourniquet palsy. In this situation, the nerve is continuous and all the layers of connective tissue are intact. As a result, there is no evidence of Tinel's sign at the site of injury. Tinel's sign will not develop because the nerve will eventually recover. With first-degree Sunderland injuries, injury management is conservative, and full recovery is expected.

Second-degree and third-degree Sunderland injuries are clinically differentiated from first-degree injuries because Tinel's sign will develop and then advance as the axons regenerate. Both second- and third-degree Sutherland injuries are managed conservatively. Full recovery is expected after a second-degree injury. Surgical intervention is indicated with fourth-, fifth- and sixth-degree injuries. In practice, however, any open wounds in which nerve injury is suspected should be explored. Closed injuries can be followed up expectantly with investigative techniques such as electromyography or nerve-conduction studies prior to exploration if nerve function does not return during the initial 3-month period following the injury.

Investigations for peripheral nerve injury

Electrophysiological assessment with nerve conduction studies and needle electromyography are useful in evaluation of closed injuries that have not recovered within the first 3 months following the injury. The electrophysiological parameters such as conduction slowing, block or failure evaluates the gross dysfunction of the peripheral nerve. However, electrophysiological assessments can falsely localise focal lesions because the proximal parts of the peripheral nerve are typically not amenable to electrophysiological evaluation. In these situations, magnetic resonance imaging is increasingly used as it has high specificity and sensitivity when evaluating focal injuries such as cervical nerve root avulsions or other brachial plexus injuries. ¹²

Current surgical procedures

The microsurgical techniques currently used for the repair of peripheral nerve injuries were pioneered by Millesi in the 1960s. 13 Over the past 40 years, surgical techniques have improved tremendously. However, the clinical outcomes following nerve repair have remained unsatisfactory. For any nerve repair, an understanding of the nerve topography will enable the surgeon to align the motor and/or sensory fascicles in the correct orientation. This will not only ensure good nerve regeneration but also optimise functional recovery. Intra-operatively, alignment of longitudinal intrinsic blood vessels and approximation of fascicles that appear similar clinically will prevent malrotation of the injured nerve. Following complete transection of a nerve, the nerve ends will retract, due to their elasticity. Primary end-to-end neurorrhaphy continues to be the most desirable approach for peripheral nerve repair when there is no nerve defect or when the gap between the two ends of the nerve is relatively short. 14 During nerve repair, it is important to appreciate the longitudinal extent of the injury so that the repair is undertaken outside this zone. The nerve

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