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Review Article

The Role of Nerve Tension on Nerve Repair Success

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Peripheral nerve injuries that are not acutely repaired may lead to a nerve gap because of the surrounding zone of injury and elastic recoil of nerve tissue after laceration. This can result in tension across the repair site during primary neurorrhaphy. Decades of basic science literature using in vivo models consistently demonstrate a relationship between increasing strain at a neurorrhaphy site and compromised microvascular blood flow. Clinical and laboratory data suggest tension-free repairs are associated with optimal outcomes; in the setting of a short segmental nerve gap, data suggest primary repair may continue to yield good functional results. In the case of high strain, nerve grafting or other methods should be considered given poor results of primary repairs performed under high tension because of local ischemia and fibrosis on a cellular level.

Rapid improvements in our knowledge of the peripheral nervous system have led to significant advances in nerve repair in the last several decades. With this enhanced understanding of neuroanatomy, multiple investigations have sought to examine the role of tension on nerve physiology and repair success.

Extrinsic mechanical forces cause functional changes in a peripheral nerve. The stress–strain relationship of a peripheral nerve may be nonlinear, meaning that after a threshold value, the strain on a nerve causes the intrafasciular environment to change rapidly.[1] Various peripheral nerves may demonstrate a characteristic modulus of elasticity based on several factors, including their local environmental, size, and mechanical properties (Fig. 1). However, after an initial loading (toe) region, nerves demonstrate an inverse relationship between stress and strain that has implications on a cellular level during periods of stretch, tension, and injury.[2]

Biomechanical forces play an important role in the modulation and growth of the native peripheral nervous system. Numerous growth factors and cellular mechanisms suggest that in the noninjured state, axons elongate through tension applied to microscopic growth cones toward specific substrates and stimuli.[3] Other studies have suggested that nerve tension also affects gene expression.[4] These small amounts of tension directly influence axonal growth and regeneration. The science of limb lengthening and distraction osteogenesis provides some evidence that there is an upper limit to the amount a nerve may be stretched; even under more controlled circumstances, this is limited to approximately 1 mm/day to prevent neuropraxia.[3]

The Basic Science of Nerve Repair Under Tension

Multiple studies that assess the effect of tension on nerve repair demonstrate that undue tension results in suboptimal healing and later function.

Initial studies in in vivo models provided early evidence of microstructural changes in repaired nerves. The early work of Sunderland[5,6] was supplemented by Terzis et al[7] in a study performed in a rat transection model in 1975. Using electrophysiological data, these authors found that optimal outcomes were achieved using tension-free repair, and regeneration through a mildly stretched repair was similar to a nerve graft. This provided foundational data regarding our understanding of nerve biomechanics in vivo, prompting investigations into the cellular factors that drove this change.

A landmark study by Clark et al used an in vivo rat model of the sciatic nerve to study microvascular changes secondary to nerve tension in immediate and delayed repairs. In this study, nerve repairs were performed without tension. Then, applied tension was applied over a 30- or 60-minute time interval. They

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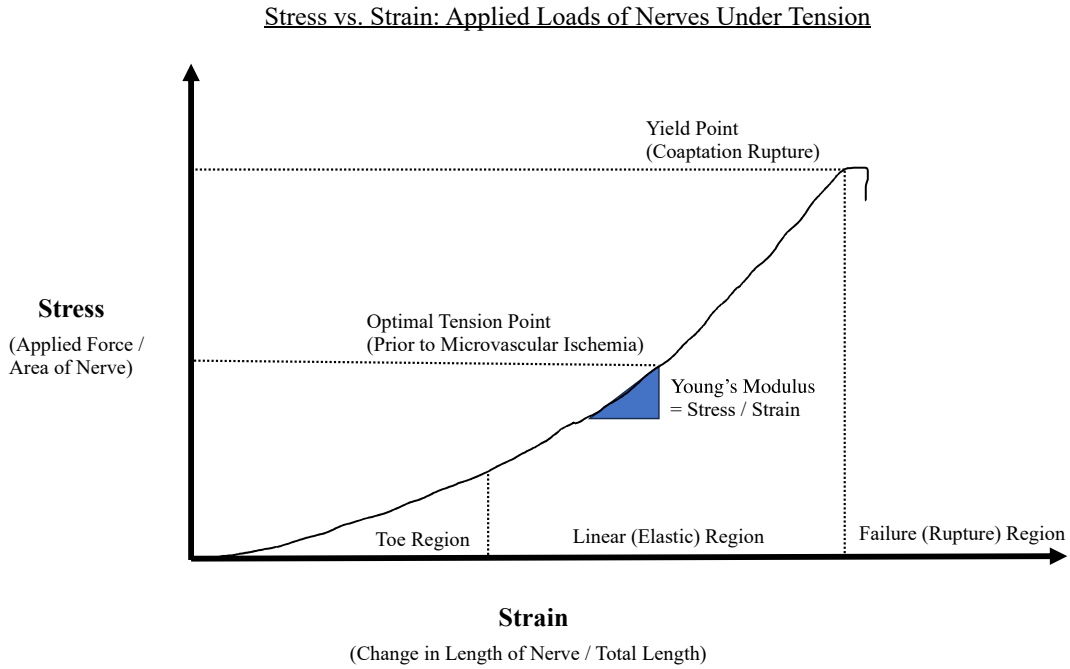

Figure 1. Stress versus strain: applied loads of nerves under tension.

found that an 8% elongation of the nerve decreased blood flow by 50%, whereas 15% elongation decreased blood flow approximately 80%.[8] Although all nerve microenvironments are different, this would suggest that tensioning and elongating a mobilized rat sciatic nerve that measured 10 mm in total length by 0.8 mm would decrease blood flow by 50%. These findings were corroborated by the study by Sunderland et al[2] in 2004, which also studied a rat sciatic nerve transection model, suggesting worse functional outcomes after a critical threshold of tension was exceeded.

Nerve ends repaired under tension lead to local ischemia, decreasing the efficacy of the repair. Seminal works by Lundborg et al[9,10] suggested intravascular clotting as a potential mechanism, as stretch or tension may increase intrafascicular pressure and therefore reduce microcirculation within a nerve. These authors similarly noted that at 8% tension there were changes observed in the microcirculation, which returned to normal if the tension was relieved within an acute time window (30 minutes). Damage to the extrinsic blood supply of nerves because of excessive mobilization, especially in the setting of pre-existing injury because of trauma, may further lower the critical threshold to inhibit regeneration.[10,11] Other authors using microelectrodes have suggested that nerve repairs performed under tension demonstrate different concentrations of extracellular electrolytes in the perineural tissue, suggesting endoneurial injury if the repair is performed under tension.[12]

At a cellular level, tension on nerve ends leads to changes in local growth factors as well as axonal regeneration. In a rat model, Yi et al[13] demonstrated that increasing tension yielded impairment in axonal outgrowth and a significant difference in activating transcription factor 3. In addition, increased Schwann cell apoptosis was noted in the models repaired under tension.

Biomechanical and Clinical Studies

Investigations of the cellular basis of nerve tension in in vivo transection models have prompted a parallel body of literature to investigate other factors to optimize nerve repair. Various techniques have been researched to optimize surgeon's intraoperative techniques to manage nerve tension in traumatic injuries. Many studies use the concept of strain, or the change in length (gap size) divided by the overall length of the nerve, as this standardizes gap size across different nerves.

Smetana et al[14] investigated the ideal suture material using human cadaveric median nerve samples. Their group used a single epineurial suture in an end-to-end repair and recorded strain at failure of the repair site. They used a threshold of average 5% strain as acceptable, with a maximum of 8% strain, finding that the average strain at failure of 9-0 suture most closely approximated the threshold value of 5% (4.9%).[14] Based on this work, the authors recommended using a single 9-0 nylon suture to perform a tension test prior to proceeding with primary neurorrhaphy.

Brogan et al[15] used a conduit splinting technique to investigate rupture rates as well as functional outcomes in a rodent defect nerve model. These authors noted a decrease in rupture rates using a conduit splinting technique, but this was accompanied by worse outcomes at 6 weeks after repair, leading to inconclusive evidence on the effectiveness when translated to a human model.[15] Another emerging method includes the prospect of nerve lengthening to facilitate a primary repair. This is an investigational technique that uses an implantable nerve internal fixator in a rat model, with an extracorporeal guidewire used to advance nerve ends over a period of 2 weeks.[16] Howarth et al[17] compared a lengthening with delayed repair to primary repair with graft, finding comparable or improved results in all functional metrics at 12 weeks in the group that underwent lengthening and subsequent end-to-end repair.

Neurolysis to mobilize proximal and distant stumps, nerve transposition, or joint immobilization in a fixed position are techniques to reduce tension at the neurorrhaphy site. Transposition of nerves may afford the ability to mobilize the nerve and facilitate a tension-free repair, particularly for large gaps. A cadaveric study of ulnar nerve lesions found that both submuscular and subcutaneous transposition were equally effective in reducing large nerve gaps (>3 mm) at the elbow.[18] Another study examined gaps at the proximal and distal forearm, finding that transposition affected the gap at the proximal forearm, but only wrist flexion improved the gap at the

wrist.[19] A recent clinical technique study described temporarily fixing the wrist in a flexed position using Kirschner wires to achieve primary nerve repair. A progressive splinting program was employed starting at 6 weeks after surgery, with acceptable results achieved.[20] Other work has demonstrated that in the setting of a tension-free repair, wrist positioning may not significantly impact nerve tension after direct repair; one study found that median and ulnar nerve repairs performed with a single 10-0 suture did not gap after positioning the wrist in 30º of wrist extension.[21]

A stepwise intraoperative approach may be useful to surgeons managing a peripheral nerve injury. Consideration should be given to a thorough initial debridement of clearly devitalized nerve tissue. For small defects without significant tension, primary repair is preferred given technical ease and superior functional results.[22] A series of 108 acute median and ulnar nerve lacerations in the forearm demonstrated superiority when primary repair was performed rather than grafting.[23] These results mirror what has been previously demonstrated in rat-based models.[24]

Several studies have demonstrated the clinical superiority of graft-based repairs in the case of undue nerve tension. However, Hentz et al demonstrated that a 15-mm nerve defect repaired in a primary epineural fashion with modest tension was superior to sutured interfascicular nerve grafts in a primate model with a primary endpoint of electrophysiological testing; no difference was noted on a histologic basis.[25] This study also employed a fascicular repair technique, which could influence outcomes. Numerous other studies have investigated the use of autograft and allograft in treating nerve gaps, and nerve grafting should be considered in nerve gaps with high strain to reduce ischemia at the repair site.

Emerging evidence may enable the use of cellularized allografts for nerve gap repair to avoid undue tension. Polyethylene glycol mediated fusion enables nerves to be coapted together immediately after injury using a monoclonal antibody to obviate the need for local immunosuppression for a cellular allograft, preventing Wallerian degeneration and allowing for immediate axonal continuity and signaling.[26,27]

Conclusions

Nerve tension should be critically evaluated at the time of repair in peripheral nerve injuries. Tension-free repair demonstrates optimal outcomes sustained over decades of experimental in vivo and clinical studies. There is moderate evidence to suggest that minimal strain at the repair site, in the setting of primary repair, should be attempted given good quality in vivo evidence of good functional results. For larger defects and high-strain repairs, nerve grafting should be considered given foundational evidence of microvascular ischemia leading to inferior clinical outcomes.

Conflicts of Interest

No benefits in any form have been received or will be received related directly to this article.

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