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Invited Commentary

Targeted Muscle Reinnervation: A Significant Advance in the Prevention and Treatment of Post-Amputation Neuropathic Pain

Kyle R Eberlin, MD
Boston, MA

"Preemptive treatment of phantom and residual limb pain with targeted muscle reinnervation at the time of major limb amputation"

is a prospective cohort study investigating the efficacy of targeted muscle reinnervation (TMR) for prevention of phantom limb pain and residual limb neuropathic pain. The authors report a dramatic decrease in postoperative pain after TMR compared with standard amputation. This is a striking finding and one that likely will (and should) have broad implications for the acute management of both upper and lower extremity amputations.

This study is timely and well executed, with a large control group and comprehensive patient-reported outcome measures. Importantly, this is the first study to demonstrate a durable reduction in post-amputation neuropathic pain with a single surgical intervention; previous attempts to identify an effective strategy have not revealed an obvious solution. In this study, the authors demonstrate a significant improvement in both Numerical Rating Scale (NRS) pain scores and Patient-Reported Outcomes Measurement Information Systems (PROMIS) instruments in patients undergoing TMR. A reduction in the use of opioid medications was also observed in the TMR cohort.

Phantom limb and residual limb neuropathic pain is unfortunately ubiquitous after major extremity amputation, with a prevalence of at least 30% to 50%, and many patients have debilitating pain.[1] Traditional techniques to address the nerves during amputation include traction neurectomy and/or suture ligature of the terminal nerve stump. Historically, little attention has been directed to the terminal ends of the transected nerves, which invariably attempt to regenerate from the site of neurotomy and often form a symptomatic neuroma. With these conventional techniques, regenerating axons have no distal target and no functional destination. This can have downstream consequences in the peripheral and ultimately the central nervous systems, as patients may eventually develop inexorable centralization of their pain symptoms.

Targeted muscle reinnervation is likely beneficial in the prevention of post-amputation pain because it confers a functional destination for the nerve endings. The field of peripheral nerve surgery has shifted to pursue a more active, rather than passive, management strategy of the terminal nerve ending in order to provide a distal target for axonal regeneration.[2] Targeted muscle reinnervation is an innovative and effective solution for this problem that satisfies the impetus for neural regeneration.

Another recently published manuscript from the authors demonstrates the efficacy of secondary (delayed) TMR in the management of chronic amputation pain.[3] Results from this manuscript suggest that earlier (ie primary, or acute) TMR may be more effective in prevention and treatment of neuropathic pain, although the specific time frame required, as well as differences in outcomes between acute and secondary TMR, still need to be clarified.

Although this study presents a remarkable advance in the acute surgical care of amputees, a number of questions remain. First, how will acute TMR be implemented on a large scale in the United States, particularly given the paucity of peripheral nerve surgeons? This procedure is technically complex and may be best performed by peripheral nerve surgeons facile with microsurgical neurorrhaphy. Another question that arises is the comparative utility for TMR in younger patients (who often have rapid neural regeneration) vs older patients (in whom nerves regenerate more slowly, and in whom symptomatic neuroma may be less common). We do not yet know the optimal patient demographics for this procedure and in what specific cadre of patients it should be performed routinely; it may have utility for all amputees regardless of age and indication for amputation. Additional study is also needed to compare the outcomes of TMR vs regenerative peripheral nerve interface (RPNI),[4] another promising treatment strategy for neuroma management in amputees. Lastly, we do not yet fully understand the effect of motor denervation (albeit temporary) of the extremity musculature as it relates to limb circumference, prosthetic tolerance, and wear patterns over time.

Overall, this important study presents a prodigious advance in the acute care of amputees, and should be strongly considered by all surgeons performing extremity amputations. It may also aid in our efforts to address the opioid epidemic, an additional advantage of this technique. Targeted muscle reinnervation has the potential to prevent development of phantom limb and residual limb pain in a large number of amputees, and the authors are to be congratulated for this seminal work.

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