Determining the Critical Time of Chronic Schwann Cell Denervation on Functional Recovery and Rna Expression

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Purpose: There is poor functional recovery following delayed peripheral nerve repair since both muscle and Schwann cells (SC) undergo denervation atrophy. We investigated the specific temporal effect of nerve/SC denervation on recovery as well as changes in RNA expression in the nerves that may elucidate changes in recovery potential. We hypothesized that functional recovery would be worse after prolonged nerve/SC denervation and that the expression profiles would differ.

Methods: Our study was conducted using a forelimb model in adult Lewis rats. Each animal underwent unilateral forelimb denervation of 8, 12, 16, or 24 weeks duration. In the functional recovery arm of the study, the ulnar nerve was denervated proximally or a sham surgery was performed. After the denervation period had elapsed, an in situ nerve transfer of median to ulnar to median nerve was performed. Functional recovery was then measured by stimulated grip strength weekly for 12 weeks. In the RNA expression arm, median and ulnar nerves were denervated. The same time points were used with the addition of a 1-week denervation period. After the denervation period, the median and ulnar nerves were harvested bilaterally. To create a comprehensive RNA-Seq dataset, the median nerve, with an average length of 3 cm, was homogenized and RNA was purified. RNA-sequencing was carried out using TrueSeq RiboZero gold kit. Samples were analyzed through FastQC, aligned to reference genome using STAR and quantified as transcripts per million (TPM) using Salmon. Principle component analysis was performed, followed by differential gene analysis using a linear mixed effects model to control for the control nerves being from the same animals.

Results: Functional recovery was statistically significantly different depending on the duration of nerve/SC denervation (P<0.01). Post-hoc tests were non-significant between the positive control and denervation periods of 8 (P=1.00) or 12 weeks (P=0.85). In contrast, when the ulnar nerve had been denervated for 16 or 24 weeks, final grip strength was significantly reduced compared to no denervation, 8, and 12 weeks of denervation (P<0.01). RNA sequence analysis showed significant differences in up- and downregulated genes depending on denervation status and duration of denervation. At a false-discovery rate >0.05, we identified 1624 genes differentially expressed, of which 327 genes were upregulated and rest (1297 genes) downregulated with denervation.

Conclusions: Prolonged nerve/SC denervation of more than 12 weeks resulted in significantly worse functional recovery. RNA sequencing demonstrated that not only were there many genes differentially expressed, but these appear to vary with duration of denervation as well. Further investigation into the specific genes and their changes over time will allow us to know why recovery potential is decreased and targets for interventions to improve recovery.

Clinical Practice Patterns and Evidence-based Medicine in Dupuytren’s Contracture: A Twelve-year Review of Continuous Certification Tracer Data From The American Board of Plastic Surgery

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**Purpose:** Since 2008, The American Board of Plastic Surgery (ABPS) has collected clinical practice data on Dupuytren’s contracture repair as part of their Continuous Certification (CC) process. Submitted twice every ten years by each plastic surgeon, this collection can help describe clinical trends in Dupuytren’s contracture repair as they relate to Evidence-Based Medicine (EBM) articles published in this timeframe.

**Methods:** Cumulative tracer data for Dupuytren’s contracture repair from February, 2008 through December, 2014 were reviewed and compared to data from January, 2015 through March, 2020 with the goal of identifying national practice trends. These trends were then evaluated alongside EBM reviews published in 2010, 2014 and 2017.

**Results:** As of March 2020, 230 cases of Dupuytren’s contracture were included in the tracer. The median age at time of surgery was 65 years (range, 38-91 years), and the average age of disease onset was 47 years. The most common surgical technique was limited fasciectomy, comprising 62% of cases. There were no postoperative adverse events reported in 77% of cases. The most common complications were loss of finger flexion (3%) and skin loss (2%). Topics addressed in EBM articles but not tracer data included adjuvant treatments and non-operative techniques such as tamoxifen administration. The use of minimally invasive procedures such as percutaneous cordotomy (0% vs. 13%) and collagenase injections (0% vs. 9%, p = .001) showed significant increases between the two time periods. More invasive procedures such as radical fasciectomy decreased in popularity (34% vs. 16%, p = .002). Use of Z-plasty also decreased between 2015 and 2020 (67% vs. 45%, p < .001). General anesthesia was the most commonly used form of anesthesia, being employed in 54% of tracer cases. There was an increase in the use of Bier block regional anesthesia (1% vs. 9%, p = 0.029) as well as in the use of epinephrine for hemostasis (0 vs. 8%, p = 0.006). Significant changes were also noted in post-operative management, including a decrease in the employment of formal postoperative hand therapy. This is consistent with evidence showing that it has no significant clinical benefit.

**Conclusion:** The tracer data collected on Dupuytren’s contracture repair over a twelve-year period allow us to describe national trends in presentation and surgical techniques, and can help plastic surgeons evaluate their surgical practice in the context of these trends and EBM.

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**WEDNESDAY, JUNE 9, 2021: CRANIOFACIAL/CONGENITAL ANOMALIES TOP SCORED ABSTRACTS**

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**The Prevalence of Normocephalic Sagittal Craniosynostosis in Young Children**

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**Purpose:** Sagittal craniosynostosis (SC) is usually diagnosed during early childhood due to the presence of an abnormal head shape termed scaphocephaly. However, patients with radiographic evidence of a prematurely fused sagittal suture but normal head shape (normocephalic) have been reported. A recent study from our group found that 3.3% of normal children under 5 years of age have partially or completely fused sagittal sutures by computed tomography but no corresponding changes in cranial form. The purpose of this paper is to validate our preliminary study with a larger cohort of patients, and to analyze factors that may be associated with incidental finding of early suture fusion.

**Methods:** We reviewed computerized tomography (CT) scans of patients from 0 to 71 months of age who presented to the emergency department (ED) of our tertiary care institution between 2008 and 2020. Patients who were found to have syndromes related with craniosynostosis, phenotypes consistent with craniosynostosis, VP shunt placement, brain or cranial abnormalities, were excluded. A panel of two craniofacial surgeons reviewed the CT scans for presence of craniosynostosis (CS). Demographic information, gestational age, past medical and family history, medications, chief complaint and fusion type were recorded as covariates. Possible medical or demographic differences between patients with and without craniosynostosis were analyzed using unpaired t-test and Chi-square/Fisher’s exact test; Firth logistic regression was performed to determine