SCIENTIFIC ARTICLE

# Outcomes of Microneurolysis of Hourglass Constrictions in Chronic Neuralgic Amyotrophy

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**Purpose** Wide variability in the recovery of patients affected by neuralgic amyotrophy (NA) is recognized, with up to 30% experiencing residual motor deficits. Using magnetic resonance imaging and ultrasound (US), we identified hourglass constrictions (HGCs) in all affected nerves of patients with chronic motor paralysis from NA. We hypothesized that chronic NA patients undergoing microsurgical epineurolysis and perineurolysis of constrictions would experience greater recovery compared with patients managed nonsurgically.

**Methods** We treated 24 patients with chronic motor palsy from NA and HGCs identified on magnetic resonance imaging and US either with microsurgical epineurolysis and perineurolysis of HGCs (11 of 24) or nonsurgically (13 of 24). Muscle strength (both groups) and electrodiagnostic testing (EDX) (operative group) was performed before and after surgery. Preoperative EDX confirmed muscle denervation in the distribution of affected nerve(s). All patients met criteria for microneurolysis: 12 months without improvement since onset or failure of clinical and EDX improvement after 6 months documented by 3 successive examinations, each at least 6 weeks apart.

**Results** Mean time from onset to surgery was 12.5 ± 4.0 months. Average time to most recent post-onset follow-up occurred at 27.3 months (range, 18−42 months; 15 nerves). Average time to latest follow-up among nonsurgical patients was 33.6 months (range, 18−108 months; 16 nerves). Constrictions involved individual fascicular groups (FCs) of the median nerve and the suprascapular, axillary and radial nerves proper (HGCs). Nine of 11 operative patients experienced clinical recovery compared with 3 of 13 nonsurgical patients. EMG revealed significant motor unit recovery from axonal regeneration in the operative group.

**Conclusions** Microsurgical epineurolysis and perineurolysis of FCs and HGCs was associated with significantly improved clinical and nerve regeneration at an average follow-up of 14.8 months compared with nonsurgical management. We recommend microneurolysis of HGCs and FCs as a treatment option for patients with chronic NA who have failed to improve with nonsurgical treatment. *(J Hand Surg Am. 2020;■(■):1.e1-e11. Copyright © 2020 by the American Society for Surgery of the Hand. All rights reserved.)*

**Type of study/level of evidence** Therapeutic IV.

**Key words** Brachial plexus, neuralgic amyotrophy, neurolysis, Parsonage Turner.

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NEURALGIC AMYOTROPHY (NA), also known as Parsonage Turner syndrome, is an idiopathic peripheral axonopathy that most frequently presents with a prodrome of severe upper-extremity pain, followed by profound muscle weakness in the distribution of one or more upper-extremity nerves.[1,2] Although its etiology is debated, there is evidence to support an immune-mediated cause.[1,3,4] Reported triggers include viral infections, vaccination, strenuous exercise, surgery, pregnancy, and traumatic injury.[5–8] Patients exhibit substantial variability in presentation, including affected nerve(s), laterality, the number of muscles involved, the extent of recovery, and recurrence. The variation in recovery remains unexplained; some patients recover spontaneously, whereas up to 30% have residual motor deficits years after onset.[5]

The presence of hourglass constrictions (HGCs) of individual nerves or nerve fascicles (fascicular constrictions [FCs]) has been reported in peripheral nerves of the upper extremity for decades, but only recent reports suggest a correlation with NA.[9–17] In 2011, Pan et al[11] documented HGCs in 5 cases of NA and proposed the HGC as an explanation for failure to recover from this syndrome. Their subsequent report described surgical treatment of HGCs or FCs in 47 spontaneous nerve palsies in 42 patients using neurolysis, repair, or grafting.[10] Using US, Arányi et al. found that 74% of affected nerves in NA patients (52 of 70) exhibited abnormalities ranging from fascicular swelling to varying degrees of nerve constriction. In their study, an increased degree of constriction correlated with lower rates of reinnervation after 6 months.[18] Sneag et al[2] studied 27 patients with clinically confirmed NA and found constrictions in 84% of affected nerves on MRI. A recent 2-center report on anterior interosseous nerve syndrome demonstrated FCs in the median nerve above the elbow using high-resolution MRI in all cases, and in 83% of cases using US.[9] Given the strong association of this pathological feature with NA and its prognostic importance, nerve or FCs may represent a therapeutic target, particularly in patients who have not recovered spontaneously.

The purpose of our study was to report outcomes of focused epineurolysis and perineurolysis of FCs and HGCs in a cohort of patients with chronic NA who did not improve with nonsurgical care. We hypothesized that patients with chronic NA would regain increased electrical and clinically important muscle function from focused microneurolysis at constriction sites identified on imaging compared with those managed nonsurgically.

## MATERIALS AND METHODS

This 2-center retrospective cohort study was approved by both institutional review boards. Patients with a diagnosis of NA presented to our centers because of failure to improve with nonsurgical care (Table 1). A diagnosis of NA was defined as the spontaneous, acute onset of muscle palsy in the distribution of one or more upper limb nerves, usually heralded by severe shoulder, periscapular or upper-limb pain, and confirmed by electrodiagnostic testing (EDX) that documented total or subtotal muscle denervation in the nerve(s) or nerve fascicle(s) distribution. Muscle denervation was defined as low discrete or no motor unit recruitment during maximal volitional activation, the presence of diffuse positive sharp waves and fibrillation potentials, and absent axonal regeneration. Recruitment categories, in order of ascending activity, were graded as none, low discrete (1 or 2 motor units with maximum recruitment), high discrete (3+ motor units), decreased, or full.[19] Motor unit configuration categories included none, nascents (representing regeneration), increased polyphasics (representing terminal collateral sprouting), and di/triphasics. Electrodiagnostic testing of all operative patients was conducted by a board-certified electrodiagnostic specialist with extensive experience in the treatment of brachial plexus injuries and NA to verify whether recovery occurred as a result of axonal regeneration or terminal collateral sprouting.

We reviewed records of 96 patients evaluated for NA. Patients were eligible for inclusion if they had at least one FC or HGC on diagnostic imaging and met either of the criteria for chronic NA: (1) lack of recovery at greater than 12 months from onset, demonstrating complete or near-complete denervation; or (2) lack of recovery at 6 months after onset with 3 successive clinical and electrodiagnostic exams at least 6 weeks apart that demonstrated complete denervation and no clinical recovery of function. A total of 24 patients met inclusion criteria. All patients who met inclusion criteria at site 1 were offered surgery or continued nonsurgical treatment; 11 of 15 opted to proceed with surgery whereas 4 opted for continued nonsurgical management. All patients at site 2 were offered nonsurgical management because the site lacked a microsurgical protocol or experience in the operative treatment of NA. Eight operative patients had confirmed NA for greater than 12 months (average of 63 weeks; range, 52–81 weeks), with complete denervation of 7 nerves and near-complete denervation of 2 nerves. Three operative patients had confirmed NA for 6, 8, and 9

**TABLE 1. Patient Characteristics and Clinical Information***

| Patient | Age (y), Gender | Involved Limb | Affected Nerve(s) Undergoing Neurolysis or Nonsurgical Treatment | Time From Onset to Surgery, mo | Time From Surgery to Most Recent Follow-Up, mo | Time From Onset to Latest Follow-Up, mo | Time From Surgery to Initial Clinical Improvement, mo | Time From Surgery to Initial EDX Improvement, mo |
|---|---|---|---|---|---|---|---|---|
| **1** | 40 M | R | Axillary | 8 | 12 | 19 | 1.3 | 1.3 |
| **2** | 21 M | R | SS | 19 | 6 | 25 | 2.0 | 5.9‡ |
| **3** | 50 M | L | SS<br>AIN<br>PT/median radial/PIN | 9 | 24 | 33 | 5.0 | 5.0 |
| **4** | 30 F | L | AIN | 18 | 6† | 24 | 2.7 | 2.7 |
| **5** | 58 F | R | AIN | 12 | 43 | 55 | 4.8 | 7.8‡ |
| **6** | 60 F | R | AIN<br>Radial | 13 | 29 | 42 | 1.6 | 4.2‡ |
| **7** | 61 M | L | Radial | 6 | 21 | 27 | 9.6 | 9.6 |
| **8** | 51 M | L | Radial | 14 | 16 | 30 | – | – |
| **9** | 52 F | R | AIN | 13 | 11 | 24 | 1.8 | 5.9‡ |
| **10** | 66 F | L | AIN | 12 | 12 | 24 | 3.9 | 4.2‡ |
| **11** | 58 M | R | AIN | 15 | 9 | 24 | 9.2 | 9.2 |
| **12** | 37 M | R | Axillary | – | – | 24 | | |
| **13** | 53 F | L | SS | – | – | 18 | | |
| **14** | 30 F | R | SS<br>AIN<br>Radial | – | – | 18<br>84<br>108 | | |
| **15** | 39 M | L | PT/Median<br>Radial | – | – | 18 | | |
| **16** | 47 F | R | AIN | – | – | 19 | | |
| **17** | 69 F | R | AIN | – | – | 18 | | |
| **18** | 41 F | L | Radial | – | – | 24 | | |
| **19** | 42 M | L | Radial | – | – | 18 | | |
| **20** | 40 M | L | Radial | – | – | 36 | | |
| **21** | 49 M | R | AIN | – | – | 72 | | |

(Continued)

**TABLE 1. Patient Characteristics and Clinical Information* (Continued)**

| Patient | Age (y), Gender | Involved Limb | Affected Nerve(s) Undergoing Neurolysis or Nonsurgical Treatment | Time From Onset to Surgery, mo | Time From Surgery to Most Recent Follow-Up, mo | Time From Onset to Latest Follow-Up, mo | Time From Surgery to Initial Clinical Improvement, mo | Time From Surgery to Initial EDX Improvement, mo |
|---|---|---|---|---|---|---|---|---|
| **22** | 71 M | R | AIN | – | – | 24 | | |
| **23** | 40 M | R | Spinal accessory nerve | – | – | 25 | | |
| **24** | 45 M | R | SS | – | – | 18 | | |

PT, pronator teres fascicle; SS, suprascapular.
*Average age, 50 y; average time from onset to surgery, 12.4 mo; average time from surgery to most recent follow-up, 14.8 mo; average time from onset to most recent follow-up (nonsurgical, 33.6 mo; average time from surgery to initial clinical recovery, 4.2 mo.
†Most recent available EMG follow-up taken earlier than 6 mo after the operation.
‡First postoperative EMG performed after the patient had demonstrated clinical recovery.

months, respectively, with complete denervation of 1 to 4 nerves each. The 11 surgical patients (15 nerves) had a minimum postoperative follow-up of 6 months (range, 6−29 months). The 13 nonsurgical patients (16 nerves) were observed for at least 18 months after onset (range, 18−108 months). All nonsurgical patients underwent physical therapy. One nonsurgical patient was also receiving corticosteroid therapy for a separate condition at the time of initial NA onset.

Clinical muscle strength in both groups was assessed by the 2 operating surgeons and the electrodiagnostic physician at site 1, and by the treating neurologist at site 2. Muscle strength was measured with the Medical Research Council (MRC) scale, graded from M0 to M5.[20] For patients with neuropathy of the axillary nerve or suprascapular nerve (SSN), shoulder abduction and external rotation was also measured to assess recovery better in dual-nerve domains. Postoperative EDX was measured for comparison with preoperative testing and to differentiate improved postoperative muscle strength owing to actual muscle reinnervation from compensation of synergistic muscles. Changes from preoperative to postoperative MRC and EDX classifications in operative patients were assessed with 2-tailed McNemar test. Differences in most recent MRC classification between operative and nonsurgical patients were assessed with 2-tailed Fisher exact test. Results were considered significant at an $\alpha$ value of $P < .05$. The power of these comparisons was calculated as 0.82.

All patients were imaged by either US or MRI to assess for HGCs. A 3.0-T MRI (General Electric Healthcare Discovery MR750, Waukesha, WI) of the affected extremity was performed in all patients at site 1 (11 operative and 4 nonsurgical) and interpreted by a radiologist specialized in nerve imaging. The MRI protocol consisted of a combination of intermediate-weighted fast-spin echo and $T_2$-weighted Dixon fat suppression 2-dimensional sequences in multiple planes, including a plane orthogonal to the longitudinal course of the nerve, and in selected cases, a 3-dimensional short tau inversion recovery sequence. Optimizing imaging parameters based on the local anatomy and nerve diameter facilitated acquisition of slice thicknesses of 1 to 2.5 mm. The radial nerve, AIN, and median nerve were imaged from the upper arm through the proximal forearm. The axillary nerve and SSN were imaged along their entire length. Magnetic resonance imaging was unavailable at site 2. Preoperative US was performed in 8 of 11 operative and 12 of 13 nonsurgical patients by one specialized radiologist

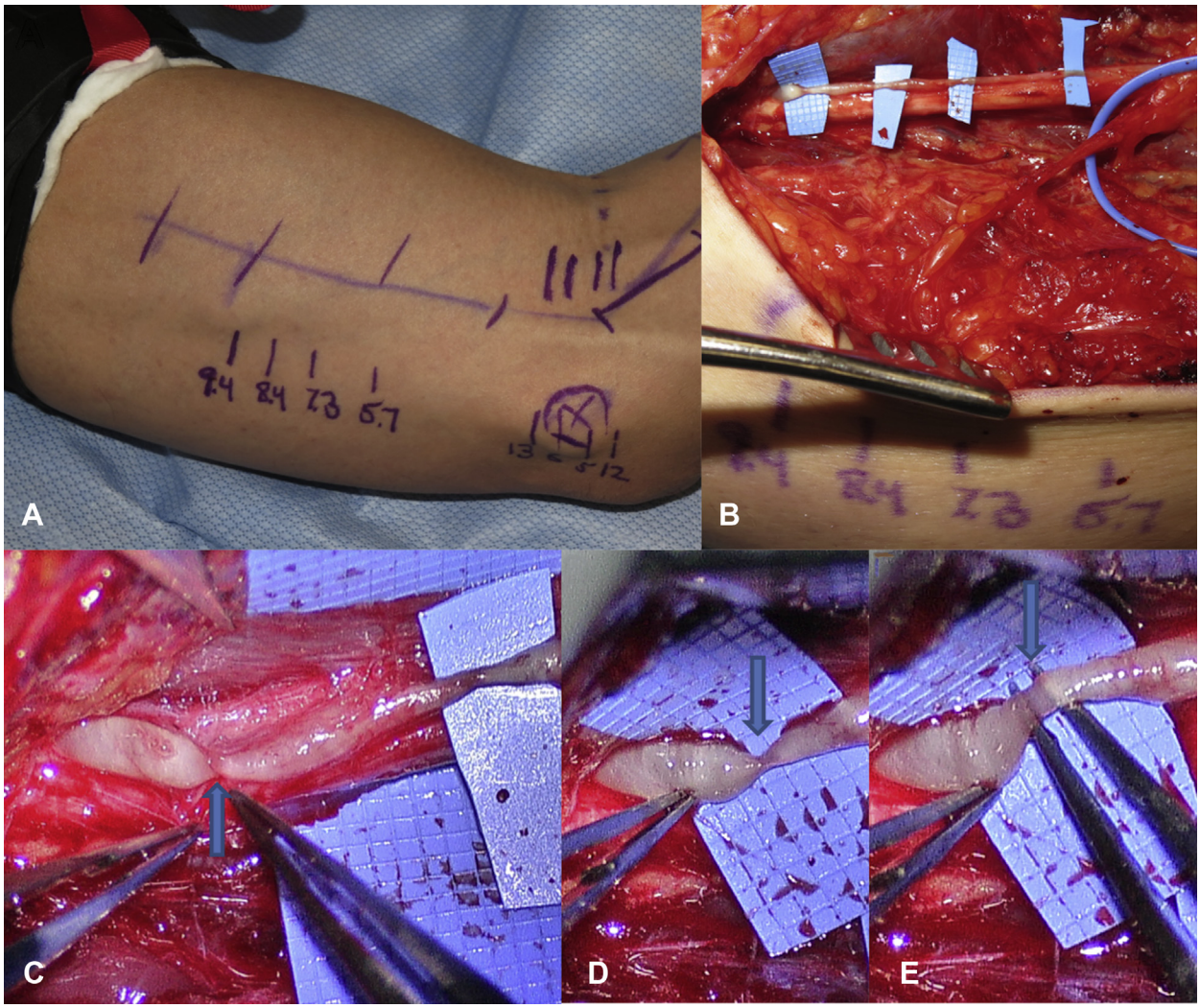


**FIGURE 1:** **A** Preoperative markings before median nerve neurolysis at MRI-predicted sites of constriction **B** Hourglass constriction sites at each predicted point (blue backgrounds) after micro-perineurolysis. **C** Severe hourglass constriction (blue arrow) of PT/FCR fascicle of median nerve before perineurolysis (×10 magnification). **D** Pronator teres/flexor carpi radialis fascicle after division of oblique perineural bands showing severe constriction (blue arrow). **E** Pronator teres/flexor carpi radialis fascicle after perineurolysis demonstrating translucency of affected portion of nerve (blue arrow) and restoration of caliber.

(site 1) or a neurologist (site 2) using targeted, high-resolution, nerve-specific imaging with 2-dimensional gray-scale and power Doppler imaging protocols (General Electric Healthcare LOGIQ E9 system; and Philips Epiq 5, Amsterdam, The Netherlands). The contralateral full-length nerve was imaged for comparison. Constriction sites in the arm (radial nerve, pronator teres/flexor carpi radialis fascicle [PT/FCR], AIN fascicular group) were localized relative to the medial and lateral epicondyles using both imaging modalities to provide coordinates for operative planning. For the SSN, HGCs were localized relative to the clavicle and omohyoid by measuring distances from the upper-trunk origin and suprascapular notch. For the axillary nerve, HGCs were localized relative to the 6-o'clock position on the glenoid.[21]

Before surgery, transverse skin markings were drawn perpendicular to the planned incision (Fig. 1A, B) at the constriction sites identified by imaging. Intraoperative nerve stimulation at 0.5 and 2 mA (Checkpoint, Cleveland, OH) proximal and distal to HGCs produced no contraction of expected muscles downstream. We performed focal epineurotomy of the parent nerve using a high-powered surgical microscope, followed by internal neurolysis to identify FCs, and finally perineurolysis to divide and excise focal circumferential, perineural bands around involved fascicles,[9,22] to release constrictions (Fig. 1C, D).

**TABLE 2. Locations of HGCs Confirmed Operatively, Grouped by Nerve**

| Patient, Nerve | HGCs, n | Locations of HGCs |
|---|---|---|
| **1, Axillary** | 1 | Distal to coracoid |
| **2, SSN** | 1 | Anterior to suprascapular notch/20 mm medial to coracoid |
| **3, SSN** | 1 | 1 cm posterior to clavicle |
| **3, AIN** | 2 | 10 mm, 4 mm proximal to ME |
| **4, AIN** | 2 | 30 mm, 8 mm proximal to ME |
| **5, AIN** | 4 | 50 mm, 43 mm, 36 mm, 24 mm proximal to ME |
| **6, AIN** | 3 | 39 mm proximal, 10 mm proximal, 8 mm distal to ME |
| **9, AIN** | 3 | 19, 10, 0 mm proximal to ME |
| **10, AIN** | 1 | 0 mm proximal to ME |
| **11, AIN** | 3 | 23 mm, 7 mm, 0 mm proximal to ME |
| **3, PT/median** | 2 | 95 mm, 4 mm proximal to ME |
| **3, Radial** | 4 | 155 mm, 24 mm, 16 mm, 7 mm proximal to LE |
| **3, Radial** | 4 | 155 mm, 24 mm, 16 mm, 7 mm proximal to LE |
| **6, Radial** | 3 | 90 mm, 60 mm proximal to LE, IM septum |
| **7, Radial** | 3 | 190 mm, 12 mm, 37 mm proximal to LE |
| **8, Radial** | 5 | 160 mm, 110 mm, 90 mm, 58 mm, 30 mm proximal to LE |

IM, intramuscular; LE, lateral epicondyle; ME, medial epicondyle.

## RESULTS

Mean age was 50 years (range, 21−66 ) for operative patients and 47 years (range, 30−71 years) for nonsurgical patients. In the operative group, average time between onset and neurolysis was 12.4 months (range, 6.0−18.6 months). Four operative and 2 nonsurgical patients presented with multinerve involvement. Fifteen nerves or nerve fascicles were involved in operative patients (1 axillary, 2 SSN, 4 radial, 1 PT/FCR, and 7 AIN) and 16 (1 axillary, 3 SSN, 5 radial, 1 PT/FCR, 5 AIN, and 1 spinal accessory nerve) in nonsurgical patients.

Among the surgical cohort, a total of 37 HGCs or FCs were discovered on imaging and confirmed operatively; each nerve averaged 2.5 ± 1.2 (range, 1−5) constriction sites (Table 2). We detected 24 HGCs or FCs (average, 1.5 ± 0.8; range, 1−3) in affected nerves of all nonsurgical patients. Each affected axillary nerve and SSN demonstrated one HGC. The number of median nerve FCs (AIN or PT/FCR fascicles) varied from 1 to 4. Radial nerves demonstrated 3 to 5 constrictions. Proximal to the constrictions, affected nerves demonstrated varying lengths of $T_2$-weighted signal hyperintensity on MRI (Fig. 2). Ultrasound revealed marked, segmental enlargement of affected nerves proximal to focal narrowing with abrupt fascicular caliber changes.

At surgery, each HGC was confirmed precisely to the preoperatively measured locations on MRI and US. Fascicular constrictions in the 7 patients with AIN syndrome were above the cubital crease (1.7 ± 1.5 cm proximal, range from 0.8 cm distal to 5 cm proximal) and confined to the AIN fascicular group (posterior/posteromedial fascicular group topographically).[9] Under microscopic examination, FCs appeared translucent (Fig. 1D) and the affected fascicle had a bluish discoloration distally. Proximal to constrictions, affected fascicles appeared swollen but of normal color and opacity. All constrictions were rated as severe at surgery, with nerve diameter at constriction sites narrowing to as little as 10% of the normal caliber. In addition to constriction, apparent torsion of the nerve[9,23] was observed in 5 patients (2 radial, 1 SSN, and 2 median [AIN fascicle]) (Fig. 3). After epineurotomy, internal epineurolysis, and excision of perineural constriction bands, affected nerves or fascicles swelled in caliber and the apparent torsion disappeared. Physical derotation of the nerve was not performed, and actual twisting of the nerve or nerve fascicles was not observed. Because there was no imaging or clinical suspicion of compressive neuropathy, decompression at theoretical entrapment points (carpal tunnel or quadrilateral space) was not routinely performed.

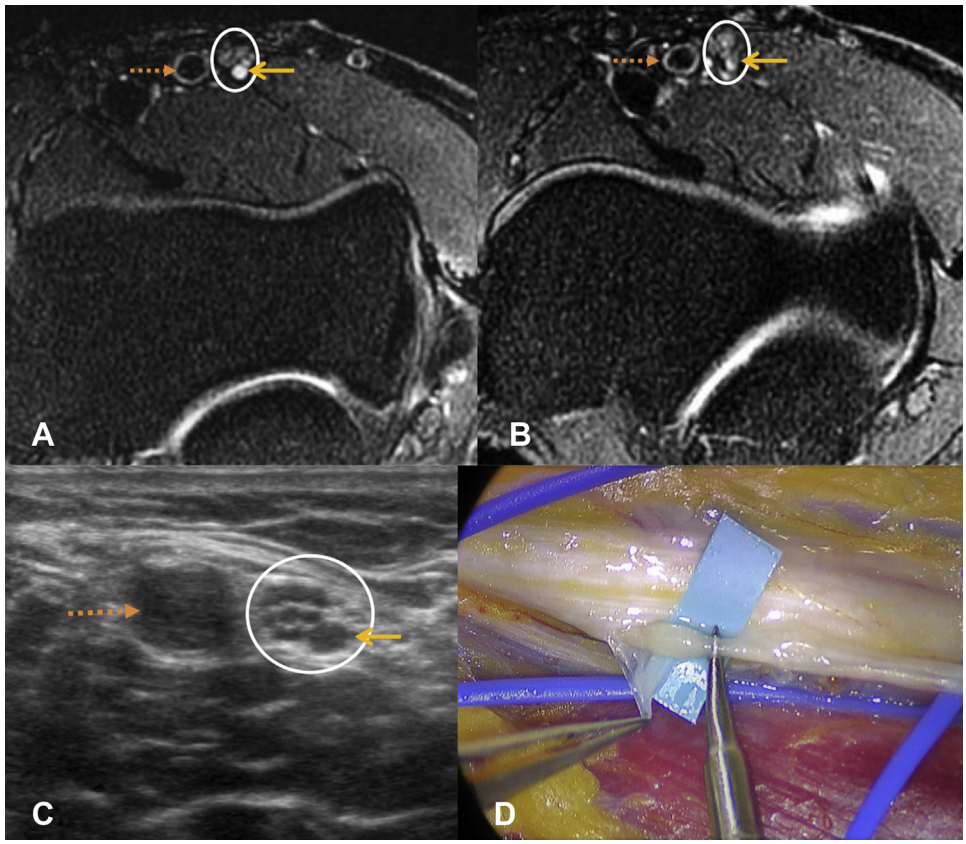


**FIGURE 2: A** Axial $T_2$-weighted fat-suppressed image demonstrates signal hyperintensity and enlargement of AIN fascicular bundle (arrow) of the median nerve (oval) at the level of the medial epicondyle **B** immediately proximal to a severe constriction of the bundle (arrow) with brachial artery (dashed arrow) marked for reference. **C** 2-Dimensional gray-scale US image demonstrating focal enlargement of AIN bundle (arrow) of median nerve (oval) adjacent to brachial artery (dashed arrow) at the same location as magnetic resonance image. **D** Corresponding AIN HGC (blue background) at level of elbow joint (×10 magnification).

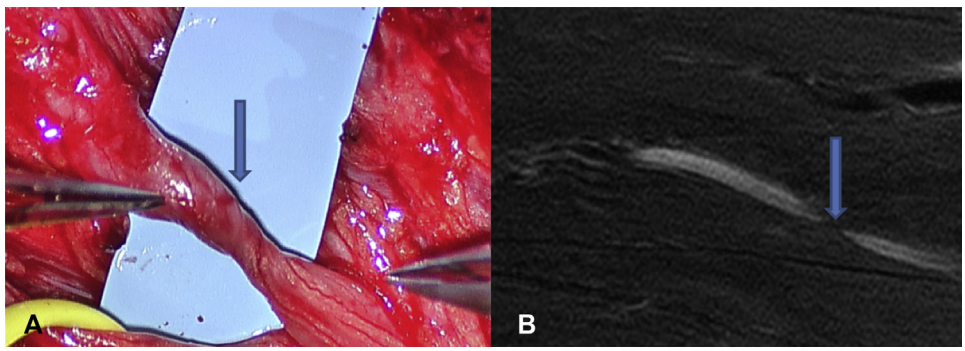


**FIGURE 3: A** Hourglass constriction of radial nerve with apparent torsion (blue arrow) 16 cm proximal to lateral epicondyle (×10 magnification). **B** Corresponding HGC (blue arrow) on MRI longitudinal view ($T_2$-weighted Dixon fat-suppressed image).

Division of the suprascapular ligament was performed in 2 cases of SSN involvement for access to the constrictions, although no compression at this notch or deformity of the nerve was identified.

The most recent clinical and EDX follow-up of the operative cohort averaged 14.8 months (range, 6–43 months) after surgery and 27.3 months after onset. Follow-up averaged 33.6 months (range, 18–108 months; median, 19 months) after onset in the nonsurgical cohort. In the surgical group, recovery of at least M3 strength was observed in 12 of 15 nerves across 9 of 11 patients, and M4 or better in 10 nerves in 8 patients at an average of 27 months (range, 19–42 months) after onset (Fig. 4). All muscles in

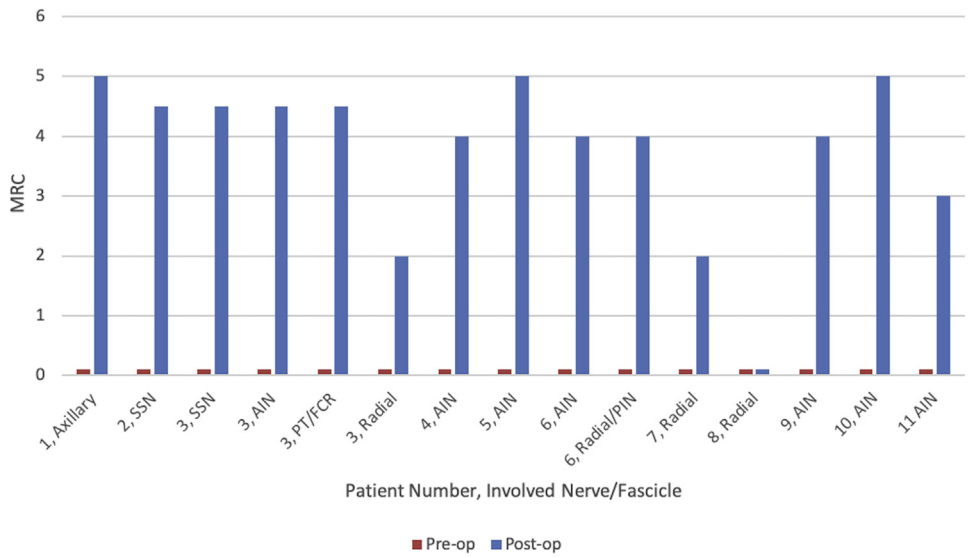


**FIGURE 4:** Preoperative to postoperative clinical recovery grouped by nerve in operative cohort. PIN, posterior interosseous nerve; Pre-op, preoperative; Post-op, postoperative.

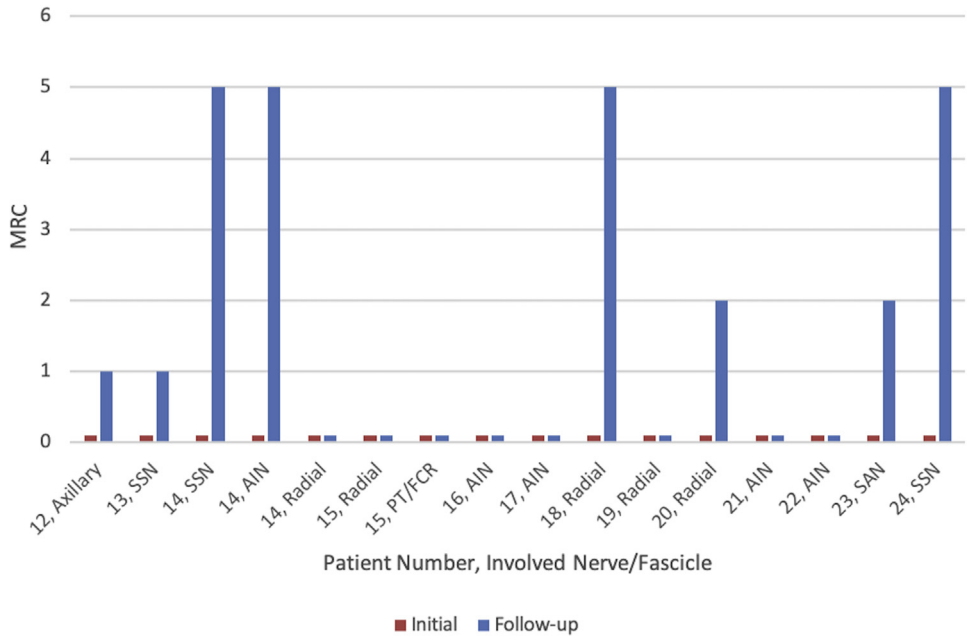


**FIGURE 5:** Clinical recovery grouped by nerve in nonsurgical cohort. PIN, posterior interosseous nerve; SAN, spinal accessory nerve.

the operative cohort that did not recover were in the radial nerve distribution. Among nonsurgical patients, 4 of 16 nerves in 3 of 13 patients experienced at least M4 recovery at 34 months (range, 18−108 months) after onset (Fig. 5). Only 1 of 5 patients with a nonsurgically managed radial nerve palsy recovered. Clinical recovery, based on MRC score, was significantly greater in the operative compared with the nonsurgical group ($P < .05$). Both the operative and nonsurgical cohorts demonstrated significant recovery ($P < .05$) at most recent follow-up. Shoulder abduction increased from 90° to 175° in the patient who underwent axillary microneurolysis and from 135° to 175° in 2 patients who underwent suprascapular microneurolysis. Improvements in axonal recovery that resulted in EMG motor unit recruitment and configuration were found in 9 of 10 operative patients who had EMG results available at least 6 months after surgery. Of 32 operative muscles treated (Table 3), 26 demonstrated significant

**TABLE 3. Changes in Electrodiagnostic Outcomes**

| Outcome | Classification Category | Before Surgery | After Surgery |
|---|---|---|---|
| **Motor unit recruitment** | None | 30 | 6 |
| | Low discrete | 2 | 4 |
| | High discrete | 0 | 5 |
| | Decreased | 0 | 14 |
| | Full | 0 | 3 |
| **Motor unit configuration** | None | 30 | 6 |
| | Nascents | 2 | 17 |
| | Increased polyphasics | 0 | 0 |
| | Di-/triphasics | 0 | 9 |

Preoperative and postoperative counts of the number of muscles demonstrating each pattern of motor unit recruitment or configuration across all operative patients.

improvements in motor unit recruitment and configuration ($P < .05$). We did not perform an electrodiagnostic analysis for nonsurgical patients because EMG evaluations after the initial assessment in this group were not performed in patients who showed no evidence of clinical recovery.

## DISCUSSION

These findings confirm the hypothesis that microsurgical neurolysis of HGCs identified by high-resolution imaging is associated with improved clinical recovery of patients with chronic NA compared with nonsurgical management. This study builds on prior studies of HGCs and their role in NA. This report is unique in using a strict definition of NA, inclusion of only chronic, unresponsive patients, the use of EDX as a recovery measure, inclusion of multiple affected nerves, and well-defined operative criteria. Pan et al,[10] Akane et al,[24] and Wang et al[25] performed neurolyses targeting HGCs with favorable results, although these were in cohorts of spontaneous nerve palsy without a strict definition of NA, and were largely limited to AIN and posterior interosseous nerve/radial nerves. In addition, neurolysis in these reports was performed earlier, at an average of 5.7, 5.5, and 2.6 months, respectively, after onset.

Intervention in our cohort was performed in nonrecovering patients at an average of 12.4 months after onset, who were unlikely to recover spontaneously based on studies of the natural history of NA and the known effects of chronic denervation on muscle.[7,26] A study of 29 NA patients treated nonsurgically and observed for a mean of 11.5 months found that 79% of patients showed initial EDX evidence of reinnervation at an average of 6 months. In addition, 69% had reached decreased recruitment at an average of 9.5 months after onset. By comparison, none of the patients in the current cohort had reached either benchmark, indicating the severity of the disease and impaired recovery.

In the operative cohort, all axillary, SSN, or AIN/median nerve musculature demonstrated electrical and physical recovery, with time to surgery ranging from 8 to 17 months after onset and recovery typically commencing 3 to 5 months after surgery. The demonstration of nascent potentials as opposed to increased polyphasics after surgery in the surgical cohort suggests that reinnervation primarily resulted from axonal regeneration after release of the constrictions, as opposed to terminal collateral sprouting of fibers already present. Muscles affected by radial nerve palsies recovered less consistently compared with those innervated by other nerves; only 5 of the 15 affected muscles recovered M3 or greater strength. Consistent with the findings of Arányi et al,[18] more constrictions were seen in the current patients with radial nerve involvement (3−5/nerve) compared with the other nerves in the series (1−3/nerve). The 3 operative patients with radial nerve involvement who did not recover also had multiple nerve involvement, and one had bilateral involvement. Interestingly, all other nerves treated in these 3 patients with surgical epineurolysis and perineurolysis recovered. Radial nerve recovery was also poor in the nonsurgical cohort; only 1 of 5 patients recovered. Tendon transfers remain an option for NA patients who do not recover after neurolysis. Given the small number of radial nerves treated, further investigation is required to determine whether there are nerve-specific differences in recovery.

Recent reports have established that anywhere from 25% to 60% of patients may fail to recover, recover partially, or experience recurrence with nonsurgical management.[5,8,27] No medical treatment,

including corticosteroids or intravenous immunoglobulin, has convincingly demonstrated efficacy for patients with NA.[28–30] The absence of a reliable intervention for NA may also result from delayed disease recognition and the lack of an objective disease marker. Hourglass constrictions have been recorded for several decades in the surgical literature but have only been recently associated with NA.[3,11,22,31,32] In the study by Arányi et al,[18] increasing nerve constriction and torsion, as visualized on US, were found to have an inverse relationship with recovery from NA at 6 months after onset.[18] Based on US findings, complete constriction was defined as a disruption of a nerve fiber or fascicle spanning its entire diameter, whereas incomplete constrictions spanned only a portion of the diameter. None of the 10 nerves with complete constriction experienced spontaneous recovery. By comparison, 18 of 29 nerves with no abnormalities, moderate nerve fascicle swelling, or incomplete constriction recovered physical and electrical function. Ultrasound allows for characterization of the proximodistal extent of nerve swelling and has been used to grade constriction severity. In a recent study of US of the SSN, long thoracic nerve, spinal accessory nerve, and phrenic nerve in the neck, US demonstrated high visualization rates and diagnostic capability.[33] Several studies reported the utility of MRI in the detection of nerve constrictions, including in areas difficult to access via US, such as posterior to the clavicle (for the SSN) or deep in the axilla (for the axillary nerve).[2,3,9] Our current practice is to obtain both imaging modalities in NA patients because we think these are complimentary studies.

The pathophysiology of HGCs is unknown, but histological studies have demonstrated loss of both myelinated and unmyelinated fibers, fibroblasts with collagen deposition, absent regeneration, microvascular occlusion, and CD8-positive T-lymphocyte infiltration in the nerve fibers.[10,34] Consistent with previous reports, AIN FCs were consistently localized in this series immediately above the elbow joint line,[9] possibly indicating a mechanical or vascular watershed phenomenon.[3,12,23,26,31] Regardless of its cause, the universal finding of one or more HGCs or FCs in chronic NA,[2,11,18] the reported correlation between HGC severity and the clinical course of NA,[3] as well as the favorable results of neurolysis of HGCs in this chronic patient cohort and other NA cohorts[10,24,25] suggest that the HGC is a unique lesion of chronic NA.

Knowing when to consider surgery is difficult, because most patients with NA exhibit spontaneous recovery. Past natural history studies of NA demonstrated that 70% of patients experienced some degree of clinical recovery by 6 months, and an additional 20% improved by 1 year. By electrodiagnostic criteria, 80% of patients presenting with complete denervation are expected to reach decreased recruitment of affected muscles by 1 year.[7] Delaying intervention carries the potential for loss of motor end plates, Schwann cell senescence, and fibrosis and fatty replacement of denervated muscle.[35] As these processes advance, the possibility of functional recovery diminishes sharply. Earlier intervention may be appropriate, depending on the extent of denervation and the particular nerves involved.[36] Because signs of initial reinnervation are present at an average of 6 months in 80% of patients with initial complete denervation, a lack of recovery at 6 to 12 months may be considered chronic and warrant intervention.[7] This is particularly applicable for the SSN and axillary nerve, which tend to recover earlier.[7] Electrodiagnostic testing, more specifically EMG, can provide valuable clinical information by demonstrating objectively when true neurological recovery has occurred. This can help clarify whether improvement in function is from nerve regeneration or recovery, because substitution patterns, the patient's varying degrees of effort, and other nonneurological factors can give the appearance that neurological recovery has occurred.

There are limitations to our study, including its small sample size, its nonrandomized, retrospective design, and our relatively short follow-up for 2 of patients after neurolysis. Nevertheless, among the patients with only 6 months' follow-up, one had reached 5 of 5 in the deltoid whereas the other had 4 of 5 strength in the flexor pollicis longus. Although patients were primarily assigned to treatment groups based on site, 4 declined surgery at site 1 and were treated nonsurgically, potentially introducing selection bias. Previous studies have established MRI and US as complimentary modalities, but we cannot draw new conclusions from this study about their relative abilities to detect constrictions because not all patients were imaged with both modalities.[3,18,22] To better understand the role that HGCs have in NA, it would be ideal to image the involved nerves with both MRI and US immediately after onset of the disease, to track the development of the pathological morphology. However, few patients present acutely to a specialty hospital with the capability to identify these lesions using high-resolution imaging.

The identification of focal nerve constrictions in a wide variety of nerves affected by chronic NA, and

the clinical and electrodiagnostic resolution of NA after surgical microneurolysis, help to draw an etiologic connection between focal constrictions and NA. These data support identification of FCs and HGCs using high-resolution MRI and/or US, and microsurgical management of patients with chronic, recalcitrant neuralgic amyotrophy.

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