Marrying Tendon and Nerve Gliding Exercises with Hydrodissection Following Injection for Carpal Tunnel Syndrome – A New Treatment Approach?

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Learning Point of the Article:
Pairing nerve hydrodissection with active tendon and nerve gliding exercises in patients with carpal tunnel syndrome receiving platelet-rich plasma injections may produce outcomes comparable to surgical release.

Abstract

Introduction: Hydrodissection has been used during injection procedures to liberate median nerve from surrounding adhesions. This investigation examined clinical and neurophysiologic impact of ultrasound-guided injections in patient with bilateral carpal tunnel syndrome (CTS) serving as own control. Novel to this investigation was performance of active tendon and nerve gliding exercises following median nerve hydrodissection and injection.

Case Report: A 37-year-old male with 6-year history of bilateral CTS presented for treatment. Wrists randomly assigned to receive platelet-rich plasma (PRP) or equal volume saline injection and median nerve hydrodissection. The patient performed active tendon and nerve gliding exercises following injection procedures. Pain ratings, CTS-related disability scores, median nerve function, and median nerve cross-section area measurements for each wrist/hand collected at baseline 2, 4, 6, and 12 months following injection procedures. 6-month follow-up. The right (saline) and left (PRP) wrists showed improvements in disability and nerve function. The left wrist (PRP) also showed improvement in pain. 1-year follow-up. The right (saline followed by PRP at 6 months) and left (PRP) wrists showed improvements in pain, disability, and nerve function.

Conclusion: Results suggest innovative treatment approach for CTS, namely, ultrasound-guided PRP injection including median nerve hydrodissection followed by performance of active tendon and nerve gliding exercises in immediate post-injection period. The patient demonstrated improvements in pain, CTS-related disability, and median nerve function comparable to surgical release and generally better than non-surgical interventions. Findings should stimulate further investigation into marrying mechanically based treatments with PRP to produce better long-term outcomes in patients with CTS.

Keywords: Electrodiagnosis, median neuropathy, physical therapy, ultrasonography.

Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy in the body [1, 2, 3, 4, 5] with an overall prevalence in the general population of 5.3% for women and 2.1% for men with certain occupations experiencing higher incidence [6, 7]. Patients with CTS complain of pain and paresthesia in the hand (often worse at night) that typically follows a median nerve distribution although symptom location varies and can include non-median innervated fingers or radiate proximally into the forearm or arm [4, 5, 8]. CTS is diagnosed based on patient history and physical examination findings [4, 5] with electrodiagnostic (EDX) testing [1, 2, 9, 10] and neuromuscular ultrasonography (NMUS) [11, 12, 13, 14, 15] routinely performed for the purposes of differential diagnoses and quantification of median nerve function and morphology. EDX testing, including neurography and needle electromyography (EMG), provides reliable and valid measures of median nerve function in patients with suspected CTS and can be used to classify...
severity of median neuropathy when present [1, 2, 10]. Point-of-
care NMUS allows for dynamic imaging of volar wrist structures
including median nerve morphology and cross-sectional area
(CSA) in addition to adjacent flexor tendons, vasculature, and
connective tissue [11, 12, 14, 15, 16, 17].

Treatment of CTS varies depending on symptom severity,
symptom duration, and patient preference [3, 8, 18, 19]. Carpal
tunnel release surgery is the most common wrist/hand surgery
performed in the USA with nearly 500 K annually and a total
economic cost exceeding $2 billion [3, 18]. Non-surgical treatment
approaches include physical therapy, splinting, NSAIDs, oral
steroids, and injection procedures [8, 19, 20, 21, 22, 23]. Physical
therapy often employs active tendon and nerve gliding exercises
[20, 24], which are mechanically based treatments seeking to
stimulate soft-tissue healing and improve median nerve
vascularization within the carpal tunnel [25, 26]. Tendon and nerve
gliding exercises can decrease edema, improve median nerve
mobility by reducing adherence of surrounding connective tissue,
and decrease nociception by decreasing concentrations of pro-
inflammatory substances and reduce peripheral and central
nervous system sensitization [3, 20, 22, 27]. In patients with CTS,
tendon and nerve gliding exercises may improve short- to mid-term
outcomes when combined with other treatments [7].

A variety of injection procedures has been to treat CTS. Steroid
injections are common and provide significant short- to mid-term
symptomatic relief in patients with mild-moderate disease but have
not been shown to provide long-term resolution [21, 23, 28, 29, 30,
31, 32] and likely have a negative impact on soft tissue and nerve
health overtime [23]. Given the limited long-term effectiveness of
steroid injections for treating CTS, recent investigations have
examined a variety of “biologic” compounds including platelet-rich
plasma (PRP) as a more suitable injectate because of the
demonstrated neuroregenerative and tissue healing effects [17, 31,
33, 34, 35, 36, 37, 38].

PRP is a safe and natural alternative to surgery for treating a variety of
soft-tissue injuries including neuropathy [35, 36, 37, 38]. Rich in
growth factors and cytokines with anti-inflammatory effects, PRP
promotes removal of degenerative and necrotic tissues and may
enhance soft-tissue healing and regeneration [34]. The potential for
PRP to provide permanent tissue healing and regeneration has
stimulated research into its use for a number of conditions including
CTS [31, 34, 35, 36, 38]. Recent studies have demonstrated the
beneficial healing effects of PRP on a variety of human tissues
including peripheral neuropathies like CTS [16, 30, 31, 32, 39, 40,
41, 42]. However, variation exists with regard to volume of injectate
used, injection approach (e.g., palmer vs. ulnar), and whether or not
median nerve hydrodissection was performed [31, 43, 44, 45, 46].

Debate exists over the value of performing median nerve
hydrodissection during an injection procedure for treating CTS
[43]. Several studies have demonstrated that in patients with CTS,
the sub-synovial connective tissue surrounding the median nerve
and adjacent tendons is thickened and fibrotic decreasing median
nerve mobility [25, 45, 47, 48]. This decreased mobility has been
hypothesized to exacerbate median neuropathy by making it more
susceptible to injury. Hydrodissection is used to liberate the median
erve from surrounding connective tissue adhesions, thereby
improving mobility, increasing vascularization, and stimulating
axoplasmic transport for improved nerve health [43, 44, 45, 46]. Wu
et al. [45] demonstrated the therapeutic value of median nerve
hydrodissection as a stand-alone treatment in patients with CTS but
it remains unclear if hydrodissection provides additional benefit
over injection alone [43].

This triple-blind case report examined the clinical and
neurophysiologic impact of US-guided injections, comparing
saline and PRP, in a patient with EDX confirmed bilateral CTS
serving as their own control. Novel to this investigation was the
addition of active tendon and nerve gliding exercises to median
nerve hydrodissection and injection.

**Case Report**

**Methods**

**Patient characteristics**

Subject: A 37-year-old male; BMI 27.7 (Height = 1.98 meters,
weight = 109 kg); right-handed; self-employed cable worker (i.e.,
heavy manual labor); reported daily tobacco and alcohol use. The
patient reported 6-year history of CTS worse on right. Prior
treatments included night splints and chiropractic 94 care. The
patient denied prior injection or surgery to either wrist/hand.

Following clinical and NMUS examinations, the patient consented
to undergo EDX testing, which confirmed bilateral CTS and
excluded other neuromuscular conditions. The patient consented
to study participation and was offered PRP injection in wrist that
received saline if PRP proved more effective at 6-month follow-up.

**Study design and procedures**

The study conducted in private outpatient orthopedic and sports
medicine clinic from early April 2018 to late March 2019. The
patient provided written informed consent before baseline data
collection, which included numeric pain rating scale (NPRS) and
Boston carpal tunnel questionnaire (BCTQ) scores for each
wrist/hand along with neurography and median nerve CSA
measurements of both wrists/hands. The patient instructed in
active tendon and nerve gliding exercises and provided a detailed
exercise handout and journal for immediate post-injection period.

**Injections**
Blood drawn and PRP prepared. Wrists randomly assigned to receive PRP or equal volume saline and blinded injections prepared. US-guided injections performed including median nerve hydrodissection. Following injections, wrists splinted and the patient provided verbal and written instructions for symptom management, avoidance of NSAIDs, and to begin prescribed exercises when symptoms allow.

**Follow-up visits**
Initial follow-up 2 months post-injection patient’s exercise journal collected and exercises discontinued. NPRS and BCTQ scores, neurography, and median nerve CSA measurements performed for each wrist/hand at 2, 4, and 6-month follow-up visits. Following data collection at 6-month follow-up wrists unblinded and injectate revealed. As previously discussed, if wrist that received PRP showed more improvement than wrist that received saline patient could elect to have PRP injection and encouraged to follow-up 6 months later (1 year since beginning of study). The patient would be prescribed same post-injection tendon and nerve gliding exercises.

**Patient-reported outcomes**

**NPRS**
Eleven-point pain scale with scores ranging from 0 “no pain” to 10 “worst imaginable pain” for current, best, and worst levels of pain over previous 24 h. Minimal clinically important difference (MCID) for NPRS is ~2.0 points [49]. Separate ratings collected for each wrist/hand.

**BCTQ**
CTS-related disability questionnaire consisting of an 11-question Symptom Severity Scale (SSS) and an 8-question Functional Status Scale (FSS). Scores in both scales range from 1 to 5 points with higher scores equating to more severe symptoms or higher levels of dysfunction and a value of 1 equating to the absence of symptoms or dysfunction. BCTQ has been shown to have good reproducibility, internal consistency, and validity in patients with CTS [50, 51, 52]. MCID for SSS is ~0.8 points and for FSS ~0.5 points [53, 54].

**Ultrasonography**
NMUS was conducted by a regenerative medicine physician with 30 years of clinical experience and who is registered in Musculoskeletal® sonography by the Alliance for Physician Certification and Advancement and was blinded to neurography findings and injection assignment throughout study. NMUS performed using GE Logiq P9 system (GE Healthcare, Chicago, IL, USA) with 12–15 MHz linear transducer. Short- and long-axis images obtained in each wrist and digitally stored including flexor retinaculum, flexor tendons, median nerve, carpal joints, and ulnar nerve in Guyon’s canal. Short-axis images stored of median nerve proximally at level of pronator quadratus muscle and distally at level of maximum enlargement for calculation of CSA using direct trace method inside echogenic epineurium [55].

For the purposes of classification, increase in median nerve CSA of >2 mm² comparing distal to proximal values considered diagnostic of CTS with 99% accuracy [15]. In addition, increase of median nerve CSA of ≥6 mm² suggests “moderate” disease and ≥9 mm² suggests “severe” disease.

**Electrodiagnosis**
EDX testing was conducted by a physical therapist with 20 years of clinical experience and who is Board Certified in Clinical Electrophysiology by the American Board of Physical Therapy Specialties and was blinded to NMUS findings and injection assignment throughout study. EDX testing was performed using Cadwell Sierra Wave system (Cadwell Laboratories, Kennewick, WA, USA). The patient underwent standardized peripheral sensory and motor neurography of median and ulnar nerves including F waves [9]. Monopolar needle EMG was performed in both upper extremities analyzing resting and volitional muscle activity representing C5-T1 nerve roots.

For the purposes of classification, prolonged distal sensory latency (DSL) only considered “mild” CTS; prolonged DSL and distal motor latency (DML) considered “moderate” CTS; and significantly prolonged or absent DSL and DML and abnormal EMG activity in the abductor pollicis brevis muscle considered “severe” CTS.

**Injection procedures**

**PRP preparation**
Thirty milliliters (mL) whole blood drawn from antecubital vein using ENDORET® Technology (BTI Biotechnology Institute, Blue Bell, PA, USA) yielding 8.0 mL of plasma-rich growth factors containing 2–3 times baseline concentration of platelets with low red and white blood cell counts. Calcium chloride (0.02 cc/mL) added to preparation before injection.

**US-guided injections**
The patient seated with forearms supinated, palms facing up, and
wrists extended over towel roll. Using in-plane approach, median nerve identified at inlet of proximal carpal tunnel at a level of pisiform bone [55] and ulnar artery identified using Doppler imaging. A 25-gauge needle passed from ulnar side of wrist toward median nerve. Each wrist received 8 mL total injection volume and underwent median nerve hydrodissection from superficial flexor retinaculum and underlying sub-synovial connective tissue. Median nerve in the right wrist adhered more strongly to surrounding soft tissues and required 6 mL of injectate to achieve hydrodissection, whereas the left wrist median nerve required 3 mL of injectate to achieve hydrodissection. Following injection, carpal tunnel visualized in long-axis ensuring proximal-to-distal diffusion of injectate occurred. The patient observed post-procedure for 20 min and provided verbal and written instructions to avoid use of NSAIDs, apply ice for 10–15 min hourly as needed for pain relief, and begin prescribed exercises when symptoms allow.

**Exercise prescription**

The patient provided verbal and written instructions along with printed illustrations for performance of the following exercises in each wrist/hand: Index and middle finger tendon gliding and median nerve gliding (Fig. 1); cervical retraction and scapular retraction (Fig. 2). The patient instructed to perform exercises until 2-month follow-up visit and was provided an exercise journal to record compliance.

**Results**

Baseline diagnostic testing suggested right median nerve more involved than left being classified as “moderate-severe” compared with “moderate” CTS, respectively (Fig. 3). At 6-month follow-up, it was revealed that the right wrist received saline and left wrist PRP.
Results for pain ratings, CTS-related disability, neurography, and CSA measurements from baseline through 1-year presented in (Table 1, 2) for the right and left wrists, respectively. Note that the right wrist, which initially received saline, subsequently received PRP approximately 1 month (Nov 2, 2018) following the 6-month follow-up visit (October 2, 2018).

6-month follow-up

The right wrist (saline) showed significant improvements in FSS score along with appearance of previously absent median sensory response and improved median DML and amplitude beginning at 2 months (Table 1). The left wrist (PRP) showed significant improvements in worst pain beginning at 4 months, improvements in SSS and FSS scores beginning at 2 months, and modest improvements in median DSL and amplitude beginning at 2 months (Table 2).

1-year follow-up

The right wrist (saline, PRP at 6 months) showed significant improvement in worst pain along with continued improvements in SSS and FSS scores. Previously absent median sensory response appearing 2 months following saline injection remained unchanged in DSL but showed 112% increase in amplitude. Median DML gradually improved overtime beginning 2 months after saline with amplitude relatively unchanged following PRP (Table 1). The left wrist (PRP) showed persistence of previously observed improvements or continued improvements in worst pain, SSS, and FSS scores. Median DSL maintained previously observed improvement in contrast to amplitude that increased 94% compared to 6-month follow-up (Table 2). No significant changes observed in median nerve CSA in either wrist throughout study. The patient denied taking additional medications or receiving additional therapies beyond those prescribed throughout study. No adverse side effects or nerve injury observed or reported for either wrist throughout study.

Discussion

This triple-blind case report examined the clinical and neurophysiologic impact of US-guided carpal tunnel injections, comparing saline, and PRP, in a patient with EDX confirmed bilateral CTS serving as their own control over a 1-year follow-up period. This is the first investigation marrying active tendon and nerve gliding exercises to median nerve hydroadissection in the immediate post-injection period regardless of injectate. We theorized that combining mechanically based treatments would result in better long-term outcomes by promoting median nerve healing and regeneration regardless of injectate. Furthermore, we theorized that combining mechanically based treatments with PRP injection would further stimulate median nerve healing and regeneration by pairing therapeutic movement with an environment rich in growth factors leading to reduced symptoms and improved function [20, 22, 24, 26, 31]. Our hypotheses were borne out in this case report based on the magnitude of improvement in pain, CTS-related disability, and median nerve function which persisted for 1-year.

Although injecting PRP was more effective than saline for reducing pain, reducing CTS-related disability, and improving aspects of median nerve function at 6 months, meaningful improvements were observed in the wrist receiving saline for CTS-related disability and median nerve function at 6 months, which may in part be explained by the therapeutic effects performing active tendon and nerve gliding exercises following median nerve hydroadissection.

### Table 1: Patient data for the right wrist that received saline from baseline through 6-month follow-up (October 2, 2018), and then PRP (~1 month later on November 1, 2018) through 1-year follow-up.

| Variables | Baseline (saline) | 2 months (saline) | 4 months (saline) | 6 months (saline) | (Baseline PRP) | 1 year (6-month PRP) |
|-----------|------------------|------------------|------------------|------------------|----------------|------------------|
| NPRS scores | 1                | 1                | 0                | 1                | 0              | 0                |
| Worst (0-10) | 4                | 3                | 4                | 3                | 2              | 2                |
| Best (0-10) | 1                | 1                | 0                | 0                | 0              | 0                |
| BCTQ scores | 2                | 2                | 1                | 1                | 1              | 1                |
| SSS (1-5) | 2.9             | 2.5             | 2.9             | 2.5             | 2.3           | 1.6             |
| FSS (1-5) | 2                | 1.3             | 1.3             | 1.4             | 1.1           | 1.1             |
| Neurography |                  |                  |                  |                  |                |                  |
| DSL (mm) | NR               | 5.5             | 5.5             | 5.5             | Not tested     | 5.5             |
| Amplitude (uV) | NR             | 5.2             | 5.2             | 5.2             | 11             | 11              |
| DML (ms) | 6.6             | 6.1             | 5.8             | 5.5             | 5.3           | 5.3             |
| Amplitude (mV) | 3.4            | 8.7             | 8.1             | 7.4             | 8.4           | 8.4             |
| CSA | 22               | 22              | 22              | 22              | 21            | 21              |
| Difference (mm²) | 10             | 11              | 13              | 12              | 10            | 10              |

### Table 2: Patient data for the left wrist that received PRP from baseline through 1-year follow-up.

| Variables | Baseline | 2 months | 4 months | 6 months | 1 year |
|-----------|----------|----------|----------|----------|--------|
| NPRS scores | 1        | 1        | 0        | 0        | 0      |
| Worst (0-10) | 4        | 3        | 4        | 3        | 2      |
| Best (0-10) | 1        | 0        | 0        | 0        | 0      |
| BCTQ scores |          |          |          |          |        |
| SSS (1-5) | 2.8      | 1.5      | 1.6      | 1.1      | 1      |
| FSS (1-5) | 1.9      | 1        | 1        | 1        | 1      |
| Neurography |          |          |          |          |        |
| DSL (mm) | 4.9      | 4.7      | 4.6      | 4.5      | 4.5    |
| Amplitude (uV) | 6.2      | 8.3      | 8.9      | 9.5      | 18.4   |
| DML (ms) | 4.5      | 4.4      | 4.4      | 4.4      | 4.5    |
| Amplitude (mV) | 7.2      | 9.5      | 9.5      | 7.5      | 7.4    |
| CSA | 15       | 12       | 17       | 16       | 14     |
| Difference (mm²) | 7        | 4        | 9        | 7        | 6      |

MCID ~2.0 points; MCID ~0.8 points (score of 1 equates to 2; MCID ~0.5 points (score of 1 equates to 2); MCID ~0.5 points (score of 2 equates to 4); MCID ~0.5 points (score of 4 equates to 8); MCID ~0.5 points (score of 8 equates to 16); MCID ~0.5 points (score of 16 equates to 32).

Abbreviations: BCTQ=Boston carpal tunnel questionnaire; CSA=Cross-sectional area; DML=Distal motor latency; DSL=Distal sensory latency; FSS=Functional status scale; mm²=Millimeters squared; ms=MILLISECONDS; mV=Millivolts; NPRS=Numeric pain rating scale; SSS=Symptom severity scale; uV=Microvolts.
Median nerve hydrodissection has been shown to provide therapeutic benefits independent of injectate. Wu et al. [45], in a randomized trial investigating US-guided median nerve hydrodissection in patients with mild-moderate CTS, demonstrated significant improvements in CTS-related disability and median nerve CSA with modest improvements in median nerve function at 6 months compared to control. The authors highlighted the role that pathological edema and inflammatory-driven synovial thickening play in pathogenesis of CTS by increasing carpal tunnel pressure and reducing median nerve mobility. They concluded that median nerve hydrodissection is a simple, minimally invasive procedure that can be effectively accomplished using saline and provides therapeutic benefit in patients with mild-moderate CTS. Given these results, it would appear that the theoretical rationale has been established for combining median nerve hydrodissection with active tendon and nerve gliding exercises in patients with CTS.

To the best of our knowledge, this case report is the first investigation of PRP for treating CTS with a 1-year follow-up. Wu et al. [42], in a single-blind clinical trial compared PRP with night splints in 60 patients with mild-moderate unilateral CTS, demonstrated significant improvements in pain, CTS-related disability, and median nerve CSA at 6 months. Because our study utilized similar methods and outcome measures, comparing our findings with those of Wu et al. is instructive. Both studies performed US-guided median nerve hydrodissection and PRP injection, although our injection volume was larger (8 mL vs. 3 mL, respectively). Baseline pain was higher in their study (6/10 vs. 4/10, respectively) with similar scores observed at 6 months (2/10 and 1/10, respectively). CTS-related disability was similar at baseline for both studies (45 points and 46 points, respectively) with similar scores observed at 6 months (25 points and 20 points, respectively). Median nerve function was similar at baseline in both studies and both studies observed modest but insignificant improvements overtime. In contrast to our study, Wu et al. showed significant improvements in median nerve CSA at 6 months (14 mm² reduced to 11 mm²) while our study showed a 1 mm² increase. Overall, our findings were similar at 6 months with observed improvements in pain, CTS-related disability, and median nerve function persisting or improving at 1 year.

Shi et al. [56], in a systematic review and meta-analysis, compared short- and long-term outcomes of surgical and non-surgical interventions for treating CTS. For CTS-related disability following surgery, they found an average SSS of 1.1 at 6 months and 1.6 points at 1 year; following non-surgical interventions, these values were 1.9 at 6 months and 1.8 points at 1 year. In our study, SSS for the left wrist (PRP) was 1.0 at 6 months and 1 year; the right wrist these values were 1.4 points at 6 months (saline) and 1.0 point at 1 year (6 months following PRP). Finally, Shi et al. found that the average improvement in median sensory latency at 6 months was −1.1 ms following surgery and −0.5 ms following non-surgical interventions. In our study, improvement in median sensory latency at 6 months for the left wrist (PRP) was −0.4 ms; the right wrist (saline) improved from no response to 5.5 ms at 2 months and remained unchanged at 6 months (no improvement 6 months following PRP). Overall, our results for CTS-related disability were comparable to or better than surgery. Notably, the persistence of our results at 1 year may be associated with the addition of active tendon and nerve gliding exercises following median nerve hydrodissection and PRP.

**Conclusion**

This triple-blind case report demonstrated that US-guided PRP injection is safe and effective for treating CTS over a 1-year follow-up period. In addition, this investigation suggests an innovative approach for the minimally invasive treatment of CTS, namely, US-guided PRP injection with median nerve hydrodissection combined with active tendon and nerve gliding exercises performed during the immediate post-injection period. Our subject demonstrated improvements in pain, CTS-related disability, and median nerve function comparable to surgical release and generally better than non-surgical interventions [56] despite having generally more severe disease than previously published reports. These findings should stimulate further investigation into marrying mechanically based treatments with PRP to produce better long-term outcomes in patients with CTS. Future research is recommended with sufficient statistical power to investigate the possible 3-way interaction between PRP injection with median nerve hydrodissection paired with performance of active tendon and nerve gliding exercises overtime in patients with CTS.

**Clinical Message**

This case report suggests an innovative approach for the minimally invasive treatment of CTS, namely, US-guided PRP injection with median nerve hydrodissection combined with active tendon and nerve gliding exercises performed during the immediate post-injection period.
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