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RESEARCH ARTICLE

# Single injection of platelet-rich plasma as a novel treatment of carpal tunnel syndrome

**Michael Alexander Malahias[1], Elizabeth O. Johnson[2], George C. Babis[1], Vasileios S. Nikolaou[1,*]**

1 Second Department of Orthopedics, Athens University, Athens, Greece
2 Department of Anatomy, School of Medicine, Athens University, Athens, Greece

***Correspondence to:**
*Vasileios S. Nikolaou, M.D., Ph.D., vassilios.nikolaou@gmail.com.*

***orcid:***
*0000-0001-7422-4195 (Vasileios S. Nikolaou)*

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## Abstract

Both *in vitro* and *in vivo* experiments have confirmed that platelet-rich plasma has therapeutic effects on many neuropathies, but its effects on carpal tunnel syndrome remain poorly understood. We aimed to investigate whether single injection of platelet-rich plasma can improve the clinical symptoms of carpal tunnel syndrome. Fourteen patients presenting with median nerve injury who had suffered from mild carpal tunnel syndrome for over 3 months were included in this study. Under ultrasound guidance, 1–2 mL of platelet-rich plasma was injected into the region around the median nerve at the proximal edge of the carpal tunnel. At 1 month after single injection of platelet-rich plasma, Visual Analogue Scale results showed that pain almost disappeared in eight patients and it was obviously alleviated in three patients. Simultaneously, the disabilities of the arm, shoulder and hand questionnaire showed that upper limb function was obviously improved. In addition, no ultrasonographic manifestation of the carpal tunnel syndrome was found in five patients during ultrasonographic measurement of the width of the median nerve. During 3-month follow-up, the pain was not greatly alleviated in three patients. These findings show very encouraging mid-term outcomes regarding use of platelet-rich plasma for the treatment of carpal tunnel syndrome.

***Key Words:*** *nerve regeneration; carpal tunnel syndrome; platelet-rich plasma; ultrasound guidance; pilot study; neural regeneration*

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## Introduction

Carpal tunnel syndrome (CTS) can be treated by both conservative (Klauser et al., 2009) and surgical interventions. Surgical decompression of the median nerve through the incision of the transverse carpal ligament (either open or mini-open or under ultrasound guidance) is the most cost-effective therapeutic option (Hui et al., 2005). However, mild to moderate CTS can be treated by conservative interventions, like functional braces and local infiltrations (Prime et al., 2010) in the carpal tunnel, mainly with corticosteroids. Local infiltration of corticosteroids easily leads to atrophy of the median nerve, subcutaneous fat, and systematic complications, such as hair loss and Cushing syndrome (Lambru et al., 2012). This treatment option is clearly inferior to surgical intervention despite the fact that it can improve clinical condition. There is evidence that local infiltration of corticosteroids is not superior to local injection of anesthetic (Karadas et al., 2012). To the best of our knowledgement, use of corticosteroids in the clinical practice has not been studied. However, a surgical treatment decision is always taken by the patient who sometimes wants to delay or avoid the surgery because of psychological or medical concerns including allergy to local anesthetic and immune deficiency and prefers a conservative treatment in the initial stage. A conservative treatment has been considered insufficient for CTS. *In vitro* and *in vivo* clinical and laboratory studies (Allampallam et al., 2000; Farrag et al., 2007; Cho et al., 2010; Anjayani et al., 2014; Park and Kwon, 2014) have demonstrated that platelet-rich plasma (PRP) has therapeutic action in several neuropathies. It would be interesting if a PPP injection is used as an alternative conservative treatment of CTS. The purpose of this study was to investigate if, and to what extent, a PPP injection, under ultrasound guidance, can improve the clinical condition of patients with CTS.

## Materials and Methods

Fourteen patients were selected from initial 32 patients who received treatment in the Department of Orthopedics of "Konstantopouleio" General Hospital, Greece because of mild to moderate CTS, with a minimum of 3-month duration of symptoms, regardless of age and gender. Patients were rejected if they had one of the following items: thrombopenia, platelet dysfunction, local infection, NSAID use (less than 48 hours prior to injury), recent illness, malignancy, hemoglobin (Hb) level $< 100$ g/L, pregnancy, rheumatologic disease, uncontrolled hormonal disorder, vibrating caused neuropathy, systematic inflammatory disease, polyneuropathy, inability to complete questionnaires (due to language unawareness or mental disability), addicted to alcohol or drugs, total loss of sensation in the fingers, prior corticosteroid injection in the same wrist, had undergone a surgical intervention for CTS in the same hand, neurological deficit,

**Table 1 General data and outcome measures of patients**

| Patient No. | Gender | Age (year) | Q-DASH prior to injection | QDASH (1 month later) | Q-DASH (3 months later) | VAS prior to injection | VAS 1 month later | VAS 3 months later |
|---|---|---|---|---|---|---|---|---|
| 1 | Female | 40 | 82.5 | 27.5 | 0 | 90 | 30 | 0 |
| 2 | Female | 56 | 30.0 | 7.5 | 0 | 60 | 0 | 0 |
| 3 | Female | 75 | 32.5 | 2.5 | 2.5 | 80 | 20 | 20 |
| 4 | Female | 75 | 32.5 | 32.5 | 32.5 | 80 | 80 | 80 |
| 5 | Female | 67 | 87.5 | 32.5 | 0 | 80 | 40 | 0 |
| 6 | Female | 47 | 40.0 | 17.5 | 5.0 | 80 | 40 | 10 |
| 7 | Female | 46 | 90.0 | 7.5 | 7.5 | 100 | 10 | 10 |
| 8 | Female | 77 | 45.0 | 15.0 | 15.0 | 60 | 20 | 20 |
| 9 | Male | 62 | 37.5 | 37.5 | 37.5 | 80 | 80 | 80 |
| 10 | Female | 42 | 72.5 | 7.5 | 7.5 | 80 | 0 | 0 |
| 11 | Female | 62 | 87.5 | 0 | 0 | 100 | 0 | 0 |
| 12 | Female | 80 | 100 | 12.5 | 12.5 | 80 | 0 | 0 |
| 13 | Female | 58 | 12.5 | 5.0 | 5.0 | 30 | 0 | 0 |
| 14 | Female | 75 | 40.0 | 40.0 | 40.0 | 70 | 70 | 70 |
| Mean rate | 92% Female | 61.5 | 564.2 | 17.5 | 11.78 | 76.4 | 27.8 | 20.7 |

Q-DASH: The disabilities of the arm, shoulder and hand (DASH) questionnaire; VAS: visual analogue scale.

**Table 2 Sonographic measurement of the cross sectional areas (CSA, cm²) of the median nerve and the delta CSA prior to and 1 month after platelet-rich plasma (PRP) infiltration**

| Patient No. | CSAa prior to PRP injection | CSAb prior to PRP injection | Delta CSA (CSAb – CSAa) prior to PRP injection | CSAa 1 month after PRP injection | CSAb 1 month after PRP injection | Delta CSA (CSAb – CSAa) 1 month after PRP injection |
|---|---|---|---|---|---|---|
| 1 | 0.06 | 0.11 | 0.05 | 0.05 | 0.08 | 0.03 |
| 2 | 0.07 | 0.11 | 0.04 | 0.05 | 0.05 | 0 |
| 3 | 0.04 | 0.07 | 0.03 | 0.06 | 0.05 | 0.01 |
| 4 | 0.05 | 0.08 | 0.03 | 0.03 | 0.06 | 0.03 |
| 5 | 0.06 | 0.09 | 0.03 | 0.06 | 0.06 | 0 |
| 6 | 0.07 | 0.16 | 0.09 | 0.07 | 0.10 | 0.03 |
| 7 | 0.08 | 0.15 | 0.07 | 0.07 | 0.15 | 0.08 |
| 8 | 0.05 | 0.12 | 0.07 | 0.05 | 0.07 | 0.02 |
| 9 | 0.07 | 0.13 | 0.06 | 0.07 | 0.13 | 0.06 |
| 10 | 0.09 | 0.12 | 0.03 | 0.07 | 0.04 | 0.03 |
| 11 | 0.04 | 0.08 | 0.04 | 0.04 | 0.04 | 0 |
| 12 | 0.05 | 0.12 | 0.07 | 0.04 | 0.09 | 0.05 |
| 13 | 0.05 | 0.17 | 0.12 | 0.04 | 0.07 | 0.03 |
| 14 | 0.05 | 0.12 | 0.07 | 0.10 | 0.05 | 0.05 |
| Mean rate | 0.06 | 0.11 | 0.05 | 0.05 | 0.07 | 0.03 |

The mean CSAb that we measured in the tunnel inlet was decreased from 0.11 to 0.07 cm² after PRP injection. This means that the mean size of the initially swollen median nerve was minimized after our treatment. CSAa: Proximal; CSAb: inlet.

cervical radiculopathy and/or cervical spinal stenosis and/or intervertebral disc herniation, nerve entrapment syndrome in the same hand.

From the initial 32 patients, three patients who had concomitant pain that derived from cervical spine disorder, one patient who showed other nerve compression unilaterally, one patient with thrombopenia, two patients with rheumatic diseases, two patients with uncontrolled hormonal disorder, and one pregnant patient were excluded. In addition, two patients who had received local infiltration of corticosteroids and one patient who failed in surgical intervention for CTS were also excluded (**Figure 1**).

The remaining 19 patients were examined clinically using Phalen and Tinnel tests (Bozek and Gazdzik, 2001) and underwent diagnostic ultrasonography for measurement of the width of the median nerve (delta CSA, as the difference – delta-between the cross sectional areas – CSA-proximal to the carpal tunnel and at the tunnel inlet) and electromyogram.

The ultrasonography was performed with a portable gray scale ultrasound machine (frequency of 10–12 MHz, A6 Portable Ultrasonic Diagnostic System, Sonoscape Company Limited, Shenzhen, China). The patients were informed with an oral and written manner for their options of treatment and they received clear explanations about the treatment with PRP that was recommended as an alternative to surgery.

For confirmation, they signed full written consent. Thus, 14 out of 19 patients who chose treatment with PRP instead of surgical intervention were included in this study. Our study protocol with written informed consent was approved by the Scientific Committee, Health Institution, School of

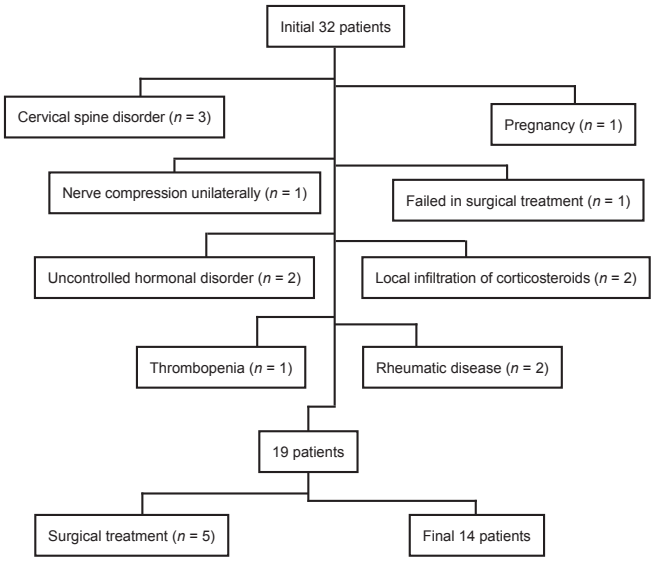


**Figure 1 Flow chart of patient selection.**

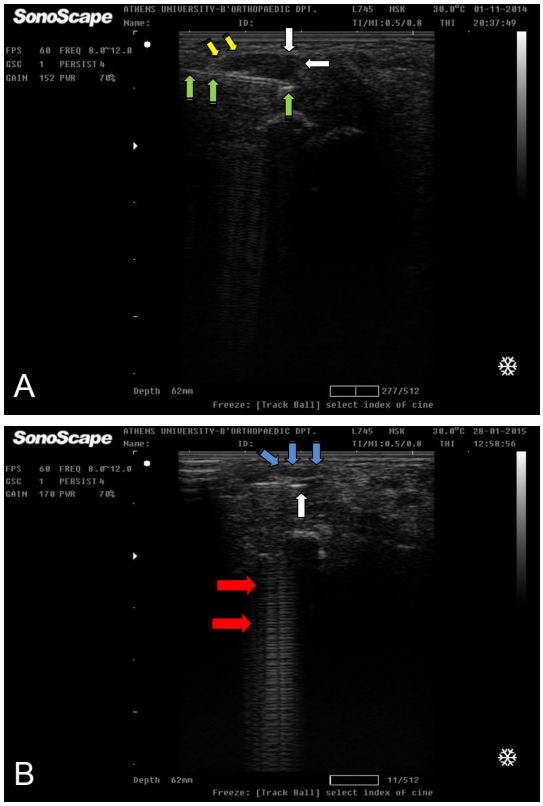


**Figure 2 Ultrasound-guided injection of PRP.**
(A) Injection of PRP around the median nerve (oval shape, honeycomb like, blue arrows) in a transverse plane at the carpal tunnel inlet. The tip of the needle (white arrow) with its acoustic shadowing (red arrows) is visible under the median nerve. (B) Injection of PRP (green arrows) at the opposite site (radial) of the needle insertion (ulnar approach). At the end of the infiltration, the hypoechoic swollen median nerve (oblique yellow arrows) is successfully hydrodissected (PRP: anechoic area, marked with the white arrows). PRP: Platelet-rich plasma.

Medicine, Athens University, Greece. Venous blood samples were obtained from subjects according to the World Medical Association outlined in the *Declaration of Helsinki*.

The severity of patient's clinical symptoms was estimated using the disabilities of the arm, shoulder and hand (DASH) questionnaire (Q-DASH; Greenslade et al., 2004) and visual analogue scale (VAS) score (0–100 mm; Karadag et al., 2010) before infiltration. Under sterile condition, 20 mL of autologous venous blood sample was taken from each patient's contralateral (non-affected) hand and then centrifuged at two consecutive density gradient centrifugations (total 3,100 runs for 10 minutes) at the laboratory of our hospital. At the first centrifugation, red blood cells were separated, and at the second centrifugation, PRP was separated from the platelet poor plasma (PPP) and then transferred to sterile tubes. The infiltration was done under sterile conditions (skin sterilization, ultrasound probe covered with sterile pad, use of appropriate gel) by a physician who simultaneously managed the ultrasound device (free hand one-man technique: a single doctor holds the syringe with one hand while he scans by moving the probe with the other hand). Under continuous imaging of the tip of the needle, the syringe was put around the median nerve at the proximal edge of the carpal tunnel (ulnar insertion of the needle (Smith et al., 2008)) where the infiltration of PRP (1–2 mL) was performed (**Figure 2A**).

The patients were encouraged to return to their daily activities immediately. Short-term outcomes were estimated and the width of the median nerve at its entry at the carpal tunnel measured by the ultrasound was compared between before and after infiltration of PRP. Short- (4 weeks) and mid-term (12 weeks) outcomes were estimated using Q-DASH and the pain scale VAS. One physician (resident) did the procedure in all patients and evaluated them prior to the PRP injection using VAS and Q-DASH. Another physician (consultant) performed the ultrasonographic evaluation by measuring the difference –delta CSA in cross sectional areas of the median nerve (Klauser et al., 2009) before and after PRP injection in all patients. A third physician (another resident) evaluated the patients during the follow-up period (VAS, Q-DASH). This physician was blinded to the procedure (PRP injection) and to the pre-injection scores of these patients. Instructions for return to work (or usual activities in elderly people) were identical in all patients.

## Results

PRP injection proved to be well tolerated, with no side effects, infections or complaints for persistent pain. We achieved well defined ultrasonographic mobilization, hydrodissection and hydrodisolution (**Figure 2B**) of the compressed median nerve through PRP simple injection.

At the end of the first month after PRP injection, the mean reduction in VAS (%) was 48.6 mm out of 100 mm in comparison to rates prior to injection. At that time, we found eight patients with full or almost full recovery (VAS: 0 – 20 mm) and three patients with great improvement (VAS decline: more than 30 mm). The mean decline of the Q-DASH score was calculated just a little less than 70% compared to the pre-injection rates (from mean Q-DASH 56.42 prior to injection to mean Q-DASH17.5 one month after). These rates slightly more improved 3 months later (**Table 1**).

At 1 month after PRP injection, we performed a new ultrasound measurement of delta CSA of the median nerve and found no ultrasonographic findings of the CTS in five patients (delta CSA: 0–0.02 cm²). We also found that delta CSA or CSAb was reduced in five patients; delta CSA was not changed after injection in three patients compared to prior to injection; delta CSA was increased after injection in one patient (**Table 2**). At 3 months of follow-up period, poor or fair improvement was found in three patients (VAS decline less than 30 mm) and an open operation for CTS was performed.

## Discussion

One double-blind randomized controlled clinical trial was reported on perineural administration of PRP in 60 patients with Hansen's disease (Anjayani et al., 2014), and positive outcomes of sensory symptoms were obtained. In another *in vitro* study, the effects of four growth factors on the transformation of cells from the impaired transverse ligament were investigated in patients with CTS using microscopy (Allampallam et al., 2000).

Three animal experimental studies also confirmed that neural tissue regeneration is attributable to PRP infiltration (Allampallam et al., 2000; Farrag et al., 2007; Cho et al., 2010; Anjayani et al., 2014; Park and Kwon, 2014). Of note, the first two studies were about regeneration of the facial nerve (the former in rats, and the latter in new guinea pigs), the last and more recent study referred to an artificially made model of CTS (Yoshii et al., 2011) at the median nerve of rabbits by infiltration of 10% dextrose (Park and Kwon, 2014). Our results showed that PRP protected patients with CTS. To the best of our knowledge, this is the first published clinical study regarding PRP injection in patients with CTS.

A limitation of our study is the small number of patients, because this is a pilot study. This choice is deliberate and was done for ethical reasons, despite the fact that there are *in vitro* and *in vivo* data from animal or laboratory studies that are in favor of our hypothesis. We deal with a rather not extensively investigated field of clinical application (Malahias et al., 2014) that would not ethically justify the direct planning and performance of a study with many patients.

To conclude, our study showed very encouraging mid-term results (12 weeks) regarding use of PRP for treatment of CTS. Based on our results, we recommend the planning and performance of a randomized double-blind controlled clinical trial to confirm the possible favorable use of PRP in patients with mild to moderate CTS.

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**Author contributions:** *MAM conducted this survey and wrote the paper. He also performed the single ultrasound-guided injection in all patients and evaluated them prior to injection using VAS and Q-DASH. VSN was in charge of ultrasonographic evaluation before and after the injection in all patients and revised the paper. EOJ retrieved the literature and evaluated the patients using VAS and Q-DASH. GCB supervised the whole study. All authors approved the final version of this paper.*

**Conflicts of interest:** *None declared.*

**Plagiarism check:** *This paper was screened twice using Cross-Check to verify originality before publication.*

**Peer review:** *This paper was double-blinded, stringently reviewed by international expert reviewers.*

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