Invited lecture/Review

New Insights into Treatment of Patients with Carpal Tunnel Syndrome

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Abstract:
Carpal tunnel syndrome (CTS) is caused by median neuropathy at wrist. Clinically is present with paraesthesia in the first three or four fingers which are more pronounced during the night and at the morning and are improved by shaking or changing the position of the hand. Diagnosis is made by clinical examination and confirmed with nerve conduction studies (NCS). Conservative treatment with wrist splints, physiotherapy and corticosteroid injections are often ineffective or have only short-term effect. Furthermore, corticosteroids injections known to have potential side effects.
Surgical treatment with open surgery or endoscopic release are only known to have long-term effect. However, iatrogenic injuries, scar formation, immobilisation and long rehabilitation is frequently present. Perineural injection therapy with 5% dextrose is highly effective for treatment of patients with CTS. Nevertheless, studies showed only short-term effect. For long-term effect, surgical treatment is advised. US guided minimally invasive carpal tunnel release is promising approach into treatment of patients with CTS with many advantages. It is true US guided procedure, it offers identification of key anatomical structures, only local anaesthesia is required, no tourniquet, immobilisation, wound or sutures or scar formation is present. Therefore, perineural injection therapy with 5% dextrose for short-term effect and US guided minimally invasive carpal tunnel release for long-term effect is recommended.

Keywords: Carpal tunnel syndrome; Treatment; Perineural injection; 5% dextrose; US guided minimally invasive carpal tunnel release

1. Introduction

Carpal tunnel syndrome (CTS) is caused by compression of the median nerve at wrist (Olney, 2001). The reported prevalence and incidence of CTS vary widely according to the diagnostic criteria used in different studies. According to some estimations one in ten people develop clinical signs and symptoms of CTS (Quality Standards Subcommittee of the American Academy of Neurology, 1993). CTS mostly affect women with mean age at diagnosis 50 years. However, these data are based on patients who self-referred to a neurophysiological laboratory or clinic and are therefore intrinsically biased (Stevens, 1997; Jablecki et al., 1993). Results of a postal survey of 3000 individuals randomly selected from the general population register of southern Sweden showed that the prevalence of CTS was similar in men and women with male to female ratio 1:1.4) (Atroshi et al., 1999). However, prevalence was highest in women aged 65–74 years and the prevalence in women was almost four times higher than in men (5.1% vs 1.3%, respectively). Suspected risk factors include diabetes mellitus, menopause, hypothyroidism, obesity, arthritis, and pregnancy (Shiri, 2014; Padua et al., 2010; Pourmemari and Shiri, 2016; Shiri et al., 2015).

The importance of clinical presentation is demonstrated by the fact that the long-accepted gold standard for diagnosis is a comprehensive and accurate clinical history along with the exclusion of other possible causes. The CTS is characterized by intermittent, nocturnal paraesthesias and dysaesthesias that increase in frequency during waking hours (Padua et al., 1999). Subsequently, loss of sensation develops along with weakness and thenar muscle atrophy later in the disease course, which result from extensive axonal degeneration (Padua et al., 1999). This sequence of symptoms is quite typical, rarely occurring in disorders other than CTS. Tinel's sign and Phalen's maneuver are popular diagnostic tests. Results are deemed positive when symptoms are evoked by percussion of the median nerve at the wrist or by forced compressive wrist posture for 1 min, respectively (Brüske et al., 2002). Although these tests are widely used because of ease of performance, their sensitivity and specificity are widely debated. Sensitivity ranges from 42% to 85% for Phalen's maneuver and from 38% to 100% for Tinel's test; specificity ranges from 54% to 98% and from 55% to 100%, respectively (Brüske et al., 2002).

Diagnosis is usually made by clinical examination with presence of typical CTS symptoms. Abnormal findings have lower sensitivity (Mackinnon et al, 2000) but higher specificity (Mackinnon et al, 2000; Gomes et al., 2006) in comparison to symptoms. Clinical diagnosis is confirmed with electrodiagnostic testing (i.e., nerve conduction studies). Extensive work by three US scientific societies (the American Academy of Neurology, the American Association of Electrodiagnostic Medicine and the American Academy of Physical Medicine and Rehabilitation) have provided physicians with recommendations for electrophysiological testing. These recommendations suggest performing median sensory and motor nerve conduction studies across the wrist and in case of normal tests performing comparative, segmental, or comparative and segmental tests, which have been shown to have high sensitivity and specificity (80–90% and >95%, respectively) (Jablecki et al., 2002). When clinical signs are present without electrodiagnostic abnormalities CTS is functionally mild, although there might be severe symptoms.

Various non-surgical treatments are available for management of CTS. The first choice should include patient's education (Huisstede et al., 2014). Changes in habits (eg, limitation of wrist movement and reduction of heavy work activities) should be considered and the use of ergonomically friendly work tools can be useful in reducing median nerve stress. However, there is little adequate evidence about the success of this approach. For example, the effectiveness of ergonomic keyboards in the treatment of CTS is unknown (Buchan and Amirfeyz, 2013; O'Connor et al., 2012). Apart from these interventions, patients should be informed about the standard surgical and non-surgical strategies for treating CTS. Surgical treatment consists of releasing transverse carpal ligament with open surgery or minimally invasive procedures (i.e. endoscopic technique).

2. Non-surgical treatment

Different methods of laser therapy exist. This term encompasses several approaches. Laser therapy is able to improve function, symptoms, and electrodiagnostic measures in short-term. Results of a randomized controlled study showed that laser treatment is more effective than placebo, especially if it is used in patients with mild to moderate CTS (Lazovic et al., 2014). In another study use of the galliumaluminium-arsenide laser with wrist splint showed higher efficacy than placebo laser therapy with wrist splint, especially in improvement of hand grip strength up to 3 months after treatment (Fusakul et al., 2014). However, results of another randomized trial (Tascioglu et al., 2012) showed that laser therapy was not more effective than placebo. Several studies have compared laser therapy with other non-surgical treatments. In a randomised controlled trial comparing laser therapy with fascial manipulation, laser therapy provided transient, short-term pain relief, whereas fascial manipulation showed pain improvement and function (BCTQ) over a longer time period (>3 months) (Pratelli et al., 2015). In another study, high-intensity laser therapy was compared with TENS. Findings showed that laser therapy was more effective than TENS (Casale et al., 2013). In a study comparing low-level laser therapy with magnetic field therapies, the effectiveness of the techniques in reducing pain was shown to be similar (Dakowicz et al., 2011).

Local corticosteroid injections are commonly used to treat CTS. The rationale for the use of this treatment is the ability of corticosteroids to reduce edema and improving the spatial relation between the carpal tunnel, median nerve and tendons. In a randomized trial of 111 patients (Atroshi et al., 2013) methylprednisolone (80 mg or 40 mg) injection into the carpal tunnel was more effective than placebo, reducing symptoms severity and rate of surgery at 1 year. However, the effectiveness of corticosteroid injections for halting disease progression was limited, because in this study three-quarters of patients had surgery within 1 year. The preferred site for local corticosteroid injection has been assessed. In a comparison of distal (palmar) with proximal (wrist) needle insertion, the palmar approach proved less painful. However, no differences were observed in nerve conduction studies (Kamanli et al., 2011). Furthermore, corticosteroid injection with the use of US guidance is better than blind administration and reduces the time to symptom resolution, even if it is more expensive (Lee at al., 2014; Makhlouf et al., 2014; Ustün et al., 2013; Kim et al., 2013).

Regarding non-invasive methods of local corticosteroid administration, a comparison of phonophoresis and iontophoresis of dexamethasone sodium phosphate showed that phonophoresis was more effective in improving symptoms and hand function (Bakhtiary et al., 2013). Phonophoresis with dexamethasone combined with splint use has been shown to provide better symptom relief than iontophoresis with dexamethasone combined with splint use or splint use alone (Gurcay et al., 2012). Corticosteroid therapy has been compared with other drugs. By use of phonophoresis for local administration, corticosteroids led to greater reductions in nerve dimensions than did non-steroidal anti-inflammatory drugs and splint use alone in patients with CTS (Soyupek et al., 2012). Triamcinolone acetonide injection and procaine hydrochloride injection were more effective than placebo, and the effectiveness of procaine hydrochloride was similar to that of triamcinolone acetonide (Karadaş et al., 2011; Karadaş et al., 2012). A comparison between 17-α-hydroxyprogesterone caproate and corticosteroid showed that both treatments were efficacious, but only patients treated with 17-α-hydroxyprogesterone caproate continued to have symptom relief after 3 months (Ginanneschi et al., 2012). Corticosteroid injection has also been compared with extracorporeal shock wave therapy, which uses acoustic waves to produce transient pressure increases in tissues with no damaging effects. No difference in symptoms or electrophysiological outcomes was seen between the two treatments (Seok et al., 2013).

Non-steroidal drugs have been assessed as an alternative treatment for CTS. Palmitoylethanolamide improved median nerve motor latency, reduced the proportion of patients with positive Tinel's sign and reduced symptoms of discomfort compared with placebo. However, further studies are needed to substantiate these results (Conigliaro et al., 2011). Gabapentin was no more effective than placebo in reducing pain, numbness, paraesthesia, weakness or clumsiness or nocturnal awakening in a randomized controlled trial (Hui et al., 2011). Repetitive local injection of lidocaine resulted in symptom reduction and electrophysiological improvement compared with single injection (Akarsu et al., 2015).

Therapeutic US is a treatment approach based on the hypothesis that mechanical waves interacting with the tissues of the carpal tunnel (including the median nerve) will reduce inflammation. No clear evidence about the effectiveness of therapeutic US exists, but the reported results are similar to those obtained with placebo and other non-surgical therapies (splint, exercises, oral pharmacotherapy) (Bakilan et al., 2014; Page et al., 2013; Page et al., 2012; Yildiz et al., 2011). However, findings from a randomized trial (Chang et al., 2014) suggest that US therapy is more effective than paraffin therapy.

Musculoskeletal manipulation is widely used. This approach includes massage, exercise and mobilization of the wrist joint. Another important non-surgical approach is the use of splints. These methods are designed to reduce the mechanical stress due to the contact between the median nerve and the surrounding tissues of the carpal tunnel. The possible mechanism of splinting and gliding exercises is edema reduction (Schmid et al., 2012). The use of a splint for 8 weeks combined with a formal education program improved hand function and reduced symptom severity compared with no intervention (Hall et al., 2013). However, a meta-analysis has shown that sufficient evidence does not yet exist to confirm the clinical usefulness of splints, its efficacy in comparison with other treatments or the efficacy of nocturnal splints (Page et al., 2012). A combination of splints and lumbrical stretches was shown to be more effective than splints and general stretches in terms of symptom severity and functional score, but further studies of this combination are needed (Baker et al., 2012). Although the use of stretches and splints might temporarily improve muscle deficits, residual strength impairments can remain 4 weeks later (Baker et al., 2013). The Madenci massage technique (30–60 s cycles of effleurage, friction, petrissage, shaking, and repeated effleurage) has been shown to be more effective than use of splints alone in a single study (Madenci et al., 2012). However, little evidence exists about the effectiveness of exercise and mobilization of carpal tunnel structures (Page et al., 2012). A combination of tendon gliding exercises and splint and paraffin therapy might be better than conventional treatments alone or in combination with median nerve gliding exercises (Horng et al., 2011).

Other non-surgical treatments have been assessed in patients with CTS. Linseed oil might provide mild or moderate improvement in symptoms severity and functional scores and median nerve conduction velocity, as assessed in a randomised trial (Hashempur et al., 2014). Acupuncture was not better than placebo for treatment of CTS, but it has been shown to improve electrophysiological measures and reduce symptom severity compared with prednisolone (Yao et al., 2012; Yang et al., 2011). The effect of acupuncture was assessed in a systematic review that showed encouraging, but not convincing results (Sim et al., 2011). Eremostachys laciniata ointment, an extract of a plant in the Lamiaceae family used in Persian traditional medicine as an anti-inflammatory and analgesic was compared with placebo ointment. However, splints were used in both groups. Treatment with E laciniata ointment resulted in improvements in pain perception and palmar prehension. Further studies are needed to confirm these findings and to understand long-term effects of this treatment (Eftekharsadat et al., 2011). Interferential current therapy (i.e., a low frequency electrical nerve stimulation) resulted in function improvement, symptom severity and electrophysiological measures compared with TENS and splint use (Koca et al., 2014). Local microwave hyperthermia was more effective than sham therapy at providing short-term improvements in pain and function in patients with carpal tunnel syndrome (Frasca et al., 2011).

2.2. *Perineural injection therapy with 5% dextrose*

Wu et al. (2017) used a single ultrasound-guided perineural injection therapy (PIT) with 5 mL dextrose water (D5W) for treating mild-to-moderate CTS in a randomized, double-blind study. They located the injection site at the proximal inlet of the carpal tunnel via short-axis ulnar approach to simultaneously hydro dissect the subsynovial connective tissue (SSCT) and flexor retinaculum from the median nerve. The results showed significant improvement in symptoms, results of the electrophysiological study and CSA of the nerve persisting for at least 6 months compared to normal saline injection. Moreover, they also ratified PIT with 5 mL D5W being superior to corticosteroid injection (3 mL triamcinolone (10 mg/mL) mixed with 2 mL normal saline) at four to six months post injection to reduce symptoms and disability (Wu et al., 2018). Likewise, they retrospectively found that body height and sensory nerve conduction velocity of the median nerve were risk factors for poor outcomes after PIT with D5W in patients with mild-to-moderate CTS. Moreover, the sensory nerve conduction velocity of the median nerve was found to be an independent prognostic factor of poor outcome (Ho et al., 2021). Nevertheless, the electrophysiological study presented a limited diagnosis of CTS with varied sensitivity (56% to 85%) and specificity (94% to 96%) (Witt et al., 2004; Jablecki et al., 2002). For example, Martin-Gruber anastomoses may lead to misinterpretation or erroneous results during routine nerve conduction studies in patients with CTS (Di Stefano et al., 2021). Hence, underestimation of CTS severity may be attributed to the failure in proficient diagnosis. This would also be reflected as conflicting results in clinical trials on CTS. Recently, Lin et al. (2020) designed a randomized, double-blinded, three-arm trial and ultrasound-guided PIT with D5W via short-axis radial approach to simultaneously dissect the median nerve from the SSCT and flexor retinaculum. The results showed that the 4 mL D5W group had superior efficacy to 1 and 2 mL D5W in symptom relief and functional improvement at the 1, 4 and 12 weeks post injection. Moreover, their extended study revealed that PIT with a higher volume of D5W also enhanced nerve mobility and reduced the CSA of the median nerve (Lin et al., 2021). The long-term effect of PIT with D5W on CTS was also satisfactory and safe, based on the latest study. Li et al. (2021) retrospectively traced 185 patients with all grades of CTS who underwent ultrasound-guided PIT with 10 mL D5W using an initial short-axis injection with subsequent long-axis injection with a follow-up period of at least 1 year after the last injection (mean 1–3 years follow-up). The results revealed that 89% of the patients showed an effective outcome (symptom relief > 50% compared to baseline), while 63% of patients showed an excellent outcome (symptom relief > 70% compared to baseline) after a mean of 2.2 injections, and there were no complications in any of the patients. Moreover, only two patients ultimately underwent surgery after the failure of injection therapy to cure the condition. In addition, 80% of the patients (12 of 15 patients) had a surgical failure or post-surgery recurrence and had an effective outcome. Additionally, the outcome is considerably related to severity grade because the severe grade is associated with poor outcome compared to mild-to-moderate grade. A mean of 1.7, 2.4, and 2.6 injections was required to achieve an effective outcome in mild, moderate, and severe CTS, respectively (Li et al., 2021).

3. Surgical treatment

Surgical decompression can be done by a traditional open technique (long longitudinal wrist incision and direct visualization of transverse carpal ligament), a minimally invasive approach (short wrist incision) or endoscopic technique. Studies have shown no significant difference between open and endoscopic release (Atroshi et al., 2015; Sayegh and Strauch, 2015; Michelotti et al., 2014; Vasiliadis et al., 2014; Chen et al., 2014; Larsen et al., 2013; Aslani et al., 2012). However, endoscopic technique shows a shorter postoperative recovery period, reduced scar tenderness and allows earlier return to work than the open technique (Atroshi et al., 2015; Sayegh and Strauch, 2015; Michelotti et al., 2014; Vasiliadis et al., 2014; Chen et al., 2014; Larsen et al., 2013; Aslani et al., 2012). However, endoscopic release is more expensive (Sabesan et al., 2012) and is associated with higher rates of transient and nerve damage (Sayegh and Strauch, 2015). Findings from a metaanalysis (Vasiliadis et al., 2014) suggest that endoscopic release is associated with fewer minor complications (such as scar pain and infection) compared with open carpal tunnel release, with similar rates of major complications (mainly complex regional pain syndrome) (Vasiliadis et al., 2014). Differences in outcome might be dependent on the expertise of the performing surgeon (Sabesan et al., 2012). In one study (Michelotti et al., 2014) the two techniques were compared in patients with bilateral CTS; each patient received both techniques, one in each hand. Although there were no differences between techniques in terms of functional outcomes, patients preferred the endoscopic approach, as shown by significantly higher overall satisfaction scores. Different open carpal tunnel release techniques are available and have shown similar effectiveness (Crnković et al., 2014). Z-type lengthening of the transverse carpal ligament results in significant improvement in function and satisfaction score compared with a standard open technique (Xu et al., 2011). Minimally invasive techniques, compared with the standard open approach seem to provide better outcomes (fewer complications, higher patient satisfaction, improvement in symptoms, results of Tinel's, Phalen's, and compression tests, electrodiagnostic assessment, grasp strength assessment, and time to recover ability to perform personal tasks) (Aslani et al, 2012; Elsharif et al., 2014; Taralo et al., 2014). A meta-analysis (Sanati et al., 2011) showed that the minimally invasive approach versus open carpal tunnel release allowed an early return to work. Further investigations are needed to recommend the best approach. Surgical complications of carpal tunnel release are reported to occur in 1–25% of patients (Soltani et al., 2014). The incidence of serious complications consisting of structural damage to nerves, arteries, or tendons is no more than 0.5% (0.5% for open carpal tunnel release and 0.19% for endoscopic methods) (Benson et al., 2006). One potential severe complication of carpal tunnel operations is complex regional pain syndrome, which presents as hand pain, increased sweating and vasomotor instability. Complex regional pain syndrome complicates recovery, delays return to work, causes deterioration of health-related quality of life and increases the probability of poor outcomes and litigation. Its incidence after carpal tunnel release varies from 2.1% to 5%. Early diagnosis and treatment of complex regional pain syndrome is essential for optimizing patient outcomes. Other complications of carpal tunnel release are scar tenderness, pillar pain (tenderness close to the ligament release), transient neuropraxia, and reoperation (with little difference between open and endoscopic carpal tunnel release) (Sayegh et al., 2015). Regarding the postsurgical phase, there is limited low quality evidence for the benefit of postoperative rehabilitation interventions (Peters et al., 2016).

As previously described, the literature shows that both non-surgical therapies and surgical intervention have clinical benefit in CTS. In a randomised trial comparing local corticosteroid injection with surgical decompression, both treatments were similarly effective at alleviating symptoms, with corticosteroids being more effective in short-term follow up (3 months), and surgical release having additional benefit for symptom resolution in the long term (2-year follow-up) (Ly-Pen et al., 2012). There is evidence that clinical outcomes significantly improve after decompressive surgery and several non-surgical treatments (e.g., splints and low-level laser therapy), but decompressive surgery shows a higher long-term effectiveness (Shi Q et al., 2011). Surgery is also more effective than non-surgical treatment at improving electrophysiological measures (Andreu et al., 2014). Furthermore, a systematic review reported in 2011 that surgical carpal tunnel release is two times more likely to result in normal nerve conduction findings and resolution of symptoms after 6 and 12 months than non-surgical treatment (Shi Q et al., 2011).

3.1 US guided minimally invasive carpal tunnel release

Technological advances have led to the use of US guidance to improve CTS therapy. US determination of the relative position of the flexor retinaculum (FR) with the neural and vascular structures in relation to the bony landmarks correlates well with the actual anatomy (Chern et al., 2009). The location of a "safe-zone" between the median nerve and the ulnar artery for the transection has been clearly demonstrated (Chern et al., 2009). Echographic localization of the target structures facilities safe and efficacious resection of the FR. Recent anatomical and clinical studies suggest that complete release of the nerve is possible by transection of only the deep fibers of the FR without cutting the superficial fibers (Stecco et al., 2010). The latter only amounts to a reinforcement that is well differentiatable histologically. This superficial layer is more richly innervated, and sparing it by not transecting it -as a result of the use of US surgery should allow local postoperative pain to be avoided. Nakamichi (1997) proposed making use of US guidance during the conventional surgical intervention (Nakamichi and Tachibana, 1997). Over time, several teams were able to show that it is possible to perform the whole procedure with ultrasound guidance only (Osterman et al., 2012; jain et al., 2014; Sayegh and Strauch, 2015; Nakamichi and Tachibana, 1997; Capa-Grasa et al, 2014; Rojo-Manaute et al., 2016). The foremost justification for the development of this new technique is its minimally invasive nature. An open surgery or limited approach requires an opening of more than 4-5 cm, mini-open surgery involves an incision of 2 cm, and endoscopic treatment employs an opening of 1 to 2 cm. US surgery allows for an incision that is up to ten times smaller, ranging from 0.1 to 0.5 cm. Comparison of surgical procedures in terms of the size of the approach route indicates that the smaller the incision the shorter the return to work time. Not surprisingly, the esthetic and functional consequences of the surgical scar are also more limited with a smaller incision. Indeed, Jugovac et al. (2002) observed that compared to a conventional open approach, a mini-open incision decreased the return to work time by half (i.e. 15 days versus 30 days). US surgery therefore appears to combine a decrease in size of the incision with an excellent surgical field of view by continuous image-based guidance.

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