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Carpal Tunnel Syndrome

surgical versus conservative treatment

Master thesis

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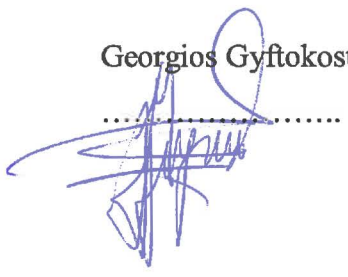

Abstract

This thesis is a systematic review of the relevant literature on the efficacy of conservative treatment of carpal tunnel syndrome (CTS) with final purpose to determine a possible consensus with regard to the choice of initial treatment for CTS. In order to be more reliable the thesis, the author choose mostly researches that used the strongest experimental design and high quality systematic reviews. The author proved that the conservative treatment provides significant benefits in the treatment of CTS in mild to moderate state of disease.

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1. Introduction

Entrapment or compressive neuropathies of upper extremity are important and widespread debilitating clinical problems, especially in patients with predisposing occupations or with certain medical disorders. By far the most common is median nerve entrapment in the wrist leading to so-called carpal tunnel syndrome (CTS).[29]

CTS is one of the most common orthopedic conditions, with an estimated incidence of nearly 1% annually in the USA, which makes almost 2.8 million new cases per year.[20] CTS is approximately three times more common in women than in men.[46] A strong correlation between workplace factors and CTS was found by Osorio et al.[57] who evaluated the prevalence of CTS among 56 grocery store workers in relation to forceful and repetitive wrist motion. This study found a strong positive association between ergonomic physical factors and CTS prevalence.[57] The wrist is a common site of overuse syndromes, and 15% of workers at risk can develop CTS.[82] Overuse syndromes are some of the most common occupational illnesses treated by primary care providers.[82]

Most cases of nerve compression begin gradually and then become chronic, so relationships to activity are not always obvious. A Washington state study indicated that carpal tunnel syndrome (CTS) was associated with a significantly longer time to return to work than were back and neck sprains, fractures, and all other injuries.[22]

To relieve the pressure on the median nerve, several treatment options, both surgical and conservative, are available.[29] The American Academy of Neurology advises non-invasive treatment first, i.e. wrist splints, modification of activities, NSAIDs or diuretics and using

invasive steroid injections or open carpal tunnel release only if non-invasive treatment have turned out to be ineffective.[2]

In the USA the surgery performed for CTS accounts for the most common operation performed on the hand.[55,46] Carpal tunnel surgery is now the fifth most common procedure performed among Medicare patients.[24] Even though surgery for CTS is generally considered safe and effective, the possible risk associated with surgery and the potential for complications may contribute to the preference of some patients for non-surgical treatment.[89] A lot of studies have been published concerning the efficacy of conservative treatment in CTS. The treatment choice seems controversial.

The large number of the patients that choose the surgical procedure for the treatment of CTS creates questions about the efficacy of conservative treatment in, mild to moderate, state of the disease. Are nonsurgical approaches to carpal tunnel syndrome effective? Are the effects of the conservative treatment comparable to surgical? Is there a consensus with regard to the choice of initial treatment for CTS? A study of the most recent clinical medical researches for the effects of the conservative treatment of CTS has to be done.

This thesis is a systematic review of the relevant literature on the efficacy of the conservative procedures in the treatment of carpal tunnel syndrome (CTS), with final purpose to determine a possible consensus with regard to the choice of initial treatment for CTS. This study will provide important findings necessary for the patients but also for the future researchers of the efficacy of the nonsurgical approach and treatment options for CTS.

2. A General Overview of the Carpal Tunnel Syndrome

2.1 Definition

Carpal tunnel syndrome (CTS) is a compression neuropathy of the median nerve at the wrist. The median nerve (figure 1) is compressed in an osteofibrous tunnel surrounded volarly by the transverse carpal ligament and laterally and dorsally by the carpal bones. [33]

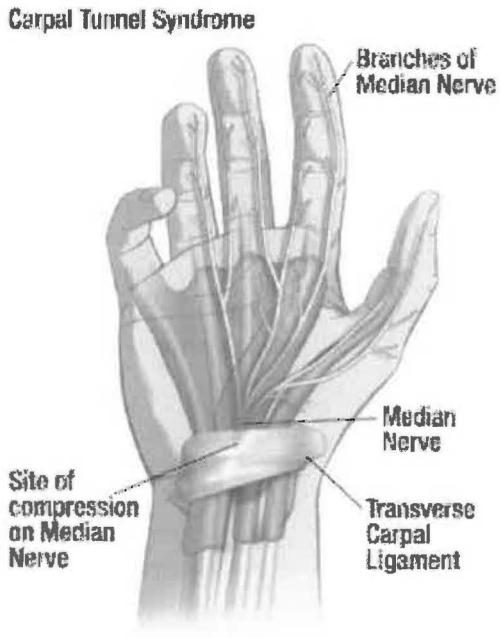

Figure 1. Site of the compression of median nerve[4]

2.2 Etiology

Nerve entrapments of the wrist have three main causes: systemic conditions, ischemia and mechanical compression, and double crush syndrome. Another separate but contributing factor is overuse syndrome.[82] Flexor tenosynovitis is the most common cause of this CTS, which is usually associated with repeated forced hand movements such as those used by typists, cashiers, electronic assembly workers, musicians, cooks, and carpenters.[84]

2.2.1 Systemic conditions

Systemic conditions affect nerve function at the wrist by way of systemic depression of peripheral nerve function or alteration of interstitial fluid equilibrium.[77] Diabetes, alcoholism, hypothyroidism, and aging can cause systemic depression of peripheral nerve function, which lowers the threshold for manifestation of a compression neuropathy. Pregnancy, myxedema, and rheumatoid arthritis are conditions that alter interstitial fluid equilibrium. Compression neuropathies may occur from the increased contents in a limited space.

2.2.2 Ischemia and mechanical compression

Nerves have a predictable response to progressing compression. At 20 to 30 mm Hg of compression, epineural blood flow is reduced. At 30 mm Hg of compression, axonal transport is impaired, while at 30 to 40 mm Hg of compression, symptoms of paresthesias appear. Greater than 60 mm Hg of compression leads to total intraneural ischemia with complete sensory and motor block.[77,78]

Pathologic changes involving the myelin sheath are the earliest indications of pressure applied to a nerve. Greater forces cause myelin loss along a longer section of the nerve; this is termed *segmental demyelination*. After nerve compression is relieved, nerve repair takes place. With lesions involving only myelin, repair can occur rapidly over days to weeks. If there is axonal

damage, recovery is much more protracted, with the regenerating axons covering 1 to 3 mm per day from the site to the target muscle.[11]

2.2.3 Double crush syndrome

Peripheral fibers are more vulnerable to pressure injury than are central ones. Nerve compression can occur at two levels. Double crush syndrome suggests that proximal compression may decrease the ability of the nerve to tolerate a second, more distal compression.[49] Thus, when a proximal cervical lesion is present, less compression of the median nerve at the carpal tunnel level is necessary to produce symptoms.

2.2.4 Overuse syndromes

The wrist is a common site of overuse syndromes, and 15% of workers at risk can develop CTS.[82] Overuse syndromes are some of the most common occupational illnesses treated by primary care providers.[82] Most cases of nerve compression begin gradually and then become chronic, so relationships to activity are not always obvious.

At the pathophysiologic level, overuse is defined as the level of repetitive microtrauma sufficient to overwhelm the tissues' ability to adapt. Microtrauma results from repetitive loading episodes at a force or elongation level well within the physiologic range. Fibrosis results from continued or repeated release of inflammatory products leading to thick, unyielding, restrictive tendon sheaths or retinacular tunnels.[82]

2.3 Risks factors

Key occupational risk factors for overuse syndromes include repetition, high force, awkward joint posture, direct pressure, vibration, and prolonged constrained posture.[82] A study conducted by Uniformed Services University of the Health Sciences demonstrated that computer keyboard operators generate significantly higher levels of force—four to five times higher—than required to operate the computer.[22] Participants who were symptomatic used even higher levels of force across the keyboard. Nerve entrapments can occur in athletes because of repetitive, vigorous use of the upper extremities; athletes are especially susceptible to compression of the peripheral nerves.

2.4 Clinical Features

2.4.1 Microscopic findings

In idiopathic CTS, the transverse carpal ligament is the point of compression. The typical progression begins as the wrist is subjected to a repeated mechanical stress. Local necrosis then develops, with subsequent edema and collagen fragmentation. Fibrous hypertrophy of the flexor tendon synovium results in compression occurring at the transverse carpal ligament. Biopsies on specimens of this ligament from patients undergoing surgical decompression demonstrated findings of edema, vascular sclerosis, and fibrosis that are consistent with repeated stress to connective tissue.[65] Lack of evidence of frank inflammation further supports this claim.

2.4.2 Symptoms

The median nerve at the wrist is 94% sensory and only 6% motor; therefore, dysfunction at the wrist usually manifests first as sensory changes; motor changes develop with severe compression.[82] Pain and paresthesias are present on the palmarradial aspect of the hand, while

the little finger is spared. CTS is usually bilateral, but in idiopathic CTS the dominant hand is usually more severely affected.[61,65]

The symptoms are exacerbated by extreme flexed or extended wrist positions during activities such as driving or typing, which increase the pressure within the carpal tunnel. Repetitive, forceful use of the hand also exacerbates the condition. In mild CTS, the findings on physical examination may be normal or show trivial sensory loss. Earliest sensory loss seems to occur over the volar tip of the middle finger.[11] Patients with advanced cases may drop items because of altered sensibility or thenar weakness. In these patients, impaired dexterity is due to the weakness of thumb abduction and opposition resulting from the motor fibers clinically involved.[65,73] Symptoms often seem worse at night. Flexion and extension positions during sleep lead to increased carpal tunnel pressure, nerve ischemia, and subsequent painful paresthesias that awaken patients and cause them to shake or wring their hands.[65] Another theory is that the same pathway is followed, but fluid redistribution caused by being in a supine position is to blame rather than hand posture.[67]

2.5 Diagnosis

CTS is diagnosed based on patients history, clinical findings and neurophysiologic evaluation.[61]

2.5.1 Patient's history

There are several broad questions that may solicit complaints of hand numbness or hand/wrist pain and/or symptoms. A detailed history should be obtained to include information about any medical conditions, prior hand/wrist injuries, and how the hands have been used during work and leisure activities.[3]

2.5.2 Physical examination

Physical examination should include the Phalen's test, Tinel's sign, and compression testing. Phalen's test involves holding the wrist in 90 degrees of flexion for 60 seconds. Numbness or tingling in median nerve distribution suggests CTS. Tinel's sign is considered positive if percussion of the median nerve at the site of compression causes tingling in the fingers. Compression testing requires the examiner to apply direct compression on the median nerve for 30 seconds. Presence of paresthesias suggests CTS.[33] Tinel's sign has a sensitivity of 60% and a specificity of 67%; the corresponding values for Phalen's test are 75% and 47%.[40,28] If the findings on both Phalen's test and Tinel's sign are positive and the history is suggestive, the diagnosis is 85% certain.[67]

When conducted in the proper setting, these tests can provide useful information. In a clinical setting, an assessment of strength, sensory loss, and pain is sufficient to monitor the progress of the syndrome.[33]

2.5.3 Electrodiagnostics

Electrophysiology localizes and aids in assessing the location, severity, and prognosis and also helps guide subsequent treatment. Two types of electrodiagnostic testing are used: nerve conduction studies and electromyography (EMG). Nerve conduction studies test for latency or asymmetry of stimulus across the wrist and represent the only completely objective evaluation for CTS. Lack of an abnormal nerve conduction test result does not exclude a diagnosis of CTS, especially early in the course of the process. EMG measures denervation of the thenar muscles in advanced motor median nerve compression.[16]

Consensus committees from the American Academy of Neurology, American Association of Electrodiagnostic Medicine, and American Academy of Physical Medicine and Rehabilitation recognize nerve conduction studies as the diagnostic standard for carpal tunnel syndrome.[39]

2.5.4 Imaging Techniques

Plain radiographs in two planes will rule out posttrauma deformity. Although magnetic resonance imaging (MRI) and computer tomography (CT) are helpful in visualizing certain anatomic factors responsible for compression, they are not useful for specifically diagnosing entrapment neuropathy at the wrist unless a mass or other lesion is suspected.[77] Fullness in the wrist or palm, or a history of a slowly progressing deficit without intermittent fluctuations, are indications for MRI and CT.[65]

2.5.5 Other diagnostic methods

Other methods of imaging the region of the carpal tunnel, like ultrasound and thermography have been evaluated.[23,35,75] The high spatial resolution and exquisite flow detection methods of ultrasound allows analysis of many superficial soft tissue structures. Thermography shows clear abnormalities in CTS, but is not reliable for the diagnosis of bilateral cases and has limited value in the differential diagnosis. [75]

2.6 Differential diagnosis

2.6.1 CTS vs cervical radiculopathy

The most common alternate diagnosis is cervical radiculopathy, most often at the level of C6, but CTS and cervical radiculopathy can coexist. (double crush neuropathy) [33,49] The presence of neck and shoulder pain, weakness in C6 innervated muscles, reflex changes such decreased tendon reflexes, neurological defects in superficial and deep sensation[80], sensory loss restricted to the thumb, the absence of nocturnal paresthesias, and the ability to reproduce the paresthesias with root compression maneuvers all favor cervical radiculopathy.[11,80,81]

During double crush neuropathy, a cervical spondylosis affecting the median nerve may not be symptomatic, but it may exacerbate a carpal tunnel syndrome.[33] The cervical spine should always be evaluated when dealing with what appears to be a local neuropathy at the shoulder, elbow, or wrist.[76] Research is revealing that CTS is not only a hand and wrist problem but is also a spinal problem. For example, when 1,000 cases of carpal tunnel syndrome were investigated it was found that a large number of them also had neck arthritis.[37]

2.6.2 CTS vs proximal median neuropathy

Proximal median neuropathy is another alternate diagnosis. The palmar cutaneous branch of the median nerve leaves the main trunk 5 to 8 cm proximal to the wrist crease. Thus, loss of sensation over the thenar eminence is not part of CTS and suggests a lesion proximal to the wrist.[49] Objervation for sensory disturbances over the thenar eminence and weakness of median muscles proximal to the wrist, especially distal thumb flexion due to the flexor pollicis longus, arm pronation (pronator teres and pronator quadratus), and wrist flexion (flexor carpi radialis).[65]

2.7 Treatment

The American Academy of Neurology advises non-invasive treatment first, i.e. wrist splints, modification of activities, nonsteroidal anti-inflammatory drugs (NSAIDs) or diuretics and using invasive steroid injections or open carpal tunnel release only if non-invasive treatment have turned out to be ineffective.[2] The severity of symptoms and the degree of abnormal test findings (on nerve conduction velocity studies) indicate the appropriate initial therapeutic approach. Surgery is generally not a first line treatment in the absence of significant clinical findings.[3,5]

2.7.1 Conservative treatment

Conservative treatment options include wrist splinting, along with cessation of aggravating activities; oral corticosteroid therapy; diuretics; local corticosteroid injections; and nonsteroidal anti-inflammatory drugs (NSAIDs).[29]

Splints

There are two types of splinting procedures used for CTS. The first is termed night splinting and assists in keeping the hand in a neutral position while the client is sleeping. The second type is termed occupational splinting and involves customizing a client's splint to the type of work the client does. The major function of both types of splints is to reduce unnecessary flexing or extending the wrist.[29]

Medication

Diuretics, nonsteroidal anti-inflammatory drugs (NSAIDs), pyridoxine (vitamin B6), and orally administered corticosteroids have been used with varying degrees of success in patients with carpal tunnel syndrome.[29]

Local injection

Combined injection of a corticosteroid and a local anesthetic drug into or proximal to the carpal tunnel can be used in patients with mild to moderate carpal tunnel syndrome.[29]

Other conservative options

Physiotherapy

A physiotherapeutic approach may help in the treatment of CTS in mild to moderate state but also after a surgery. Physiotherapy could help by the use of: ice therapy for the treatment of swelling and inflammation, anti-inflammatory therapeutic modalities like ultrasound and laser, strengthening exercises, passive stretching exercises to maintain or improve the range of motion (ROM) of wrist and peripheral to the wrist joints, mobilization techniques like joint play[43] for wrist joint and activity modification instructions for avoiding exacerbation of the symptoms. A physiotherapist will evaluate the muscles and joints around the wrist. Joints of hand, elbow, shoulder and cervical part of spine will be evaluated in order to avoid or treat possible compensation changes to other parts of body. A physiotherapist also will create an auto-therapy schedule that the patient will follow it at home. This schedule may include strengthening and stretching exercises of the wrist and peripheral to the wrist joints and activity modification instructions.[33,43]

Laser therapy

Low-level lasers are also known as "cold lasers" and non-thermal lasers. Low-level lasers refer to the use of red-beam or near-infrared lasers with a wavelength between 600 and 1000 nm and Watts from 5-500 milliwatts. (In contrast, lasers used in surgery typically use 300 Watts.) When applied to the skin, these lasers produce no sensation and do not burn the skin. Because of the low absorption by human skin, it is hypothesized that the laser light can penetrate deeply into the tissues where it has a photobiostimulative effect. The exact mechanism of its effect on carpal tunnel and other pain syndromes is unknown: hypotheses have included improved cellular repair and stimulation of the immune, lymphatic, and vascular systems.

One low-level laser device, the MicroLight 830 Laser, has received clearance for marketing from the U.S. Food and Drug Administration (FDA) specifically for the treatment of carpal tunnel syndrome. In the data submitted to the FDA as part of the FDA 510(k) approval process, the treatment consisted of application of the laser over the carpal tunnel three times a week for five weeks. The labeling states that the "MicroLight 830 Laser is indicated for adjunctive use in the temporary relief of hand and wrist pain associated with carpal tunnel syndrome." Other protocols have used low-level laser energy applied to acupuncture points on the body. This technique may be referred to as "laser acupuncture." [64]

Ultrasound therapy

Ultrasound is assumed to have thermal effects on the target tissue resulting in an increase in blood flow, local metabolism and tissue regeneration and also reducing inflammation, oedema and pain, thereby facilitating the recovery of nerve compression.[29]

Chiropractic approach

The chiropractic treatment involved manipulation of the hand, wrist, forearm, and cervical spine to ease the passage of the median nerve through its sheath at the wrist.[18]

Exercises

Tendon-Gliding exercises: Isolated tendon gliding exercises of the flexor digitorum superficialis and flexor digitorum profundus to each digit passing through the carpal tunnel has also shown to be effective in recent studies. Each exercise series starts with the wrist and digits in full extension, then the digits are held in a hook grip, followed by a straight fist, followed by a full fist. These exercises are to be preformed five times each, five times daily.[34]

Alternative therapeutic methods

Yoga and acupuncture are also used to provoke relief of symptoms in mild to moderate state of CTS.[25,52]

2.7.2 Surgical treatment

Indications [5]

Medically Necessary:

Carpal tunnel release surgery is considered **medically necessary** without the need for a trial of conservative treatment measures if there is documentation of both the diagnosis of carpal tunnel syndrome and thenar atrophy or carpal tunnel syndrome following significant acute trauma. Carpal tunnel release surgery is considered **medically necessary** when conservative medical treatment has been ineffective at relieving the symptoms of significant pain or functional impairment with numbness in the distribution of the median nerve, which is:

- refractory to adequate wrist splinting of at least 4 weeks duration; or
- unresponsive to additional conservative treatment measures, such as anti-inflammatory medications, of at least 4 weeks duration, or steroid injections, etc; and
- confirmed by electrodiagnostic testing (nerve conduction velocity studies); and
- not associated with other treatable or time-limited conditions, such as current pregnancy, treatment-responsive arthritis, or hypothyroidism.

Not Medically Necessary:

Carpal tunnel release surgery is considered **not medically necessary** when the criteria listed above are not met.

Surgical procedures

Open Carpal Tunnel Release Surgery

Carpal tunnel release surgery (figure 2) is an outpatient procedure that is performed using regional anesthesia. The goal of this procedure is to increase the space in the carpal tunnel in order to remove pressure on the median nerve, which is compressed in the tunnel at the wrist. The procedure involves dividing the ligament that forms the roof of the tunnel. This allows the nerve to pass freely through the tunnel without being compressed.[70]

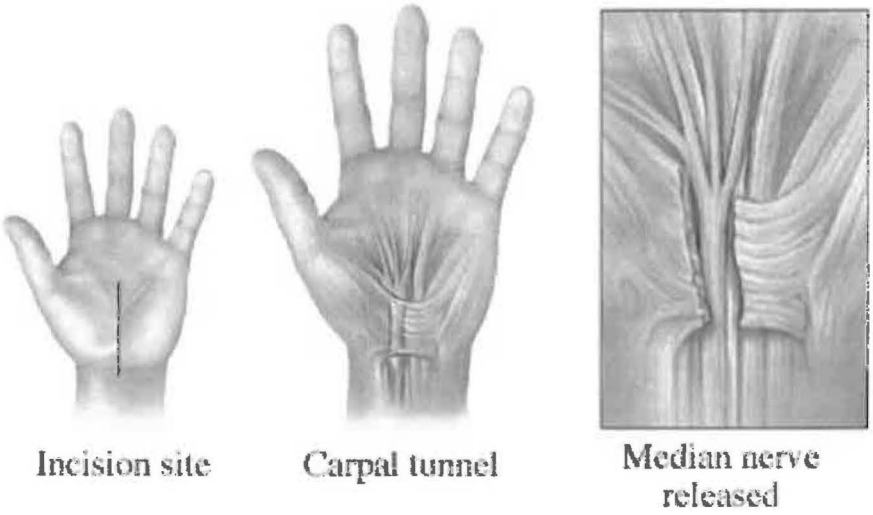

Figure 2. Open carpal tunnel release[4]

Endoscopic carpal tunnel release

A newer procedure using a very small incision at the wrist allows the surgeon to pass fiber-optic tools through an endoscope (a device consisting of a pencil-thin tube and an optical system) into the tunnel. (figure 3) Then, using specialized tiny instruments, the surgeon divides the ligament. The surgeon views the carpal tunnel area and the median nerve on a video monitor. Use of this procedure purportedly lessens scar formation and allows an earlier return to work and activities of daily living. The wrist is generally splinted for three to four weeks after surgery.[42]

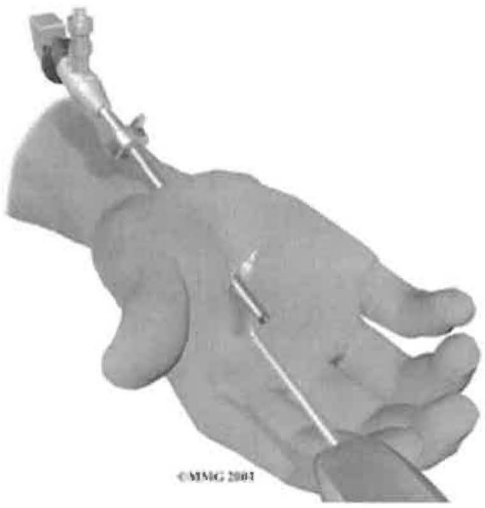

Figure 3. Endoscopic carpal tunnel release[4]

Complications of surgery

Complications of surgery include injury to the palmar cutaneous or recurrent motor branch of the median nerve, hypertrophic scarring, laceration of the superficial palmar arch, and tendon adhesion.[42] Postoperative infection, hematoma, arterial injury, stiffness, and reflex sympathetic dystrophy are other possible complications.[88] If carpal tunnel release is incomplete, symptoms may recur.

3. Methodology

3.1 Process Overview

This thesis completed a systematic review of the relevant literature on the efficacy of conservative treatment of carpal tunnel syndrome (CTS). In order to be more reliable the thesis, the author choose mostly researches that used the strongest experimental design and high quality systematic reviews.

3.2 Clinical Research Designs

A clinical trial is an *experiment* conducted with patients as subjects. The principles of good experimental design apply to clinical trials. The strongest experimental design (the "gold standard") is the randomized design in which subjects (patients) are randomly assigned to treatment groups. An important distinction in the purpose of clinical trials is that between therapeutic trials (comparing treatment methods) and prophylactic (or prevention) trials.[58]

Key Features of the Randomized Clinical Trial

The randomized clinical trial is characterized by two or more therapeutic treatment groups. These groups are sometimes referred to as *arms*. One treatment may be a placebo control in which a biologically-inert substance (in a drug trial) is used. Placebo controls cannot always be used because of ethical or practical constraints. Often, the "control" condition is the treatment is the standard of care which is then compared to experimental treatments.[58]

Psychologic and other potentially confounding variables can be controlled by coding the treatment in such a way that the subject cannot tell what it is; this is called a single-blind trial. The best control is where neither the subjects nor the investigators know which treatment a given subject is receiving; this is called a double-blind trial. Again, ethical or practical constraints may make blinding impossible.[58]

3.3 Rating the Quality of Evidence

The quality of therapeutic evidence was rated using an evidence hierarchy that exists for each of four different study types: **therapeutic**, **prognostic**, **diagnostic**, and **economic** or **decision-modeling**. This hierarchy is shown in **Appendix: Literature Searches** and on the American Academy of Orthopaedic Surgeons (AAOS) website.[4]

3.4 Study Phase[58]

Most clinical trials are designated as phase I, II, or III, based on the type of questions that study is seeking to answer:

- In Phase I clinical trials, researchers test a new drug or treatment in a small group of people (20-80) for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.
- In Phase II clinical trials, the study drug or treatment is given to a larger group of people (100-300) to see if it is effective and to further evaluate its safety.

- In Phase III studies, the study drug or treatment is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the drug or treatment to be used safely.
- In Phase IV studies, the post marketing studies delineate additional information including the drug's risks, benefits, and optimal use.

These phases are defined by the Food and Drug Administration in the Code of Federal Regulations.

4. Conservative treatment efficacy researches

4.1 Wrist Splints

Splinting is the most popular method among the conservative treatments of CTS.[10,26,86] Among the conservative treatment, splinting the wrist in a neutral position will help reduce and may even completely relieve CTS symptoms.[74] There are many studies stressing the effectiveness of neutral angle wrist splinting in CTS. An initial trial of full-time splinting for 3-4 weeks followed by part-time night splinting is recommended similar to full-time splinting for 3 weeks. [21, 27]

Splinting the wrist at a neutral angle helps to decrease repetitive flexion and rotation, thereby relieving mild soft tissue swelling or tenosynovitis. Splinting is probably most effective when it is applied within three months of the onset of symptoms.[41] The optimal splinting regimen depends on the patient's symptoms and preferences. Nightly splint use is recommended to prevent prolonged wrist flexion or extension.[69] Manente et al. in a randomized controlled trial, mention that when worn at night for four weeks, a specially designed wrist brace was found to be more effective than no treatment in relieving the symptoms of carpal tunnel syndrome.[47] This brace has not yet been compared with traditional splints. Some patients choose to wear a wrist splint all of the time. Compared with nighttime-only splint use, full-time use has been shown to provide greater improvement of symptoms and electrophysiologic measures; however, compliance with full-time use is more difficult.[85]

In the year 2005 in order to determine the effectiveness of nocturnal splinting, in a randomized controlled study[87], Werner et al. studied 112 active workers at a Midwestern automotive assembly plant with symptoms consistent of carpal tunnel but who had not sought medical treatment. Subjects were selected if they experienced numbness, tingling, burning or pain in the median nerve of the hand for more than a week or for more than three times in the past six months. Werner notes that automotive assembly workers are five to ten times more likely to

develop carpal tunnel than people than the general population and people who type for a living. Workers in the group too, miss, on average, a month of work, especially those who seek surgical intervention for advanced symptoms of carpal tunnel. As part of the randomized controlled study, 63 study participants were fitted with a custom wrist-hand splint that maintained the wrist in a neutral posture overnight and were instructed to wear the splint at night for a period of six weeks. This group, along with the remaining 49 participants, also viewed a 20-minute video on carpal tunnel syndrome and how to reduce ergonomic stressors at work and home. After the six week trial, about half of the splinted group reported significant improvement in their symptoms, with one participant reporting complete relief of symptoms. Compared to the group assigned to just watch the video, the splinted group had significantly decreased hand, wrist, elbow and forearm discomfort after three months. After 12 months, the improvement seen in each group was greatly dependent on the individual's level of hand/wrist nerve damage. Of those in the non-splinted group, participants with healthy nerves noted reduced hand/wrist discomfort, while those with injured nerves felt no improvement over time. Those who used the splint – both with healthy and injured nerves – saw significant improvement in hand/wrist discomfort, and participants who initially reported higher levels of discomfort at the start of the study saw the greatest improvements with splint use. Additionally, 10 percent of the participants in this group continued to wear the splint at night beyond the initial six-week trial. Prior to the study, nearly half of the participants used non-steroidal anti-inflammatory drugs and ice/heat treatments to treat their hand and wrist discomfort, while less than 25 percent had previously sought physical therapy for their carpal tunnel symptoms. Despite relief from NSAIDs and other home remedies, Werner says using a custom fit or store-bought splint for night-time use is the best first line of defense when symptoms of carpal tunnel begin. Splinting, he notes, has minimal effect on those with advanced carpal tunnel. "Early intervention with splinting is key to effective management of carpal tunnel syndrome," says Werner. "It's very cost-effective and the odds are very good that you will feel the benefits." Werner hopes to build on the findings from this study by

conducting a larger study to determine the cost-effectiveness of splinting and its long-term benefits for patients.

In the year 2006 Mishra et al. in a prospective randomized clinical and electrophysiological study[50] with 3-month follow-up, study the efficacy of splinting and oral steroids in the management of carpal tunnel syndrome (CTS). Forty patients with CTS were randomly divided into splint group (N-20), wearing splint in neutral position for 4 weeks; and steroid group (N-20), who received oral prednisolone 20 mg/day for 2 weeks followed by 10 mg/day for 2 weeks. Clinical and electrophysiological evaluations were done at baseline and at 1-month and 3-month follow-up. Independent 't' test and paired 't' test were used for statistical analysis. There was significant improvement in both groups, clinically as well as electrophysiologically, at 3 months. On comparing the efficacy of the two treatment methods, except for the functional status score, there was no significant difference between the two groups. [50]

Two high quality systematic reviews[51,56] was conducted to determine the effectiveness non-surgical interventions for carpal tunnel syndrome (CTS) based on the best available evidence. Current evidence shows a significant benefit (grade B recommendations) from splinting.[51,56]

Sevim et al. [71] evaluated the long-term efficacy of non-surgical treatment methods for mild and moderate carpal tunnel syndrome, 120 patients with clinical symptoms and electrophysiological evidence were included in a prospective, randomizes blinded trial: 60 patients were instructed to wear splints every night, 30 received injection of betametasone 4 cm proximal to the carpal tunnel , and 30 received injection distal to the carpal tunnel. After approximately 1 year (mean, 11 months; range, 9-14), 108 patients were available for final evaluation. They assessed clinical symptoms an performed detailed electrophysiological examinations before and after treatment. Splinting provided symptomatic relief and improved sensory and motor nerve conduction velocities at the long-term follow-up when the splints were worn almost every night. Proximal

and distal injections of steroid were ineffective on the basis of both clinical symptoms and electrophysiological findings.

4.1.1 Splinting vs Surgery

Gerritsen et al. conducted a randomized controlled trial [30] in order to compare the short-term and long-term efficacy of splinting and surgery for relieving the symptoms of CTS. A total of 176 patients with clinically and electrophysiologically confirmed idiopathic CTS were assigned to wrist splinting during the night for at least 6 weeks (89 patients) or open carpal tunnel release (87 patients); 147 patients (84%) completed the final follow-up assessment 18 months after randomization. The main outcome measures were: general improvement, number of nights waking up due to symptoms, and severity of symptoms. In the intention-to-treat analyses, surgery was more effective than splinting on all outcome measures. The success rates (based on general improvement) after 3 months were 80% for the surgery group (62/78 patients) vs 54% for the splinting group (46/86 patients), which is a difference of 26% (95% confidence interval [CI], 12%-40%; $P<.001$). After 18 months, the success rates increased to 90% for the surgery group (61/68 patients) vs 75% for the splinting group (59/79 patients), which is a difference of 15% (95% CI, 3%-27%; $P = .02$). However, by that time 41% of patients (32/79) in the splint group had also received the surgery treatment. The authors conclude that the treatment with open carpal tunnel release surgery resulted in better outcomes than treatment with wrist splinting for patients with CTS.

Verdugo et al. (Cochrane) conducted a systematic review.[83] The objective of this review was to compare the efficacy of surgical treatment of carpal tunnel syndrome with non-surgical treatment in improving clinical outcome. The selection criteria were: all randomised and quasi-randomised controlled trials comparing any surgical and any non-surgical therapies. The authors conclusion

was that surgical treatment of carpal tunnel syndrome relieves symptoms significantly better than splinting and that further research is needed to discover whether this conclusion applies to people with mild symptoms.

4.2 Oral Medications

Diuretics, nonsteroidal anti-inflammatory drugs (NSAIDs), pyridoxine (vitamin B_6), and orally administered corticosteroids have been used with varying degrees of success in patients with carpal tunnel syndrome. Unfortunately, few high-quality trials have evaluated these treatments.

Herskovitz and colleagues[36] demonstrated a short term improvement in global symptom scores for CTS with oral corticosteroid compared to placebo, but Chang et al. could not find a dose response.[13,14] While these finding suggest some potential therapeutic benefits, none of these therapies either alone or in combination have been rigorously compared to surgery.

Gerritsen et al. in a recent systematic review[29] of conservative treatments for carpal tunnel syndrome found 14 randomized controlled trials (RCTs), including five trials of oral medications. The authors concluded that NSAIDs, diuretics, and pyridoxine are no more effective than placebo in relieving the symptoms of carpal tunnel syndrome.[29]

Orally administered corticosteroids have been shown to be more effective than NSAIDs or diuretics in the short-term treatment of carpal tunnel syndrome. The optimal corticosteroid dosage remains to be determined. In one prospective, randomized, double-blind, placebo-controlled trial (73 patients), global symptom scores for carpal tunnel syndrome were significantly improved at two weeks and four weeks in patients randomized to receive prednisolone in a dosage of 20 mg per day for two weeks, followed by 10 mg per day for two weeks.[13] No major adverse effects were noted. The study also found that NSAIDs and diuretics conferred no greater benefit than placebo.

In the year 2007, Piazzini et al. in a systematic review[62] found thirty-three RCTs. The studies were analysed to determine the strength of the available evidence for the efficacy of the treatment. The review shows that: vitamin B6 is ineffective, steroids are better than non-steroidal anti-inflammatory drugs (NSAIDs) and diuretics, but they can produce side-effects. The conclusion of this study was: There is: (1) strong evidence (level 1) on efficacy of local and oral steroids; (2) moderate evidence (level 2) that vitamin B6 is ineffective and (3) limited or conflicting evidence (level 3) that NSAIDs, diuretics, are effective.

4.3 Local Injection

Combined injection of a corticosteroid and a local anesthetic into or proximal to the carpal tunnel can be used in patients with mild to moderate carpal tunnel syndrome. Such injections can be diagnostic as well as therapeutic. While most studies evaluating local injection have been retrospective or uncontrolled, two recent systematic reviews of RCTs concluded that local corticosteroid injection provides greater clinical improvement at one month compared with placebo.[29,48]

A randomized, double-blind trial [90] compared oral corticosteroid therapy and local corticosteroid injection in 60 patients with electrophysiologically confirmed carpal tunnel syndrome. In this study, 30 patients were treated with local injection of 15 mg of methylprednisolone plus oral placebo; the other 30 patients received 25 mg of orally administered prednisolone for 10 days plus a saline injection. Mean global symptom scores for the two groups did not differ significantly at two weeks. At eight and 12 weeks, however, significant improvement was evident only in the methylprednisolone injection group.

In one double-blind, placebo-controlled trial,[17] 60 patients older than 18 years with electrophysiologically confirmed carpal tunnel syndrome and symptoms for longer than three

months were randomized to receive 10 mg of lignocaine (lidocaine) or 10 mg of lignocaine plus 40 mg of methylprednisolone. In all patients, the injection was administered proximal to the carpal tunnel. Improvement was defined as no symptoms or minor symptoms requiring no further treatment. At 1 month 6 (20%) of 30 patients in the control group had improved compared with 23 (77%) of 30 patients the intervention group (difference 57% (95% confidence interval 36% to 77%)). After 1 year, 2 of 6 improved patients in the control group did not need a second treatment, compared with 15 of 23 improved patients in the intervention group (difference 43% (23% to 63%). Of the 28 non-responders in the control group, 24 (86%) improved after methylprednisolone. Of these 24 patients, 12 needed surgical treatment within one year. No side effects were reported. Superior symptom relief for corticosteroid injection compared with placebo (lignocaine only) injection was not adequately demonstrated beyond one month of follow-up. All injections in the study were performed by one neurologist, which may limit the reproducibility of the results.

Local injection of corticosteroid into the carpal tunnel improves short-term clinical outcomes, as compared with oral corticosteroids, intramuscular corticosteroid injections, NSAIDS, or splints alone. [12,17,31,36,59] Celiker et al. found also that corticosteroid injection into the carpal tunnel was superior to NSAIDs therapy.[12]

4.3.1 Local injection vs surgery

Ly-Pen et al. in a 1-year, prospective, randomized, open, controlled clinical trial [45], studied the effects of surgical decompression versus local steroid injection. According one of the authors this is the first randomized controlled clinical trial comparing the two most common therapies for CTS. The research effort focused on the results of 163 wrists belonging to 101 patients 93 women, 8 men who were referred by their primary care physician to a CTS unit specifically

created for this study. All the patients had experienced CTS symptoms most notably, nightly attacks of extreme tingling and burning in the hand and fingers, which disrupted their sleep for at least 3 months. Of the total wrists, 80 were randomly assigned to the standard surgical procedure: decompression of the median nerve. The remaining 83 wrists were treated with local steroid injection. Patients in both groups were similar in age the median was 50 for the surgery group and 53 for the injection group as well as in the duration and severity of their symptoms. All wrists were evaluated 14 days after the initial treatment. At that time, 69 of the wrists that had been treated with steroids received a second local injection. Researchers then assessed the symptoms of both groups at 3, 6, and 12 months, using visual analog scale scores to measure improvement. At the 3-month mark, 94 percent of the wrists in the injection group achieved significant improvement a response of 20 percent or better for the nocturnal symptoms, compared with 75 percent of wrists in the surgery group. At the 6-month mark, 85.5 percent of wrists in the injection group achieved a 20 percent or better response for the nocturnal symptoms, compared with 76.3 percent in the surgery group. At the 12-month mark, 69.9 percent of the wrists in the injection group achieved a 20 percent or better response for the nocturnal symptoms, compared with 70 percent in the surgery group. Throughout follow-up, results for two other symptoms measured daily pain in the wrist area and self-perceived functional impairment were similar. The authors conclusion was that over the short term, local steroid injection is better than surgical decompression for the symptomatic relief of CTS. At 1 year, local steroid injection is as effective as surgical decompression for the symptomatic relief of CTS.

4.4 Ultrasound therapy

There are conflicting results on the efficacy of therapeutic ultrasound in the treatment of CTS, and only a few studies reported the benefit of ultrasound in CTS treatment.[6,10,19,29,60] Ultrasound therapy may be beneficial in the longer term management of carpal tunnel syndrome. A double-blind, randomized trial [19] found that compared with "sham ultrasound" treatment (control), 20 sessions of carpal tunnel ultrasound therapy administered over approximately seven weeks resulted in significantly greater improvement of symptoms at two weeks, seven weeks, and six months. However, a smaller study showed no benefit for this treatment.[60]

In the year 2004 a randomized controlled trial [63] conducted to investigate the efficacy of low intensity ultrasound thermotherapy, as conservative option of treatment of mild to moderate carpal tunnel syndrome (CTS). The patients were eighteen women, 30 hands who had clinical and electrophysiologic evidence of mild to moderate CTS. Patients were divided into two groups; A and B of 15 hands by random sampling. Group A was given placebo and continuous ultrasound therapy with the intensity of 0.5 W/cm2 applied to the palmar carpal tunnel for 10 minutes. Group B was given Diclofenac 75 mg/day in divided doses and sham ultrasound. The ultrasound was applied 5 days a week for 4 weeks. Each patient was clinically and electrophysiologically evaluated before and after treatment. There were statistically significant improvements ($p < 0.05$), in the clinical parameters of both groups after treatment. In the electrophysiologic study, the median SNAP amplitude was increased significantly after the treatment in ultrasound group (group A). When both groups were compared, group A had significant difference in increasing of median SNAP amplitude after treatment. The authors coclusion was that the therapeutic efficacy of low intensity ultrasound thermotherapy was satisfied for mild to moderate CTS. However, the electrophysiological changes after ultrasound treatment need further investigation

In the year 2007, Piazzini et al. in a systematic review [62] found thirty-three RCTs. The studies were analysed to determine the strength of the available evidence for the efficacy of the conservative treatment of CTS. In the conclusion of this study included that there is limited or conflicting evidence (level 3) that ultrasound is effective.

4.5 Laser therapy

Naeser et al. [53] randomized eleven patients with carpal tunnel syndrome to low-level laser therapy (LLLT) or sham laser therapy. In addition to LLLT, the investigational group also received TENS. Significant improvement in pain scores median nerve sensory latency, and Phalen and Tinel signs were reported for the LLLT group compared to those receiving sham therapy. However, the number of patients was too small to reach firm conclusions and the authors state that further studies with larger numbers of patients are needed. Studies are also needed in which LLLT is compared to outcomes of standard treatments of carpal tunnel syndrome including treatment with non-steroidal antiinflammatory medications with splinting and/or surgery.

Irvine et al. [38] reported on the results of a small double-blind study of fifteen patients with carpal tunnel syndrome who were randomized to receive either low-level laser therapy or sham laser therapy. There was a significant improvement in both groups, but there was no significant difference between the groups.[38] Bakhtiary and Rashidy reported on the outcomes of 50 consecutive patients with carpal tunnel syndrome who were randomized to receive ultrasound therapy or low-level laser therapy. Improvement was significantly better in those randomized to ultrasound. [6]

Gerritsen et al. provided a systematic review [29] in order to determine the efficacy of the various conservative treatment options for relieving the symptoms of CTS. Found that laser seem to be ineffective in providing short-term symptom relief (varying levels of evidence).

Piazzini et al. recently in a systematic review [62] found limited or conflicting evidence (level 3) that laser is effective as a conservative therapy in carpal tunnel syndrome.

4.6 Exercise therapy

Of the many studies of conservative treatment of CTS, only a few has used exercise treatment. Tendon- and nerve-gliding exercises have been used particularly for the management of postoperative CTS [79], while only two studies in the literature has used tendon- and nerve-gliding exercises in conservative management of CTS. The value of these exercises in conservative management of CTS is not well understood.[1,68]

Tendon- and nerve-gliding exercises have been mostly used in the postoperative CTS.[72,78,79] Totten and Hunter[79] proposed a series of exercises enhancing the gliding of the median nerve at the carpal tunnel for management of postoperative CTS. They also suggested these exercises for non-operative CTS. Szabo et al.[78] showed that the relationship between median nerve and flexor tendon excursion was consistently linear. They suggested active finger motion of the median nerve and flexor tendons in the vicinity of the wrist to prevent adhesion formation even if the wrist is immobilized. Seradge and colleagues[72] demonstrated that intermittent active wrist and finger flexion-extension exercises reduce the pressure in the carpal tunnel. Tendon- and nerve-gliding exercises may maximize the relative excursion of the median nerve in the carpal tunnel and the excursion of flexor tendons relative to one another.[66]

Of the many studies of conservative treatment of CTS, only two have used exercise treatment.[1,68] Rozmaryn et al. [68] have used nerve- and tendon-gliding exercises in conservative treatment models to decrease adhesions developed in the carpal tunnel and regulate venous return in the nerve bundles. They reviewed more than 200 hands under consideration for carpal tunnel decompression. Altogether 71% of the patients who were not offered gliding exercises went forward to surgery; only 43% of the gliding exercise group were felt to require surgery. Although they had a large number of patients and a long follow-up period, their control group's treatment was not standardized.[68] Throughout the extremity movement, mobility of the peripheral nerve changes and longitudinal movement of the median nerve mostly occur in the carpal tunnel. In CTS, this physiologic mobility of the median nerve disappears.[44] During the exercise, there may be redistribution of the point of maximal compression on the median nerve. This milking effect would promote venous return from the median nerve, thus decreasing the pressure inside the perinerium.[66] Akalin et al. compared the group of wrist splint alone to the group with wrist splint in combination with nerve- and tendon-gliding exercises for the efficacy of the treatment. They reported significant improvement in clinical parameters, functional status scale and symptom-severity scale in both groups. They also reported significant improvement only in pinch strength in the group with wrist splint in combination with exercises compared with the wrist splint group.[1]

Hayes et al. found in their study a significant improvement in patients' carpal tunnel symptoms when tendon-gliding exercises were performed in conjunction with traditional treatment. [34]

4.7 Chiropractic treatment

Davis et al.[18] in a randomized clinical trial compared chiropractic treatment of carpal tunnel syndrome (CTS) to nonsurgical medical treatment. Their study included ninety-one subjects who reported symptoms that were confirmed by clinical exam and nerve conduction studies. The study design was two-group, randomized, single-blind trial with 9 weeks of treatment and a 1-month follow-up interview The chiropractic group used manipulation, ultrasound, and wrist supports while the medical group used wrist supports and ibuprofen. While both treatment groups improved significantly, the authors noted that chiropractic represents an alternative conservative treatment for CTS, especially for patients "who are unable to tolerate ibuprofen"

Bonebrake, et al. [8,9] compared several objective measures and subjective pain ratings between an experimental group of individuals with CTS and a control group without CTS. These same measures were then compared, following a treatment program designed to address CTS in 25 subjects. The treatment was designed to decrease muscular and fibrotic restriction. Osseous and soft-tissue manipulation were applied to cervical, thoracic, and lumbar regions of the spine, upper and lower extremities, shoulder girdle, and rib cage. Dietary modifications were addressed, along with exercises specific to the wrists, thumbs, and neck for increased flexibility. Ultrasound was also used in several cases. This study indicated improvements in strength and ROM measures at the conclusion of treatment. The average number of treatments was 27, and ranged from three to 96 treatments. Most subjects were treated daily, five times per week, while some received two treatments per day, three times per week. A 15 percent reduction in pain and distress rating were also noted, and subjects were able to perform many tasks of daily living and return to hobbies that they were unable to do prior to treatment. All subjects maintained the same job positions and had no lost work time throughout the duration of the study.1 In a six-month follow-up study, 22 of the initial subjects were reevaluated and demonstrated to have maintained

improvements in most of the objective measures and pain and distress ratings over the pretreatment level.

4.8 Alternative therapies

Acupuncture

Acupuncture may be useful in the treatment of CTS. In a preliminary trial, people with CTS (some of whom had previously undergone surgery) received either acupuncture or electro-acupuncture (acupuncture with electrical stimulation). Eighty-three percent of the participants in this trial experienced complete relief that lasted through two to eight years of follow-up.[15] After reviewing all available scientific literature on the topic, a consensus conference convened in 1997 by the National Institutes of Health concluded that acupuncture for CTS "may be useful as an adjunct treatment or an acceptable alternative or be included in a comprehensive management program.[54]

Yoga

Garfinkel et al. in a randomized controlled trial [25], randomised forty-two patients with CTS to yoga or standard practice. Subjects assigned to the yoga group received a yoga-based intervention consisting of 11 yoga postures designed for strengthening, stretching, and balancing each joint in the upper body along with relaxation given twice weekly for 8 weeks. Patients in the control group were offered a wrist splint to supplement their current treatment. Subjects in the yoga groups had significant improvement in grip strength (increased from 162 to 187 mm Hg; P = .009) and pain reduction (decreased from 5.0 to 2.9 mm; P = .02), but changes in grip

strength and pain were not significant for control subjects. The yoga group had significantly more improvement in Phalen sign (12 improved vs. 2 in control group; P = .008), but no significant differences were found in sleep disturbance, Tinel sign, and median nerve motor and sensory conduction time. The authors conclusion was that in this preliminary study, a yoga-based regimen was more effective than wrist splinting or no treatment in relieving some symptoms and signs of carpal tunnel syndrome.

4.9 Combination therapy

Baysal et al. provided a randomized controlled trial [7], involving 36 female patients (72 wrists) with clinical and electrophysiological evidence of bilateral CTS. The aim of this study was to investigate and compare the therapeutic effect of three different combinations in the conservative treatment of carpal tunnel syndrome (CTS) by means of clinical and electrophysiological studies. The combinations included tendon- and nerve-gliding exercises in combination with splinting, ultrasound treatment in combination with splinting and the combination of ultrasound, splinting, tendon- and nerve-gliding exercises. Study was limited by the small number of patients but results showed significant improvement in tinels and phalens signs and pain at end of treatment and at 8 week follow-up, improvement in grip and pinch strength at 8 week follow-up. The results of the long-term patient satisfaction questionnaire revealed that symptomatic improvement is more prominent in the group treated with splinting, exercise and ultrasound therapy combination. Results suggest that a combination of splinting, exercise and ultrasound is a preferable and efficacious type of treatment in CTS. [7]

Graham et al. performed a prospective study[32] to assess the role of steroid injections combined with wrist splinting for the management of carpal tunnel syndrome. A total of 73 patients with 99 affected hands were studied. Patients presenting with known medical causes or muscle wasting

were excluded. Diagnosis was made clinically and electrodiagnostic studies were performed only when equivocal clinical signs were present. Each patient received up to three betamethasone injections into the carpal tunnel and wore a neutral-position wrist splint continuously for 9 weeks. After that period, symptomatic patients received an open carpal tunnel release, and those who remained asymptomatic were followed up regularly for at least 1 year. Patients who relapsed were scheduled for surgery. At a minimum follow-up of 1 year, seven patients (9.6 percent) with 10 affected hands (10.1 percent) remained asymptomatic. This group had a significantly shorter duration of symptoms (2.9 months versus 8.35 months; $p = 0.039$, Mann-Whitney test) and significantly less sensory change (40 percent versus 72 percent; $p = 0.048$, Fisher's exact test) at presentation when compared with the group who had surgery. It is concluded that steroid injections and wrist splinting are effective for relief of carpal tunnel syndrome symptoms but have a long-term effect in only 10 percent of patients. Symptom duration of less than 3 months and absence of sensory impairment at presentation were predictive of a lasting response to conservative treatment. It is suggested that selected patients (i.e., with no thenar wasting or obvious underlying cause) presenting with mild to moderate carpal tunnel syndrome receive either a single steroid injection or wear a wrist splint for 3 weeks. This will allow identification of the 10 percent of patients who respond well to conservative therapy and do not need surgery.

5. Conclusion

This thesis completed a systematic review of the relevant literature on the efficacy of conservative treatment of carpal tunnel syndrome (CTS). Forty nine clinical trials and seven systematic reviews were found and evaluated according their results.

Splinting provides significant benefits in the treatment of CTS in mild to moderate state of disease. The key for an effective treatment with splinting is the early intervention, within 3 months of the onset of symptoms and the full-time application. In later stage and for long term benefits splinting is better to used almost every night. In comparison with surgery, surgical procedure results better outcomes than conservative treatment with wrist splinting, especially long term outcomes.

Oral administered medicaments like oral steroids provide short term improvements but the non steroidal anti-inflammatory drugs (NSAIDs), diuretics and pyridoxine (vitamin B6) are no more effective than placebo in relieving the symptoms of carpal tunnel syndrome.

Local corticosteroid injection provides significant short term improvement, better than oral steroids or splinting alone. In comparison to surgery, over the short term, local steroid injection is better than surgical decompression for the symptomatic relief of CTS.

Ultrasound therapy may provide some short term benefits in mild to moderate state of CTS, but more high quality clinical trials are necessary to be done, as the most recent high quality systematic reviews found limited or conflicting evidence that ultrasound is effective in the treatment of CTS.

Laser therapy seems to be ineffective in providing short term symptoms relief, due to limited or conflicting evidence as a conservative therapy of CTS. Further high quality clinical trials have to be done.

Exercise therapy seems to be ineffective as a conservative treatment of CTS, according the small number of clinical trials. Further clinical trials are necessary in order to determine the efficacy of exercise therapy. Significant improvement of symptoms reported when exercises performed in combination with splinting. Exercise therapy provides significant benefits post operatively.

Alternative therapies like chiropraxy, yoga and acupuncture, may provide some short term benefits in the treatment of CTS, but, due to the small number of clinical trials, more clinical trials are necessary to performed in order to establish their efficacy.

Combination therapy, like ultrasound with splinting and exercises, seems to be a preferable and efficacious type of treatment in CTS. Significant improvement of symptoms reported when exercises performed in combination with splinting Also, the combination of steroid injections with splinting is effective to relief the symptoms of CTS. More clinical trials are necessary to be done, in order to determine the long term efficacy of combination therapy.

Conservative treatment provides significant benefits in the treatment of CTS in mild to moderate state of disease. Conservative treatment offers short-term benefit (1-3 months) similar to surgery and many patients' symptoms may resolve for at least a year after conservative treatment. More severe cases, when thenar atrophy is present, or carpal tunnel syndrome following acute trauma, need surgical intervention.

6. Discussion

Many patients suffer from carpal tunnel syndrome. The question that arises is: conservative or surgical treatment for the CTS? This thesis proved that the conservative treatment plays an important role in the treatment of CTS, especially in mild to moderate state of the disease. A trial of conservative therapy offers the opportunity to avoid surgery for some patients. Most severe cases need surgical intervention.

During the research on the efficacy of conservative treatment of CTS, many clinical trials of alternative therapeutic methods like yoga and acupuncture were found. This means that the patients trying to find other that the usual therapeutic approaches and the most important is that these techniques have some therapeutic results. Scientifically is very important an open-minded approximation of the disease and a combination of eastern and western therapeutic techniques could be useful.

As a physiotherapist, I am glad because I saw that ultrasound, laser therapy, exercises and activity modification instructions may provide benefits in the treatment of CTS. These procedures are parts of a standard physiotherapeutic session. Dr. Lewit in his book mentions that for the treatment of CTS, mobilization techniques of carpal bones like joint play could be very effective. Mobilization techniques are also a part of physiotherapeutic session. It will be very interesting to see in the future a clinical trial that examines the efficacy of the combination therapy, formed only by physiotherapeutic techniques.

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Appendix

Levels of Evidence for Primary Research Question[1]

	Types of Studies			
	Therapeutic Studies Investigating the results of treatment	**Prognostic Studies** Investigating the effects of a patient characteristic on the outcome of disease	**Diagnostic Studies** Investigating a diagnostic test	**Economic and Decision Analyses** Developing an economic or decision model
Level I	• High quality randomized trial with statistically significant difference or no statistically significant difference but narrow confidence intervals • Systematic review[2] of Level I randomized controlled trials (RCTs) (and study results were homogenous[3])	• High quality prospective study[4] (all patients were enrolled at the same point in their disease with ≥80% follow-up of enrolled patients) • Systematic review[2] of Level I studies	• Testing of previously developed diagnostic criteria on consecutive patients (with universally applied reference "gold" standard) • Systematic review[2] of Level I studies	• Sensible costs and alternatives; values obtained from many studies; with multiway sensitivity analyses • Systematic review[2] of Level I studies
Level II	• Lesser quality RCT (e.g., <80% follow-up, no blinding, or improper randomization) • Prospective[4] comparative study[5] • Systematic review[2] of Level II studies or Level I studies with inconsistent results	• Retrospective study[6] • Untreated controls from an RCT • Lesser quality prospective study (e.g., patients enrolled at different points in their disease or ≤80% follow-up) • Systematic review[2] of Level II studies	• Development of diagnostic criteria on consecutive patients (with universally applied reference "gold" standard) • Systematic review[2] of Level II studies	• Sensible costs and alternatives; values obtained from limited studies; with multiway sensitivity analyses • Systematic review[2] of Level II studies
Level III	• Case control study[7] • Retrospective[6] comparative study[5] • Systematic review[2] of Level III studies	• Case control study[7]	• Study of nonconsecutive patients; without consistently applied reference "gold" standard • Systematic review[2] of Level III studies	• Analyses based on limited alternatives and costs; and poor estimates • Systematic review[2] of Level III studies
Level IV	• Case series[8]	• Case series	• Case-control study	• Analyses with no sensitivity

Types of Studies				
	Therapeutic Studies Investigating the results of treatment	**Prognostic Studies** Investigating the effects of a patient characteristic on the outcome of disease	**Diagnostic Studies** Investigating a diagnostic test	**Economic and Decision Analyses** Developing an economic or decision model
			• Poor reference standard	analyses
Level V	Expert opinion	Expert opinion	Expert opinion	Expert opinion

[1] A complete assessment of quality of individual studies requires critical appraisal of all aspects of the study design.
[2] A combination of results from two or more prior studies.
[3] Studies provided consistent results.
[4] Study was started before the first patient enrolled.
[5] Patients treated one way (e.g., cemented hip arthroplasty) compared with a group of patients treated in another way (e.g., uncemented hip arthroplasty) at the same institution.
[6] The study was started after the first patient enrolled.
[7] Patients identified for the study based on their outcome, called "cases"; e.g., failed total hip arthroplasty, are compared to those who did not have outcome, called "controls"; e.g., successful total hip arthroplasty.
[8] Patients treated one way with no comparison group of patients treated in another way.