# Thesis Title: A Concise Review of Carpal Tunnel Syndrome: Anatomy, Epidemiology, Pathophysiology, Diagnosis and Management.

**BY**

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# A Concise Review of Carpal Tunnel Syndrome: Anatomy, Epidemiology, Pathophysiology, Diagnosis and Management.

## Abstract

Carpal tunnel syndrome (CTS) is the most common peripheral nerve entrapment syndrome, accounting for approximately 90% of all focal entrapment neuropathies. CTS is caused by compression of the median nerve as it travels through the wrist's carpal tunnel. Traditionally, patients with CTS experience pain, numbness, and paresthesia along the distribution of the median nerve. CTS costs the United States billions of dollars annually. Therefore, it is vital that the primary care physician fully understands this syndrome, so they can diagnose it and guide proper treatment. This review provides an overview of CTS with emphasis on anatomy, epidemiology, pathophysiology, diagnosis, and management.

## 1. Introduction

Carpal Tunnel Syndrome (CTS) is a common medical disorder affecting the general patient population. It is the most common peripheral nerve entrapment syndrome, accounting for approximately 90% of all focal entrapment neuropathies[1,2]. CTS occurs when the median nerve is compressed as it travels though the wrist, leading to decreased function of the nerve at that level. The syndrome is associated with early symptoms like pain, numbness, and paresthesia in the distribution of the median nerve, namely the thumb, index finger, middle finger, and the radial half of the ring finger (**Figure 1**). Pain can also radiate up the involved arm. With further advancement of the disease, weakness and clumsiness of the hand, poor grip strength, decreased fine motor coordination and thenar muscles atrophy can occur. Earlier, symptoms tend to be more common at night, but they become more constant with further progression. In the United States, CTS is the most expensive upper extremity musculoskeletal disorder, with costs exceeding $2 billion yearly[3]. Most patients with CTS are industrial workers, females and elderly who are presenting to their general practitioners or primary care physicians for the first time. Consequently, it is important for such practitioners to fully understand the syndrome so they can diagnose it and guide proper treatment. This review article discusses anatomy, epidemiology, pathophysiology, diagnosis, and management of CTS.

**Figure 1.** The palmar distribution of the median nerve.

## 2. Anatomy of the carpal tunnel

The carpal tunnel is located at the proximal palmar area of the wrist where it serves as a passageway that connects the forearm to the hand. Superiorly, it is bounded by a sheath of tough connective tissue, the flexor retinaculum. The floor of this tunnel is formed by carpal bones. The eight carpal bones are arranged in two transverse rows (proximal and distal) and form an arch which is convex on the dorsal side and concave on the palmar side. From the lateral to the medial side of the hand, the four carpal bones on the proximal row are scaphoid, lunate, triquetrum, and pisiform. In a similar order, the four carpal bones on the distal row are trapezium, trapezoid, capitate, and hamate. The flexor retinaculum is attached to the tubercle of the scaphoid bone and the ridge of the trapezium on the radial side of the hand while on the ulnar side it is attached to the pisiform bone and the hook of the hamate. Running through this tunnel from the forearm to the hand are ten structures: nine long flexor tendons (flexor pollicis longus, four tendons of flexor digitorum superficialis and four tendons of flexor digitorum profundus) and the median nerve. The median nerve is one of the major peripheral nerves of the upper limb. It lies just below the flexor retinaculum as the most superficial structure of the carpal tunnel (**Figure 2 & 3**). It journeys from the anterior compartment of the forearm through the carpal tunnel into the wrist, where it forms branches to provide motor innervation to the thenar muscle group (abductor pollicis brevis, flexor pollicis brevis and opponens pollicis) and sensory innervation to the palmar surface of the thumb, index, middle and radial half of the ring finger (**Figure 1**). CTS results from any lesion that significantly narrowed the size of the carpal tunnel or that causes the swelling of the synovial sheaths of the long flexor tendons. This significant constriction of the carpal tunnel leads to compression of the median nerve, producing early symptoms like pain, numbness, and paresthesia in the distribution of the median nerve. With further progression of the disease, weakness and clumsiness of the hand, poor grip strength, decreased fine motor coordination and thenar muscles atrophy can occur.

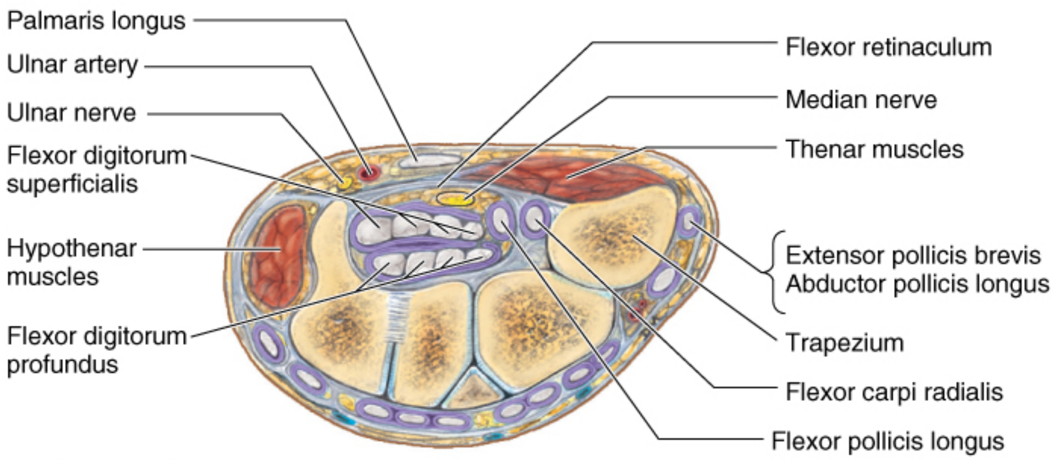
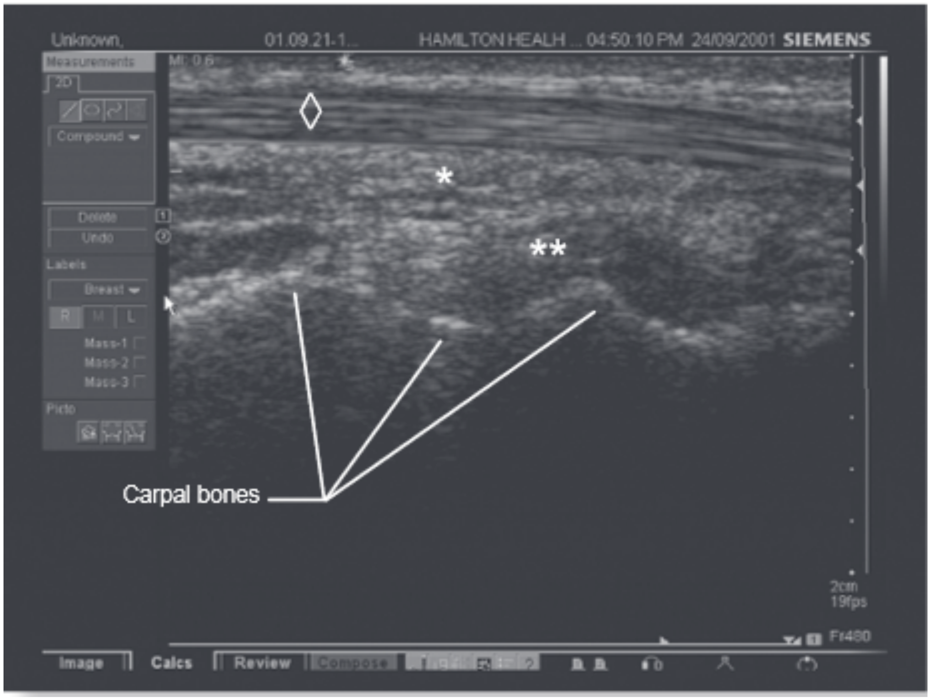



**Figure 2.** Anatomical diagram of the carpal tunnel in transverse section.

**A.**

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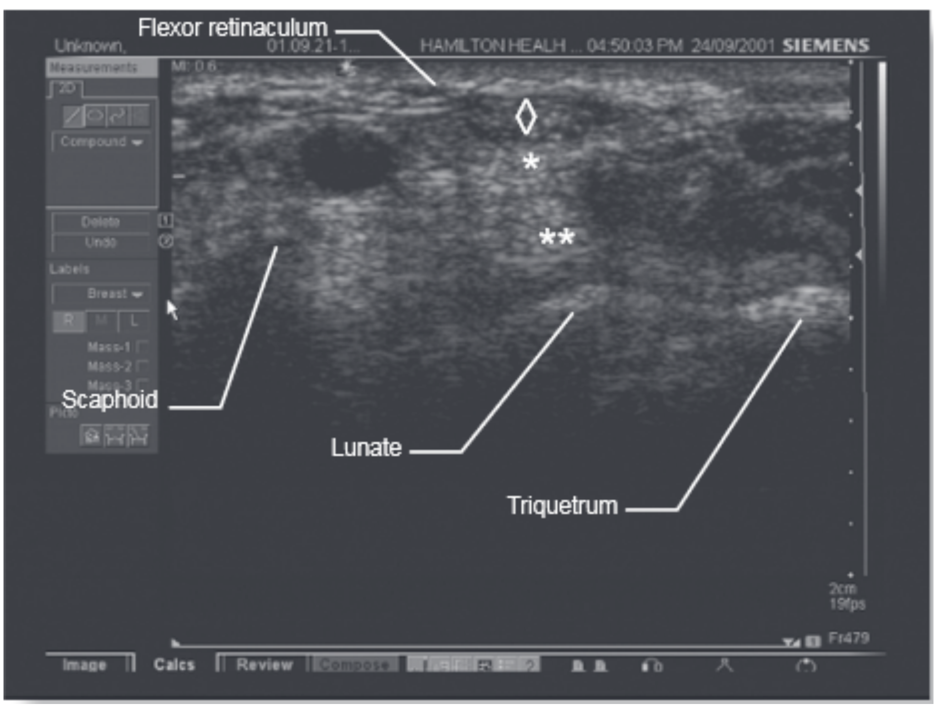


**C.**

**Figure 3.** Ultrasound imaging of the normal carpal tunnel at the volar aspect of the wrist. (A) Transducer placement technique for longitudinal imaging. (B) On this longitudinal scan, the median nerve (◊) is seen overlying the relatively hyperechoic superficial (∗) and deep (∗∗) flexor tendons of the wrist. The median nerve, like tendons, appears as a hyperechoic fibrillar structure.

(C) On this transverse scan, the hyperechoic median nerve is located deep to the hyperechoic flexor retinaculum and has a characteristic cyst-like appearance[51].

## 3. Epidemiology

The estimates of the prevalence and incidence of CTS vary widely in the literature. Worldwide, an estimated 4-5% suffers from CTS and the most liable population being elderly individuals aged between 40 and 60 years[4,5]. The UK General Practice Research Database in 2000 reveals that the prevalence of CTS was 88 per 100,000 in males and 193 per 100,000 in females showing that CTS is more common amongst women as compared to men[6,7]. CTS is a work-related musculoskeletal disorder (WMSD) caused by strain and repeated movement thus it is quite common amongst manual workers. The associated work absence and healthcare cost is a significant socioeconomic burden to the UK economy[6]. In the United States, the incidence of CTS is 1-3 persons per 1000 subjects per year, with a prevalence of 50 cases per 1000 subjects in the general population[2]. CTS most commonly affects whites and appears to be rare in some racial groups (e.g., nonwhite South Africans)[8]. In North America, the rate of CTS is 2-3 times more common among the white US Navy personnel compared to their black counterparts[9].

## 4. Etiology and Risk Factors

Most cases of CTS are idiopathic[10]. Several risk factors and diseases associated with this medical condition have been identified. These include female gender (peak age 45-54 years), genetic predisposition, aging, obesity, alcoholism, drug toxicities and exposure to toxins[2,7,11-12] . If a woman has not experienced the symptoms of CTS in her middle age years, she is less likely to experience them for the first time in old age. Contrastingly, the incidence in men seems to increase with age. Hormonal factors play a role in the gender differences observed in CTS. Accordingly, the incidence of CTS is higher in pregnancy, breastfeeding women, women in their first menopausal year, women on oral contraceptives pills or hormone replacement therapy[11,13-14]. However, oophorectomy reduces the incidence of CTS[11]. Obese individuals are 2.5 times more likely to be diagnosed with CTS compared to non-obese ones[15]. Some CTS cases are linked with endocrine disorders such as hypothyroidism, acromegaly, diabetes mellitus[11]. In hypothyroidism, the resulting myxedema can cause the deposition of mucopolysaccharides and water within both the perineurium of the median nerve and the tendons of the carpal tunnel. With acromegaly, the hypersecretion of growth hormones causes excessive growth of the soft tissues and bones around the carpal tunnel leading to compression of the median nerve. Trauma (like fracture of the wrist) and diseases that cause inflammation may increase the volume within the carpal tunnel and thus lead to CTS[11]. A good example is rheumatoid arthritis, where the resulting pannus formation or synovitis can lead to an increase in carpal tunnel pressure. Additionally, space occupying lesions in the carpal tunnel like tumor, lipoma, ganglion cysts, infection and scar tissue can lead to compression of the median nerve[12].

A lot of studies have been carried out to show the association between CTS and occupational activities. A review of these studies reveals a positive association between CTS and occupations involving highly repetitive wrist motion, use of vibratory tools, increased hand force, and prolonged or repetitive flexion/extension of the wrist[11,16-19]. Most patients have often associated the onset of CTS with excessive computer keyboarding and mouse use. Surprisingly, up to date, the literature shows no clear evidence to support this association[20-21]. In the systematic review published by Thomsen et al in 2008 and Mediouni et al in 2014, it was concluded that some certain work circumstances involving computer mouse use may increase the incidence of CTS and although, carpal tunnel pressure does increase with computer keyboarding and mouse use, however, the pressure was still below harmful levels[20-21]. Thus, keyboarding and mouse use should be viewed as aggravating factors for CTS rather than as a risk factor.

## 5. Pathophysiology

As discussed in the section above, CTS is associated with many epidemiological risk factors, including genetic, social, occupational, medical, and demographic. An interplay between these factors eventually leads to the development of CTS.

The pathophysiology of CTS is related to a merger of two processes, compression, and traction mechanisms. The compression mechanism results from an increase in carpal tunnel pressure. Normally, in a healthy subject, the pressure in the carpal tunnel ranges between 2.5 to 13mmHg[16,22]. However, in CTS patients, the pressure may rise to critical levels above 20-30mmHg[16]. The abnormally high carpal tunnel pressure leads to obstruction to venous outflow, back pressure, increasing local edema, and eventually, ischemia of the median nerve. The latter results due to the compromise to the blood flow to the endoneurial capillary system. The resulting alteration in the blood-nerve barrier interferes with the structural integrity of the median nerve, leading to demyelination and axonal degeneration. The traction mechanism is due to the repetitive traction and wrist movements. Flexion and extension of the wrist can cause eight and ten times increase in the carpal tunnel's fluid pressure respectively[23]. Thus, repetitive wrist movements will further worsen the nerve damage in CTS patients. Accordingly, splinting of the wrist to hold it in a neutral position is widely considered the first line of treatment for mild to moderate CTS cases.

## 6. Diagnosis

The diagnosis of CTS involves a combination of thorough history and physical examination in conjunction with adjunctive tests like electrodiagnostic studies and ultrasonography.

### 6.1 **History**

A detailed history is a very vital component of the diagnostic workup towards the identification of CTS in a patient. With regards to the symptoms, the clinician should ask the patient about its duration, frequency, location, character, radiation (e.g., Do symptoms radiate from the shoulder?), progression (better, worse, or stable?), timing (night, day, or both), frequency, severity, aggravating factors (certain positions or movements), relieving factors (ice, rest, shaking/flicking the hand and wrist or use of splints). The shaking or flicking of the hands to provide relief from CTS symptoms is known as the flick sign. The flick sign is 93% sensitive and 96% specific[24]. Additionally, the clinicians should ask about the patients' lifestyle/activities, whether they use vibratory tools for their tasks, predisposing factors and any comorbidities such as diabetes, obesity, pregnancy, or inflammatory arthritis. History may reveal the classic features of CTS, that is, pain, numbness, and paresthesia in the distribution of the median nerve, namely the thumb, index finger, middle finger, and the radial half of the ring finger. Numbness existing in the fifth finger or extending to the dorsum of the hand should suggest other diagnoses (**Table 1**). Additionally, there can be associated history of decreased strength with pinching or grip with patients reporting that their hands fall asleep, or things slip through their fingers unintentionally. Patients may describe difficulty in holding objects, buttoning a shirt, or opening jars. They may also report that the symptoms are worse at night and are associated with certain activities that fully flex/extend the wrist, such as driving, holding a telephone, reading newspapers or painting.

| **Table 1. Differential Diagnosis of Carpal Tunnel Syndrome** |
| --- |
| • Cervical radiculopathies at C6-C7 |
| • Arthritis of the wrist |
| • Carpometacarpal arthritis of the thumb |
| • de Quervain tendinopathy |
| • Peripheral neuropathy |
| • Pronator syndrome |
| • Raynaud syndrome |
| • Ulnar compressive neuropathy |
| • Tendonitis |
| • Tenosynovitis |

### 6.2 **Physical Examination**

This involves a complete examination of the upper limb, including neck, shoulder, elbow, and wrist, to exclude other neurologic or musculoskeletal diagnoses (**Table 1**). Initial inspection of the hand and wrist may reveal evidence of precipitating factors such as arthritic changes and other signs of prior injuries like abrasions, ecchymosis, deformities, swelling and other skin changes. Inspection can also reveal wasting and atrophy of the muscles of the thenar eminence. Sensory examination may show lack of two-point discrimination and abnormalities in sensation on the palmar aspect of the first three digits and radial one half of the fourth digit of the affected hand. This will help to localize the symptoms to the median nerve distribution. Motor examination may reveal wasting of the thenar eminence muscle groups and weakness of thumb abduction and opposition.

In clinical practice, the physical examination includes some special provocative tests with varying degrees of sensitivities and specificities[24]. Nevertheless, these tests are easy to perform, and a combination of positive findings from them can increase the possibility of CTS[24,25].

- Median nerve (Carpal tunnel) compression test: It is considered the best of all the provocation tests for CTS[2,12]. Examiner applies firm pressure directly over the carpal tunnel for 30 seconds. A positive test is demonstrated when the symptoms (pain, numbness, and paresthesia) are reproduced in the distribution of the median nerve.

- Phalen's maneuver: Patient fully flexes both wrists to 90 degrees by placing dorsal surfaces of both hands together for 60 seconds. A positive test is demonstrated when the symptoms are reproduced in the distribution of the median nerve.
- Reverse Phalen's maneuver (Prayer test): Patient extends both wrists by placing palmar surfaces of both hands together for 60 seconds (as if praying). Again, a positive test is demonstrated when the symptoms are reproduced in the distribution of the median nerve.
- Tinel sign: Examiner percusses/taps the volar surface of the patient wrist over the carpal tunnel. A positive test is demonstrated when the symptoms are reproduced in the distribution of the median nerve.

### 6.3 **Adjunctive Tests**

In a classic case of CTS, diagnosis is clinical (History and Physical Examination). Nonetheless, electrodiagnostic studies can assist in confirming the diagnosis, especially in atypical cases. Ultrasonography has been shown to be useful in diagnosing CTS.

#### 6.3.1 **Electrodiagnostic studies**

Electrodiagnostic or electrophysiological studies involve nerve conduction studies (NCS) and electromyography (EMG). With NCS, you can measure the speed and strength of impulses propagated through the length of a peripheral nerve. Thus, it can confirm CTS by revealing an impaired conduction through the median nerve. EMG records and analyzes electrical activity in the muscles. It can reveal pathological changes in the muscles innervated by the median nerve. However, electrodiagnostic studies have their limitations. For CTS, electrodiagnostic studies have a sensitivity and specificity of 56% to 85% and 94% to 99% respectively[26]. False positives and negatives have been reported with electrodiagnostic studies. Witt JC et al in 2004 reveals that NCS results were normal in up to one-third of patients with mild CTS[27]. Thus, electrodiagnostic studies are not a perfect gold standard for the diagnosis of CTS and cannot replace the clinical examination. However, in combination with clinical examination, they can serve as a powerful confirmatory tool for the diagnosis of CTS. Most importantly, electrodiagnostic studies can help in ruling out other neurologic diagnoses and to determine the severity of CTS. Limited evidence exists in support of a correlation between findings from electrodiagnostic studies alone and functional recovery from CTS following carpal tunnel release surgery[28]. This limits the prognostic use of electrodiagnostic studies. However, if a repeat NSC test after the carpal tunnel release surgery shows improvement in median nerve function, this can help to reassure the patient. The American Academy of Orthopedic Surgery (AAOS) guidelines for diagnosing CTS recommend that physician obtain electrodiagnostic studies if clinical examination and/or provocative tests are positive and surgical management is being considered[29].

#### 6.3.2 **Ultrasonography**

Recently, ultrasonography has gained more popularity in the diagnosis of CTS. An increase in the cross-sectional area of the median nerve has been correlated with the diagnosis of CTS. In their meta-analysis study, Tai et al reveals that a cross-sectional area of 9 $mm^2$ or more of the median nerve is 87.3% sensitive and 83.3% specific for CTS[30]. Ting et al reveals a positive association between ultrasound measurement and electrodiagnostic studies in CTS patients[31].

Additionally, Wessel et al reveals a positive association between the severity of CTS and increased cross-sectional area of the median nerve[32]. The advantages ultrasonography offers include patient comfort; lower cost; non-invasiveness; and its ability to rule out etiologies like mass lesion, tendinopathies etc. However, local expertise is a requirement since ultrasound imaging is highly-operator dependent. Additionally, ultrasound cannot determine the severity of CTS or rule out etiologies such as polyneuropathies[24].

## 7. Management

Following the suspicion or the establishment of the diagnosis of CTS, primary care physicians should refer their patients to an orthopedic hand specialist. The management of CTS will depend on the severity of the disease. In mild and moderate cases of CTS, conservative treatment options are recommended. These include wrist splinting, local and systemic corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), physical therapy, therapeutic ultrasound, and yoga[24]. Conservative management options encourage improved symptoms in two to six weeks and reaches maximal benefits at three months[24,33]. Initially, patients are instructed on how to reduce their symptoms by modifying their movement at the wrist. Patients should practice proper hand ergonomics. Repetitive wrist movements should be avoided if possible.

A properly fitted splint that holds the wrist in a neutral position is widely recommended. Splinting is even more advisable for use in reversible cases of CTS, such as pregnancy, where it can be used to supplement other treatment options. Splints are low cost, tolerable, simple, and effortless. A Cochrane review conducted in 2012 found nighttime wrist splinting to be more effective than placebo[34]. Additionally, the review found insufficient evidence to endorse one splint design over another or compare effectiveness of splinting to another conservative treatment options.

Oral and local corticosteroids may be recommended for patients with mild to moderate CTS. An oral prednisone at a dosage of 20 mg daily for 10 to 14 days (about 2 weeks) was shown to be effective for the symptomatic treatment of CTS compared with placebo, with its improvement lasting up to eight weeks[24,35,36]. However, oral corticosteroids are associated with some serious side effects, and they are less effective than corticosteroid injection. A 2007 Cochrane review reveals that local carpal tunnel corticosteroid injection produced symptomatic benefit for up to one month compared with placebo[35,37]. Ultrasound-guided injections are more effective and safer than blind injections[38]. Although local carpal tunnel corticosteroid injections are safe, misplaced injections can lead to median nerve injury and tendon rupture. Other medications like non-steroidal anti-inflammatory drugs, diuretics, and vitamin $B_6$ are not effective and evidence does not support their use[35,39,40].

Another conservative treatment option for mild to moderate CTS is physical therapy. Physical therapy includes carpal bone mobilization, therapeutic ultrasound, and nerve glide exercises. There is limited evidence to show that physical therapy is effective in the treatment of CTS[41,42]. Therapeutic ultrasound and carpal bone mobilization require an experienced therapist and several sessions[42]. Nerve glide exercises are quite simple and easy to learn exercises that can be done at home. A video showing the demonstration of these exercise techniques is available at https://www.youtube.com/watch?v=B5goXA9MqCA. Garfinkel et al reveals that yoga offers some benefits in CTS compared to wearing a wrist splint[43].

### 7.1 **Carpal tunnel release (CTR) surgery**

Patient with severe CTS (such as when there is wasting of the thenar muscles or weakness of thumb opposition) or nerve damage (axonal degeneration) on nerve conduction studies should be offered surgical intervention with carpal tunnel release (surgical decompression). Patients should also be referred for surgical treatment when conservative measures fail or if the symptoms persist. CTR is usually performed by a neuro/orthopedic/plastic surgeon or hand surgeon. The procedure involves cutting the transverse carpal ligament or flexor retinaculum, thus opening more space in the carpal tunnel, and reducing the pressure on the median nerve. CTR has a lasting, good outcome in 70% to 90% of cases[44]. Furthermore, studies have shown that surgery is more effective and beneficial than conservative, non-surgical management options[45,46,47]. The surgical procedure can be performed either with an open approach, or endoscopically. Although open CTR remains the traditional, and most popular method of CTR, endoscopic CTR is gaining more popularity due to its more rapid recovery and improved safety profile[48]. Studies have shown that open and endoscopic CTR are equally effective; however, patients who had endoscopic CTR are able to return to work on average a week earlier than with open surgery[49,50].

## 8. Conclusion

CTS is the most common compressive neuropathy of the upper limb. It costs the United States billions of dollars annually. The hallmark of typical CTS is pain, numbness, and paresthesia along the distribution of the median nerve. Conservative management and limitation of repetitive wrist movements is warranted in mild and moderate cases of CTS. Surgical decompression is effective for severe CTS, and it involves the release of TCL to reduce the pressure on the median nerve within the carpal tunnel. Primary care physicians must understand this syndrome, so they can diagnose it and guide proper treatment.

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