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Risk Factors, Diagnosis, and Treatments for Carpal Tunnel Syndrome: A Review

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Abstract

Carpal tunnel syndrome (CTS) is a common medical condition that is usually caused by the compression of the median nerve at the level of the carpal tunnel. The mechanism leading to carpal tunnel syndrome is not completely understood. In general, CTS develops when the tissues around the median nerve swell and exert pressure on the median nerve. Symptoms present as tingling and numbness in the thumb, index, middle fingers and lateral half of the ring finger, pain in the anterior part of forearm and wrist, and awkwardness of hand. In early stages, the process leading to CTS is usually reversible. However, with the passage of time, the insulation over the surface of median nerve branches may wear away, and permanent damage to the nerve may develop. Several risk factors such as age >30 years, female sex, fractured carpal bones, rheumatoid arthritis, diabetes, high BMI, specific occupations involving repetitive twisting, bending or vibrations of wrists, congenital carpal tunnel stenosis, dialysis, pregnancy, etc. are responsible for CTS. The incidence of CTS in the US has been reported to be 3.5/1000 person-years, with a prevalence rate up to 3.7%. Rates of CTS have risen remarkably and rapidly over the recent years, but it is uncertain whether this is due to rising risk factors or a better awareness of the disease. CTS is uncommon in developing countries and has a different propensity for different ethnic groups. The purpose of this review article is to provide up-to-date information about the risk factors, diagnosis, and treatment strategies of CTS.

Introduction

Compression of the median nerve at the level of the carpal tunnel gives rise to signs and symptoms of carpal tunnel syndrome (CTS) [1]. Symptoms present as tingling and numbness in the thumb, index, middle fingers and lateral half of the ring finger, pain in the anterior part of the forearm and wrist, and awkwardness in the hand [2]. The incidence of CTS in the US has been reported to be 3.5/1000 person-years, with a prevalence rate up to 3.7% [3, 4]. The incidence and prevalence rates of CTS in many other developed countries are almost similar to the reported rates of the US [5–8]. CTS is uncommon in developing countries and has no different propensity for different ethnic groups. For instance, in South Africa white ethnic group has similar rates of CTS as those reported in Europeans, whereas it has almost never been heard of in the black ethnic group of South Africa [9]. Rates of CTS have risen remarkably and rapidly over the recent years, but it is uncertain whether this is due to rising risk factors or a better awareness of the disease. The syndrome is three times more frequent in females than in males [10].

This syndrome is correlated with various potential risk factors, these may include any factor that can cause alterations in the anatomical component of the carpal tunnel, pregnancy, age >30 years, high body mass index (BMI) [11], repetitive activities and movements of the wrists such as in some occupations, besides genetic and psychosocial factors [12]. Conclusively in most of the cases, the causation is more likely to be multi-factorial, and it is rare to have a single definite etiology [13]. Most of the potential risk factors may result in elevated pressure within the carpal tunnel and therefore, compression of the median nerve part that lies inside the tunnel (Fig. 1) [14]. The raised pressure can provoke a series of unfavorable events that eventually leads to disturbance of blood flow to the median nerve presenting as ischemia, and in some cases, scarring of the nerve may also take place [15]. In CTS patient, ischemia is likely to result in the typical intermittent sensation of pain and numbness (Fig. 2). Compression of the nerve will also cause demyelination and eventually axonal loss, and patients may present with no symptoms, but with abnormal findings on nerve conduction studies [16, 17]. The purpose of this review article is to provide up-to-date information about the risk factors, diagnosis, and treatment strategies of CTS.

Chronological approach for the diagnosis of CTS

CTS diagnosis is made by the combination of symptoms and abnormal findings of electrodiagnostic testing [18]. The history of CTS includes the gradual onset of the symptoms, intermittent pain and/or numbness of one or both hands, causing patients to wake up at night time, and usually relieved by wrist flicking or shaking. The typical history is highly specific for diagnosing CTS [19]. Numbness is typically presented in the arm, forearm, and in the wrist, it is restricted to the palmar aspect of the thumb, the index, the middle, and lateral half of the ring finger [20]. On awakening, most patients are likely to have difficulty in flexing or extending their fingers. In the daylight, symptoms are frequently associated with activities as holding an object (i.e., book, newspaper, and telephone), driving, or using a screwdriver. The patient may also complain of clumsy hand, particularly during performing fine-motor skills. Vasomotor manifestations and cold intolerance may present in some patients. Involvement of both wrists is an important hint of suspecting CTS, as many other conditions (strokes, radiculopathy, plexopathy, and proximal median neuropathies) are almost always unilateral. In ulnar neuropathy, sensory symptoms present in the little finger, whereas, in radiculopathy, sensory symptoms present proximal to the wrist crease [21].

It is important to perform the musculoskeletal examination of the upper extremity and the cervical spine to rule out many other musculoskeletal disorders that may mimic or coexist with CTS. The weakness of the muscles at the base of the thumb (thenar eminence) is a common finding. Nevertheless, wasting of the thenar eminence is the last stage of median nerve injury and is considered as an important sign in severe CTS [22]. A common differential diagnosis for CTS is a condition known as radiculopathy which can be confirmed or ruled out by performing some special tests of the neck such as

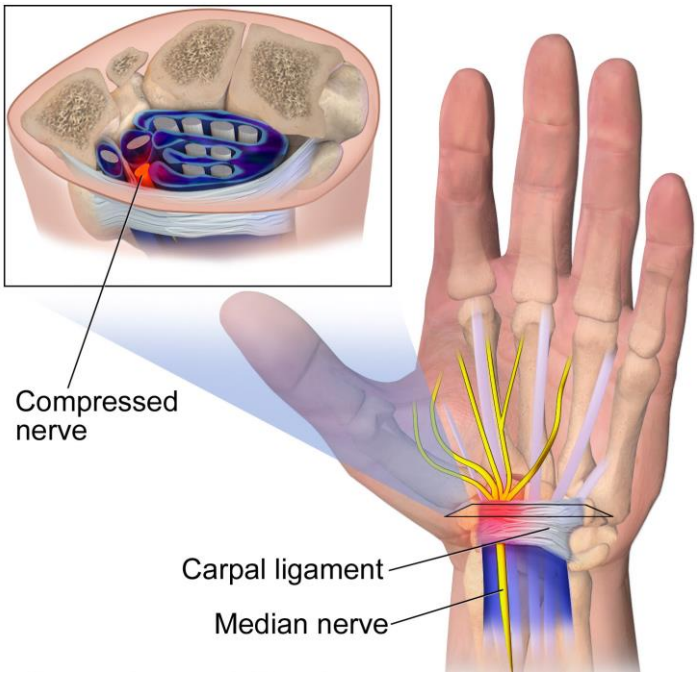

Fig. 1 Illustration of carpal tunnel syndrome.
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Spurling's test and range of motion. The examination should be held to exclude other conditions such as De Quervain's tenosynovitis, wrist flexor and extensor tendonitis and first carpometacarpal joint osteoarthritis since those conditions can be the cause of patient's symptoms and may also contribute to entrapment of median nerve [23]. A space-occupying lesion should be suspected when there is a focal swelling adjacent to the carpal tunnel and/or pain sensation in the nondominant hand [24].

It is necessary to perform a neurological examination to rule out other disorders such as radiculopathy and motor neuron disease. The most useful finding in CTS patients is the abnormal sensation to pinprick that exclusively presents over the palmar side of first three fingers and the radial half of the fourth finger, without the involvement of the thenar eminence. Clinicians should not rely on the thenar muscles weakness or bulkiness in determining the diagnosis of CTS since those signs are unreliable. Testing the reflexes is of great value in ruling out other conditions and they are typically normal in CTS [25]. Nerve conduction study (NCS) is the most specific and sensitive available test to make the diagnosis of CTS, and it is recommended in a patient who was clinically diagnosed with the syndrome. NCS is easily performed, able to confirm and localize abnormalities of the median nerve in the tunnel; moreover, it can provide categorization to the degree of damage to the nerve making it more possible to decide the route and kind of management. Additionally, the NCS can be performed to rule out other conditions such as C6-radiculopathy or to prove the presence of other co-existing pathologies such as polyneuropathies [26–28].

Recently, ultrasonography of the median nerve has been used as a complementary diagnostic tool for CTS. A ganglion cyst or tendinitis is structural abnormalities that may impact the median nerve and can be identified by ultrasound. An ultrasound can also support the diagnosis of CTS by detecting swelling and enlargement of the damaged median nerve. Additionally, ultrasound can be used to make it easier and more accurate when placing the needle for injecting the corticosteroid into the carpal tunnel [29, 30]. When suspecting space-occupying lesions in the wrist, then performing high-resolution ultrasound will be of great value in confirming or excluding such

lesions. MRI is also useful in cases where space-occupying lesions are suspected [31]. There are many different clinical tests used for the clinical diagnosis of CTS, those include: (1) Tinel's sign [32]; (2) Phalen's test [33]; (3) hand elevation test [34, 35]; (4) carpal compression test [36]; (5) tourniquet test; (6) pressure aesthesiometer and (7) two-point discrimination tests [37]. When clinically diagnosing CTS, the hand elevation test shows superiority if compared to questionnaires and other physical tests [38]. Tourniquet test has shown a poorer value in sensitivity when compared to Phalen and Tinel's test [39]. None of the mentioned clinical tests is optimal to detect CTS [36].

Risk factors for CTS

Age group below 30 years old is uncommon to have CTS, whereas it is most common in patients aged 40-60 years old. CTS is less common in ages 60-65 years old. In the population of working age, the probability of having CTS rises by 30% per decade [9, 10, 12]. This supports the hypothesis that the median nerve is compromised by degenerative events resulting from increased activity of the hands [30, 40–42]. It was reported that there is a positive relationship between high BMI and high risk of having CTS. In patients with obesity (BMI greater than 29.9), the risk of CTS is double the non-obese. The reasons for that association are unknown [43–45]. Mauro Mondelli et al. [46] have concluded that the waist: stature ratio is an important index that should be considered when studying the relationship between obesity and CTS. When compared to men, women are three times more likely to have CTS, for unclear reasons [5, 47]. Abnormalities within the space of the carpal tunnel (such as space-occupying lesions, tumors as lipoma of the hand, anomalous muscles) serve as clear unambiguous etiologies of CTS. Patients with such anomalies are more likely to complain of pure unilateral symptoms (mostly in non-dominant hand) [48–52].

Patients with a prior wrist fracture are two times at risk of developing CTS. Moreover, CTS can acutely co-exist with wrist fracture; this can result from direct trauma to the median nerve and/or from hemorrhage and edema leading to a subtle rise in pressures inside the tunnel. The external pressure applied by splints and casts may be the cause of subacute presentation of CTS. Chronic CTS might result from deformities which are responsible for decreasing the space in the tunnel [12, 41, 53]. There is a positive relationship between squares wrist and CTS, particularly when the ratio of wrist thickness to wrist width is more than 0.7 then the risk rates of CTS can be more than triple. It is worth mentioning that those ratios are significantly higher in women than in men [54–59]. It was reported that 10% - 20% of patients diagnosed with rheumatoid arthritis are likely to develop CTS. Probable mechanisms involve an increased thickness of tendon sheaths and synovium inside the wrist joint, leading to a tightening of the carpal tunnel [60, 61]. Patients with diabetes are 2-3 times more likely to develop CTS when compared to non-diabetic ones [62]. It was recently reported that the lifetime risk of developing CTS in patients with diabetes type I is around 85% [63]. Presumably, the mechanism is due to polyneuropathies and musculoskeletal anomalies that compress the median nerve causing restricted joint motion and tenosynovitis [64, 65].

The risk of developing CTS is high (80-90%) in patients who are undergoing for a long–term kidney dialysis. The potential cause may include the deposition of amyloid on transverse carpal ligaments, flexor tendon sheaths, and other structures within the carpal tunnel [66–68]. About 1 out of 4 pregnant women can present with CTS symptoms [69]. The risk of CTS is highest in the third trimester (60%) compared to first trimester (20%) and second trimester (20%). Moreover, older maternal age is associated with a greater risk of developing CTS. Pregnant women are more prone to develop edema and hypertension, and these factors may also contribute to developing CTS. Nulliparity is also an additional risk factor [70]. The condition regularly resolves within few weeks after delivery, but can also persist, especially in breastfeeding women [71]. In some individuals, anatomical abnormalities in the carpal tunnel can be inherited. Those anomalies may include aplasia of the median nerve and/or thickened transverse carpal ligament [72, 73]. Michaud et al. [74] has reported an autosomal dominant

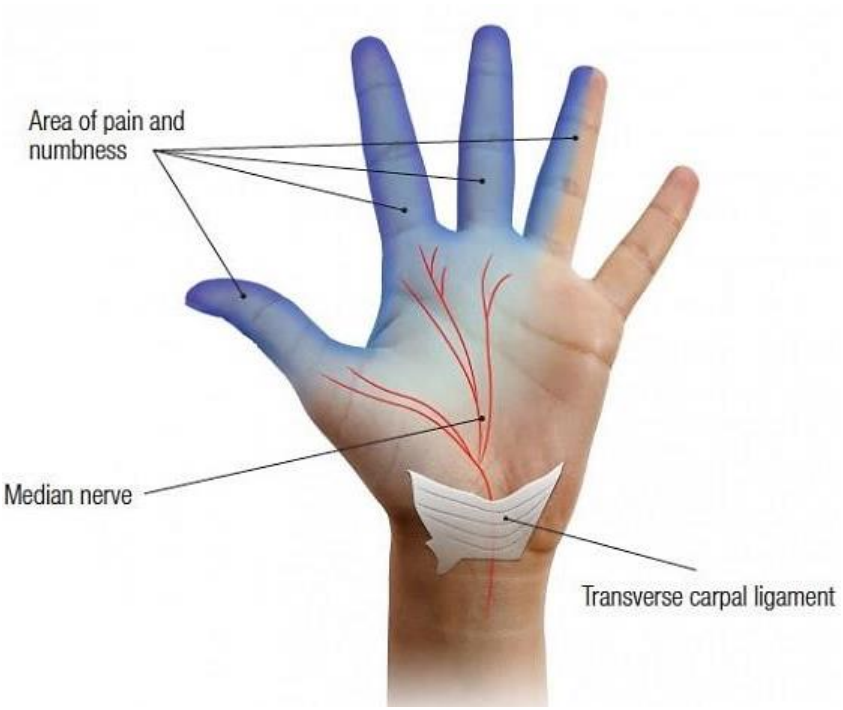

Fig. 2 Sensory manifestation of carpal tunnel syndrome. This figure is used with permission from the following source: (Source: www.practicalpainmanagement.com)

transmission of CTS in three consecutive generations, and a rare case (uncommon in age<30) of a 7-years old male with congenital carpal tunnel syndrome. It is suggested that damage to the median nerve can progress over time when performing some repetitive activities with hands (such as bending, twisting, or using vibrating tools) notably in predisposed people. If the dominant hand is affected firstly and severally, the likelihood that activity is the cause becomes highly accepted [75–79].

CTS is common in wheelchair athletes [80]. Body mass index (BMI) and period of wheelchair use are important factors that contribute to the development of CTS in wheelchair basketball players [81]. The use of mobility aids (walking stick, walking frame, or wheelchair) may carry an increased risk of CTS. Among wheelchair users, 49%- 63% experience CTS. The mechanism may be secondary to large forces transmitted through the wrist and prolonged extremes of posture [82, 83]. The risk of CTS in smokers is two folds of that in non-smokers [84]. CTS is most common in white people and is less common in black people [9]. Thyroid disorders such as hypothyroidism and Grave's disease are associated with CTS. It was reported that in patients with the Grave's disease, the symptoms of CTS and the NCS findings were resolved once the Grave's disease is treated with radioactive iodine [85, 86]. The cause of CTS in hypothyroidism patients is thought to result from elevated body weight [87]. Limited physical movement is a risk factor for CTS [88]. However, exercises may indirectly help in symptom relief by weight reduction [89]. Some certain sports (such as crocheting, long–term body building, racket sports, and cycling) could cause stress through joint of the wrist and might increase the rates of CTS [90].

Leading diagnostic signs and symptoms for CTS

Numbness present earlier in the dominant hand and is usually more severe than the non-dominant one [20]. CTS is highly suspected if the symptoms (pain, tingling, paresthesia of hands) are causing patients to wake up from their sleep at night. It is important to mention that in some patients, these complaints are relieved by flicking the wrists [91]. Numbness or tingling present classically in the palmar part of the first three fingers with the radial half of the ring finger. Thenar eminence is spared, and areas supplied by ulnar and radial nerves are also preserved, but in

many cases, the whole hand or even forearm can have symptoms [20]. Typically, intermittency of symptoms in CTS patients differentiates it from other conditions where symptoms are constant. In CTS, the condition slowly progresses over time, unlike other conditions (such as radiculopathy) where onset arises acutely. Decreased ability to perform some activities or movements such as rotating an object as seen when the patient tries to open jars or turns a wrench. The clumsiness of the hand particularly noticed when patients drop objects or have difficulty performing fine motor skills [92]. Mostly, the pain will radiate from the anterior side of the wrist proximally to forearm and upper arm [20]. Decreased strength of the thenar muscles is usually evident [93]**.** Reflexes of the upper limb (biceps, brachioradialis, triceps, and long finger flexor) are normal in CTS, and if abnormal reflexes present, then another diagnosis such as radiculopathy should be suspected [21]. The stiffness of the fingers is also present in CTS but it is not a common finding, it can present in some CTS cases. The presentation is likely to be worsened flexion and extension of the fingers when the patient wakes up in the morning [21]. Cold intolerance is not the very common symptom. A few patients may have the complaint of vasomotor symptoms mimicking the presentation in patients with Raynaud's phenomenon, eventually due to the injury of sympathetic fibers passing through the median nerve [94]. Atrophy of thenar muscles will indicate the presence of a severe degree of CTS. If there is an existing joint deformity such as in carpometacarpal osteoarthritis, then the thenar eminence may have flattened morphology [22].

Diagnostic modalities for CTS

Electromyogram/nerve conduction studies are the best available tool to make the diagnosis of CTS [26–28]. This tool is also useful for the evaluation of the severity of damage to the median nerve, it can assist in determining the suitable management, additionally, it can judge the outcome of interventions, and determines the prognosis of CTS. Moreover, it can also exclude or identify other neurological conditions [83]. CTS can be classified according to NCS results as follow: (1) Negative CTS: no evidence of any abnormalities in both comparative and segmental tests; (2) minimal CTS: abnormality in either comparative or segmental test; (3) mild CTS: deceleration in sensory conduction velocity (SCV) in the finger-wrist tract with normal ranges of distal motor latency (DML); (4) moderate CTS: deceleration in sensory conduction velocity (SCV) in the finger-wrist tract with raised (DML); (5) severe CTS: absent sensory response in the finger-wrist tract with increased DML, and (6) extreme CTS: the thenar muscle's motor response is absent [95].

Ultrasonography of the median nerve has been used as a complementary diagnostic tool for CTS [96], though some studies suggested that ultrasonography can be the initial test and can replace NCS when diagnosing CTS [97]. A ganglion cyst or tendinitis is structural abnormalities that may impact the median nerve and they can be identified by ultrasound. Ultrasound can also support the diagnosis of CTS by detecting swelling and enlargement of the damaged median nerve [29, 98, 99]. MRI is useful in cases where space-occupying lesions are suspected, particularly pre-operatively. MRI is superior to ultrasound for depicting the carpal tunnel, but its expense and availability restrict its use as a routine [31].

Differential diagnosis and diagnostic criteria for CTS

Differential diagnosis of CTS includes: (1) osteoarthritis; (2) stroke; (3) C6 radiculopathy; (4) C7 radiculopathy; (5) ulnar neuropathy; (6) amyotrophic lateral sclerosis/motor neuron disease; (7) De Quervain's tenosynovitis; (8) lateral epicondylitis; (9) Rotator cuff tendonitis; (10) polyneuropathy; (11) brachial plexopathies; (12) proximal median neuropathies and (13) multiple sclerosis [100]. Severity of CTS can be evaluated by EMG grading: (1) mild condition: sensory nerve irregularity without axonal loss; (2) moderate condition: a combination of sensory nerve irregularities with motor nerve irregularities but without axonal loss and (3) severe condition: if axonal loss present in sensory and/or motor nerves [101,102]. Furthermore, grading of CTS severity can be evaluated by scaling of symptoms and functional status (Boston questionnaire). The symptom severity scale consists

of 11 elements, each element should be graded 1-5, the higher the grade the more serious is the syndrome. Those items includes: (1) severity of wrist pain at night; (2) frequency of waking up at night because of wrist pain in the last two weeks; (3) having hand pain during daytime; (4) frequency of hand pain during the daytime; (5) the duration of each pain episode during daytime; (6) having hand numbness; (7) having weakness of the hand; (8) having tingling in the hand; (9) severity of numbness and tingling of the hand; (10) frequency of waking up at night time because of numbness or tingling in preceding two weeks and (11) having difficulty of grasping or using objects such as keys, pens, etc. Scaling of the functional status consists of eight elements and is also graded 1-5. Those elements includes: (1) writing; (2) buttoning of the clothes; (3) holding a book during reading; (4) holding a telephone handle; (5) performing rotational movements such as opening jars; (6) housework; (7) carrying of storage basket and (8) dressing and bathing. These scales are used to evaluate and control the severity of CTS [103,104].

Treatment strategies for CTS

If the patient's clinical presentation suggests the diagnosis of CTS, then performing NCS is the next step to be taken in the evaluation of the severity and management plan. The findings of EMG are essential in classifying the condition as mild, moderate and severe. Hand splinting shouldn't be delayed, and have to be initiated even before performing EMG [102]. Conservative management with wrist splints should be initiated while waiting for EMG [105,106]. In 1/3 of cases, the condition improves on its own with no treatment [107]. CTS of mild condition based on EMG findings will present as sensory nerve irregularity without axonal loss, and in moderate condition, there is a combination of sensory nerve irregularities with motor nerve irregularities but without axonal loss. Patients in these categories will be treated conservatively. Patients with mild CTS should have a prolonged conservative treatment [108]. In moderate cases, the splint should be used for 1-2 months, and in cases that splint shows no improvement, then both splints and steroid injections can have benefits to the patient [109]. It is not clear which dose and class of steroid will have the best benefits, but usually, a dose of 40 mg of methylprednisolone acetate is used, and the volume is around 1 ml plus the volume of the anesthetic agent [110].

It was reported that higher doses of steroid may provide better results [111]. When applying the steroid injection, caution should be taken to avoid the injury to tendons, vessels or even the median nerve itself, and EMG should be performed to evaluate any damage to the median nerve since steroid injection can mask the ongoing nerve damage. A high volume of fluid in injection should be avoided since it can worsen the condition by increasing pressure in the tunnel [112]. In most cases, injection is just applied once, and no benefit has been reported when injecting the patient more than one time. The improvement can be perceived 3-4 weeks after injection [113]. It was reported by Mohammad et al. [114] that the use of topical chamomile oil in patients with mild and moderate stages of CTS has been shown to have a significant improvement in the severity of symptoms, hand function in addition to the improved findings of EMG as the oil resulted in a significant decrease of compound latency measured for the median nerve. It is important to notice that chamomile oil has been used as a complementary agent in the treatment of CTS.

Other conservative treatments such as vitamin B6 and diuretics are not proved for the improvement of CTS, and more studies are needed in this area [115–118]. Oral steroids can improve the condition and are more effective than other drugs (such as NSAIDs and diuretics), but they may cause systemic negative effects, and moreover, they are not as effective as steroid injections [119]. In moderate cases, if splint and/or corticosteroid injections show no improvement in the patient's condition, then carpal tunnel release is recommended [120]. CTS of severe condition based on EMG findings will present with axonal loss present in sensory and/or motor nerves. In such case, surgical release is recommended [121]. In CTS cases where edema is evident in the hand and the wrist area, both splint and the use of diuretic should be considered. If the patient doesn't respond, then the steroid injection is recommended, and in the

case where all previous treatments fail, the carpal tunnel release operation can be considered [106,108].

In CTS cases of evident inflammation such as arthritis or tendonitis, both splint and nonsteroidal anti-inflammatory drugs can be used. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as celecoxib is recommended for 7-10 days if the patient doesn't respond, then steroid injection can be applied, if still not responding to treatments then the operation can be considered [109,113,119]. In pregnant patients, the complaints of CTS may rise rapidly and get worse quickly, that is thought to be caused by fluid retention, it is important to keep a very close monitoring and intervene aggressively. Typically, the symptoms fade away within few weeks post-delivery. In most cases, only splints are used. Medications such as diuretics and NSAIDs are better to be avoided in pregnant women [122]. In one study held by Demiryurek et al. [123], it was shown that vitamin D deficiency has increased the severity of pain in patients with CTS, and as a result, the management of those patients with supplementary vitamin D has been shown to decrease the pain severity. More studies are required to investigate the possibility of adding vitamin D to the list of available conservative treatments of pain in CTS patients even without the presence of vitamin D deficiency. In patients with long-term symptomatology, the prognosis is not favorable. Additionally, if the Phalen's test is positive on examination, then the prognosis is predicted to be poor. Another important finding is the thenar muscle wasting, which suggests the worst outcome [124].

Recommendations

Patients obtaining conservative treatment should be rechecked once a month until their conditions improve. Nerve conduction studies are the main useful tool to provide information about progression over time; this progression can present as improvement or decline in the patient's condition. Patients should consider seeking medical consultation if one or more of the following findings, existing in hand and wrist (numbness, tingling, painful sensation, and weakness), although the increased activity of the hands can cause symptoms to worsen, decreasing or limiting activity is not recommended. CTS is a slowly progressive disease which can take a few years to develop, and the symptoms may fade on their own for months or even years. Patients must be cautioned that findings at the wrist haven't to be ignored, because median nerve is very necessary for the well-being of hand function, particularly for performing fine motor tasks. It is of importance to mention that symptom disappearance may be a sign of greater damage to the median nerve.

Conflict of interest

The authors declare that they have no conflict of interest.

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