Carpal tunnel syndrome related to rheumatic disease (Review)

LENUȚA BÎRSANU[1,2], GEORGIANA-ANCA VULPOI[1,3], DAN IULIAN CUCIUREANU[1,4], CRISTIAN DORIN ANTAL[1,2], IONUT RADUCU POPESCU[1] and DANA MIHAELA TURLIUC[1,5]

[1]Faculty of Medicine, University of Medicine and Pharmacy 'Grigore T. Popa', Iași 700115, Romania; [2]Department of Neurology, Clinical Rehabilitation Hospital, Iași 700081, Romania; [3]Dorna Medical Clinic, Iași 700022, Romania; [4]Neurology Department 1, Clinical Emergency Hospital 'Prof. Dr. Nicolae Oblu', Iași 700309, Romania; [5]Neurosurgery Department 2, Clinical Emergency Hospital 'Prof. Dr. Nicolae Oblu', Iasi 700309, Romania

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Abstract. Carpal tunnel syndrome (CTS) is the most commonly occurring type of entrapment neuropathy in the world. Several conditions may contribute to the development of CTS, such as obesity, repetitive wrist movements, pregnancy, genetic predisposition and rheumatoid arthritis (RA) inflammation. CTS is characterized by a wide range of pathophysiological factors, including increased pressure, mechanical trauma and ischemic damage to the median nerve that runs through the wrist tunnel. In the present narrative literature review, the way rheumatic diseases (RDs) contribute to CTS occurrence is investigated. The epidemiological, clinical, paraclinical and pathogenesis aspects of the relationship are examined. CTS is the most common neurological finding in RA, and incidences of RA, psoriatic arthritis and CTS are closely related. The association of CTS with systemic lupus erythematosus, Sjögren's syndrome, Behcet's disease and systemic sclerosis is weaker. In these cases, the prevalence of CTS is similar to that in the general population. As the occurrence of CTS is increasing, understanding the common mechanism and making an early diagnosis are required to limit pain and costs. When patients with RD present with symptoms such as wrist pain, tingling sensations or numbness in their fingers, CTS should be suspected. This suspicion should not be interpreted in terms of RD. To accurately evaluate patients with RD, a detailed electrophysiological examination should be included in the evaluation process. A diagnostic algorithm should include neuromuscular ultrasound or magnetic resonance imaging for patients with RD.

Correspondence to: Dr Georgiana-Anca Vulpoi, Faculty of Medicine, University of Medicine and Pharmacy 'Grigore T. Popa', 16 University Street, Iași 700115, Romania
E-mail: vulpoi.anca@yahoo.com

Abbreviations: BD, Behcet's disease; CSA, cross-sectional area; CTGF, connective tissue growth factor; CTS, carpal tunnel syndrome; EDX, electrodiagnostic examination; MRI, magnetic resonance imaging; NCS, nerve conduction study; NMUS, neuromuscular ultrasound; OA, osteoartritis; PsA, psoriatic arthritis; PNP, polyneuropathy; PNS, peripheral nervous system; RD, rheumatic disease; RA, rheumathoid arthritis; SLE, systemic lupus erythematosus; SS, Sjogren syndrome; SSc, systemic sclerosis

Key words: carpal tunnel syndrome, rheumatoid arthritis, psoriatic arthritis, scleroderma, Behcet's disease, systemic lupus erythematosus, epidemiology

Contents

1. Introduction

Carpal tunnel syndrome (CTS) is a common peripheral nervous system disorder and is the most frequent entrapment neuropathy. CTS is more common in women than men, and it is most often diagnosed at 45-60 years of age (1,2). A compression of the median nerve in the wrist causes entrapment neuropathy. The cause of CTS is not completely understood, despite the previous identification of risk factors. Several factors contribute to the development of CTS, including old age, smoking, obesity, repetitive hand movements and vibration tools. Rheumatic diseases (RDs), hypothyroidism and diabetes are also common factors. CTS has a high prevalence and a significant impact on the quality of life of patients. The condition is associated with numbness, weakness and pain in the hand and arm, and is a marked cause of disability (3).

RDs and musculoskeletal diseases affect millions of people worldwide due to degenerative, inflammatory and immune conditions. Chronic pain, joint damage and increasing disability may occur in patients with these diseases (4). There are several RDs associated with CTS, including osteoarthritis (OA), rheumatoid arthritis (RA), psoriatic arthritis (PsA) and some connective tissue conditions, such as systemic lupus

erythematosus (SLE), systemic sclerosis (SSc) and Sjögren's syndrome (SS). In general, RDs and related musculoskeletal disorders are prevalent throughout the world, but when their prevalence was compared, in different countries, for each disorder, variations in their prevalence were identified (e.g. the prevalence of OA may vary from 2.3-20.4%) (5-7).

The pathogenesis of RDs such as SLE, SSc, SS or RA appears to be associated with the presence of autoantibodies (8,9). The causes of neurological involvement in RD are not fully understood (10,11). In the present narrative review, neurological complications related to the peripheral nerve system (PNS) in RD are discussed. As the prevalence of CTS is on the rise, understanding the common mechanism and making an early diagnosis are necessary to limit unnecessary pain and cost. When patients with RD manifest symptoms such as wrist pain, tingling sensations or numbness in their fingers, CTS should be suspected. This suspicion should not be interpreted in terms of RD. Strong interdisciplinary collaborations would benefit the patient, since an early diagnosis can result in full recovery of the median nerve lesion. However, late diagnosis in severe CTS cases has limited recovery prospects. Collaborations can only be achieved by identifying common problems. The current review aims to raise awareness about these issues, which are often overlooked.

2. Epidemiological data

CTS. It is estimated that 3.8% of the general population worldwide suffer from CTS, with a higher prevalence among women (male to female ratio, 1.4) (12). A study published by Atroshi *et al* (12) found that 1 in 5 symptomatic patients had CTS on clinical examination and electrophysiology testing. According to a recent study, CTS diagnoses and surgical decompressions are on the rise in the general population (13). While a CTS diagnosis is approximately two times more common in women than in men and increases with age, surgical intervention rates are similar between men and women (13).

RDs. A total of >200 RDs affect the joints, bones, muscles and connective tissue, with major categories including inflammatory conditions, such as RA, and non-inflammatory conditions, such as OA (14). Almutairi *et al* (15) revealed a global prevalence of RA of 0.46% between 1980 and 2018. This was approximately two times higher than the estimated RA prevalence of 0.24% reported by the Global Burden of Disease study (16,17). The prevalence and incidence of SS vary depending on diagnostic criteria and study designs used, and it can be challenging to estimate trends in SS prevalence and incidence at different geographic and temporal levels (18). The prevalence of hand OA is high, ranging between 2.0 and 6.2% in adults, but range between 4.7 and 20.4% in elderly individuals (19).

CTS related to RD. Hand OA is a heterogeneous group of disorders and not a single disease; it can be classified into three distinct types: i) Erosive; ii) nodal; and iii) first carpometacarpal joint OA (20). OA is a common degenerative condition that often co-exists with CTS (21). Shin *et al* (22) concluded that the prevalence of basal thumb OA was not higher in a CTS group compared with that in a non-CTS group, despite several previous studies reporting a causal link between CTS and basal thumb OA (23,24). The results of an extensive systematic review and meta-analysis revealed the risk of CTS to be approximately two times as high among subjects with RA or OA, compared with individuals who don't suffer from these RDs (11).

In RA, autoantibodies, persistent synovitis and widespread inflammation are common (25). Entrapment, vasculitis and drug toxicity can also cause neuropathy in RA. CTS is the most common neurological finding in RA (26). According to a study by Agarwal *et al* (27), 10.1% of 108 patients with RA had CTS. In a study by Gray and Gottlieb (28), those patients with RA and flexor tendinopathies develop CTS more frequently than those with RA without flexor tendinopathies (47% vs. 13%). In a recent study by Sakthiswary and Singh (29), there was no conclusive and convincing evidence of a link between laboratory or clinical parameters in RA and the involvement of the median nerve. The study pooled data from eight studies with a random selection of patients with RA, and it was revealed that 86/1,561 (5.5%) patients with RA had CTS. By contrast, subclinical CTS exhibited a pooled prevalence of 14.0%. The study concluded that the prevalence of CTS in RA is no different from the prevalence in the general population, and no correlation was observed between the median nerve characteristics and the clinical parameters of the disease. A recent cross-sectional study showed that 95.9% of the wrists of patients with RA had CTS (30). There was a high incidence of CTS in this study compared with that in other studies using neuromuscular ultrasound (NMUS) to assess CTS in patients with RA; The NMUS can provide a greater level of accuracy in the diagnosis of CTS in patients with clinical symptoms and negative NCS results (31). Smerilli *et al* (32) revealed that CTS was diagnosed in 26.3% patients with RA, and Karadag *et al* (33) also reported CTS in 18% of patients with RA (32,33). By contrast, Lee *et al* (34) found that the incidence rate of CTS in patients with RA was similar to the incidence rate of CTS in the general population, and CTS occurrence was not correlated with RA duration or activity.

PsA is an inflammatory erosive arthritis that affects the peripheral joints as RA does (26). PsA occurs in ≤30% of patients with psoriasis and can have severe debilitating effects on the peripheral joints, tendon insertions and spine (35). Tezcan *et al* (36) showed that the CTS frequency was higher in PsA compared with that in healthy control groups. In 30.76% of patients with PsA, an electrodiagnostic examination (EDX) detected CTS. In addition, NMUS or magnetic resonance imaging (MRI) was used to support the diagnosis in patients who could not undergo EDX (36). As reported in a recent study by Subaşı *et al* (26), electrophysiological and ultrasonographic findings indicated that CTS occurred more frequently in patients with RA and in patients with PsA compared with that in controls; CTS was detected in 13.2 and 15.4% of patients with RA and PsA with hand involvement, respectively, and in 3.5% of controls (26).

SS belongs to the group of autoimmune RDs. Patients with SS often experience peripheral neuropathies. Symptoms of autoimmune disease may precede the onset of neuropathy (37). An estimated 0.2-1% of the population is affected by SS, and it appears to be as common as RA (38,39). Based on a retrospective, comparative study by Hsu *et al* (10) in 2021, patients with

RA and SS have a high risk of CTS. The rate of CTS in SS patients is high (54%), and Jaskólska *et al* hypothesized this is due to inflammation and synovitis overgrowth (37).

As an autoimmune disorder, scleroderma causes inflammation, blood vessel injury and organ fibrosis. The condition can be divided into two groups: SSc and localized scleroderma. Patients with SSc most frequently suffered from myopathy (51.8%), trigeminal neuropathy (16.52%), peripheral sensorimotor polyneuropathy (PNP; 14.25%) and CTS (6.56%) (40).

Behcet's disease (BD) is a multisystemic disorder with unknown pathogenesis (41). Recurrent oral and genital ulcers, skin lesions, recurrent uveitis, articular, vascular and neurological symptoms are the clinical symptoms of BD. In patients with BD, neurological involvement occurs in 2.2-49% of cases and is a major cause of morbidity (42). BD, a chronic, widespread inflammatory condition, can be associated with peripheral nerve involvement, therefore CTS can occasionally occur in those with BD (41). An analysis of 1,750 patients with BD in a study by Lee *et al* (42) found a 0.8% prevalence of CTS. The clinical severity of CTS or nerve conduction study (NCS) findings of CTS was not notably correlated with the disease activity of BD (42). In total, 45-60% of patients with musculoskeletal involvement experience arthritis or arthralgia; it can be observed in the knees, elbows, hands and ankles, and can mimic RA due to non-erosive, oligoarticular or monoarticular involvement (43).

A chronic, autoimmune disease known as SLE has heterogeneous clinical manifestations that may affect every system and organ in the body (44). In certain cases, SLE damages the central nervous system and PNS for numerous years before other symptoms appear. CTS could be the first sign of SLE (45). In the study by Sivri *et al* (46), 23.6% of patients with SLE had peripheral nerve conduction slowing and almost half of them were asymptomatic. The study also suggested that electrophysiological tests should be conducted during early SLE in asymptomatic patients to detect nervous system involvement. The proportion of patients with CTS in this study was 44.7%. In another study, patients with SLE without clinical or electrophysiological neuropathy showed marked differences with respect to several NCS parameters of the upper and lower limbs compared with matched healthy controls of the same age and sex. According to these findings, SLE may have an early effect on PNS. However, it may also suggest the beginning of an insidious and gradual process leading to PNS, the mechanisms of which are unknown (47). Omdal *et al* (48) conducted a retrospective study on 30 patients with SLE and assessed the neurological complications caused by the disease. In 23% of the patients, there was CTS and muscular weakness. A study by Toledano *et al* (49) found a 17.7% overall prevalence of PNS involvement (93 out of 524 patients presented with manifestation of PNS). PNS involvement was the only manifestation of SLE in ~50% of the study participants. In the study, CTS was reported by only 4.2% of patients with SLE, a value that is within range found for the general population (3.8-4.9%). According to this study, SLE is not, generally, the direct cause of CTS (49).

Table I summarizes the most relevant epidemiological studies on CTS and its association with RDs that have been published in the last 30 years.

3. Diagnosis of CTS in patients with RDs

Clinical. The symptoms of acroparesthesia include tingling, numbness, reduced sensation and prickling in the extremities (fingers and toes). Despite the frequency of the condition, data regarding a diagnostic approach and its management are limited. There are several diseases that can be revealed by acroparesthesia (50). Some patients may experience acroparesthesia along with rheumatic complaints such as arthritis, or it may result from mononeuropathies such as CTS (50).

CTS involves a constellation of signs and symptoms caused by different pathogenetic mechanisms, all resulting in median nerve compression. A clinical history and physical examination are the first steps in diagnosing CTS (51). It is possible to categorize CTS symptoms and signs into three stages. At the beginning of the disease, patients with typical CTS often experience paresthesia, numbness and tingling in 1-3 fingers and the radial half of the ring finger, especially at night. The second stage involves the appearance of symptoms during the day. They may be experienced by patients performing repeated hand or wrist movements or remaining in the same position for a long period of time. Reduced grip strength is one of the symptoms experienced by patients. Atrophy or hypotrophy of the thenar eminence constitutes the third stage. At this stage, sensory symptoms may not be felt at all (52). Among the numerous tests that can be used to diagnose CTS clinically, Tinel's sign and Phalen's maneuvers are two of the most widely used (53). The Boston carpal tunnel questionnaire is a widely used, self-administered questionnaire that assesses symptom severity and functional status in patients with CTS (53).

RA is characterized by symmetric polyarthritis, but the disease often involves extra-articular structures, and it does not only affect the joints. PNS may be asymptomatic in its early stages, or it may present with a variety of symptoms such as pain, paresthesia and weakness of the muscles. There may be similarities and overlaps between these symptoms and those associated with arthritis (27).

Patients with OA also experience considerable pain, with reduced grip strength and joint mobility, as well as impaired functional abilities, particularly when grip strength is required to twist the hands (19,54).

Fig. 1 shows a patient suffering from specific RA changes and deformities of the joints, with an exclusive focus on the proximal interphalangeal joint, localized rheumatoid nodules on the skin and bilateral thenar atrophy (secondary to severe bilateral CTS).

Pain and paresthesia at night as well as weakness, loss of dexterity and thenar atrophy, are common complaints in the patients with RA, and they are presented late for the EDX study, as CTS in patients with RA is not always obvious (55).

Paraclinical

EDX. Considering the limited diagnostic value of clinical tests, complementary EDX is recommended when CTS is suspected in a patient with RD. These tests include NCS and if necessary, electromyography. Due to high specificity (at least 94%) and sensitivity (56-85%) percentages, NCS is the gold standard for diagnosing CTS (52). EDX is used to diagnose the severity of CTS in RA and PsA based on NCS results, emphasizing the importance of this test for treatment (26,30).

Table I. Most relevant epidemiological studies on CTS and RD in the last 30 years.

First author, year	Total patients, n	Patients with RD, n	CTS, %	(Refs.)
Karadag *et al*, 2012	100	100 RA	17.0	(33)
Agarwal *et al*, 2008	108	108 RA	10.1	(27)
Smerilli *et al*, 2021	82	57 RA	26.3	(32)
Lee *et al*, 2015	1,060	1,060 RA	3.5	(34)
Sakthiswary and Singh, 2017	1,561 (8 studies)	1,561 RA	5.5	(29)
Subaşı *et al*, 2021	179	70 RA/39 PsA	13.2/15.4	(26)
Mahmoud *et al*, 2022	74	74 RA	95.9	(30)
Tezcan *et al*, 2023	67	39 PsA	30.8	(36)
Jaskólska *et al*, 2020	50	50 SS	54.0	(37)
Amaral *et al*, 2013	9,506 (182 studies)	1,628 SSc	6.56	(40)
Lee *et al*, 2015	1,750	1,750 BD	0.8	(42)
Sivri *et al*, 1995	58	38 SLE	44.7	(46)
Toledano *et al*, 2017	524	524 SLE	4.2	(49)
Florack *et al*, 1992	246	256 OA	43.0	(23)

RD, rheumatic disease; CTS, carpal tunnel syndrome; RA, rheumatoid arthritis; OA, osteoarthritis; PsA, psoriatic arthritis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; SS, Sjögren's syndrome; BD, Behcet's disease.

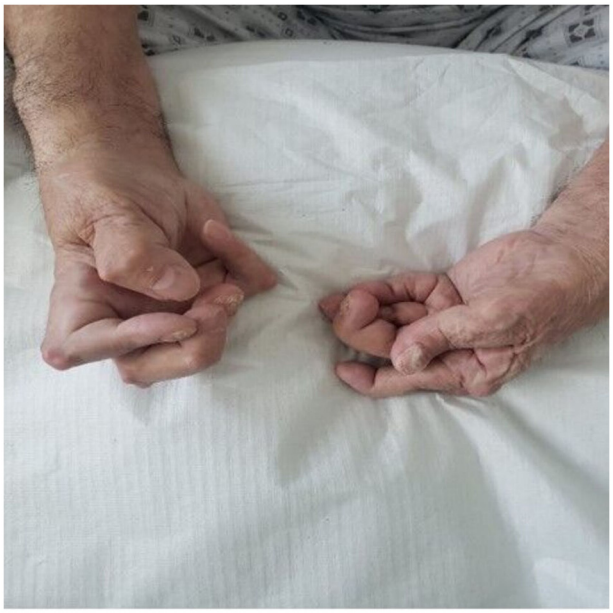

Figure 1. Patient with rheumatoid arthritis and bilateral severe carpal tunnel syndrome.

EDX can be used to determine the location and severity of nerve compression, monitor its course after therapy and exclude other causes of median pain, including cervical radiculopathies, brachial plexopathies, PNPs and mononeuropathies (1).

It is recommended that EDX should be performed when quantifying the severity of CTS in individuals aged >70 years (56). In patients with clinical symptoms and NCS results, the NMUS provides a more accurate diagnosis of CTS (56). In a study of patients with clinical CTS but normal NCS, Aseem *et al* (57) reported abnormal NMUS findings, which were compatible with CTS, such as median nerve enlargement at the wrist (mean area 16.3 mm^2) and an increased wrist-forearm ratio.

Role of NMUS in studying CTS in patients with RD. The use of NMUS has grown over the past 20 years, and several diagnostic laboratories are now routinely performing the technique. For the diagnosis of CTS, it has been shown to be sensitive and specific (57).

Through NMUS examinations, the morphological changes to the nerve can be evaluated, as well as their severity. Furthermore, the examination can identify some anatomical conditions or variants that may be contraindicated by minimally invasive treatments, and it is also useful in evaluating patients whose surgical outcomes were unfavorable (1). The test can also identify secondary causes of CTS, such as serous or hyperplastic tenosynovitis, carpal tunnel lesions, including ganglion cysts, giant cell tumors of the tendon sheath and vascular malformations, and gout and pseudogout crystallized deposits (1). A limited number of studies (26,30,32,36) have applied NMUS to evaluate the local causes, with a greater focus on wrist arthritis and tenosynovitis as the main causes of entrapment neuropathy of the median nerve in RA (30). Also, clinicians can use NMUS to diagnose CTS in patients with clinical symptoms but negative nerve conduction test results (31).

The use of NMUS has proven to be beneficial in identifying the etiopathogenesis of CTS, especially in patients with OA or RA, for which causes other than synovial inflammation must be considered (19,30). According to Smerilli *et al* (32), patients with RA and CTS have distinct

sonographic patterns compared with patients with idiopathic CTS. CTS in patients with RA exhibits a characteristic inflammatory pattern, defined by finger flexor tenosynovitis and/or radio-carpal joint synovitis. On the other hand, idiopathic CTS is characterized by a marked swelling of the median nerve (32). According to Yagci *et al* (58), the median nerves in patients with SSc lose their elasticity, while the cross-sectional area (CSA) is in the normal range. This suggests that the increased peripheral nerve involvement in SSc is due to increased nerve stiffness.

MRI in studying CTS in patients with RD. Recently, MRI of the peripheral nerves has been used as a complementary diagnostic modality in patients with CTS to assess nerve and carpal tunnel anatomical parameters (59). With MRI, the flexor retinaculum and carpal bones could be reliably mapped, thus defining the borders of the carpal tunnel. Carpal tunnel flexor tendons are distinguished from median nerves in all cases by their ovoid shape and moderate signal intensity (60).

MRI is used less in clinical practice than electrophysiological evaluation in CTS diagnosis. This is because it is very costly, time-consuming and not readily available (52). When clinical and EDX findings are inconsistent, MRI can be helpful in identifying patients who could benefit from surgery. Also, it may be an important tool for assessing the persistence and recurrence of CTS (52).

In RD, MRI plays a marked role. As part of OA, PsA or RA, synovitis plays a key role, particularly in the inflammatory phenotype (61,62). MRI findings for patients with PsA usually include periostitis and synovitis of the proximal interphalangeal joints, while MRI findings for patients with RA typically include synovitis with erosions of the wrist, and the midcarpal, carpometacarpal and metacarpophalangeal joints (61). In patients with RA, MRI can also detect abnormalities such as bifid median nerves, persistent median arteries and accessory muscle bundles that contribute to CTS (34).

4. Pathogenesis of CTS and RD

The development of CTS can be caused by a variety of factors, including thickening of the tendon or flexor retinaculum, synovitis, the accumulation of fluid and alterations of the subsynovial connective tissue (63). CTS results from mechanical trauma or increased pressure (carpal tunnel shrinkage or increased median nerve size), which subsequently leads to ischemic injury to the median nerve (64).

All the aforementioned RDs have a complex autoimmune substrate that has not been fully elucidated. The rheumatoid wrist experiences synovial expansion, joint erosions and ligamentous laxity. This results in a reduction in the size of the carpal tunnel and an increase carpal tunnel pressure. Consequently, median nerve and vessel compression in the perineurium result in impaired axonal transport and median nerve ischemia. Another plausible cause of CTS in RDs is drug toxicity, vasculitis and amyloidosis (29).

A combination of synovial inflammation and local causes such as persistent median artery and accessory muscle bundle may contribute to the etiology of CTS in patients with RA (30). With time, inflammation of the joints results in their destruction, with loss of cartilage and bone erosions, which changes the conformation of the carpal tunnel (65). The carpal tunnel is formed from the carpal bones and the transverse carpal ligament. Within the tunnel, there are nine flexor tendons, as well as the median nerve (52).

Filippucci *et al* (66) found that ~50% of the 90 recruited patients with RA had at least one inflamed tendon, and an equivalent percentage of those had at least one damaged tendon. A variety of pathological conditions can lead to neurotendinous abnormalities, including edema of the tendon, invasion of the synovial tissue, tear of the tendon and scar formation Filippucci *et al* (66) found a high rate of both inflammation and tears in the flexor tendons of fingers II, III and IV, as well as in the extensor carpi ulnaris tendon in 90 patients with RA.

RA for a long period can result in histopathological changes to the wrist tendon, including synovial proliferation and tendon damage (66). In RA, synovial hyperplasia and the formation of invasive synovial tissue, called the pannus, occur. CTS compression can be caused by an infiltrating pannus narrowing the space in the tunnel (55,67). Demyelination, on the other hand, is a notable reaction to nerve injury in the median nerve. As a result of compression, demyelination spreads to the intermodal segment, where the axons remain intact. In continuous compression, there is an interruption of the blood flow to the endoneurial capillary system, resulting in changes in the blood-nerve barrier and endoneurial edema. The result is ischemia, venous congestion and local metabolic changes (3).

In Fig. 2, the pathogenesis of CTS related to RA is briefly illustrated. Symptoms of CTS appear to resolve quickly after surgery for carpal tunnel release, indicating ischemic injury (64).

Studies conducted on RA and PsA that focused on vascular changes showed that synovial membrane vascularity and modification of the vascular morphology in patients with PsA were markedly increased compared with those in patients with RA (68,69). The symptoms of CTS are more common in patients with psoriatic arthritis due to increased inflammation and angiogenesis in the synovium, which causes narrowing of the carpal tunnel and compression of the median nerve in the wrist area (68,69).

Several fibrotic disorders are associated with connective tissue growth factor (CTGF) expression, according to Pierce *et al* (70). It has also been demonstrated that tenosynovial samples from patients with CTS and certain associated comorbidities, specifically SLE and RA, show marked increases in CTGF levels compared with those found in patients with idiopathic CTS (35).

As a chronic inflammatory autoimmune disease, SS is characterized by infiltrating lymphocytic cells in the exocrine glands, such as the salivary and lacrimal glands. Primary SS is the result of an independent condition, while secondary SS occurs in other autoimmune diseases, such as RA, SSc and SLE (37).

Patients with SSc may experience involvement of the nerve connective tissue, suggesting multisystem involvement (58). Patients with SSc experience an increase in the stiffness of the median nerve. There are still several questions regarding the involvement of the median nerve in SSc and how it differs between patients with CTS and healthy individuals (58).

CTS can also develop in patients with BD secondary to inflammation in the connective tissues, tendons and vessels, as well as nerve involvement in BD itself (41,42).

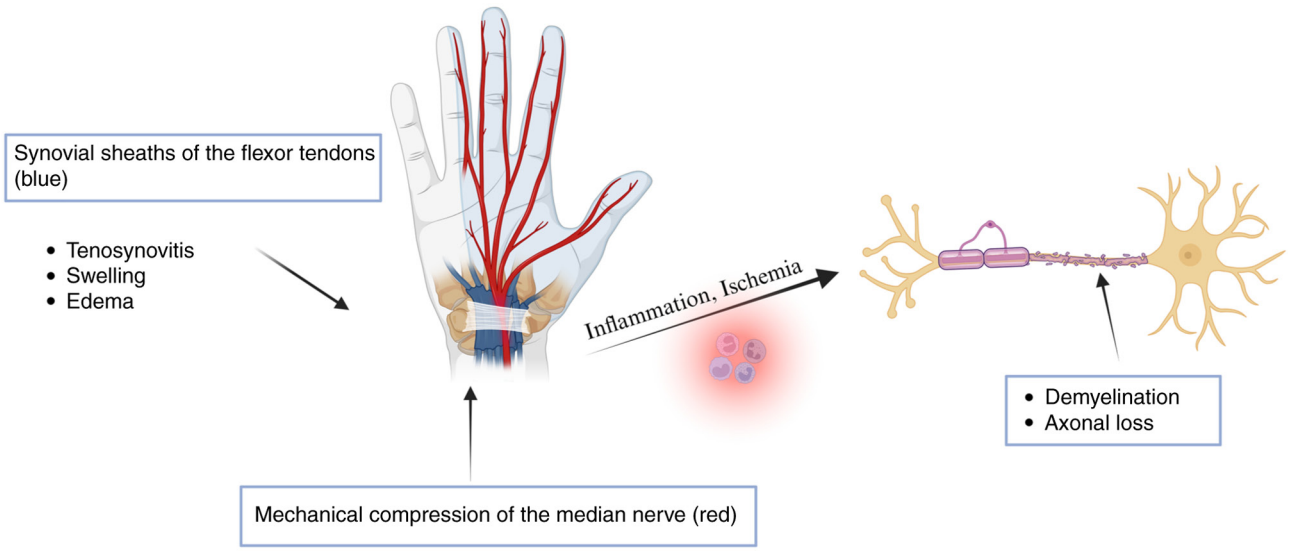

Figure 2. Pathogenesis of carpal tunnel syndrome and rheumatoid arthritis. Created with BioRender.com.

5. Discussion

According to numerous published studies (23,26,27,29, 30,32-34,36,37,40,42,46,49), CTS is more common in patients suffering from RD compared to those without these conditions In addition, other risk factors or diseases may contribute to CTS, as some researchers have discovered that the incidence rate of CTS in patients with RA is similar to that in the general population (29).

Several of the studies included in the present review have limitations due to their retrospective nature (34). As a result, some of the data may have been underestimated. Certain studies also included a small patient group, which was partially justified by the low incidence of some of the diseases in the general population, such as BD or SSc (41,42).

The incidence of RA is closely associated with that of CTS (67). Patients with PsA have a higher risk of CTS compared with healthy individuals, as evidenced by increased median nerve CSA on NMUS and MRI (36). CTS can occur due to BD inflammation and can also be the presenting symptom of nerve involvement in BD. Therefore, there should be a high level of suspicion for CTS in patients with BD and vice versa, although the exact association is uncertain (42).

EDX evaluation is essential in the diagnostic process for first determining whether there is a lesion of the median nerve, and then ruling out other pathologies causing similar symptoms, and assessing the severity of the lesion and treatment accordingly. The diagnosis of CTS in RD mostly depends on electrophysiological assessment. NMUS has become a crucial complementary test to electrophysiological examinations in CTS detection. When used together, EDX and NMUS are more informative than when used separately (56). MRI and NMUS are the two primary imaging modalities used to assess synovitis in OA, PsA and RA (61,71).

As concluded by Agarwal *et al* (27), neuropathy in RA is common and mostly subclinical. To evaluate patients with RA accurately, a detailed electrophysiological examination should be part of the evaluation process.

CTS and other neurological manifestations such as PNP may be the first symptom of RD, and patients are initially referred for neurological evaluation. Considering the marked association between CTS and RD, some studies recommend that rheumatologists refer patients with RD for neurological assessment, and neurologists who diagnose CTS should refer patients for rheumatological examination.

6. Conclusions

There are more studies that examine the associations between CTS and PsA, RA and OA than those that examine the associations between CTS and SLE, BD, SS and SSc. In part, this can be explained by the lower incidence of the latter diseases, but also by the prevalence of CTS associated with them. The pathogenic mechanisms of RA, PsA and OA are similar, which may explain why CTS is associated more often with these diseases. According to previous research, SS, BD and SLE are not directly associated with CTS. However, CTS should be investigated in these patients due to their systemic nature and impact on other connective tissue disorders.

A patient with RD and symptoms suggestive of CTS will undergo similar paraclinical investigations to a patient without such conditions. The diagnosis of CTS is based on clinical symptoms, physical examination and electrophysiological findings. EDX is helpful in identifying CTS frequency and the correlation with disease activity in patients with RD. NMUS is useful for identifying local causes, such as synovial inflammation and anomalous variations contributing to CTS; however, EDX remains essential for comprehensive evaluation and management. Due to the ability of ultrasound to detect inflammatory patterns and nerve swelling, it is essential for assessing CTS in RD, particularly in OA, RA and PsA. The use of MRI in the diagnosis and assessment of CTS in patients with RD is generally considered to be a valuable tool, as it provides detailed insights into the inflammatory and anatomical factors contributing to this condition.

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Authors' contributions

LB, GAV, CDA and DIC were responsible for study conceptualization. LB and DIC were involved in validation of the study. LB and GAV prepared the original draft. LB, GAV, IRP and CDA reviewed and edited the manuscript. DMT supervised the study. All authors have read and agreed to the final version of the manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for the use of the image in Fig. 1.

Competing interests

The authors declare that they have no competing interests.

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