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Article

PATHOGENETIC MECHANISMS OF CARPAL TUNNEL SYNDROME AS A SECONDARY CONDITION: A LITERATURE REVIEW

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Annotatsion: Carpal tunnel syndrome (CTS) is a condition caused by compression of the median nerve within a narrow osteofibrous canal at the wrist, leading to pain, numbness, and sensory impairment in the hand and fingers. It represents the most common form of entrapment neuropathy and constitutes a significant medical and social problem due to its high prevalence, chronic course, and negative impact on daily functioning and work capacity. Despite the relative uniformity of clinical manifestations, CTS develops in the context of a wide range of local and systemic disorders, reflecting substantial pathogenetic heterogeneity. This article provides an analytical review of current concepts regarding the pathogenesis of carpal tunnel syndrome, with particular emphasis on the diverse pathogenetic pathways involved in its development depending on the underlying condition. Anatomical and functional prerequisites for median nerve compression, as well as the common final compression–ischemic mechanism of neuropathy, are discussed. The importance of a comprehensive clinical and instrumental diagnostic approach is highlighted, along with the need for individualized, pathogenetically oriented prevention and treatment strategies aimed at correcting the underlying disease and reducing the risk of progression of compression neuropathy.

Keywords: carpal tunnel syndrome; median nerve; tunnel neuropathies; hand; decompression; repetitive wrist movements; hormonal factors; risk factors.

Introduction. Carpal tunnel syndrome (CTS), also known as median nerve entrapment at the wrist, is a symptomatic compressive neuropathy caused by increased pressure within the carpal tunnel, resulting in impaired median nerve function [1,2] Among all entrapment neuropathies, carpal tunnel syndrome is the most prevalent, accounting for approximately 50–90% of cases [3,7,16,17]. The incidence of CTS in the general population is estimated at 150–300 cases per 100,000 individuals annually [3]. According to Mumenthaler (1990), among 5,938 patients with non-traumatic peripheral nerve disorders, carpal tunnel syndrome was diagnosed in 4,051 cases [6]. Epidemiological data reported by Agasarov L.G. and Chuzavkova E.A. in the Russian Medical Journal indicate that the highest incidence of CTS is observed in individuals aged 40–60 years. However, the condition is not uncommon in younger populations, with approximately 10% of cases diagnosed before the age of 31. The lifetime risk of developing CTS is estimated at around 10%, while the annual risk among adults ranges from 0.1% to 0.3%. Overall prevalence in the general population reaches 1.5–3%, increasing to up to 5% in specific high-risk groups [8]. Particular attention should be paid to the etiology and pathogenesis of CTS, especially in the context of technological advancement and increased computer use. Wrist movements during computer mouse and keyboard operation—specifically wrist extension exceeding 20 degrees relative to the forearm—have been identified as a direct mechanical factor contributing to damage of carpal tunnel

structures, as demonstrated in studies by Liu et al. [5,9]. According to the clinical guideline Diseases of the Nervous System by Yakhno N.N. and Shtulman D.R., CTS may develop in association with myxedema, acromegaly, diabetes mellitus, menopause, pregnancy, lactation, and the use of oral contraceptives. Predisposing conditions include mucopolysaccharidosis, obesity, forearm and hand trauma, tenosynovitis, and rheumatoid arthritis. Median nerve entrapment may be further facilitated by nerve thickening in conditions such as amyloidosis, leprosy, and Guillain–Barré syndrome. In addition, congenital narrowing of the carpal tunnel, detectable by computed tomography of the wrist, plays a significant role and may partially explain the higher prevalence of CTS among women, who generally have smaller carpal tunnel dimensions [6].

Etiology and Pathogenesis According to Primary Conditions

Numerous studies indicate that frequent, monotonous wrist motions, especially when combined with forceful exertion and extreme wrist positions, lead to increased intracanal pressure and microtrauma of tendon structures [11,26,28]. In response to chronic mechanical overload, aseptic inflammation of the synovial sheaths of the flexor tendons develops, accompanied by thickening and interstitial edema, which contributes to a reduction in the volume of the carpal tunnel [27,28]. Elevated pressure in this confined space causes median nerve compression, disruption of endoneurial blood flow, and ischemic changes [25,28]. Prolonged exposure to these factors results in demyelination of nerve fibers and the development of chronic compressive neuropathy [26,28]. Thus, in the context of repetitive hand use, CTS develops via a microtraumatic mechanism, combining mechanical compression with ischemic injury of the median nerve [25,27,28]. Carpal tunnel syndrome is significantly more common in women than in men, highlighting the important role of sex- and hormone-related factors in its development [28,13]. During pregnancy, hormonal shifts and fluid retention exacerbate tissue edema, increasing pressure within the carpal tunnel and inducing median nerve compression, particularly in the third trimester [27,12]. In postmenopausal women, decreased estrogen levels are associated with impaired microcirculation and connective tissue trophism, which may contribute to the progression of chronic compressive neuropathy [12,11]. Therefore, CTS in women represents a multifactorial secondary pathology, primarily resulting from hormone-induced edema, structural alterations of connective tissue, and median nerve compression [27,29,13]. Epidemiological studies and meta-analyses have demonstrated a dose-dependent relationship between increased BMI and the risk of CTS, highlighting a proportional rise in the probability of median nerve compression with greater adiposity [12]. The pathophysiological mechanisms underlying CTS in obesity include elevated intracanal pressure due to fat deposition, as well as chronic low-grade systemic inflammation, which promotes perineural edema and microcirculatory disturbances [10,14]. Metabolic derangements associated with obesity, including insulin resistance, may further impair neural trophism and increase the vulnerability of the median nerve to compressive injury [10,15]. Therefore, obesity should be considered an independent etiological and pathogenetic factor for CTS, exerting its effects through a combination of mechanical, inflammatory, and metabolic mechanisms [12,10,15]. Diabetes mellitus (DM) is an important risk factor for CTS, as it is associated with an increased incidence of the syndrome compared to non-diabetic individuals [20,23]. A meta-analysis of 36 studies showed that both type 1 and type 2 diabetes nearly double the risk of developing CTS (odds ratio approximately 1.7–1.9), indicating a significant association between diabetes and median nerve compressive neuropathy. Pathogenetically, hyperglycemia induces microcirculatory impairments and metabolic alterations, such as the formation of advanced glycation end products (AGEs) and increased expression of vascular endothelial growth factor (VEGF), exacerbating ischemia and degeneration of nerve fibers and rendering the median nerve more susceptible to compression within the carpal tunnel [21]. Thus, diabetes mellitus contributes to CTS development through a combination of metabolic, microvascular, and neurotoxic mechanisms, increasing the susceptibility of the median nerve to compressive injury [20,23,21].

Clinical Presentation

Carpal tunnel syndrome (CTS) clinically manifests as pain, numbness, and paresthesia in the median nerve distribution, predominantly affecting the first three fingers (I–III) and the radial half of the fourth finger, with symptoms often worsening at night and during repetitive hand movements [5]. The median nerve is a mixed nerve containing motor, sensory, and autonomic fibers, which accounts for the combined sensory and motor deficits observed in the hand when the nerve is affected [5].Patients most commonly report dull, aching pain in the radial half of the palm and the first three fingers, often occurring at night and alleviated by active movements or shaking of the hand [5]. As the disease progresses, clinical features may include decreased grip strength, impaired fine motor skills, and thenar muscle atrophy, particularly in chronic cases or in patients with concomitant systemic disorders [23]. In individuals with obesity or diabetes mellitus, CTS symptoms are generally more pronounced and tend to progress more rapidly, likely due to metabolic and microcirculatory disturbances [10,16].

Diagnosis

The heterogeneity of pathogenic mechanisms in carpal tunnel syndrome (CTS) often complicates timely diagnosis. In clinical practice, CTS is frequently misinterpreted as cervical radiculopathy, hand osteoarthritis, neurasthenia, or anterior scalene syndrome, among other conditions, leading to inappropriate therapy and progression of the pathological process. During the initial clinical evaluation, specific provocative tests aimed at detecting median nerve compression play a key role. The most commonly used tests include Tinel’s sign, in which percussion over the median nerve elicits radiating paresthesia in the fingers, and Phalen’s test, characterized by the onset of paresthesia during wrist flexion held

for 60 seconds. Additional diagnostic maneuvers include Gillet's test, the elevation test, and the opposition test, which identifies weakness in the thenar muscles. Of particular note is the "shaking" symptom, in which patients report relief of pain and numbness after actively shaking the hand; this test has a reported sensitivity of 95.9% and specificity of 93.2% [3]. The Goloborodko test, based on transient tension of the transverse carpal ligament with temporary symptom relief, is also occasionally employed. Ultrasonography is used to visualize anatomical changes within the carpal tunnel. Key sonographic findings of CTS include thickening of the median nerve proximal to the tunnel, flattening or reduced thickness distally, decreased echogenicity as the nerve enters the canal, and thickening or increased echogenicity of the flexor retinaculum. According to meta-analyses, the sensitivity and specificity of ultrasonography for CTS diagnosis are 77.6% and 86.8%, respectively [5]. Electroneuromyography (ENMG) remains widely used for instrumental confirmation, with a sensitivity of 49–84% and specificity of 95–99%. However, in some patients with clinically confirmed CTS, ENMG may not reveal functional impairments of the median nerve, or observed changes may not correlate with symptom severity. Therefore, definitive diagnosis and prognostic assessment should rely on a comprehensive analysis of clinical findings combined with ENMG results [19]. Magnetic resonance imaging (MRI) of the wrist is primarily indicated in atypical clinical presentations, to exclude secondary causes of CTS, for differential diagnosis of space-occupying lesions, and when symptoms persist after unsuccessful surgical treatment. MRI allows visualization of the median nerve, the anterior interosseous nerve, their innervated muscles, and the ligamentous structures of the wrist [2].

Treatment

The management of carpal tunnel syndrome (CTS) is determined by the severity of clinical symptoms, disease duration, and the presence of comorbid conditions, and includes both conservative and surgical approaches. In mild to moderate cases, particularly in the early stages, conservative treatment is preferred. This typically involves wrist immobilization in a functionally optimal position, reduction of repetitive strain, administration of nonsteroidal anti-inflammatory drugs (NSAIDs), application of physiotherapeutic modalities, and local corticosteroid injections aimed at reducing median nerve compression and alleviating clinical symptoms [1,2,5,8]. The highest efficacy of conservative measures is observed in patients with a short disease history and no persistent motor deficits [3,6]. Surgical intervention is indicated in cases of symptom progression, persistent pain, grip weakness, thenar muscle atrophy, or lack of response to conservative therapy. The standard procedure involves decompression of the median nerve through division of the transverse carpal ligament. Surgery is considered a pathogenetically justified treatment, providing stable clinical improvement in the majority of patients [1,3,5]. The choice of treatment strategy should be individualized and based on a comprehensive evaluation of clinical and instrumental data, including functional scales and patient-reported outcome measures that reflect hand function and quality of life [7].

Prevention

Prevention of CTS includes modification of occupational activities, reduction of repetitive hand movements, ergonomic optimization of the workplace, and regular work breaks [5]. In patients with overweight or diabetes, preventive measures should focus on weight management and optimal control of the underlying disease, as these factors significantly increase the risk of CTS development [10,16]. For patients with endocrine and systemic disorders, including hypothyroidism, rheumatoid arthritis, and acromegaly, CTS prevention should consider disease activity and the need for adequate pharmacological management [22,23,24].

Conclusion

Carpal tunnel syndrome (CTS) represents a clinically uniform form of median nerve compression neuropathy; however, its development is driven by heterogeneous etiological and pathogenetic mechanisms. A review of the literature demonstrates that, despite similarities in clinical manifestations, the primary pathogenic pathways may vary significantly — ranging from mechanical and inflammatory microtrauma of carpal tunnel structures due to repetitive physical activities, to hormonally mediated interstitial edema, metabolic and microcirculatory disturbances in obesity and diabetes, as well as inflammatory, infiltrative, and storage processes in systemic and endocrine disorders. Despite the diversity of primary pathogenic factors, the final common pathway in all cases is increased intracanal pressure, resulting in compression and ischemia of the median nerve. Differences in initial mechanisms, however, determine clinical course characteristics, rate of disease progression, severity of neurological deficits, and potential reversibility of the pathological process. Functional and edematous changes associated with hormonal states and repetitive strain may be transient, whereas metabolic, inflammatory, and storage-related processes are more often linked to chronic and progressive CTS. These findings underscore the importance of considering the pathogenetic heterogeneity of CTS when interpreting clinical presentations and selecting diagnostic and therapeutic strategies. Understanding the role of the underlying pathology supports a differentiated, pathogenetically oriented approach to prevention and treatment, including modification of occupational activities, correction of metabolic and endocrine disturbances, and timely management of inflammatory and systemic diseases. Implementation of such an approach may reduce the risk of CTS development, slow disease progression, and improve clinical outcomes.

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