Barw Medical Journal | 2025;3(2):36-44
Journal home page: https://barw.krd/index.php/BMJ

Review

Differential Diagnosis of Neurogenic Thoracic Outlet Syndrome: A Review

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Keywords:
Neurogenic
Thoracic outlet
Diagnosis
Musculoskeletal disorders
Neurological disorders

Received: January 22, 2025
Revised: January 31, 2025
Accepted: February 17, 2025
First Published: February 25, 2025

Citation: Kakamad FH, Asaad SK, Ghafour AK, Sabr NS, Namiq HS, Mustafata LJ et al. Differential Diagnosis of Neurogenic Thoracic Outlet Syndrome: A Review. Barw Medical Journal. 2025;3(2):36-44.
https://doi.org/10.58742/bmj.v3i2.161

Abstract

Thoracic outlet syndrome (TOS) is a complex and often overlooked condition caused by the compression of neurovascular structures as they pass through the thoracic outlet. This compression can result in pain, numbness, tingling, muscle weakness, and vascular complications, with severe cases leading to thrombosis or embolism.

TOS is classified into three types based on the affected structure: neurogenic, venous, and arterial. Neurogenic TOS is the most prevalent, accounting for over 90% of cases, and is more commonly seen in females. Venous TOS represents 3–5% of cases, while arterial TOS is the rarest, comprising only 1%. Diagnosing TOS is challenging due to its symptom overlap with various musculoskeletal and neurological disorders, often leading to misdiagnosis. The absence of universally accepted diagnostic criteria further complicates identification, relying primarily on clinical evaluations and inconsistent diagnostic methods.

Neurogenic TOS, in particular, is difficult to distinguish from other conditions with similar presentations. This study provides a comprehensive review of the differential diagnosis of neurogenic TOS, comparing it with musculoskeletal and neurological disorders that share overlapping clinical features.

1. Introduction

Thoracic outlet syndrome (TOS) is a group of conditions caused by the compression of neurovascular structures passing through the thoracic outlet, first described in 1956 [1]. The thoracic outlet is an anatomical region in the lower neck, extending from the supraclavicular fossa to the axilla [2].

Typically, TOS occurs in three anatomical regions: the scalene triangle, the costoclavicular space, and the subcoracoid space. The structures involved may include the subclavian and axillary arteries, veins, and the brachial plexus. Compression of these structures can result in various symptoms, such as pain, paresthesia, pallor, weakness, a sensation of fullness, and muscle atrophy [3]. Accurately determining the prevalence of TOS is difficult due to its non-specific symptoms. However, the estimated incidence varies widely, ranging from approximately 3 to 80 cases per 1000 people [4].

The classification of TOS includes three types based on the compressed structure: neurogenic (nTOS), venous (vTOS), and arterial (aTOS) [5]. The nTOS is the most common type, representing over 90% of cases, and is more frequently observed in females [4]. The vTOS constitutes 3–5% of cases, while aTOS is the least common, making up only 1% [2]. In aTOS and vTOS, patients typically show clear signs of vascular compromise in the upper extremities, such as venous thrombosis, swelling, or arterial emboli affecting the fingers. In contrast, the diagnosis of nTOS relies more on the clinical history and the patient's symptoms [6].

This condition may develop due to congenital, acquired, or traumatic factors. Secondary causes include clavicle fractures and trapezius muscle weakness, which lead to shoulder depression, further narrowing the thoracic outlet and raising the pressure in the area [4].

Diagnosing nTOS presents a significant challenge due to its wide range of symptoms, which often resemble other conditions, leading to frequent misdiagnoses. The lack of a universally accepted diagnostic standard further complicates matters, resulting in a heavy reliance on clinical assessments and inconsistent use of diagnostic tests [7, 8]. These conditions include numerous musculoskeletal and neurological disorders, which may act as primary causes or as additional factors contributing to the patient's symptoms [9]. This study thoroughly reviews the differential diagnosis of nTOS, with all references carefully assessed for eligibility [10].

2. Differential diagnosis of nTOS

2.1. Cervical Radiculopathy

Cervical radiculopathy is a fairly common condition caused by dysfunction of the spinal nerves or nerve roots, often due to mechanical compression or inflammation [11]. The primary contributing factor is likely foraminal stenosis resulting from osteoarthritic changes in the cervical spine's joints rather than disc herniation [11]. Degenerative disc disease can reduce the foraminal height and lead to osteophyte formation. Additional factors that narrow the intervertebral foramen include trauma, infections, and tumors [12].

Cervical radiculopathy can manifest with a wide range of symptoms, including pain, muscle weakness, and reduced reflexes, that can mimic nTOS. Taking a thorough patient history is essential for diagnosing radiculopathy, with emphasis on the location and patterns of pain, paresthesias, sensory changes, and motor deficits. In many cases, the diagnosis can be made based solely on the patient's history [13].

Distinguishing points: Arm elevation above the shoulder usually relieves pain in cervical radiculopathy while exacerbating the symptoms in nTOS. Spurling's test is frequently utilized to diagnose cervical radiculopathy by reproducing symptoms through neck extension, titling, and compressing towards the affected side. Magnetic resonance imaging (MRI) plays a key role in confirming cervical disc disease or nerve root compression. In contrast, TOS is evaluated using tests like Adson's or Roos's, which involve specific arm movements to detect thoracic outlet compression. Nerve conduction studies (NCS) can also aid in diagnosing cervical radiculopathy [11, 14].

2.2. Carpal Tunnel Syndrome

The carpal tunnel is a narrow anatomical passageway bordered on the dorsal and lateral sides by the curved carpal bones and on the palmar side by the transverse carpal ligament. It contains nine flexor tendons for the fingers and thumb, along with the median nerve. However, the radial and ulnar arteries and the ulnar nerve do not pass through it. The transverse carpal ligament connects to the scaphoid and trapezium on the radial side and the pisiform and hamate on the ulnar side [15].

Carpal tunnel syndrome (CTS) results from median nerve compression as it travels from the forearm to the palm beneath the transverse carpal ligament. Typical symptoms include paresthesia, pain, numbness, and tingling affecting some or all of the thumb, index, middle, and ring fingers. Many patients experience symptoms that disrupt sleep, often finding relief by shaking or rubbing their hands [15].

Multiple factors contribute to the development of CTS, often leading to median nerve compression. Anatomical variations, such as a smaller carpal tunnel, along with repetitive wrist movements, increase susceptibility. Systemic conditions like diabetes, rheumatoid arthritis, and thyroid disorders are also significant risk factors. Hormonal changes during pregnancy and menopause, as well as wrist injuries like fractures or cysts within the tunnel, can further exacerbate the condition. Additionally, CTS is more common in women and typically affects adults between 40 – 60 years old [16].

Distinguishing points: In CTS, usually, the pain is found below the elbow joint, sparing the shoulder and neck. Also, a positive Tinel's sign is typically noted over the median nerve at the wrist, where compression occurs as it passes through the carpal tunnel. In contrast, in nTOS, a positive Tinel's sign may be elicited over the ulnar nerve or brachial plexus, which can be found at the cubital tunnel, interscalene triangle, or axilla [17]. However, the modified Phalen's test serves as a highly effective screening tool for diagnosing CTS [18].

NCS across the wrist are essential for distinguishing CTS from nTOS. In CTS, these studies help diagnose median nerve compression by assessing the conduction velocity and latency of the median nerve as it travels through the carpal tunnel. A decrease in conduction velocity or an increase in latency across the carpal tunnel indicates the presence of CTS [19].

To determine the relative impact of nTOS versus CTS in a patient with multifocal disease, it's essential to evaluate specific diagnostic and treatment responses. A scalene test block can confirm nTOS by temporarily relieving brachial plexus compression. For CTS, wrist splinting and steroid injections are commonly used for symptom management, with splinting effective in mild-to-moderate cases and injections providing short-term relief [20-22].

2.3. Suprascapular Nerve Entrapment

The suprascapular nerve is a mixed motor and sensory nerve originating from the brachial plexus (C5–C6). It travels through the suprascapular notch, passes under the superior transverse scapular ligament, and reaches the posterior aspect of the scapula, where it mainly innervates the supraspinatus and infraspinatus muscles [23].

This nerve is commonly compressed at two specific locations: the suprascapular notch and the spinoglenoid notch. Compression at the suprascapular notch leads to weakness in both the supraspinatus and infraspinatus muscles, while entrapment at the spinoglenoid notch results in weakness isolated to the infraspinatus muscle [24].

Injury to the suprascapular nerve can occur due to repetitive overhead movements, trauma, or in association with rotator cuff injuries. Patients with suprascapular nerve entrapment often experience shoulder pain, typically localized to the top and back of the shoulder, along with weakness during forward flexion and external rotation. Although relatively uncommon, this condition should be considered in cases of poorly defined posterior shoulder pain [23].

Distinguishing points: In contrast to TOS, the symptoms of suprascapular nerve entrapment are primarily confined to the shoulder. MRI is helpful in detecting the pathology associated with suprascapular nerve entrapment [25].

2.4. Cervical Dystonia

Cervical dystonia (CD) is a neurological disorder characterized by involuntary and abnormal neck movements due to repetitive or sustained muscle contractions, leading to unusual head and neck postures. It includes postural abnormalities such as torticollis, retrocollis, anterocollis, and laterocollis, although most patients exhibit a combination of these. CD is the most prevalent form of dystonia in younger adults, typically developing spontaneously without a clear cause. However, it can also arise secondary to trauma, the use of certain medications like anti-dopaminergic or neuroleptics, or as part of another neurological condition, with some cases linked to genetic mutations. Common symptoms include pain, muscle stiffness, limited range of motion, and abnormal postures [26]. In some instances, patients with mild dystonia, accompanied by significant pain or numbness, may be assessed for nTOS [9].

Distinguishing points*:* The symptoms of CD mainly involve involuntary movements and abnormal postures of the head and neck, sometimes accompanied by tremors. In contrast, the symptoms of nTOS are typically concentrated in the shoulder and arm, manifesting as pain, numbness, and weakness, primarily when the arm is raised. The diagnosis of CD is mainly clinical, based on observing abnormal head and neck movements [27]. However, combining electromyography (EMG) with ultrasound guidance can better assess the specific muscles involved in the condition and contribute to the patient's pain. Patients with CD often respond well to botulinum toxin injections targeting the affected muscles [9].

2.5. Brachial Neuritis

Brachial neuritis, also known as neuralgic amyotrophy or Parsonage-Turner syndrome, is a neuromuscular disorder affecting the peripheral nerves. The condition is not fully understood and is often underdiagnosed. The hallmark symptoms include the sudden onset of unilateral or bilateral shoulder girdle pain, followed by muscle weakness. Some patients may also experience sensory deficits. Typically, the pain radiates to the neck, arms, and forearms, with symptoms lasting from a few days up to an average of 4 weeks [28].

The exact cause of brachial neuritis remains unknown, although most experts suggest that immune-mediated conditions are the primary underlying factor, with other contributory factors potentially predisposing certain individuals to develop this neuromuscular disorder. The specific susceptibilities have not yet been identified. Additionally, mechanical and genetic factors have also been linked to brachial neuralgia [29].

Brachial neuritis predominantly affects middle-aged males, with the average age of onset being around 40 years, though it can occur in both males and females of any age. The reported incidence of brachial neuritis is 1 in 1000 individuals, a rate higher than previously reported [29, 30].

Distinguishing points: The sudden onset of severe shoulder pain, typically on one side and lasting from days to weeks, followed by muscle weakness in the shoulder and upper arm, distinguishes brachial neuritis from nTOS, which usually does not present with an initial phase of intense pain [28].

2.6. Brachial Plexus Tumors

Brachial plexus tumors are rare, with studies showing that 91% are benign and 9% are malignant. Schwannomas (61%) and neurofibromas (18%) are the most common benign tumors, whereas malignant peripheral nerve sheath tumors (MPNSTs) constitute 7% of all cases. Although uncommon, metastases to the brachial plexus can originate from primary cancers such as breast cancer and lymphomas [31].

Brachial plexus tumors present with a wide range of signs and symptoms, often significantly impacting motor and sensory functions in the upper limb. Pain is the most common symptom, reported by around 70% of patients, and can be localized or radiated to the shoulder and arm, sometimes worsening with movement [32]. A palpable mass in the supraclavicular region is another frequent finding, occurring in up to 95% of cases, and may be firm, sometimes leading to misdiagnosis. Sensory disturbances, such as numbness, tingling (paresthesia), and dysesthesia, affect approximately 54.5% of patients [33]. Additionally, upper limb weakness is notable, with motor deficits observed in 40-52% of cases [32, 33].

***Distinguishing points**:* The symptoms of brachial plexus tumors are usually persistent and not influenced by arm position. They are often accompanied by a palpable supraclavicular mass, such as schwannomas or lipomas [34]. Brachial plexus tumors can be differentiated from nTOS using Computed tomography (CT) or MRI imaging. MRI is considered the gold standard for evaluating these tumors due to its exceptional soft-tissue contrast and ability to provide high-resolution views of the entire plexus. It enables identifying distinct masses, analyzing their features, and examining their relationship with nearby structures [35].

2.7. Acromioclavicular Osteoarthritis

The acromioclavicular (AC) joint is a planar diarthrodial joint formed by the junction of the anteromedial acromion and the lateral clavicle. Osteoarthritis of this joint is a common and potentially disabling shoulder condition, leading to pain and restricted movement, particularly with overhead and cross-body activities. Clinically, osteoarthritis is the most prevalent AC joint disorder and can arise from various causes. Therefore, recognizing, diagnosing, and managing this condition is essential when evaluating patients with shoulder pain [36].

The degenerative joint disease of the AC joint can result from age-related wear of the intra-articular disk, post-traumatic changes, distal clavicle osteolysis, inflammatory arthritis, septic arthritis, joint instability, and impingement. Like the meniscus in the knee, the intra-articular disk undergoes degeneration through fraying, tearing, and defects in the cartilage surface, ultimately contributing to osteoarthritis. However, the frequency of these degenerative changes in asymptomatic individuals remains uncertain, which can complicate diagnosis. Additionally, trauma is a significant factor in joint-related pain, most often caused by an axial impact on an adducted arm [36].

Diagnosing AC joint osteoarthritis can be challenging, as common symptoms include pain during passive and active shoulder movements, particularly with overhead or cross-body motions [36].

Distinguishing points: Pain of AC joint osteoarthritis is primarily felt in the AC joint, with tenderness commonly detected through direct palpation. Patients frequently experience discomfort when pressure is applied to the area, which can be further evaluated using the cross-body adduction test. This test requires the arm to be moved across the body toward the opposite shoulder, and a positive result is indicated by pain in the AC joint, suggesting osteoarthritis. Imaging, particularly X-rays, often reveals joint space narrowing, bone spur formation, and other degenerative changes in the AC joint [36, 37].

2.8. Neurogenic Pectoralis Minor Syndrome

Brachial plexus compression can occur either above the clavicle in the thoracic outlet region or below it, beneath the pectoralis minor muscle. Because the symptoms of these conditions are similar, the history-taking and physical examination process is identical for nTOS and neurogenic pectoralis minor syndrome (nPMS). Hand paresthesia and arm pain should raise suspicion of brachial plexus involvement. A detailed history and thorough physical examination are crucial to determine whether the compression occurs above the clavicle in the thoracic outlet or below it under the pectoralis minor muscle. In many cases, both conditions are present simultaneously. Studies have shown that at least 75% of patients diagnosed with nTOS also have nPMS. Therefore, during the physical examination, it is essential to assess for tenderness in both the anterior scalene muscle and the pectoralis minor muscle [38].

The development of nPMS is influenced by multiple factors, including repetitive stress injuries, trauma, poor posture, occupational risks, and anatomical differences [39].

***Distinguishing points**:* Unlike nTOS, patients with nPMS typically show little to no response to neck rotation or head tilt maneuvers. This is because nPMS is caused by brachial plexus compression from the pectoralis minor muscle, which is not significantly influenced by neck movements. However, pain or tenderness in the axilla and the anterior chest wall just below the clavicle strongly suggests nPMS [38].

Both local anesthetic blocks and botulinum toxin injections play a crucial role in diagnosing and managing nPMS. They assist in determining whether symptoms result from compression by the pectoralis minor muscle, helping to guide appropriate treatment decisions [40].

2.9. Rotator Cuff Pathology

The term "rotator cuff" describes the group of muscles and tendons that encircle and provide stability to the shoulder joint during movement. Rotator cuff injuries and disorders are common causes of shoulder pain [41]. While these conditions can affect individuals of all ages and activity levels, they are more prevalent among those who repeatedly stress their shoulders and in middle-aged or older adults [41]. Rotator cuff diseases encompass a spectrum of conditions, including tendonitis, bursitis, impingement syndrome, as well as tears and lesions affecting the muscles and/or tendons in this region [41].

The most common symptoms of rotator cuff tears include pain caused by subacromial impingement, shoulder muscle weakness, and functional limitations, such as reduced range of motion. These symptoms primarily arise from a loss of superior stability in the glenohumeral joint due to dysfunction of the rotator cuff muscles [42]. On physical examination, patients with rotator cuff disorders often experience pain during overhead movements (similar to individuals with nTOS) and demonstrate weakness during external rotation of the shoulder [9].

***Distinguishing points**:* Patients with rotator cuff disorders may experience pain when the shoulder joint and deltoid are palpated; however, unlike nTOS, they typically do not exhibit significant tenderness in the scalene triangle. Rotator cuff disorders are characterized by pain primarily localized to the anterior and lateral shoulder. In contrast, nTOS presents with more widespread symptoms, including pain in the neck, upper chest, shoulder, and arm, often accompanied by numbness, tingling, and weakness in the hand, particularly affecting the pinky and ring fingers. Diagnostic tests such as the Hawkins-Kennedy, Neer, and Jobe tests are frequently positive in rotator cuff dysfunction and impingement cases. Imaging techniques

like MRI and ultrasound are useful for identifying rotator cuff tears and tendinopathy, while radiographs can reveal degenerative changes or variations in acromial morphology [9, 43].

2.10. Scapular Dyskinesis

The scapula plays a crucial role in optimal shoulder and arm function, contributing to scapulohumeral rhythm and being linked to various clinical shoulder injuries [44]. Scapular dyskinesis refers to abnormal scapular movement patterns during shoulder motion, which can adversely affect upper extremity function and contribute to various shoulder disorders. This condition is commonly observed in athletes, especially those engaged in overhead sports, where shoulder mechanics are subjected to greater demands. Recent research highlights that scapular dyskinesis should be considered a physical impairment rather than a standalone diagnosis, as it can result from diverse factors such as muscular imbalances, neurological conditions, and anatomical differences. Clinically, scapular dyskinesis is associated with reduced shoulder strength, altered glenohumeral joint mechanics, and an elevated risk of injury in athletes [44, 45].

Distinguishing points: In scapular dyskinesis, pain is typically localized around the shoulder blade or upper back and is often associated with shoulder movement or repetitive overhead activities [46]. The diagnosis of scapular dyskinesis involves a clinical examination that assesses abnormal scapular motion during shoulder movement, focusing on scapular positioning, rhythm, and movement patterns. This involves several tests, including visual observation, where the clinician examines the scapula during arm elevation or other movements to identify winging, tilting, or asymmetry. The Scapular Assistance Test helps determine whether manual assistance of the scapula improves motion or reduces pain, indicating dysfunctional scapular involvement in shoulder symptoms. Similarly, the Scapular Dyskinesis Test assesses scapular motion during repetitive arm movements, such as flexion or abduction, to detect dyskinetic patterns. Additionally, muscle strength testing identifies weaknesses in stabilizing muscles like the serratus anterior or lower trapezius, which may contribute to scapular dyskinesis [44].

2.11. Complex Regional Pain Syndrome

Complex regional pain syndrome (CRPS) is a persistent neurological disorder that affects the limbs and is characterized by intense pain along with sensory, autonomic, motor, and trophic dysfunction [47]. CRPS is classified into two types: CRPS-I, which occurs without a confirmed nerve injury, and CRPS-II, where nerve injury is present. Female gender is a known risk factor for CRPS, along with conditions such as fibromyalgia and rheumatoid arthritis. The exact cause of CRPS remains unclear [48]. This condition can be triggered by surgery, trauma, or even minor injury, and its progression varies, ranging from mild and self-limiting to chronic, potentially affecting daily activities and overall quality of life [47].

Distinguishing points: CRPS is marked by persistent regional pain that appears excessive in relation to the typical progression of any known injury or lesion. Key clinical features include allodynia (pain from a non-painful stimulus), hyperalgesia (heightened pain sensitivity), sudomotor and vasomotor issues (sweating and blood vessel abnormalities), and trophic changes (alterations in skin, hair, and nails). The Budapest Criteria are the most commonly used for diagnosing CRPS. According to these criteria, a patient must experience ongoing pain disproportionate to any triggering event, along with at least one symptom from three out of four categories (sensory, vasomotor, sudomotor/edema, and motor/trophic) and at least one sign from two or more of these categories [49].

2.12. Biceps Tendinitis

Biceps tendinitis is a condition affecting the tendon of the long head of the biceps muscle. When inflammation occurs within the intertubercular (bicipital) groove, it is referred to as primary biceps tendinitis, which accounts for approximately 5% of all cases. The remaining 95% of cases are typically associated with a rotator cuff tear or a superior labrum anterior to posterior (SLAP) lesion [50].

This condition is most commonly observed in individuals aged 18 to 35 who participate in throwing and contact sports, swimming, gymnastics, and martial arts. Many of these athletes experience secondary impingement of the bicep tendon, often linked to factors such as scapular instability, shoulder ligamentous laxity, anterior capsule looseness, or posterior capsule tightness. Additionally, secondary impingement may result from soft tissue injuries like labral or rotator cuff tears, which can expose the biceps tendon to the coracoacromial arch [50].

Individuals with biceps tendinitis often experience a deep, throbbing ache in the front of the shoulder. The discomfort is typically centered around the bicipital groove but may extend toward the deltoid muscle insertion or radiate down the arm in a radial pattern. Symptoms tend to worsen at night, particularly if the affected shoulder is compressed during sleep. Activities involving repetitive overhead movements, pulling, or lifting can also trigger or intensify the pain [50].

Distinguishing points: Biceps tendinitis is characterized by localized tenderness over the bicipital groove. Patients often experience significant pain when direct pressure is applied to this area. Various provocative tests, such as Yergason, Neer, Hawkins, and Speed tests, are used to identify biceps tendon pathology. A positive result in any of these tests suggests the presence of impingement, which can contribute to the development of biceps tendinitis. However, biceps tendon sheath injections serve as both a diagnostic and therapeutic approach for anterior shoulder pain associated with biceps tendinopathy. Ultrasound guidance enhances their accuracy and minimizes the risk of complications [50].

2.13. Ulnar Entrapment Syndrome

The ulnar nerve follows a long and intricate anatomical path, originating from the brachial plexus in the neck, where its trunk forms within the posterior triangle before extending into the axilla. Due to this complex course, the nerve is vulnerable to compression, direct trauma, and traction injuries. A thorough patient history, detailed neuromuscular examination,

appropriate imaging, and electrophysiological studies can precisely identify the site of conduction blockage and the underlying pathological cause [51].

Ulnar nerve entrapment is the second most common compression neuropathy in the upper limb, following CTS. While the nerve can be compressed at various points along its path, the elbow is the most frequent site of entrapment. A comprehensive understanding of ulnar nerve anatomy is essential for accurate diagnosis and effective treatment planning [38].

This condition is three to eight times more common in males due to the anatomical course of the ulnar nerve, which makes it more susceptible to repetitive strain injuries and work-related impairments. The causes range from physiological compression during elbow flexion to structural abnormalities such as tumors within the tunnel, bursae, ganglion cysts, inflammatory conditions affecting the elbow joint, and osteophytes [51].

In the early stages of the condition, numbness and paresthesia are the primary symptoms, while pain is less frequently reported. Sensory disturbances in the ulnar digits are common, though patients often struggle to identify the affected area precisely. A thorough history and clinical examination are essential for individuals presenting with medial elbow pain to exclude other potential causes. While pain is usually confined to the cubital tunnel region, it may also extend to the medial epicondyle and forearm [52].

Distinguishing points*:* Ulnar nerve entrapment primarily affects the ulnar side of the forearm and hand, leading to tingling, numbness, or weakness, particularly in the ring (4th) and little (5th) fingers. Tinel's sign at the elbow is an essential clinical test during physical examination, performed by tapping over the ulnar nerve in the cubital tunnel between the olecranon and medial epicondyle. A positive result is indicated by tingling or paresthesia radiating to the fourth and fifth fingers, which are supplied by the ulnar nerve [53]. Electrodiagnostic studies are crucial in confirming the diagnosis, particularly at the elbow. NCS and EMG are key assessments used to determine the presence and severity of nerve damage [54].

2.14. Pancoast Tumors

Pancoast syndrome is characterized by a distinct set of symptoms, including shoulder and arm pain along the distribution of the eighth cervical and first and second thoracic nerves, Horner's syndrome, and hand muscle weakness with atrophy. It is primarily caused by the local extension of an apical lung tumor into the superior thoracic inlet. These tumors, referred to as superior pulmonary sulcus tumors or Pancoast tumors, are the leading cause of the syndrome [55].

The earliest and most frequent symptom is shoulder pain, which arises from tumor infiltration into the brachial plexus, parietal pleura, endothoracic fascia, vertebral bodies, and the first three ribs. This pain may extend toward the head and neck or radiate downward to the medial scapula, axilla, anterior chest, or ipsilateral arm, typically following the ulnar nerve distribution [55].

Pancoast tumors are predominantly non-small cell lung cancers (NSCLC), with squamous cell carcinoma being the most frequent type (52%), followed by adenocarcinomas (23%) and large cell carcinomas (20%). Small cell carcinoma accounts for only about 5% of Pancoast tumors. While bronchogenic carcinoma is the primary cause of superior sulcus tumors, these tumors represent less than 5% of all bronchogenic carcinomas [55, 56].

The risk factors for developing Pancoast tumors are similar to those of lung cancer, with cigarette smoking being the most significant cause. Additional contributing factors include secondhand smoke exposure, long-term asbestos exposure, and contact with industrial elements. The condition typically presents in the sixth decade of life and is more common in men than in women [56].

Distinguishing points: Around 40% of individuals with Pancoast tumors show signs of Horner's syndrome, typically marked by the triad of ipsilateral ptosis, miosis, and anhidrosis. This condition occurs when the tumor affects the paravertebral sympathetic chain and the inferior cervical (stellate) ganglion, causing oculosympathetic paresis. Unlike TOS, systemic symptoms such as weight loss, cough, and hemoptysis are commonly seen in the later stages of the disease [56]. CT scan is considered the gold standard for diagnosing Pancoast tumors, while MRI is crucial for evaluating local invasion. Using both imaging methods together with histological confirmation from a biopsy is vital for an accurate diagnosis and effective treatment planning [57].

2.15. Fibromyalgia Syndrome

Fibromyalgia syndrome is a prevalent condition marked by ongoing, widespread pain, often accompanied by debilitating fatigue, sleep issues, reduced cognitive and physical function, and emotional distress. It is recognized in the International Classification of Diseases as chronic primary pain. Various names, such as fibrositis or fibromyositis, have previously referred to fibromyalgia syndrome. However, these terms are now considered inaccurate, as they wrongly suggest that muscle inflammation is the primary source of pain. While the exact cause remains unclear, recent research indicates that changes in pain processing within the nervous system are likely responsible [58].

Fibromyalgia affects an estimated 2-4% of the population, predominantly women [59]. Diagnosing Fibromyalgia syndrome can be difficult, as there are no specific clinical tests to confirm the condition, and its symptoms fluctuate, often not aligning with established medical diagnostic categories [58]. The exact cause and pathogenesis of fibromyalgia remain unclear, but it appears that several factors, such as dysfunctions in the central and autonomic nervous systems, neurotransmitters, hormones, the immune system, external stressors, and psychiatric factors, may all play a role. Central sensitization is considered the primary mechanism involved, defined by an increased response to stimuli mediated by central nervous system signaling. This phenomenon results from spontaneous nerve activity, expanded receptive fields, and heightened stimulus responses transmitted by primary afferent fibers [60].

Distinguishing points: In contrast to TOS, fibromyalgia syndrome is characterized by widespread musculoskeletal pain, accompanied by symptoms like fatigue, sleep disturbances, and cognitive difficulties. Fibromyalgia diagnosis, according to the American College of Rheumatology (ACR) guidelines, relies on two key criteria: the Widespread Pain Index (WPI) and the Symptom Severity Scale (SSS). The WPI assesses pain across specific body regions, while the SSS evaluates symptoms like fatigue and cognitive difficulties. To meet the diagnostic requirements, a patient must have either a WPI score of 7 or higher, an SSS score of 5 or higher, or a WPI score between 3 and 6 with an SSS score of 9 or higher (Table 1) [58, 61].

Table 1. Summary of the distinguishing points.

#	Differential diagnoses	Distinguishing points
1	Cervical Radiculopathy	**a)** Pain reduction by arm elevation. **b)** Positive Spurling's test. **c)** MRI and EMG/NCS.
2	Carpal Tunnel Syndrome	**a)** Confined pain to below the elbow. **b)** Positive Tinel's sign over the median nerve at the wrist. **c)** Positive modified Phalen's test. **d)** NCS.
3	Suprascapular Nerve Entrapment	**a)** Localized pain in the shoulder. **b)** EMG/NCS.
4	Cervical Dystonia	**a)** Involuntary head and neck movements, abnormal postures, and sometimes tremors. **b)** EMG/NCS.
5	Brachial Neuritis	**a)** Sudden onset of severe shoulder pain, lasting from days to weeks, followed by muscle weakness. **b)** EMG/NCS.
6	Brachial Plexus Tumors	**a)** Symptoms unaffected by arm position. **b)** CT scan and MRI.
7	Acromioclavicular Osteoarthritis	**a)** Acromioclavicular joint tenderness. **b)** Positive cross-body adduction test. **c)** X-ray and US.
8	Neurogenic Pectoralis Minor Syndrome	**a)** Minimal to no response to neck rotation. **b)** Tenderness in the axilla and below the clavicle.
9	Rotator Cuff Pathology	**a)** Tender shoulder joint. b) Positive Hawkins-Kennedy, Neer, and Jobe tests. **c)** MRI and US.
10	Scapular Dyskinesis	Pain around the scapula and upper back.
11	Complex Regional Pain Syndrome	a) Excessive regional pain. b) Budapest Criteria.
12	Biceps Tendinitis	**a)** Tenderness localized over the bicipital groove. **b)** Positive Yergason, Neer, and Speed tests.
13	Ulnar Entrapment Syndrome	**a)** Pain in the ulnar side of the forearm and hand. **b)** Positive Tinel's sign at the elbow. **c)** NCS/EMG.
14	Pancoast Tumors	**a)** Horner's syndrome. **b)** CT scan and MRI.
15	Fibromyalgia Syndrome	Widespread musculoskeletal pain, fatigue, sleep disturbances, and cognitive difficulties.

MRI*: magnetic resonance imaging,* NCS*: nerve conduction study,* EMG*: electromyography,* CT *scan: computed tomography scan,* US*: ultrasound*

3. Future perspectives

The development of more objective and reliable diagnostic tests for nTOS is crucial, potentially involving advanced imaging techniques to visualize neurovascular structures and compression sites. Research into biomarkers could aid in differentiating nTOS from conditions with similar symptoms. Personalized treatment approaches tailored to the specific cause and severity of TOS should be investigated, potentially combining physical therapy, medication, and surgical interventions. Further understanding of the role of posture and ergonomics is needed to develop effective prevention strategies, especially considering conditions like nPMS. Exploring the effectiveness of combined therapies, such as botulinum toxin injections alongside TOS treatments, could provide synergistic benefits for patients with overlapping conditions. Increased awareness and education among healthcare professionals and the public are essential to improve early diagnosis and management of this often-overlooked condition.

4. Conclusion

Diagnosing TOS can be complex due to its varied symptoms, which often overlap with other musculoskeletal and neurological conditions. Advanced imaging techniques, electrophysiological studies, and thorough clinical examinations are key to improving diagnostic accuracy.

Declarations

Conflicts of interest: The author(s) have no conflicts of interest to disclose.

Ethical approval: Not applicable.

Patient consent (participation and publication)**:** Not applicable.

Funding: The present study received no financial support.

Acknowledgements: None to be declared.

Authors' contributions: FHK, BAA, and SSA were significant contributors to the conception of the study and the literature search for related studies. SKA, AKG, NSS, HSN, LJM, ASH, SHT, AHA, SOA, and OMH were involved in the literature review, the study's design, and the critical revision of the manuscript, and they participated in data collection. HAN, MNH and BAA were involved in the literature review, study design, and manuscript writing. FHK and FHK confirm the authenticity of all the raw data. All authors approved the final version of the manuscript.

Use of AI: AI was not used in the drafting of the manuscript, the production of graphical elements, or the collection and analysis of data.

Data availability statement: Not applicable.

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