

# Thoracic outlet syndrome: wide literature for few cases. Status of the art

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**Abstract** Despite its low prevalence and incidence, considerable debate exists in the literature on thoracic outlet syndrome (TOS). From literature analysis on nerve entrapments, we realized that TOS is the second most commonly published entrapment syndrome in the literature (after carpal tunnel syndrome) and that it is even more reported than ulnar neuropathy at elbow, which, instead, is very frequent. Despite the large amount of articles, there is still controversy regarding its classification, clinical picture, diagnostic objective findings, diagnostic modalities, therapeutical strategies and outcomes. While some experts believe that TOS is underrated, overlooked and very frequent, others even doubt its existence as a nosological entity. In the attempt to shed more light on this condition, we performed a systematic review of the literature and report evidence and opinions around this controversial subject. Only articles focused on neurogenic TOS were considered. Understanding the status of the art and the underlying reasons of doubts and weaknesses could help clinical practice and set the stage for future research.

**Keywords** Thoracic outlet syndrome · Nerve entrapments · Brachial plexus · Literature review · Neuropathy · Neurogenic TOS

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## Introduction

Nerve entrapment syndromes are a group of conditions that share a unique common pathophysiology and pathogenesis that results in a predictable pattern of neurological symptoms (pain, numbness, tingling, weakness, and muscle wasting in peripheral nerve distribution). While some of these conditions are very common from the epidemiological point of view (e.g., carpal tunnel syndrome), others are very rare (e.g., pronator teres syndrome). One of these disorders, the thoracic outlet syndrome (TOS), is not even universally accepted as a nosological entity. Despite its low prevalence and incidence, a large amount of articles in the literature deal with this neuropathy. From analysis of literature on nerve entrapments (Table 1), we realized that TOS is the second most commonly published entrapment syndrome in the literature (after carpal tunnel syndrome) and that it is even more reported than ulnar neuropathy at elbow, which, instead, is very frequent.

Assuming that the magnitude of debate reflects not only prevalence and incidence, but also interest, doubts and attempts to reach certainties, we decided to provide the state of the art of TOS. In the attempt to shed more light on this condition, we reviewed the most recent articles and report evidence and sometimes opinions (specifying if the concepts are based on the former or on the latter) around this controversial clinical entity.

## Search strategy and selection criteria

In the first phase, to provide as much as possible evidence-based data, we performed a comprehensive search of PubMed using the MeSH term: “thoracic outlet syndrome” with the following additional filters: article types (meta-analysis; systematic reviews), text availability (abstract

**Table 1** PubMed search results of the number of articles published on each nerve entrapment syndrome (from January 1, 2006 to June 30, 2016)

Nerve entrapment syndromes	Number of articles in PubMed
Carpal tunnel syndrome	2450 (MeSH)
Thoracic outlet syndrome	446 (MeSH), 658 (no MeSH)
Ulnar neuropathy at elbow	547 (no MeSH)
Ulnar neuropathy at wrist	142 (no MeSH)
Tarsal tunnel syndrome	134 (MeSH)
Superficial peroneal entrapment	24 (no MeSH)

MeSH terms were used when available

*MeSH* MeSH terms, *no MeSH* without using MeSH terms

available), publication dates (from January 1, 2006 to June 30, 2016), species (humans) and language (English). Following this methodology, we found 0 meta-analysis and 7 systematic reviews [1–7]. Then next, due to the scarce literature of meta-analysis on the topic, other article types were included, i.e., “clinical trials”, “reviews”, “multi-center studies”, “guidelines”, and “practice guidelines”. Extending the search: 40 reviews, 4 clinical trials, 0 multicenter studies, 0 guidelines, 1 practice guideline were found. For each article, pertinence was considered. Articles solely focused on vascular TOS were excluded. Finally, four systematic reviews [1, 3, 5, 6], six clinical trials [8–13] and 36 reviews were included [14–49].

### Pathophysiology and epidemiology

TOS is a nerve entrapment syndrome characterized by different neurovascular signs and symptoms due to compression of neurovascular bundle passing through the thoracic outlet, proximally or at the first rib. Compression may occur in different segments of the brachial plexus, trunks or cords: the interscalene triangle (the most frequent), the space and the retropectoralis minor space.

TOS is usually classified into arterial TOS, venous TOS and neurogenic TOS. In this review, we deal with the neurogenic TOS, which includes the vast majority of cases [30], and is typically found in patients with a history of excessive repetitive activity or trauma of the upper extremity [31]. Neurogenic TOS includes the rare “true” TOS (the “classic” form with objective findings, 1% of neurogenic cases, prevalence of approximately 1 case per million persons [27]), and the “nonspecific” or “disputed” TOS (the “common” form, with chronic pain but without objective findings, the remaining 99% of cases) [27, 30].

TOS is more frequent in women than in men (3–4:1 ratio) and usually occurs in the third and fourth decades [30]. As with all entrapment neuropathies, anatomic predisposition seems to play a crucial role in TOS, whose occurrence is often triggered by an injury. According to some authors, a

history of traumatic injury of the neck, shoulder girdle and upper extremity is common [16, 19, 20, 24–32, 34–36, 42, 45] and is reported by about 70–80% of patients [32]. Virtually, any chronic cervical muscle spasm (primary, or more often secondary to cervical trauma) may induce this condition. As with the other nerve entrapments, habits, work and posture may have a crucial role [15, 16, 19, 20, 24, 26, 27, 30–32, 34–36, 38, 42–47]. Other acquired causes are rare but must be systematically considered: tumors, hyperostosis, osteomyelitis, lipomas [20], accessory muscles [41], and soft tissue anomalies [29, 46].

### Clinical features

The clinical picture of TOS varies from positive sensory symptoms (most frequent in the “disputed form”) to motor and sensory deficits (most common in the “true form”). Sometimes, symptoms may be both neurogenic and vascular due to a possible over-activation of the sympathetic nervous C8–T1 fibers [22, 24, 32].

Patients with the disputed TOS usually complain of pain, paresthesias and numbness in the shoulder, arm, hand (most commonly in the ring and small fingers) and occipital region. Symptoms are usually worsened by elevated, overhead, or outstretched positions of the arm. Limb fatigue and heaviness in the affected arm are common. Symptoms are often vague, inconsistent and poorly defined [29]. Although sensory symptoms are predominant in this form, motor complaints and functional impairment are frequently reported [27]. Neurological examination is usually negative and characterized only by subjective findings (tenderness over the scalene muscles and subcoracoid space, reported hypoesthesia to light touch, positive Tinel’s sign over brachial plexus area). Four provocative diagnostic maneuvers (Adson test, Roots test, Wright test, and costoclavicular test), traditionally, have been used to diagnose TOS, although they have a very low specificity [9, 14, 28, 32, 36, 38] and their reliability is unknown [30].

In the true TOS, motor abnormalities are considered much more pronounced than the sensory ones [27, 29]. Most patients with this form come to medical attention late, usually complaining of intrinsic hand muscle weakness and wasting. Progressive inability to use the hand and loss of dexterity are other common complaints. Pain and paresthesiae are often moderate or may even be absent. On examination, upper extremity weakness and wasting in a lower trunk distribution is apparent, involving the thenar eminence to the greatest degree, the ulnar hand intrinsic muscles less, and the medial forearm muscles even less.

The severity and debilitating nature of signs and symptoms in TOS is supported by a recent study, which demonstrated that untreated patients with neurogenic TOS have physical component summary (PCS) scores on the

12-Item Short Form Health Survey (SF-12) quality-of-life instrument, similar to PCS scores in patients with chronic heart failure [31].

## Diagnosis

The clinical presentation of TOS is highly variable, and no reproducible study exists to confirm the diagnosis, which, instead, is mostly based on physician's judgment after a meticulous history and physical examination [16, 19, 24, 29, 30, 32, 35, 45, 46]. There is also a lack of clarity in the literature about the typical neurophysiological pattern of TOS. In this regard, while some authors distinguish between true TOS and disputed TOS [15, 21, 27, 28, 36, 39], others consider this aspect indistinctly [3, 16, 19, 23, 24, 26, 29–32, 38, 42].

In the disputed form, neurophysiology is generally of little help (apart from excluding other diagnoses) and usually normal [15, 27–29, 36, 39], although some authors believe that medial antebrachial cutaneous nerve conduction can detect abnormalities [16, 42]. Concerning the true form, although abnormal neurophysiological results are expected, there is controversy over what is the typical pattern. Nerve conduction abnormalities are observed in patients with long-standing TOS that results in muscle atrophy [40]. Some authors reported that conduction velocity may be decreased in the case of permanent nerve compression [19, 23, 25, 26, 29, 36], while others underline the reduced median, ulnar, and distal radial amplitude of CMAP, with ulnar and medial antebrachial cutaneous SNAP absent [27, 28, 36, 38]. Regarding F-wave studies, which should theoretically reflect brachial plexus involvement, inconsistent results are reported, and so, their role is controversial [28]. Somatosensory evoked potentials are considered not useful in TOS, being non-specific, non-localizing, and rarely abnormal [28, 29, 36]. Needle electromyography is useful to assess possible neurogenic damage (usually chronic) [15, 19, 26, 28, 29, 38, 39].

The lack of a reproducible neurophysiological dysfunction, that any nerve compression causes, often leads neurologists/neurophysiologists to consider TOS a “neuro-myth”. In support of this disbelief is also the absence of supportive neuroimaging data. Ultrasonography (US) is unable to show nerve changes at the costoclavicular space. Magnetic resonance (MR) imaging may occasionally depict fibrous bands causing nerve distortion (often associated with cervical rib or an elongated transverse C7 process). However, the finding of a cervical rib is not diagnostic considering that for every 20,000–80,000 individuals with a cervical rib, only 1 has true neurogenic TOS [27]. Evaluation of anatomical spaces (interscalene, costoclavicular and retropectoralis minor space) and the results from postural maneuvers (dynamic MR) may increase the diagnostic sensitivity [10, 46]. Some authors

believe that MR can confirm the clinical suspicion of TOS [17, 19, 20, 23, 25, 34], while according to others, MR results in these patients are generally normal [16, 31]. Moreover, MR may only show indirect signs, such as distortion of brachial plexus nerves, and many times fails to demonstrate unequivocal anatomical or functional nerve impairment. Among all studies evaluating the role of MR in the diagnosis of TOS, to our knowledge, there are not controlled or blinded studies available. A recent prospective study evaluated the value of 3T-MR neurography in the assessment of patients with a “clinical diagnosis or at least high suspicion of TOS” [11]. Seven out of 30 patients were identified with unambiguous morphological correlates of TOS (presence of an anatomical structure compressing the brachial plexus and an associated abnormal focus on T2 W within the compressed plexus portions), which were confirmed by surgical exploration [11]. Even in this study, limitations included the small number of patients, that the surgeon was not blind, surgical exploration in patients with negative findings was not performed, and a long-term follow-up was not reported.

Finally, some authors suggest that the intramuscular anterior scalene block, through neuromuscular blocking agents injection, may be a diagnostic test with temporary benefit due to reduced muscle spasm compressing the thoracic outlet [16, 25, 30, 31, 36, 48]. Klaassen et al. proposed that anterior scalene block should be used as a screening tool for selecting candidates for undergoing subsequent decompression surgery [25]. Indeed, the degree of symptom relief achieved from intramuscular injections in patients with neurogenic TOS correlates with a successful response to subsequent treatments including physical therapy [31] and surgical intervention [19, 25, 26, 30, 31]. However, this test has poor specificity for TOS, and there is no substantial evidence that it can reliably confirm the diagnosis.

The differential diagnosis for TOS includes musculoskeletal diseases (e.g., arthritis or tendinitis) of the cervical spine, shoulder girdle, or arm; cervical radiculopathy or upper extremity nerve entrapment; neuralgic amyotrophy; fibromyalgia [31]; and brachial plexus compression due to an infiltrative process or space-occupying mass (e.g., Pancoast tumor). Distal compression neuropathy, such as carpal tunnel or cubital tunnel, is another important alternative diagnosis to consider. However, as reported by some authors [24, 32], nearly 40–50% of patients with TOS have associated peripheral nerve compression symptoms; therefore, this finding does not exclude the diagnosis of TOS.

## Therapy

The first treatment option for TOS is usually conservative [3, 15, 16, 19, 24–26, 28–32, 36, 45, 46]: rest, correct posture, and avoidance activities and behaviors that may worsen

symptoms. Limited data support the use of rehabilitation and physical therapy [30, 33] and no randomized controlled trials have been conducted to measure its efficacy [15]. Ferrante and colleagues believe that “there is no role for conservative therapy with true neurologic TOS, because, due to the slowly progressive nature of this disorder, maximal reinnervation via collateral sprouting has already occurred” [27]. Personally, we do not understand the correlation between the aim of conservative therapy (which is to prevent further damages and to reduce disabling symptoms) and maximal reinnervation (which also has not been demonstrated). According to Brooke and colleagues, approximately 60–70% of patients may be successfully managed non-operatively, when physical therapy is constantly performed for at least eight weeks [31]. Moreover, a 2007 systematic review of the available literature concluded that conservative treatment seems effective in reducing symptoms, improving function, and facilitating return to work [1]. Evidence-based data are, however, lacking. A clinical trial showed that therapeutic exercises provide relief of symptoms of TOS, although the lack of a control group and the aspecificity of the inclusion criteria make the results inconclusive [8]. Concomitant pharmacological approach may be suggested [30, 31, 38], despite limited efficacy in muscle relaxation and nociceptive and neuropathic pain reduction.

In case of failed conservative therapy, some authors suggest anesthetic [28], steroid [28] or botulinum toxin injection [26, 28, 30] into the cervicothoracic musculature, in spite of conflicting evidence and possible side effects/complications. A double-blind, randomized, controlled trial [12] and a recent Cochrane review, concluded that there is no evidence that treatment with botulinum toxin injection is better than placebo for TOS [5].

After failed conservative therapy, some authors suggest surgery to relieve extrinsic compression of cervical nerve roots or brachial plexus [15, 16, 19, 24–26, 28–32, 35, 36]. Three main surgical approaches have been described: transaxillary first rib resection, scalenectomy (supraclavicular neuroplasty) and rib resection with scalenectomy (combined approach). While some authors suggest that the combined surgical approach for TOS is the best [24, 32], others are in favor of the supraclavicular approach [3, 35] or of the transaxillary first rib resection [29, 31]. There is very low quality evidence that transaxillary first rib resection decreases pain more than supraclavicular neuroplasty [5].

All the approaches are not devoid of risks, and complications are not exiguous including phrenic nerve (most frequently), long thoracic nerve, cervical sympathetic chain, nerve roots injury and Horner’s syndrome during supraclavicular operations; wound infections, hematoma, irritation of the intercostal brachial nerves, pneumothorax (10%) and temporary radial nerve palsy following first rib resection [30]. Finally, endoscopic-assisted transaxillary first rib resection is a novel

approach in the management of TOS and, in a single clinical trial on 22 surgical interventions, appeared to be safe [13].

In summary, although excellent in-hospital outcomes are reported by some authors [31, 32, 38], the role of surgery remains controversial even because there is not randomized evidence that surgery is better than no treatment for TOS [5]. Two Cochrane reviews (2010 and 2014), aiming to evaluate the available interventions for the treatment of TOS, were complicated by a lack of generally accepted diagnostic criteria and concluded also that there is a need for agreed outcome measures and high quality randomized trials [5, 6].

## Conclusions

Distinction between true TOS and disputed TOS is crucial both in clinical practice and in research planning. These two forms must be considered as two different clinical entities with regard to aetiology, clinical picture, and diagnostic findings and modalities. In the disputed TOS, symptoms are vague and subjective, clinical picture is heterogeneous, objective findings are lacking and diagnosis is of exclusion. This form is still considered a controversial subject by both neurologists and surgeons. Although diagnostic tests are typically unrevealing in this form, it is always mandatory to identify individuals with an alternative disorder before making the diagnosis. In the true TOS, symptoms are localizing and diagnostic tests usually reveal abnormalities. However, despite these advantages, even in this form, there are still unmet clinical needs, such as universally recognized diagnostic criteria and agreement on therapeutical approach.

In conclusion, TOS is a nerve entrapment syndrome with peculiar features, among which:

1. TOS is subject to an extensive literature debate, out of proportion in relation to its actual incidence.
2. The current concept of TOS varies according to different perspectives: neurophysiologists and neurologists often deny the existence of TOS, while surgeons claim that it is very frequent and responsive to surgical therapy. The controversial opinions are favored by the lack of gold standard diagnostic tests.

## Compliance with ethical standards

**Conflict of interest** There are no conflicts of interest to declare.

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