Thoracic Outlet Syndrome (Costoclavicular Syndrome)

Acknowledgment: this article has been produced with a large contribution by Kjetil Larsen. His work is reproduced with his permission. Details of the impact of posture and management are seen on his website: https://trainingandrehabilitation.com/how-truly-treat-thoracic-outlet-syndrome/

Thoracic outlet syndrome (TOS) is not the name of a single entity, but rather a collective title that encompasses a variety of conditions produced by compression of nerves, arteries and or veins (or all) because of an inadequate passageway through an area (thoracic outlet) between the base of the neck and the armpit. The thoracic outlet is bordered by the scalene muscles, first rib, and clavicle.

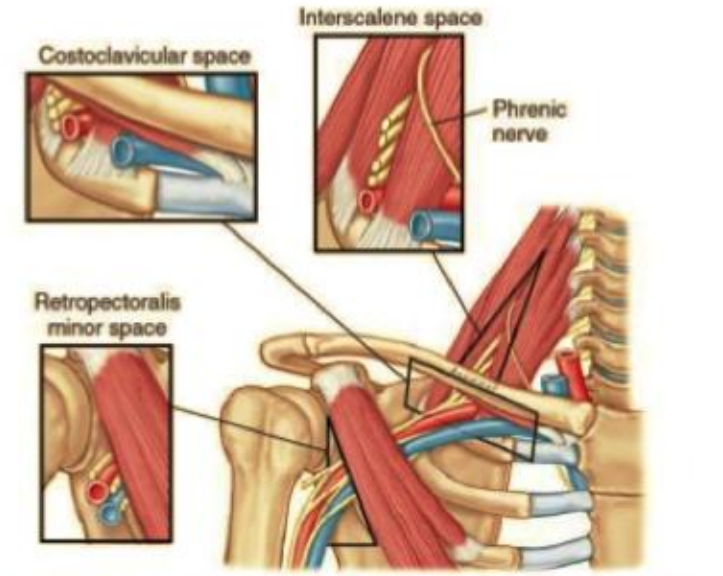
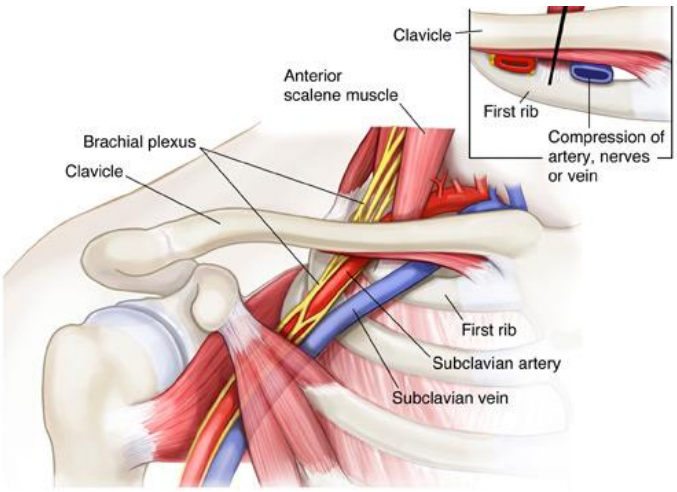


FIGURE 59-2 Three spaces in the thoracic outlet that may be responsible for thoracic outlet syndrome.

Source: https://www.slideshare.net/swatcats2013/thoracic-outlet-syndrome-62735055 (10)



Thoracic Outlet Syndrome

Source: http://sportmedschool.com/thoracic-outlet-syndrome/ (22)

Shoulder disorders, which include unspecific shoulder pain and specific disorders, are commonly diagnosed in primary care and often lead to prolonged disability. Their 12-month

prevalence in the population of working age range between 7 to 47% for shoulder pain, depending on the population studied. The impacts for workers are important in industry such as in office, especially for chronic shoulder pain. (19)

"Although neck and arm pain is a frequent presenting complaint in the general population, the controversial and difficult to diagnose Thoracic Outlet Syndrome should always be considered especially if the risk factors and occupational situations associated with it as assessed. The neurogenic forms are by far the most frequent as they represent more than 95% of all cases of TOS, and these can be classified in the "true" neurological form associated with neurological deficits (mostly muscular atrophy), and painful neurological forms (with no objective neurological deficit). These painful forms are very frequent, especially when patients are systematically screened for these symptoms. The existence of these forms of TOS remains controversial in part because muscular and neurological manifestations are strongly interrelated. (19)"

"Nearly all cases of TOS (95%) are neurogenic in origin. NTOS is an underappreciated and often overlooked cause of shoulder and neck pain and numbness. Like patients with other chronic pain conditions, patients with untreated neurogenic TOS experience a diminished quality of life, reduced financial well-being, functional limitations, and an increased risk for depression and anxiety.(20)"

"Although the notion of NTOS as a complex spectrum disorder provokes some controversy in the field, its impact on patients is beyond dispute. Data indicate that the quality of life for a patient with untreated TOS is as impaired as that of someone with chronic heart failure. (20)"

"True NTOS, which is confirmed with objective findings, accounts for only 1% of cases, whereas common NTOS, which has symptoms suggestive of brachial plexus compromise but no objective findings, makes up 99% of neurogenic cases of TOS. The remaining cases of TOS are arterial (1%) and venous (3%-5%).(20)"

"Neurogenic TOS occurs in an estimated 3 to 80 per 1,000 individuals, the wide range reflecting the lack of confirmation in many patients with signs and symptoms indicative of the condition. Women with NTOS outnumber men by 3 to 4:1. The syndrome is particularly common in people who perform repetitive tasks with their upper extremities, such as violinists, data entry personnel, and workers on assembly lines. Athletes with repetitive overhead arm motion, including volleyball players, swimmers, baseball pitchers, and weightlifters, also are at increased risk, as are people who have experienced neck trauma. (20)"

Any condition that results in enlargement or movement of these tissues of or near the thoracic outlet can cause the thoracic outlet syndrome. Other risk factors include shoulder trauma, occupations or sports that involve heavy usage of the upper extremities against resistance, including jack-hammer operators and dental hygienists, weight lifting, pregnancy, poor posture and obesity. Rarely lung tumours can affect the outlet.

"Histologic studies suggest that injury to either the anterior scalene muscle (ASM) or the middle scalene muscle are the main causative factors of NTOS. Muscle fibrosis is a prime finding on examination of excised scalene muscles, with NTOS patients having 3 times as much scar tissue as unaffected subjects. The ASM derives from the transverse processes of the C3-C6 vertebrae. The muscle, which attaches to the first rib, serves as an accessory muscle of respiration, and also rotates the neck slightly. Spasm of the ASM puts traction on the brachial plexus and causes oedema of the muscle and nerves, which, in turn, limits the space of the outlet. Development of scar tissue and fibrosis of the ASM further worsen neural compromise and perpetuate pain. (20)"

Thoracic outlet syndrome symptoms include neck, shoulder pain, arm pain, numbness and paraesthesiae (pins and needles) fingers and impaired circulation of the extremities (so there

may be for example, discolouration of the hands.) Symptoms can be constant or intermittent depending on what activities are being performed.

“Painful neurological forms of TOS account for 97% of all cases of TOS according to Roos [21]. They are typically responsible for symptoms in the C8-T1 distribution (medial aspect of the arm, ulnar border of the forearm and hand), but the C7 nerve root and sometimes the superior trunk of the brachial plexus (C5-C6) may be responsible. Clearly systematized symptoms are rarely present. [19]”

“It has been reported that the 3 most disturbing preoperative symptoms are pain at rest (87% of cases), feeling of numbness (66% of cases) and decreased strength (55% of cases). In practice, the patient often reports vague, poorly defined, and inconsistent symptoms, but clinical interview often reveals difficulties during activities requiring elevation of the arms (hanging up the washing, brushing one’s hair, etc.). [19]”

“Functional impairment and pain related to carrying heavy loads are frequent but less specific. Pain of the neck and shoulder region is at least partly due to muscle imbalance but can sometimes be due to a proximal form of TOS (C5-C6). Decompensation fairly frequently occurs after a change of job or in a context of carpal tunnel syndrome (double crush syndrome). These patients present with complex upper limb pain. Carpal tunnel symptoms appear rapidly due to pre-existing irritation of the nerve fibres by TOS. However, the pathophysiology of the association between upper-limb distal nerve entrapment and TOS is complex, and may not be only on irritation of nerve fibres. For instance, median nerve sensory fibres do not travel with the C8 fibres that are being hypothesized as the site of the double crush. Therefore, other mechanisms could be considered in relationship to increase median or ulnar nerve pressure and scalene muscle activity, or a hypothesis of centralization of pain. The associated TOS must be identified, as it can be responsible for persistent symptoms after treatment of carpal or ulnar tunnel syndrome.”

“Apart from double crush syndrome, other secondary painful diseases may be associated, such as epicondylar pain secondary to medial or lateral insertion tendinitis. However, referred pain is not always easy to distinguish from a possible associated tendinitis (medial aspect of the elbow, which also raises the problem of the real (or at least the initial) cause of the pain . Nevertheless, some of these forms of medial or lateral epicondylitis may resolve in response to rehabilitation for TOS. [19]”

Kjetil Larsen describes “TOS is considered to be one of modern medicine’s most difficult issues, because of the complex and variable nature of its symptoms. It has potential to cause numerous types and areas of pain, such as neuralgia in the arms, chest, between the shoulder blades and in the back (figure 1), dizziness, brain fog, migraine, headaches, a feeling of being “heavy-headed”, etc.” [1]”

“The reason why the potential symptoms are all over the spectrum, is because it in addition to compression of the entire brachial plexus nerve network which innervates the arms as well as parts of the chest, neck and back, also may compress the subclavian artery & vein. A branch of the subclavian artery include a key vessel, the vertebral artery. The vertebral artery supplies the brain with blood and is therefore especially important to assess for symptoms of vertebrobasilar insufficiency. It has also been shown that TOS may cause secondary dysautonomic symptoms.” [1]

“Despite more than 2600 references to TOS on PubMed, there is still wide controversy regarding TOS; no concrete diagnostic criteria have been established, and many practitioners claim that the whole problem is a fad which does not really exist.” [1]

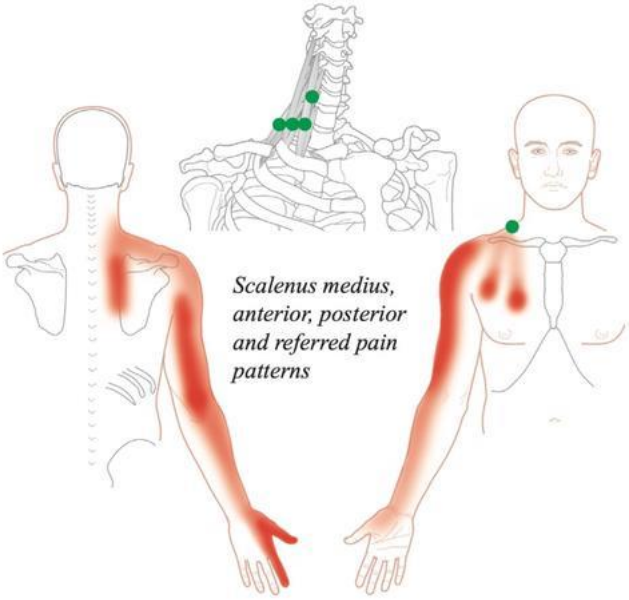
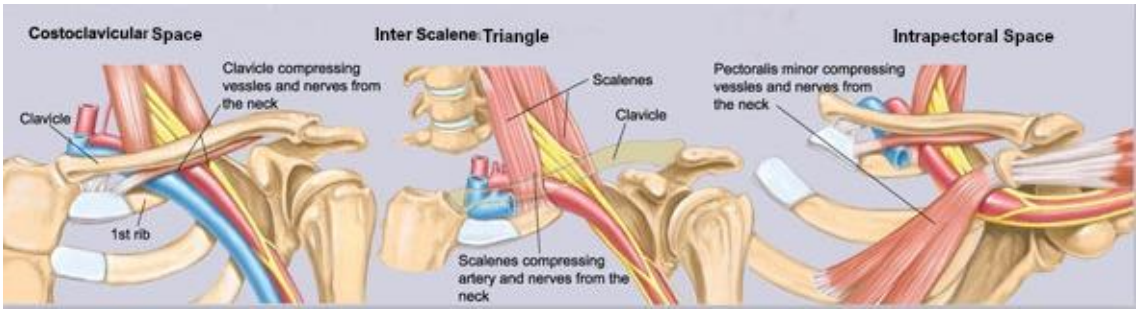


Figure 1:

“The name thoracic outlet syndrome suggests chronic irritation (compression) of the brachial plexus and the subclavian vessels, as mentioned initially. “Thoracic” means region of the thorax (chest), and “outlet” is self-explanatory. Why do they become irritated or compromised? Due to continuous compression within spaces that the nerves and vessels pass through. The cause of the compression is mainly tightness of the surrounding muscles and clavicular depression, strangulating the thoracic outlet vascular and nervous structures.”(1)



“In turn, the main cause of the muscle tightness and clavicular depression, is faulty movement and postural strategies. This can be rooted in habits alone, or triggered by injuries such as a clavicular fracture, whiplash injury or similar. Slouching of the neck (forward head posture) and shoulder, belly-(only)-breathing and lack of diverse movement will cause the scalenes that form the interscalene triangle of which the brachial plexus pass through, to inhibit/deactivate. This in turn may cause severe tightening of the scalenes, compressing all of the thoracic outlet’s structures and may thus (potentially) cause all of the initially mentioned symptoms.” (1)

“The (anterior and medial) scalenes are involved in many actions. They elevate the ribs during inspiration (inhalation), ipsilaterally rotate, cause lateral translation, laterally flex and forward flex (bend) the neck. In normal breathing patterns, the ribs and clavicle should elevate slightly during inspiration, and this is done in syncronization by the scalenes, trapezius and several other muscles. Severe slouching habits will inhibit this pattern as well as proper cervical (axial) rotation, causing degeneration of the involved muscles. In turn, severe inhibition of the scalenes will often develop over time.” (1)

“Because the trapezius muscle holds the scapula and clavicle, the loss of optimal function of this muscle will cause chain reactions of muscular inhibition down the line (arm), creating the

potential for several nervous and vascular entrapment points, such as the triangular interval in the posterior shoulder. This is especially important when there is pre-compression within the scalenes and costoclavicular passage, as this sensitize the whole nervous chain and make the distal branches more vulnerable to additional irritation." (1)

"Additionally, because the scalenes attach to the ribs, they may elevate the first rib, greatly increasing the potential of secondary compression between the 1st rib and the clavicle. Compression within the scalenes often attribute to between 60-80% of the patients' direct symptoms in my experience; a considerable amount." (1)

Table 1

History and examination features in ATOS, VTOS, and NTOS.

TOS Subtype	History	Examination
ATOS	Claudication/rest pain of upper limb, excluding shoulder/neck Numbness, coolness, pallor	Raynaud's phenomenon Upper limb ischaemia, digital ulceration, peripheral embolisation Pulsatile mass ± bruit on auscultation Blood pressure differential >20 mmHg Positive EAST, ULTT, Adson's test
VTOS	Deep pain on movement or rest pain in upper limb, chest, shoulder Swelling and cyanotic discoloration	Upper limb swelling Cyanosis Positive EAST, ULTT, Adson's test
NTOS	Pain in neck, trapezius, shoulder, arm, chest, occipital headache Variable pattern upper limb weakness, numbness, paraesthesias	Tenderness on palpation: scalene triangle, subcoracoid space Upper plexus (C5-C7): sensory disturbance of arm. Weakness/atrophy of deltoid, biceps, brachialis Lower plexus (C8-T1): sensory disturbance ulnar forearm & hand. Weakness/atrophy of small muscles of the hand, weak wrist & finger flexion Positive EAST, ULTT, Adson's test

Source: **Polvsen,S., Povlsen,B.: Diagnosing Thoracic Outlet Syndrome: Current Approaches and Future Directions.** Published online 2018 Mar 20. doi: 10.3390/diagnostics8010021: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5872004/(14)
TOS Subtypes: ATOS= arterial TOS, VTOS= venous TOS, NTOS= neurogenic TOS

History:

Thoracic outlet syndrome was first described in in 1942 in soldiers with loaded backpacks who developed pain, numbness and arm fatiguability as they stood at attention, and results published in 1943.(2) "The mechanism of compression involved downward movement of the clavicle against the first rib, with a resultant tendency to shearing of the neurovascular bundle." (3) This same mechanism was thought to explain subclavian vein thrombosis precipitated by prolonged heavy exercise of the upper extremities- Paget-Schroetter Syndrome. De Silva then described the same mechanism occurring in heavy breasted women with tight bra straps again shearing the neurovascular bundle. Peet et al formalized the diagnosis in 1956. (16)

Association with Migraine

Thoracic outlet compression has been associated with intractable migraine.[9] From ongoing research underway at present in the association between popliteal vein compression syndrome and migraine, this TOS association may be from cascades of inflammatory chemicals from compression of baro (pressure) receptors in and around the vessels and other structures, but also there is clinical evidence that the scalene muscles that insert onto C3 vertebra also affect the C2/3 region, triggering migraine as described by Dean Watson.

Most migraine appears to be driven by cervical nerve root sensitivity. Physio researcher from Adelaide, Dean Watson, found "The cervical afferents of C1-3 are the reason we get increased sensitization of the brainstem. The common pathway with the Trigeminal nerve will present as the head pain or facial pain plus associated symptoms of dizziness and nausea etc (C2/3). The head pain is a representation of the input from the cervical afferent nerves C1-3. This constant input will reduce the latency period (ie someone will get symptoms earlier than the normal person). This constant input then causes the brainstem to become sensitized and effectively "ready to go" with small input. This is why small variations (small C2 rotation perhaps from bad posture) or triggers will bring on large changes so quickly. The changes of this C2 rotation can very subtle and hard to find unless therapists are experienced in assessing these." [4]

Neural sensitivity

Dovetailing into this concept of neural sensitivity is the increasing realization of glial hypersensitization causing the pain of Fibromyalgia Syndrome (FMS). FMS is characterized by widespread musculoskeletal pain, fatigue and cognitive difficulties. Central nervous system sensitization is a major component where various external stimuli eg infection, trauma and stress contribute to symptoms. The pain is neuropathic in nature, with changes in dermal unmyelinated nerve fibre bundles, while myelinated fibres are not affected.

Recent research has made some significant progress in the probable mechanism of this neuroinflammation, both central and peripheral. FMS has been "linked to inflammatory reactions and changes in the systemic levels of pro-inflammatory cytokines that modulate responses in the sympathetic nervous system and hypo-pituitary-adrenal axis"**.** Mendieta et al found higher levels of IL-6 and IL-8 than in healthy volunteers, and these 2 interleukins were 2 of the most constant inflammatory mediators in fibromyalgia, with levels corresponding to the severity of fibromyalgia symptoms, and that IL-6 and IL-8 could have additive effects in the continuous pain in fibromyalgia. [13]

Hypersensization in FMS is felt to be part of threat receptor hypersensitivity. There appears to be an array of TRP and Acetylcholine receptor polymorphisms that results in nerve hypersensitivity, altered calcium influx and cellular function - even immune responses.

Autonomic Variability

Heart rate variability studies in patients with TOS symptoms have shown unexpected changes when provocation studies are undertaken, with both sympathetic and parasympathetic activation, probably from Thoracic Sympathetic Chain, Phrenic and Vagal Nerve activation.

In patients with Postural Orthostatic Tachycardia Syndrome (POTS) where the autonomic instability is exaggerated, we find marked increases in heart rate as well as parasympathetic activation, creating a "wired but tired" response. There is increasing evidence from our work in this area, that has associated the inflammatory changes found in TOS with autoimmune disease, anxiety and depression.

Thrombosis and microemboli from the subclavian and axillary veins

Thrombosis of the subclavian and axillary veins have been associated with pulmonary emboli, just as popliteal vein compression is a cause of DVT and pulmonary emboli. In the migraine research from Drs David Grosser and Ross Sharpe, they found microemboli from the occluded popliteal veins in the legs can pass through a Patent Foramen Ovale (PFOs) to affect the brain, and the same risk is present from the TOS vein compression. [5] In recent research from USA

looking at people seen at emergency departments after syncope or sudden collapse, 20% have been found to have had pulmonary emboli.[6]

Dyspnoea in patients with known chronic obstructive pulmonary disease (COPD) can be a clinical challenge due to the nonspecific nature of atypical presentations. Typical features of fever, productive cough, and wheezing on presentation support COPD exacerbation, while absence of such findings may warrant further evaluation for underlying aetiologies, including pulmonary embolism (PE). It is suspected that one in four patients with atypical COPD exacerbation may have PE as an underlying or concomitant cause of acute dyspnoea. [7]

The very real risk of microemboli and emboli from occluded subclavian veins in the thoracic outlet plays an important role in the cause of “unexplained” pulmonary emboli, as an underlying cause of “asthma” where adequate investigation has not been performed, in emphysema, idiopathic pulmonary hypertension, and probably disease such as sarcoidosis.

The lungs should filter out any microscopic emboli from the compression areas, unless a PFO is present. I strongly suspect many of the people with “asthma” not confirmed on formal lung function testing, sometimes presenting at emergency departments with chest pain and shortness of breath, have had microscopic embolic cascades. In other patients it appears to be a cascade of inflammatory chemicals rather than microemboli, and any microembolic phenomena would also produce an inflammatory response. Sometimes there is a positive D-Dimer test suggesting a pulmonary embolus, but with no sign of DVT or embolus in VQ lung scans, the usual tests, they are discharged. In all patients where we consider this a possibility, we have started regular lung function testing, and if appropriate, HS-CT lungs.

Researchers are now looking at “microtrauma” in the veins, and that concept is very appealing to me, with particular importance for unexplained chest pains (also from cascades of catecholamines and simple nerve compression at the axillae. With the evolving concept of microembolic and inflammatory cause of cardiovascular disease (MINOCA) it is highly probably TOS will be shown to have a significant role. It all becomes very murky and complex but does allow a path to recovery from the problems by addressing the mechanical issues, certainly until we have clear confirmation of the exact pathogenesis of the diseases. Another area of clear association we have found is in aortic arch dilatation. Our research has shown this problem to have a very high association with TOS and sportsmen. This is discussed elsewhere in “Aortic Arch Dilatation.”

Myofascial Pain Syndrome

Complicating the issue is the presence of myofascial pain where the fascia that surrounds the muscles is affected, most notably with the trigger points where muscles fibres that when compressed is painful and can give rise to referred pain elsewhere and is associated with motor dysfunction and autonomic changes. Trigger points might be “active” or “latent.” An active trigger point is always sore and can prevent the full use of the muscle, leading to weakness and decreased range of motion. A latent trigger point does not cause pain during normal activities but is tender when touched and can be activated when the muscle is strained, fatigued, or injured.

Other authors look at the syndrome as “Scalene Myofascial Pain,” where patients present “with unilateral neck and shoulder pain associated with typical referred pain in the radial distribution of the affected arm/hand, simulating C6 radicular pain. When the referred pain is due to MPS of the scalene muscle, the referred pain and numbness can be due to brachial plexus irritation as a result of direct compression between two scalene muscles. This phenomenon justifies the established fact that MPS of the scalene muscle is one of the causes of TOS. [17]”

The cause of myofascial pain syndrome is uncertain in traditional medical literature. Causes appear to include mechanical factors — such as having one leg longer than the other — poor posture, stress, and overuse of muscles. Exercising or performing work activities using poor techniques can also put excessive strain on muscles seem most likely. Prior injury, poor sleep patterns, stressful life situations, and depression are common underlying conditions that may play a role in inciting and exacerbating myofascial pain syndrome. It is currently felt that risk

factors such as these may lead to a change in the ability of the brain to properly process pain perception, but it implicates the linking with the autonomic changes that are found in TOS.

The close association between adhesive capsulitis (frozen shoulder) and TOS is most likely associated with autonomic changes associated with this. There is a high association between TOS, myofascial pain and fibromyalgia. It becomes an esoteric discussion what label is applied as long as the mechanical causes and physical signs are identified, and other pathology excluded.

Population studies

As yet we have simply no idea of what percentage of compression is in the normal population – in arm movements it must be said that venous compression is probably a normal occurrence. In the very biased population of migraine, fibromyalgia, POTS and auto-immune patients seen at this clinic, TOS of various types is found in around 80% of patients. Rodante et al identified a myofascial component of pain in 30% of all patients, and up to 95% at a chronic pain centre. [15] It is quite likely that this myofascial component accounts for the bulk of the neurogenic symptoms, and as traditional investigations such as nerve conduction studies are normal, the diagnosis is missed.

Sport Specific Biomechanics

Thoracic outlet syndrome is most often seen in patients who engage in repetitive motions that place the shoulder at the extreme of abduction and external rotation. An example of such activity is swimming, especially with the freestyle, butterfly, and backstroke. When a swimmer reports tightness and pain around the shoulder, neck, and clavicle as his or her hand enters the water, thoracic outlet syndrome should be suspected. Other athletes affected include water polo, baseball, and tennis players and athletes in any other activity that places repetitive stress on the shoulder at the extremes of abduction and external rotation. It is also found in musicians, waiters and others working above their shoulders.

Povlsen and Povlsen describe “It is becoming increasingly recognised that high-level repetitive physical activity involving the upper extremity may put individuals at risk for development of thoracic outlet syndrome. Indeed, in one centre >40% of patients requiring first rib resection and scalenectomy for NTOS relief were competitive athletes. This risk also appears to extend to the vascular subtypes of TOS, where such events may be antecedents for effort-induced thrombosis. Although cases of thoracic outlet syndrome in musicians have been documented, until now it had not been rigorously studied.

A recent paper prospectively evaluated 64 high-performance string instrument musicians and 52 healthy age-matched controls. They found positive elevated arm stress test (EAST) or upper limb tension test (ULTT) in 44% of musicians compared with 3% in the control group. Abnormal ultrasound scan with vascular compressions was detected in 69% of musicians versus 15% of controls. Interestingly, they also noted abnormal ultrasound scans with vascular compression were more commonly noted in violinists and viola players than cellists. Furthermore, in violinists and viola players, the left arm, which is elevated to hold up the instrument, was more commonly affected than the right bow-holding hand. This underscores the theory that it is the overhead repetitive-strain aspect of these activities that predisposes to thoracic outlet syndrome. [14]”

Illig and Doyle[8] write: “the subclavian vein is highly vulnerable to injury as it passes by the junction of the first rib and clavicle in the anterior-most part of the thoracic outlet. In addition to extrinsic compression, repetitive forces in this area frequently lead to fixed intrinsic damage and extrinsic scar tissue formation. Venous thoracic outlet syndrome progressing to the point of axillosubclavian vein thrombosis, variously referred to as Paget-Schroetter syndrome or effort thrombosis, is a classic example of an entity which if treated correctly has minimal long-term sequelae but if ignored is associated with significant long-term morbidity.”

Management

Surgery in cases of thoracic outlet syndrome is indicated for acute vascular insufficiency and progressive neurologic dysfunction. Neurological symptoms may persist in patients following surgery to remove the first ribs, thus freeing the venous compression, but scarring of the nerves that envelop the vessels causes the prolonged symptoms after surgery, and which would mean that the observed vein compression seen in vascular scanning is only a guide to the presence of the compression producing the sensitization.

Increasingly botox into the scalene muscles is being used as a diagnostic tool in this sub-group of patients, and increasingly literature suggests it may be effective as a therapeutic one. It is being used primarily in neurogenic TOS, and as yet I can find no use in venous TOS, so I await responses to botox trials when used in mixed forms of TOS. John Hopkins provides a useful graphic to demonstrate the surgical and botox procedures, although I feel the site presents an overly glowing presentation https://www.hopkinsmedicine.org/heart_vascular_institute/vascular-surgery/our-specialties/thoracic-outlet-syndrome/index.html

Physiotherapy focuses on pain control and range of motion with specific stretching exercises that addresses postural abnormalities and muscle imbalance relieves symptoms in most patients with thoracic outlet syndrome by relieving pressure on the thoracic outlet. Once pain control and cervical motion are regained, strengthening exercises of the lower scapular stabilizers are begun, as is an aerobic conditioning program. When surgery is performed, best results do appear to be in those where appropriate physiotherapy is undertaken.

Postural correction focuses on positions of most risk and least risk for compression, with integration into the patient's activities of daily living at work, home, and sleep. In addition, the impact of obesity and general physical conditioning should be assessed. Treating TOS is not simple and requires a dedicated physiotherapist or a musculo-skeletal trained physician or suitable other therapist. TOS may be treated successfully with myofascial release manipulation and stretching. Self-stretching exercises complement all other treatment modalities for TOS. Stretching must be demonstrated "hands on" with the patient and reviewed and modified regularly[18]. The work described by Kjetil Larsen in: https://trainingandrehabilitation.com/how-truly-treat-thoracic-outlet-syndrome/ is I believe a step forward to help therapists in other areas where specialized teams do not exist, deal with the complexity of this problem.

References:

1. Larsen,K. How to truly identify and treat thoracic outlet syndrome (TOS). 2017, https://trainingandrehabilitation.com/how-truly-treat-thoracic-outlet-syndrome/
2. Falconer, M., Weddel,G.,Costoclavicular Compression of the Subclavian Artery and Vein. Lancet, 1943: ii: 539-44
3. De Silva, M. The Costoclavicular Syndrome: a “new cause.” Annals of Rheumatic Diseases, 1986; 45, 916-920
4. Watson,D., https://watsonheadache.com/
5. Grosser, D.: Popliteal Vein Compression syndrome the main cause of DVT, unrecognized. https://www.arteries-veins.com/single-post/2017/01/07/Popliteal-vein-compression-syndrome-the-MAIN-cause-of-DVT-unrecognised
6. Prandoni P et al. Prevalence of pulmonary embolism among patients hospitalized for syncope. N Engl J Med 2016 Oct 20; 375:1524.
7. Teng Moua[1] and Kenneth Wood[2] COPD and PE: A clinical dilemma, Int J Chron Obstruct Pulmon Dis. 2008 Jun; 3(2): 277–284.
8. Illig,k., Doyle, A.: A Comprehensive Review of Paget-Schroetter Syndrome, Journal of Vascular Surgery, Volume 51, Issue 6, June 2010, https://www.sciencedirect.com/science/article/pii/S074152140902518X
9. Chahwala V, Tashiro J, Li X, Baqai A, Rey J, Robinson HR. Venous Thoracic Outlet Syndrome as a Cause of Intractable Migraines. https://www.ncbi.nlm.nih.gov/pubmed/27531080
10. Narra, C. Thoracic Outlet Syndrome. https://www.slideshare.net/swatcats2013/thoracic-outlet-syndrome-62735055

11. Rosenbaum, D.A., Thornburg, M.,Silvis,M.L., Thoracic Outlet Syndrome. http://emedicine.medscape.com/article/96412-overview
12. Sheil, W.C. Thoracic Outlet Syndrome (TOS) http://www.medicinenet.com/thoracic_outlet_syndrome/article.htm
13. Mendieta,D, Barrera-Villalpando,M., de la Cruz Aguilera, D., Villanveuva, L., IL-8 and IL-6 primarily mediate the inflammatory response in fibromyalgia patients. Journal of Neuroimmunology 290(1):22 - 25 · November 2015. https://www.researchgate.net/publication/284722475_IL-8_and_IL-6_primarily_mediate_the_inflammatory_response_in_fibromyalgia_patients
14. Polvsen,S., Povlsen,B.: Diagnosing Thoracic Outlet Syndrome: Current Approaches and Future Directions. Published online 2018 Mar 20. doi: 10.3390/diagnostics8010021: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5872004/
15. Rodante,J., Al HGassan,Q., Almeer,A.: Myofascial Pain Syndrome: Uncovering the Root Causes. 2019. Practical Pain Management. https://www.practicalpainmanagement.com/pain/myofascial/myofascial-pain-syndrome-uncovering-root-causes
16. Peet,R., Henriksen,J., Anderson,T., Martin,G. Thoracic-outlet syndrome: Evaluation of a therapeutic exercise program. Proc. Staff. Mayo Clin. 1956,31, 281-287
17. Nizar Abd Jalil, Mohammad Saufi Awang, Mahamarowi Omar. Scalene Myofascial Pain Syndrome Mimicking Cervical Disc Prolapse: A Report of Two Cases. Malays J Med Sci. 2010 Jan-Mar; 17(1): 60–66.
18. Sucher,B. Thoracic outlet syndrome--a myofascial variant: Part 2. Treatment. J Am Osteopath Assoc. 1990 Sep;90(9):810-2, 817-23.
19. Laulan,J., Fouquet,B., Rodaix, A., Jauffret,P., Roquelaure, Y., Descatha,A.: Thoracic outlet syndrome: definition, aetiological factors, diagnosis, management and occupational impact. J Occup Rehabil. 2011 Sep; 21(3): 366–373.
20. Christo,P.: New Perspectives on Neurogenic Thoracic Outlet Syndrome. Practical Pain Management. https://www.practicalpainmanagement.com/pain/neuropathic/new-perspectives- neurogenic-thoracic-outlet-syndrome
21. Roos DB. Thoracic outlet syndromes : Update 1987. Am J Surg. 1987;154:568–73. [PubMed: 3425795]
22. Thoracic Outlet Syndrome: http://sportmedschool.com/thoracic-outlet-syndrome/