Thoracic outlet syndrome (TOS) is a condition arising from compression of the subclavian vessels and/or brachial plexus as the structures travel from the thoracic outlet to the axilla. Despite the significant pathology associated with TOS, there remains some general disagreement among experts on the specific anatomy, etiology, and pathophysiology of the condition, presumably because of the wide variation in symptoms that manifest in presenting patients, and because of lack of a definitive gold standard for diagnosis. Symptoms associated with TOS have traditionally been divided into vascular and neurogenic categories, a distinction based on the underlying structure(s) implicated. Of the two, neurogenic TOS (nTOS) is more common, and typically presents as compression of the brachial plexus; primarily, but not exclusively, involving its lower trunk. Vascular TOS (vTOS) usually involves compression of the vessel, most commonly the subclavian artery or vein, or is secondary to thrombus formation in the venous vasculature. Any anatomical anomaly in the thoracic outlet has the potential to predispose a patient to TOS. Common anomalies include variations in the insertion of the anterior scalene muscle (ASM) or scalenus minimus muscle, the presence of a cervical rib or of fibrous and muscular bands, variations in insertion of pectoralis minor, and the presence of neurovascular structures, which follow an atypical course. A common diagnostic technique for vTOS is duplex imaging, which has generally replaced more invasive angiographic techniques. In cases of suspected nTOS, electrophysiological nerve studies and ASM blocks provide guidance when screening for patients likely to benefit from surgical decompression of TOS. Surgeons generally agree that the transaxillary approach allows the greatest field of view for first rib excision to relieve compressed vessels. Alternatively, a supraclavicular approach is favored for scalenotomies when the ASM impinges on surrounding structures. A combined supraclavicular and infraclavicular approach is preferred when a larger field of view is required. The future of TOS management must emphasize the improvement of available diagnostic and treatment techniques, and the development of a consensus gold standard for diagnosis. Helical computed tomography offers a three-dimensional view of the thoracic outlet, and may be valuable in the detection of anatomical variations, which may predispose patients to TOS. This review summarizes the history of TOS, the pertinent
HISTORY OF THORACIC OUTLET SYNDROME

Throughout the course of medical history, thoracic outlet syndrome (TOS) has developed a reputation as a condition based on convoluted neurological and vascular symptoms. Physicians have continually disagreed about the relevance and pathogenesis of TOS, leading to a wide spectrum of opinions and research directions. This disagreement is augmented by the presence of anatomic anomalies and abnormal diagnostic tests observed in an asymptomatic population, resulting in further dispute about the specificity and sensitivity of commonly used diagnostic measures (Jordan and Machleder, 1998). Regardless of opinion, the history of TOS represents a chronicle of the difficulties involved in the diagnosis, management, and treatment of this condition.

The symptoms attributed to TOS were first described in 1818 by the English surgeon and anatomist Sir Astley Cooper (Ranney, 1996), and yet it was not until 1956, Peet et al. (1956), coined the term “thoracic outlet syndrome.”

The list of etiological agents and causative mechanisms for TOS is extensive, yet one of the earliest and most consistent is the presence of a cervical rib. Galen first documented the presence of cervical ribs in 2 AD and further elaboration by the anatomist Vesalius during the first dissections of human bodies in 1543 provided additional insight (Roos, 1996; Nannapaneni and Marks, 2003). In 1842, Gruber contributed to the classification of cervical ribs by designating four categories, namely, (i) hypertrophic transverse process of C7, (ii) rudimentary rib with no connection to the rib of T1, (iii) an incomplete rib connected to the rib of T1 by a fibrous band, and (iv) a complete first cervical rib fusing with the rib of T1 (Gruber, 1869; Nannapaneni and Marks, 2003). The development of radiography during the early twentieth century dramatically increased the number of cervical rib diagnoses that presumably would have been largely ignored in the past (Claggett, 1962).

Additional causes for TOS have been postulated. In 1912, Todd was the first to relate a postural abnormality to the symptoms of TOS. He suggested that a drooping shoulder could lead to compression of the subclavian vessels and the brachial plexus between the clavicle and the first rib. Todd further explained that the reason for the drooping shoulder was inadequate muscular support of the scapula secondary to changes in maturation during the third decade of life, leading to a realignment of the shoulder girdle. Furthermore, Lord and Stone (1956) were the first to propose that the pectoralis minor tendon may impinge on the nerves of the brachial plexus. Supporting this theory is the fact that one of the common regions of brachial plexus nerve entrapment is within the subcoracoid tunnel (Charon et al., 2004).

One of the oldest surgical interventions for decompressing TOS symptoms is removal of the first rib. First documented in 1910 by Thomas Murphy, a procedure involving excision of the first rib provided significant decompression of TOS (Murphy, 1910). This procedure has been improved in the last century, most notably through the development of a transaxillary approach to the first rib, and in 1966 Roos’ efforts to refine this approach provided adequate decompression of TOS, as well as broader visualization of the pertinent structures involved in TOS from the transaxillary point of view. The transaxillary approach represents the most common and successful technique for decompression of TOS, with the supraclavicular approach indicated for compression of the median nerve distribution, and the combination of both supraclavicular and infracoracoid approaches for vascular TOS (vTOS) involving a cervical rib or large cervical vertebral transverse process (Merrel and Wolfe, 2002).

The introdution of magnetic resonance imaging (MRI) and computed tomography (CT) in the 1970s revolutionized the methods of diagnosis and management of TOS. Prior to this time, more conservative and subjective bedside clinical techniques, such as the Adson’s test (1947), were the basis for diagnosis of TOS, whereas MRIs and CTs now provide greater precision in predicting an anatomical predisposition to TOS, but may lack specificity because of various anatomical variations present in the thoracic outlet in an asymptomatic population. Additionally, there is evidence to indicate that there is a correlation between detection of cervical ribs, enlarged transverse processes, fibrous scarring of the scalene muscles, and variations in the course of nerves and vessels with the development of TOS (Nannapaneni and Marks, 2003).

CLINICAL PRESENTATION

TOS has been generally divided into vascular and neurogenic categories, with the majority of cases (nearly 95%) being neurogenic (nTOS) in nature. Physical examination for TOS should include four tests, they are Adson or scalene test, the Halstead maneuver, Wright hyperabduction maneuver, and Roos test. A positive result on any single test is not reliable according to a report by Warrens and Heaton (1987) who concluded that 58% of random volunteers...
had at least one positive test result. Faced with the wide variations and nonspecific nature of the typical presenting symptoms of TOS, clinicians must carefully exclude cardiac, pulmonary, traumatic, degenerative, cervical spinal, and distal neuropathic etiologies, particularly in the elderly and female population.

An arterial TOS generally results from compression of the subclavian artery in individuals with a history of vigorous arm activity above the head, and may present with the typical signs and symptoms of ischemia, including pain, pallor, paresthesia, pulselessness, and extremity poikilothermia. The presence of a cervical rib or other bony abnormality is a frequently reported finding in these cases (Lindgren, 1993; White et al., 2009). Venous TOS often manifests because of acute thrombosis of the subclavian and axillary veins in young men after strenuous exercise. In these cases, the diagnosis is suggested by the presence of pain, edema, and cyanosis. Occasionally, in the case of chronic venous thrombosis, one may note the presence of extensive collateral circulation, although many cases are intermittent in nature, making for an elusive diagnosis. Confirmation of a vascular etiology is aided by the use of duplex ultrasound, which has been found to be 92% sensitive and 95% specific (Longley et al., 1992). Surgery is indicated when true vascular compromise is identified, although vascular etiologies represent fewer than 5% of TOS cases (Urschel and Razzuk, 1998).

The typical patient with TOS is a young, thin female with a long neck and drooping shoulders, who presents with chronic pain in the neck or shoulder and paresthesias in the medial aspect of the arm and hand (Clein, 1976; Swift and Nichols, 1984; Pang and Wessel, 1988; Zager, 2000; Huang and Zager, 2004). Rarely is there objective evidence of chronic nerve compression. One of the classic findings of true nTOS is Gilliatt–Sumner hand, characterized by severe atrophy of the abductor pollicis brevis muscle, as well as less severe atrophy of the intersosseous and hypothenar muscles of the ipsilateral side (Gilliatt et al., 1970; Huang and Zager, 2004). Beyond these physical signs, the only reliable objective test is a measured reduction in nerve conduction velocity across the affected nerves to a value less than 85 m/s. In advanced cases of nTOS, common observations include decreased sensory potential along the ulnar nerve and decreased compound motor potential along the median nerve (Huang and Zager, 2004).

It was recently reported by Ambard-Chalela et al. (2004), that 17 out of 500 patients in their study redeveloped the classic nTOS signs between 3 and 80 months after their initial operation. They reported that 9 of the 17 with recurrent symptoms suffered from residual muscle and scar tissue resulting from anterior and medial scalene muscles adhering to the brachial plexus. As a course for treatment, Ambard-Chalela et al. (2004) indicated that complete excision of cervical and/or first thoracic ribs, in combination with partial scalene muscle excision, was sufficient in eliminating recurrent nTOS symptoms.

Disputed nTOS cases are usually differentiated from true nTOS cases based on a lack of the classical symptoms typifying true nTOS, namely, atrophy of the abductor pollicis brevis muscle and typical paresthesia patterns. The most common cause of disputed nTOS is trauma, as Roos (1987) reported whiplash injuries resulting from motor vehicle accidents as a common etiology for disputed nTOS. A patient will present with general neck and arm pain, often accompanied by shoulder pain, and the variation in symptomatic presentation of nTOS adds difficulty in making the distinction from a more distal nerve compromise, and complicates definitive diagnosis. In a study by Seror, of 100 upper limbs with definitive CTS, he reported no major symptoms suggestive of TOS or nTOS, although mild symptoms suggestive of disputed nTOS were commonly found (Seror, 2005). Of particular note is the potential for misdiagnosis of nTOS as carpal tunnel syndrome, leading to inappropriate surgical decompression of the median nerve at the wrist: an intervention which fails to address the root pathology (Seror, 2005).

Two recent case reports are of clinical relevance to TOS. Matsuyama et al. (2002) reported a patient with atrophy of the right biceps muscle, as well as weakness in the deltoid, triceps, supraspinatus, and infraspinatus muscles. The case was diagnosed as upper plexus TOS because of C5–C7 nerve root compression. Traditionally, TOS will implicate the nerves of the lower plexus, as they are compressed between the anterior and medial scalene muscles and the first rib. Upper plexus TOS is only seen in 3–12% of nTOS cases and usually presents as sensory changes in the first three digits (Roos, 1982; Wood and Ellison, 1994; Urschel and Razzuk, 1998; Matsuyama et al., 2002). In addition, the historical literature contains three accounts of neurilemmomas causing TOS symptoms, including a 2005 report of a neurilemmoma originating from the lateral fascicles of the brachial plexus (Nakazawa et al., 2005).

ANATOMY AND EMBRYOLOGY

Anatomically, the thoracic outlet and corresponding neurovascular compression is considered to incorporate three areas, namely, the interscalene triangle, the costoclavicular space (cervicoaxillary canal), and the pectoralis minor space or subcoracoid space (Merrel and Wolfe, 2002; Charon et al., 2004) (Fig. 1).

Typically, the left and right subclavian arteries ascend into the neck before arching laterally to the medial border of the anterior scalene muscle (ASM). After traveling behind this muscle, they descend laterally from the lateral margin of ASM to the outer border of the first rib, at which point they become the axillary arteries (Gabella, 1995) (Fig. 2). There are many variations described in the literature concerning the course of the subclavian artery and the ASM. These include the right subclavian artery passing anterior, within, or posterior to the ASM (Fig. 3) (Stauffer and Pote, 1946; Sealy, 1951; Nathan and Seidel, 1983; Stone et al., 1990; Gabella, 1995). These variations may be because of a hypertrophic muscle, muscle strain, or accompanying soft tissue problems such as fibrosis or congenital bands (Konuskan et al., 2005).
The frequency of abnormal ASM insertion on the first rib was demonstrated by Wayman et al. (1993). In this study, 3 cadavers out of 21 had abnormal insertion of the ASM. As a result, the subclavian veins were compressed at the costoclavicular angle, contributing to compression of these veins. This observation suggests that an abnormal anterior insertion of the ASM represents a contributory factor in the compression of the subclavian vein.

The ASM is also implicated in the distribution of nerves comprising the brachial plexus. As previously mentioned (Roos, 1982; Wood and Ellison, 1994; Urschel and Razzuk, 1997; Matsuyama et al., 2002), upper plexus TOS is seen in 3–12% of nTOS cases. This is likely a result of the multitude of variations seen between C5/C6 and the ASM. Roos (1982) observed during 93 scalenectomies every brachial plexus had a variation with respect to the ASM. The variations included (i) C5 anterior to the ASM, (ii) C5 and C6 anterior to the ASM, (iii) C5 and C6 through a double ASM, (iv) C5 anterior and C6 through the ASM, and (v) C5 and C6 through the ASM, which was the predominant finding (Roos, 1982; Natsis et al., 2006). Harry et al. (1997) confirmed the variation of C5 and C6 through the ASM in a report of 51 cadaveric specimens. Thus, penetration of C5 and C6 through the ASM may lead to compression of these nerves, contributing to symptoms of upper plexus TOS.

Cervical ribs occur in <1–6% of the general population and in approximately 10% of patients with TOS (Roos, 1976; Gruss et al., 2002; Charon et al., 2004; Brewin et al., 2009). In these cases, the brachial plexus is usually formed from the fourth through the eighth cervical nerves. However, the first thoracic
ventral ramus may also join the plexus, but must ascend a considerable distance in order to do so. Additionally, the inferior trunk of the brachial plexus must take the most acute course and is thus predisposed to compression and traumatic neuritis. A cervical rib normally raises the thoracic outlet; so that in order to leave the thoracic cavity and enter the axilla, the subclavian artery must ascend to a more superior level. Whether this artery travels with the brachial plexus over a cervical rib depends on the precise anatomy of this abnormal rib, with blunt ribs it is less likely to involve the artery (Tubbs et al., 2006). Additionally, some cases of symptomatic cervical rib may be compressed by the dorsal scapular artery as it arises from the third portion of the subclavian artery (Tubbs et al., 2006).

**DIAGNOSIS AND TREATMENT**

One of the issues with TOS is the lack of a gold standard for definitive diagnosis. MRI provides for detection of cervical ribs and fibrous bands, for the identification of potential factors causing TOS and indicates individual anatomical variations that have been associated with the development of TOS (Nannapaneni and Marks, 2003). In most situations, it is
useful to hypothesize whether the patient is suffering from vTOS or nTOS in order to select the proper diagnostic technique. However, still radiographs and CT scans remain the routine diagnostic modalities in most of the centers (Figs. 4 and 5).

When TOS is presumed to be vascular in origin, a number of techniques are commonly used. Conventional angiography has been the mainstay for diagnosis of TOS in the arterial system and currently CT angiography is the most common imaging study to diagnose and plan treatment in patients with vTOS (Figs. 6–8) (Kadir, 1986; Charon et al., 2004). Concurrently, venography is used for detecting thrombus formation. Duplex ultrasound imaging, however, represents a noninvasive, relatively inexpensive method of detection of the stenosis and vascular compression associated with TOS, and is associated with both high-sensitivity and high-specificity results in the diagnosis of vTOS (Longley et al., 1992). The value of the study is particularly enhanced when combined with the Adson’s test, leading to a 0% positive response rate in people without TOS (Hachulla et al., 1990; Lee et al., 2006). Duplex ultrasound is a noninvasive, inexpensive way to detect stenosis and compression is commonly seen in vTOS. For these reasons, it is likely to replace angiography and venography in diagnosing vTOS.

When TOS is presumed to be neurogenic in origin, there are different techniques for diagnosis compared to those used for vTOS. Electrophysiological nerve conduction studies are a common procedure, as they allow detection of decreased action potential conductance because of nerve compression (Dawson, 1993; Charon et al., 2004). This is an effective way to select patients for surgical decompression of nTOS. An additional method for diagnosing nTOS utilizes ASM blocks involving injection of a local anesthetic directly into the ASM, temporarily relaxing the muscle, and approximating the relaxation of muscular tension achieved by more invasive decompression surgery. A
study by Jordan et al. (1998) reported that 94% of people with a positive block had good outcomes following decompression of TOS in comparison to 50% who underwent surgery in spite of a negative block. Thus, these results point to ASM blocks as a screening tool for selecting candidates for undergoing subsequent decompression surgery.

As is the case with diagnosing TOS, treatment is also variable in approach and management. Patients with nTOS may conservatively manage their symptoms through physiotherapy and anticoagulation directed at postural adjustments to alleviate strain on the brachial plexus. Recently, botulinum toxin injection has been used for treatment of nTOS, and the measure was reported by Torriani et al. (2010) to provide symptomatic improvement of nTOS complaints in 69% of the 41 patients receiving injections in the anterior scalene, pectoralis minor, or subclavius muscle. In patients with vTOS and patients with nTOS with unresolved symptoms, surgical treatment is the management of choice.

One of the main decisions is whether to take a transaxillary, supraclavicular, or posterior surgical approach. The transaxillary approach is favored by a number of surgeons for treating venous and arterial compression (Greenhalgh, 2002; Charon et al., 2004; Degeorges et al., 2004). If the compression is because of the first rib and de Leon et al. (2009) recommend a first rib resection with a scalenectomy, followed by a postoperative venogram and anticoagulation, as the preferred method of treating TOS.

Additional surgical approaches include an anterior supraclavicular approach and a posterior approach. The supraclavicular approach is favored by surgeons performing scalenotomies to relieve nTOS symptoms and for those removing cervical ribs (Adson, 1951; Leffert, 2002). It is, however, a less appropriate approach to resect the first rib because of the difficulty in visualization of the structure. The posterior approach is the most technically demanding of the three surgical techniques because of the need for traversing the sensory muscles of the scapula, potentially causing structural damage and subsequent shoulder morbidity. Yet, it provides the advantage of exposing an excellent visual field of the lower trunk of the brachial plexus in context with the first rib (Claggett, 1962; Leffert, 2002). This approach may be preferred when the supraclavicular and transaxillary approaches do not provide adequate resolution of the clinical situation.

One of the most extensive studies of treatment of TOS is a 50-year analysis by Urschel and Razzuk (1998) of the Baylor University experience. More than 15,000 patients were evaluated for TOS including 3,914 patients who underwent primary neurovascular procedures. Two hundred and forty patients were treated successfully for axillary–subclavian artery aneurysm or occlusion and of 264 patients with Paget–Schroetter syndrome, 211 were treated by first rib resection and immediate urokinase thrombolysis (Urschel and Razzuk, 1998). Of 2,210 patients treated consecutively for nTOS, 250 had upper plexus compression, 1,508 had lower plexus compression, and 452 were symptomatic for both. All three groups were treated with a transaxillary first rib resection with >95% of patients in all three groups becoming asymptomatic postoperatively (Urschel and Razzuk, 1998). In 1,221 patients who presented with recurrent symptoms following their first procedure, Urschel and Razzuk (1998) took a posterior approach with a concomitant dorsal sympathectomy in patients who had not received one during their initial surgical treatment (Urschel and Razzuk, 1998).

**NOMENCLATURE**

A precise system of nomenclature surrounding descriptions of TOS has been a source of contention between anatomists and clinicians. Anatomists refer to the thoracic orifice as the thoracic inlet, citing the fact that this is the only opening in the thorax that allows passage of food and air (Rowland, 2000). Clinicians, by contrast view the thoracic aperture as the thoracic outlet, emphasizing the emergence of the great vessels and the ventral ramus of T1 as they travel to the neck and upper extremity. In terms of clinical outcomes, however, the debate remains an academic one. Patients presenting with symptoms consistent with TOS, and with initial suspicions supported by physical examination, diagnostic imaging, and/or nerve conduction testing, are generally treated with a similar approach: transaxillary rib resection with or without anterior scalenectomy of the thoracic outlet and 3D reconstruction of the anatomy, including bone detail. Prior to the development of this technique, CT images could only be viewed in the transverse plane. In a study by Matsumura et al. (1997) they demonstrate the potential diagnostic application of MDCT by observing impingement on the subclavian vein and artery in a number of arm positions. MDCT may increase the efficacy of TOS diagnosis for each type of TOS, as this procedure offers a more complete view of the thoracic outlet.

The burgeoning field of minimally invasive surgery has recently impacted the treatment of TOS.
et al. (2005) reported that starting in 2003 they used the robotic da Vinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA) for 42 patients to improve visualization during transaxillary rib resection, noting no mortalities or permanent neurovascular injuries in these patients. Abdellaoui et al. (2007) described an endoscopic technique for improved intrathoracic visualization, by making a 6–7 cm axillary incision and introducing a camera and instruments through the incision. Candia-de la Rosa et al. (2010) reported their experience with endoscopic management of TOS, noting that this approach improves identification and dissection of the neurovascular bundle. Furthermore, percutaneous angioplasty has been used in conjunction with thoracic outlet decompression to treat subclavian vein compression because of TOS (Azakie et al., 1998; Kreienberg et al., 2001; Schneider et al., 2004). Schneider et al. (2004) reported 16 patients presenting with residual subclavian vein compression, and reported a technical success rate of 100% with treatment involving intraoperative percutaneous angioplasty. In the study, two patients had recurrent thrombosis leading to percutaneous mechanical thrombectomy, and the overall 1-year primary patency rate was 92% with a secondary patency rate of 96%. Coupling decompression with angioplasty may decrease risk of recurrent thrombosis and eliminate the need for open surgical venous repair (Schneider et al. 2004).

Current histopathological findings may help elucidate the basis for nTOS. In a recent report by Tubbs et al. (2008), compression of distal proximal brachial plexus by the presence of a cervical rib demonstrated epineurial fibrosis, vascular hyalinization, mucinous degeneration, and frequent intraneural collagenous nodules. These histological changes are similar to those reported elsewhere in known cases of other forms of compression neuropathy. They conclude that “cervical ribs may cause histological changes in the lower trunk of the brachial plexus,” which may provide further insight into the neurogenic changes leading to clinical compression neuropathy. It should be noted that none of their studied specimens were known to present nTOS symptoms during life (Tubbs et al., 2008).

The future of TOS will likely revolve around improving diagnostic procedures and criteria, as well as the continued improvement of treatment techniques. The value of conservative management in the form of physical therapy regimens should not be overlooked, yet definitive treatment of TOS generally relies on surgical intervention to yield optimal patient relief and satisfaction (Urschel and Patel, 2008; Chang et al., 2009). Surgeons should be competent in identifying symptoms related to TOS, even though diagnosis remains difficult because of the subjective variability of presenting symptoms and patient complaints. Greater emphasis on diagnostic evaluation will lead to improved treatment outcomes for those suffering from TOS.

REFERENCES


