Variability in electrodiagnostic findings associated with neurogenic thoracic outlet syndrome

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Abstract

Introduction/Aims: Neurogenic thoracic outlet syndrome (NTOS) is a heterogeneous and often disputed entity. An electrodiagnostic pattern of T1 > C8 axon involvement is considered characteristic for the diagnosis of NTOS. However, since the advent of high-resolution nerve ultrasound (US) imaging, we have encountered several patients with a proven entrapment of the lower brachial plexus who showed a different, variable electrodiagnostic pattern.

Methods: In this retrospective case series, 14 patients with an NTOS diagnosis with a verified source of compression of the lower brachial plexus and abnormal findings on their electrodiagnostic testing were included. Their medical records were reviewed to obtain clinical, imaging, and electrodiagnostic data.

Results: Seven patients showed results consistent with the “classic” T1 axon > C8 pattern of involvement. Less typical findings included equally severe involvement of T1 and C8 axons, more severe C8 involvement, pure motor abnormalities, neurogenic changes on needle electromyography in the flexor carpi radialis and biceps brachii muscles, and one patient with an abnormal sensory nerve action potential (SNAP) amplitude for the median sensory response recorded from the third digit. Patients with atypical findings on electrodiagnostic testing underwent nerve imaging more often compared to patients with classic findings (seven of seven patients vs. five of seven respectively), especially nerve ultrasound.

Discussion: When there is a clinical suspicion of NTOS, an electrodiagnostic finding other than the classic T1 > C8 pattern of involvement does not rule out the diagnosis. High resolution nerve imaging is valuable to diagnose additional patients with this treatable condition.

KEYWORDS
brachial plexopathy, clinical neurophysiology, electrodiagnostic studies, nerve ultrasound, neurogenic thoracic outlet syndrome

Abbreviations: ADM, abductor digiti minimi muscle; APB, abductor pollicis brevis muscle; BicB, biceps brachii muscle; CMAP, compound motor action potential; ED, extensor digitorum muscle; FCR, flexor carpi radialis muscle; FF, finger flexors; IH, intrinsic hand muscles; IO, interossei muscles; MABC, medial antebrachial cutaneous nerve; NTOS, neurogenic thoracic outlet syndrome; SNAP, sensory nerve action potential; TOD, thoracic outlet decompression; TOS, thoracic outlet syndrome; US, ultrasound.

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1 | INTRODUCTION

The thoracic outlet syndromes (TOSs) are a group of disorders caused by compression of the brachial plexus and/or the subclavian vessels as they traverse the thoracic outlet. Neurogenic TOS (NTOS), caused by displacement and entrapment of the lower plexus elements, is rare, with an estimated incidence of 2–3 per 100,000 individuals.5

The diagnosis of NTOS can be challenging as upper extremity symptoms are very common, while NTOS as their cause is rare.6 Although the causative anatomy in NTOS patients can originate from different anatomical structures in the thoracic outlet, NTOS is often thought to be caused by either a rudimentary cervical rib or a fibrous band arising from an elongated C7 transverse process. However, the prevalence of a cervical rib is approximately 1% of the general population, meaning that the finding of a cervical rib in a patient with upper extremity complaints is often incidental.3,4 Consequently, both under- and overdiagnosis of NTOS are common.5,6

At present, the diagnosis of NTOS is based mainly on characteristic clinical features and electrodiagnostic testing results. A distinct electrodiagnostic pattern is often described as pathognomonic for NTOS, summarized as an absent or very low sensory response of the medial antebrachial cutaneous nerve (MABC) (mostly T1 innervated), a low sensory nerve action potential (SNAP) amplitude over the ulnar nerve to the fifth digit (mostly C8 innervated), and/or a low compound motor action potential (CMAP) amplitude of the median nerve recorded from the abductor pollicis brevis muscle (APB; mostly T1 innervated), that is more affected than the CMAP of the ulnar nerve recorded over the abductor digiti minimi muscle (ADM; mostly C8 innervated).7–10

While this typical electrodiagnostic pattern has been very helpful for detecting patients with a certain anatomic abnormality, recent studies showed that nerve imaging (MRI and ultrasound [US]) may be an important complementary tool that can identify the actual site and cause of compression.9,11–13

Whereas earlier reports on electrodiagnostic testing in NTOS mainly described the most frequent findings, data on variability of these results is scarce. Therefore, we performed a retrospective study on a cohort of patients with NTOS, and systematically compared the distribution of electrodiagnostic abnormalities with findings at imaging and surgery.

2 | METHODS

2.1 | Patients

We searched the databases of the Neurology department of the Radboud University Medical Center, Nijmegen, the Netherlands, and the TOS-expert center (a joint effort from the Vascular Surgery and Neurology departments) of the Catharina hospital, Eindhoven, the Netherlands, for patients diagnosed with NTOS from 2010 to 2021 who underwent EMG at one of these centers and imaging of the thoracic outlet. Both centers host tertiary referral clinics for brachial plexopathies, and both can perform nerve US of the brachial plexus for this diagnosis. Inclusion criteria for this study were clinical signs and/or symptoms consistent with at least a lower cervical root and/or lower trunk brachial plexopathy, a verifiable anatomical structure causing compression of the lower plexus on imaging studies and/or confirmed intra-operatively, and electrodiagnostic studies that showed at least one abnormal nerve conduction or needle EMG test result. Patients with a history of traumatic or iatrogenic injury of the brachial plexus, or with a history of a concomitant neurological condition involving the upper extremities (eg, radiculopathy or mononeuropathy), were excluded. Patient medical records were systematically reviewed to obtain clinical, imaging and electrodiagnostic data. All patients had indicated no objection to the use of their de-identified personal information for further research, as noted in our electronic health record system. As this was a retrospective chart review of prospectively maintained databases, per our institutions policy no further ethical approval was required.

2.2 | Electrodiagnostic testing

Before the electrodiagnostic studies, the upper limbs were warmed in a water bath if necessary, and a surface temperature was maintained at a minimum of 30°C Celsius by resting the patient on a warm surface. For both nerve conduction studies and needle electromyography, the specific structures assessed during the recordings were at the discretion of the clinical neurophysiologist performing the tests, based on the clinical information available at the time of electrodiagnostic testing. Sensory nerve conduction studies were performed antidromically and in most patients bilaterally, except for unilateral measurements to evaluate possible carpal tunnel syndrome (digit 3 segmental median sensory conduction velocity of wrist-to-palm compared to palm-to-digit segments; and digit 4 median vs. digit 4 ulnar peak latency difference). SNAP amplitudes were measured peak-to-peak. In one patient, only the symptomatic side was assessed.

SNAP and compound muscle action potential (CMAP) amplitudes and nerve conduction velocities were defined as abnormal either based on their absolute values if they were below the fifth percentile or above the 95th percentile (age-stratified) of our locally obtained normal values. SNAP amplitudes were also considered abnormal if less than 50% of the contralateral value.14

2.3 | Nerve imaging

Nerve US of the brachial plexus was performed, generally only on the symptomatic side (in six out of nine patients), according to the recommended protocol.15 with systematic visualization of the extrarominal nerve roots from C5 to T1 if accessible, the interscalene trunks, and the supraclavicular brachial plexus elements. Transverse measurements were made of all elements at each level, measuring the cross-sectional area within the hypoechoic epineurial rim, and compared to our local reference values.16
| ID | Sex | Age (y) | Age at onset (y) | Side | Weakness | Atrophy | Hypesthesia | Imaging findings | Surgical treatment | Follow-up |
|----|-----|---------|------------------|------|----------|---------|------------|-----------------|-------------------|-----------|
| 1  | F   | 46      | 26               | Right| APB, IO, OP, FF | APB, IO, ADM | MABC area | MRI-plexus: hyperintense inferior trunk on STIR sequence US: WSS, elongated proc trans C7, enlarged inferior trunk | Referred for surgical intervention | n/a       |
| 2  | F   | 16      | 14               | Right| APB, ADM, IO, FE, FF, WE, WF, SE, EE | APB, ADM, IO | Diffuse total arm | MRI-plexus: cervical rib, enlarged inferior trunk | Transaxillary TOD | 3 mo: improvement |
| 3  | F   | 17      | 17               | Right| APB, ADM, IO, FE, FF, WE, WF, SE, EF, SA, SE | APB, IO, ADM, forearm flex & ext | MABC > median and ulnar nerve distribution | MRI-CWK: cervical rib with fibrous band; US: elongated proc trans C7 with enlarged nerve root and enlarged and hypoechogenic inferior trunk | Resection fibrous band | 16 mo: improvement |
| 4  | F   | 70      | 55               | Right| APB       | APB       | Superficial radial nerve domain | US: fibrous band from elongated proc trans C7 compressing inferior trunk | No | n/a       |
| 5  | F   | 22      | 15               | Right| APB, ADM | n/a       | MABC area | US: WSS, elongated proc trans C7 with fibrous band compressing inferior trunk | Transaxillary TOD with tenotomy m. PM | 2 mo: improvement |
| 6  | F   | 37      | 36               | Left | OP, FF, FE | APB       | T1 dermatoma | MRI-plexus: cervical rib, fibrous band from C8 to T1 | Transaxillary TOD | n/a       |
| 7  | M   | 28      | 17               | Right| Hand     | APB, ADM, IO | MABC domain and dig IV-V | X-thorax: cervical rib | Transaxillary TOD | 12 mo: improvement |

Abbreviations: dFF, deep finger flexors; dig, digit; EE, elbow extensors; EF, elbow flexors; F, female; FE, finger extensors; FF, finger flexors (not further specified); FP, flexor pollicus muscle; IH, intrinsic hand muscles (not further specified); IO, interossei muscles; M, male; n/a, not available; OP, opponens pollicis muscles; PM, pectoralis minor; SA, shoulder abductors; SE, shoulder external rotators; supFF, superficial finger flexors; TOD, thoracic outlet decompression; WE, wrist extensors; WF, wrist flexors; WSS, wedge sickle sign (a hyper-echoic fibromuscular structure at the medial edge of the middle scalene muscle that indents the lower trunk of the brachial plexus).
| ID | Sex | Age (y) | Age at onset (y) | Side | Weakness | Atrophy | Hypesthesia | Imaging findings | Surgical treatment | Follow-up |
|----|-----|---------|-----------------|------|----------|---------|-------------|-----------------|-------------------|-----------|
| 8  | F   | 16      | 15              | Right | APB, ADM, IO, FP, FE, FF | APB, forearm flex | None | MRI-plexus and US: swollen inferior trunk; CT-thorax: elongated proc trans C7 | Transaxillary TOD | 14 mo: improvement |
| 9  | M   | 45      | 44              | Right | IO, FE | None | MABC domain, dig IV-V | MRI-plexus: cervical rib | Resection fibrous band | 2 mo: improvement |
| 10 | F   | 51      | 10              | Right | IO, APB, ADM, dFF, FF, FE | APB, ADM, forearm | MABC domain | MRI-plexus: cervical rib with fibrous band; US: enlarged inferior trunk, fibrous band, WSS, elongated proc trans C7 | Resection fibrous band | 2 mo: improvement |
| 11 | F   | 17      | 15              | Right | None | None | Diffuse forearm, dig II-IV | US: WSS, swollen and hypoechoic middle and inferior trunk | Transaxillary TOD with tenotomy m. PM | 12 mo: complete recovery |
| 12 | F   | 69      | 63              | Right | None | APB, ADM, IO | Diffuse arm | US: WSS; X-thoracic elongated proc trans C7 | Transaxillary TOD | 12 mo: improvement |
| 13 | F   | 34      | 26              | Right | OP, ADM, FP, supFF, FE | APB, ADM, IO | Ulnar side hand and dig V | US: cervical rib, WSS, enlarged and hypoechoic C8 and T1 | Transaxillary TOD with tenotomy m. PM | 12 mo: improvement |
| 14 | F   | 41      | 18              | Right | Hand | APB | dig III-IV | US: WSS; X-thoracic cervical rib | Transaxillary TOD | 3 mo: improvement |

Abbreviations: ADM, abductor digiti minimi muscle; APB, abductor pollicis brevis muscle; dFF, deep finger flexors; dig, digit; EE, elbow extensors; EF, elbow flexors; F, female; FE, finger extensors; FF, finger flexors (not further specified); FP, flexor pollicus muscle; IH, intrinsic hand muscles (not further specified); IO, interossei muscles; M, male; n/a, not available; OP, opponens pollicis muscles; PM, pectoralis minor; SA, shoulder abductors; SE, shoulder external rotators; supFF, superficial finger flexors; TOD, thoracic outlet decompression; WE, wrist extensors; WF, wrist flexors; WSS, wedge sickle sign (a hyper-echoic fibromuscular structure at the medial edge of the middle scalene muscle that indents the lower trunk of the brachial plexus).
MRI scans had been performed clinically without a specific protocol, at the discretion of the radiologist, usually prior to referral to our centers. MR images included coronal T1, T2, and STIR images in all patients. In some patients additional sequences were included such as T1 gadolinium contrast enhanced images, and/or images in transverse or sagittal plane.

The diagnosis of NTOS was confirmed when there was enlargement of elements of the lower trunk of the brachial plexus, including patients with nerve enlargement in whom an anatomical structure causing compression of plexus elements was seen.

3 | RESULTS

Fourteen patients were included in this study. Demographic and clinical information are shown in Tables 1 and 2. Of note, data on the involvement of certain isolated muscle groups such as the specific finger flexors (FF) could not be retrieved from the medical records of all patients. Tables 3 and 4 show the results of the nerve conduction studies and needle electromyography, respectively, in each patient.

Examples of characteristic imaging findings are shown in Figures 1 and 2 and Supporting Information Video S1, which is available online.

Seven patients (patients 1–7) showed results consistent with a T1 > C8 pattern of axonal damage. One of these patients (patient 5) had a normal CMAP amplitude of the APB, but her needle EMG revealed more pronounced neurogenic changes in the abductor pollicis brevis (APB) than the FDI muscle, fitting the T1 > C8 pattern.

The other seven patients (patients 8–14) had electrodiagnostic findings that can be seen with a lower brachial plexopathy, but different from the classic pattern. In three patients (patients 10, 13 and 14) the SNAP amplitude of the MABC was normal. In addition to C8 and T1 involvement, one patient had neurogenic changes in the C7 innervated flexor carpi radialis (FCR) muscle (patient 10), one had neurogenic changes in both the FCR and the C6 innervated biceps brachii muscle (BicB; patient 13), and one had a low SNAP amplitude for the median nerve response recorded from the third digit (patient 14).

In two other patients (patients 8 and 11) we only found motor abnormalities, and all SNAP amplitudes were within the reference ranges. The motor abnormalities found in one of these patients fit the classic pattern with T1 > C8 involvement. In the other patient, T1 and C8 motor axons were equally affected, and additionally neurogenic changes with reinnervation and denervation potentials were found in the FCR muscle. One patient (patient 9) showed sensorimotor involvement of C8 axons, without any evidence of T1 axon involvement. Finally, one patient (patient 12) only showed an abnormal SNAP.
| Patient | APB | ADM | FDI | ED | FCR | BicB | Delt | EPL | FCU |
|---------|-----|-----|-----|----|-----|------|------|-----|-----|
| Classic pattern | | | | | | | | |
| 1 | DE | | | | | | | | |
| 2 | DE | DE | nl | | | | | | |
| 3 | DE | RE | nl | nl | nl | nl | | | |
| 4 | DE | RE | RE | | | | | | |
| 5 | RE | RE | nl | nl | | | | | |
| 6 | RE | RE | RE | RE | | | | | |
| 7 | DE | RE | | | | | | | |
| Other pattern | | | | | | | | | |
| 8 | | | RE | RE | DE | | | | |
| 9 | nl | nl | RE | nl | RE | RE | | | |
| 10 | DE | DE | nl | RE | nl | | | | |
| 11 | DE | RE | RE | RE | nl | | | | |
| 12 | nl | nl | nl | | | | | | |
| 13 | | | DE | RE | RE | RE | RE | nl | | |
| 14 | RE | RE | RE | | | | | | |

Note: Bold: abnormal values. nl = (sampled and) normal; RE = neurogenic changes showing reinnervation potentials; DE = neurogenic changes with reinnervation but also denervation potentials.

Abbreviations: ADM, abductor digiti minimi muscle; APB, abductor pollicis brevis muscle; Delt, deltoid muscle; EPL, extensor pollicis longus muscle; FCU, flexor carpi ulnaris muscle; FDI, first dorsal interossei muscle.

**FIGURE 1**  Nerve US of the right brachial plexus of patient 10. Elongated C7 transverse process (A, *) with enlarged C7 root (B, cross-sectional area 0.17 cm²). Enlarged lower trunk of the brachial plexus (cross-sectional area 0.17 cm²) with wedge sickle (C, protruding edge of the middle scalene muscle as a layer between the supraclavicular plexus and pleura) with kinking of the C8 root (D).
amplitude for the median sensory response recorded from the third digit.

Imaging of the brachial plexus was performed with US in 10 and with MRI in seven patients (Tables 1 and 2). Patients 1, 3 and 13 underwent MRI of the cervical spine that did not show neural foraminal narrowing.

Twelve patients underwent surgical treatment. One patient (patient 1) was only recently referred for surgical intervention at the time of writing of this article. Patient 4 had very severe atrophy and weakness of the hand muscles and it was decided not to perform surgery as this was unlikely to result in improvement.

The median time of post-surgery follow-up was 12 mo. All surgically treated patients experienced an improvement in their symptoms, mostly relief of pain and sensory symptoms.

4 | DISCUSSION

In our retrospective case series we found that half of the confirmed NTOS patients had a classic electrodiagnostic pattern of abnormalities, but the other half did not. In the literature the SNAP amplitude of the MABC is regarded as the most sensitive electrodiagnostic marker for NTOS, but in our study it was normal in 6/14 patients.\textsuperscript{8,9} These non-classic patients showed variable electrodiagnostic patterns, characterized by equally severe involvement of T1 and C8 nerve fibers, or more severe or even isolated involvement of C8 nerve fibers. We hypothesize this is related to the individual anatomic configuration of the thoracic outlet that determines whether the T1 or C8 nerve roots sustain the most severe injury by mechanical entrapment.

A notable finding was the involvement of the FCR muscle in four patients and of the extensor digitorum muscle (ED) in four patients in our study, which are both considered to contain innervation from the C7 root. All of these had an elongated C7 process or a cervical rib that could possibly explain the middle trunk involvement. However, the reason for the occurrence in these patients and not in the others who also demonstrated the same anatomic findings is uncertain, and again most likely due to individual variations in local anatomy and mechanical strain. Several studies have reported variability or anomalies of the basic contents of the thoracic outlet, as well as considerable variability between connections of brachial plexus elements and arm nerve anatomy.\textsuperscript{16-18} To add to the complexity, muscles are often innervated by two spinal segments with one level dominating, and electrodiagnostic studies cannot provide detailed information on these segmental variations.\textsuperscript{18-20}

The involvement of the median sensory response recorded from digit three was found in two patients and can be explained by the fact that the cutaneous domain of the lower plexus in approximately 20% of individuals also includes the median nerve-innervated skin of the middle finger.\textsuperscript{21} In two patients we only found motor abnormalities, a finding for which we have no ready explanation at this point.

In our series, nerve imaging with either MRI or US was important in half of the patients to arrive at the final diagnosis. Plexus US has an advantage over MRI in having a higher resolution and a better ability to detect fibromuscular bands that may compress or constrict the plexus.\textsuperscript{11,12,22} Its use has been indicated before, in a study showing that it can be useful in detecting early stage NTOS patients, in whom axonal damage is still only mild and electrodiagnostic studies subsequently (near) normal.\textsuperscript{9} Our study now adds information that US detects not only these early or mildly affected patients, but also more
severely affected patients who do not have the classic pattern of compressive damage.

Of note is that the Reporting standards of the Society for Vascular Surgery for thoracic outlet syndrome state that “electrodiagnosis and brachial plexus imaging studies are not required” in reporting on NTOS.23 Though these reporting standards are valuable to harmonize the reporting on clinical features of NTOS, they do not discriminate between disputed and true NTOS. The current definition of NTOS in the neurological literature still includes a typical clinical syndrome and a classic electrodiagnostic pattern.21,24 However, the current study shows that electrodiagnostic results in NTOS can be more variable than previously published. In addition, imaging studies serve to discriminate between disputed and true NTOS, as patients with disputed NTOS generally have no clear pre-operative anatomical source for their entrapment.12,25 We would advocate to always combine electrodiagnostic and imaging studies to correlate the anatomy with the neurophysiology.

A limitation of this study was the use of non-uniform protocols in the diagnostic evaluation of patients, inherent to the retrospective design of the study. In our practice, the amount of time allotted for each electrodiagnostic study is determined by the diagnosis for which the patient is referred. This means that in practice the physician needs to make choices regarding nerves and muscles to be examined, and to what extent to both answer the referral question and search for an alternative diagnosis when appropriate. This type of practice limits the number of muscles that can be sampled in one study, and therefore not all muscles that were clinically weak were evaluated on needle electromyography. Furthermore, technical factors related to the performance of nerve conduction studies cannot be entirely excluded. Of note, as the combination of the electrodiagnostic and imaging study performed already yielded the diagnosis in our patients, no patients was referred for further additional electrodiagnostic testing. Ideally, our results would be verified in a prospective study that compares a complete and standardized EMG protocol to a complete and standardized quantitative imaging protocol, using the surgical findings as the gold standard for the presence or absence of nerve entrapment in the thoracic outlet area.

We conclude that when there is a clinical suspicion of NTOS, the finding of a non-classic electrodiagnostic pattern does not rule out the diagnosis, but warrants additional imaging studies, for which high resolution US of the brachial plexus is very well suited.

CONFLICT OF INTEREST
None of the authors has any conflict of interest to disclose.

ETHICAL PUBLICATION STATEMENT
The authors confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION
Additional supporting information may be found in the online version of the article at the publisher’s website.

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