The use of ultrasound in neuromuscular diagnoses

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Abstract

Purpose of review: The use of ultrasonography for diagnosis of neuromuscular disorders is a relatively new but rapidly expanding field. This review covers key ultrasound findings in primary disease of muscle and nerve. **Recent findings:** Ultrasonography is used routinely for evaluation of entrapment neuropathies, hereditary and inflammatory neuropathies, polyneuropathies, myopathies, and motor neuron disease. When used in association with other electrodiagnostic testing, ultrasound has allowed physicians to increase the yield of clinical evaluation in diagnostic laboratories. **Summary:** While ultrasonography has not yet replaced the need for electrodiagnostic studies, it has become a useful accompaniment. *Neurol Clin Pract* 2017;7: 266-273

Ultrasound has been commonly used in medicine since the mid-20th century, but its use for diagnosis in neuromuscular disorders is relatively new.¹ Improvements in ultrasound resolution and display have made it increasingly helpful in the diagnosis of neuromuscular disorders; furthermore, the technique is readily available, inexpensive, and, unlike electrodiagnostic studies, painless. This review will cover key ultrasound findings in primary diseases of muscle and nerve.

Basic principles

An ultrasound image is based on sound waves and echoes. The ultrasound transducer is responsible for emitting sound wave pulses through the biological tissues and recording their resultant echoes. As human tissue is mostly water, it transmits most sound but reflects a small portion related to anatomic barriers and tissue boundaries. The echoes that return the earliest are from the most superficial structures, while those that return later are from deeper structures.

The resolution of the image is directly proportional to the frequency of the transducer. However, it is important to note that the depth of penetration is inversely proportional to the frequency.^{1,2} Therefore, the higher the frequency of the transducer, the less detail of deeper structures can be obtained. As such, higher frequency transducers are used for

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more superficial structures, and lower frequency transducers are used to study deeper structures.² Transducer frequencies in the neuromuscular laboratory typically range from 12 to 18 MHz for nerve studies and as low as 2–7.5 MHz for some muscle studies and deep nerves (figure 1).^{1,3}

Healthy muscle, when viewed in the axial plane, demonstrates a background of echolucency interspersed with small punctate echoes, giving it a heterogeneous appearance. Based on this picture, normal muscle is often referred to as having a starry night appearance.^{2,4} Healthy nerve tissue viewed in the same plane also has background of echolucency that is interspersed with brighter, smaller echoes. This honeycomb appearance represents nerve fascicles. The important difference in determining tendons from nerve in ultrasound relies on anisotropy, referring to the extent that echogenicity varies with the angle of insonation of the transducer. Tendons demonstrate a large amount of anisotropy, while nerves do not.^{2,5}

One of the easiest and quickest uses of ultrasound in the electrodiagnostic laboratory is assessing muscle size. One caveat, however, is that muscles are highly compressible, so care must be taken to avoid applying too much force while maintaining an even pressure on the transducer.² A side-to-side comparison using a dual screen projection can reveal even subtle size differences in unilateral disorders. In symmetric disorders, a comparison control muscle can usually be found among EMG laboratory staff.² In addition, the diseased muscle typically demonstrates increased echogenicity and loss of

Figure 1 Ultrasound devices

(A) Cart-based GE ultrasound device (GE Healthcare, Little Chalfont, UK) used to create images in figure 2. (B) Linear array transducer 6–15 MHz for imaging nerves, and a curvilinear 1–5 MHz transducer for imaging deeper structures.

Figure 2 Imaging of median nerve

(A) Normal left median nerve at the distal wrist crease with a cross-sectional area measuring 7 mm² obtained with a 15 MHz linear array transducer GE Logiq 7 (GE Healthcare, Madison, WI). (B) For comparison, an abnormal left median nerve at the distal wrist crease shows hypoechogenicity and an enlarged cross-sectional area measuring 22 mm².

heterogeneity.^{1,2,4} The Heckmatt scale is commonly used to grade muscle intensity, in which grade I represents normal muscle and grade IV represents very increased muscle echogenicity and loss of bone echo.¹

Muscle atrophy can be seen in CNS disorders secondary to disuse, primary muscle diseases, and peripheral neurogenic disorders.⁵ Subtle myopathies and mild disuse atrophy are difficult to distinguish, as they may show no or minimal changes in echogenicity. End stage neurogenic and myopathic disorders are also difficult to distinguish, as they show profoundly increased echogenicity and loss of resolution of deeper structures such as bone. However, in such cases, the distribution of muscles affected may be helpful as neuropathies often involve distal muscles and proximal myopathies.² At the level of the individual muscle, in moderate cases of myopathy, changes tend to be more homogeneous than neurogenic, as seen for example in motor neuron disorders.^{1,4} The increase in echogenicity in diseased muscle typically results from replacement of the muscle fibers with fibrosis and fat.^{2,5} One study was able to demonstrate that these findings were accurate for differentiating nerve and muscle disease, with positive predictive value of 86% and negative predictive value of 84%.¹

Mononeuropathies

Perhaps the most widely described application for neuromuscular ultrasound is its use in entrapment neuropathies.⁶ Most commonly discussed in the literature is median mononeuropathy at the wrist, or carpal tunnel syndrome, the most common entrapment disorder. Seen with ultrasound, the median nerve at the distal wrist crease has a stippled honeycomb appearance, with bright punctate echoes on a background of hypoechogenicity. Both distally and proximally the nerve has a more hypoechoic appearance, with easily distinguished fascicles. The change of appearance at the distal wrist crease is thought to be relative to its background, which is made up of more hyperechoic tendons. The nerve tends to flatten as it travels distally, and as it dives under the flexor retinaculum it becomes a bit more difficult to see, but it again becomes superficial as it divides into its smaller branches. At the distal wrist crease, tendons can be distinguished from the median nerve both by anisotropy and by observing their movement; the tendons move actively with flexion and extension but the nerve tends to remain in place.²

The most common finding in carpal tunnel syndrome is median nerve cross-sectional area enlargement at the distal wrist crease.² Many studies have shown that this is an accurate indicator of disease, with sensitivity and specificity >85%.³ It has been demonstrated that a wrist-to-forearm arm ratio of greater than 1.4 is highly sensitive for the diagnosis of carpal tunnel syndrome.⁷ Other common abnormal findings in this disorder

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include loss of echogenicity, decreased mobility, and increased vascularity of the median nerve at the wrist (figure 2).^{2,6}

Focal nerve enlargement is common to almost all entrapment neuropathies, including ulnar neuropathy at the elbow, radial neuropathy at the spiral groove, and fibular (peroneal) neuropathy at the fibular head. Unlike electrodiagnosis, where nerve conduction study responses become increasingly difficult to detect as the nerve become more diseased, nerve enlargement often makes affected nerves easier to detect by ultrasound.

Polyneuropathies

In addition to diagnosing entrapment neuropathies, ultrasound is useful in characterizing hereditary and inflammatory neuropathies. Several studies have evaluated the varying neuropathies of Charcot-Marie Tooth disease.^{8–10} While this is a diverse population, with over 45 distinct genetic mutations,¹¹ these neuropathies overall demonstrate diffusely enlarged nerves throughout the extremities. Demyelinating forms of hereditary neuropathy tend to have more significantly enlarged nerve cross-sectional areas when compared to normal controls.^{8–10} Hereditary axonal neuropathies have nerve cross-sectional areas that are smaller compared to their demyelinating counterparts, but are still enlarged compared to healthy controls.⁸

Immune-mediated neuropathies such as chronic inflammatory demyelinating polyneuropathy (CIPD), acute inflammatory demyelinating polyradiculoneuropathy, and multifocal motor neuropathy typically reveal patchy focal nerve enlargements along the course of the nerve,⁸ which increase the cross-sectional area intranerve variability.¹² Just as nerve conduction findings often reveal focal and asymmetric abnormalities in these disorders, the same is seen with

Figure 3 Imaging of radial nerve

(A) Normal radial nerve distal to the spiral groove measuring 4 mm² in cross-sectional area obtained with a 15 MHz linear array transducer GE Logiq 7 (GE Healthcare, Madison, WI). (B) Abnormally enlarged radial nerve below the level of the spiral groove measuring 16 mm² in cross-sectional area, with one abnormally enlarged fascicle seen within the nerve. This nerve was isolated in a patient with multifocal motor neuropathy.

Figure 4 Imaging of diaphragm

(A) Normal diaphragm measuring 2.3 mm in thickness obtained with a 15 MHz linear array transducer GE Logiq 7 (GE Healthcare, Madison, WI). (B) Atrophic and hyperechoic diaphragm measuring only 1.3 mm in thickness.

ultrasound. Focal nerve enlargements can be both proximally and distally located and are not confined to areas of common entrapments (figure 3). While previous studies have described focal nerve enlargement associated with areas of conduction block, another study has shown cross-sectional area enlargements at sites both with and without electrophysiologic abnormalities.¹³ This suggested that areas of focal swelling may be more pathologically complex than originally thought. Onion bulb pathology may account for some of these changes, but the histopathology of nerve enlargement in inflammatory neuropathy is poorly understood in part due to reluctance to biopsy nerves in a treatable disorder. Interestingly, regions of enlarged cross-sectional area seen in CIDP are not necessarily permanent, as cross-sectional area may decrease with effective treatment.¹⁴

Diabetic polyneuropathy is frequently encountered in general practice. While electrodiagnostic studies remain the gold standard for diagnosing these pathologies, emerging research has reported ultrasound findings of potential clinical use. In a study evaluating the sural nerve, ultrasound revealed that the sural nerve in electrodiagnostically proven diabetic neuropathy was enlarged compared to diabetic controls without neuropathy.¹⁵ While differences in cross-sectional area were minimal, these results indicate a potential adjunctive use for ultrasound in diagnosing diabetic neuropathy. Other studies have shown that the diabetic cross-sectional area at common entrapment sites is often increased compared to controls. A caveat is that these changes may be due to underlying nerve entrapment or to the polyneuropathy itself.⁸ A further use for ultrasound in diagnosing diabetic polyneuropathy involves evaluating the foot muscles. One study has demonstrated that the plantar muscles in patients with diabetic polyneuropathy were atrophied compared to controls.¹⁶ While all the above studies demonstrate interesting potential for the use of ultrasound in diabetic neuropathy, further research is necessary to develop sonographic markers of the disease.

Motor neuron disease

Although primarily a disorder of motor nerves, most distinguishing ultrasound findings in motor neuron disease involve the muscles. For instance, ultrasound reveals a prominent heterogeneous pattern of increased muscle echogenicity, muscle atrophy, and increased subcutaneous tissue thickness in patients with motor neuron disease.⁸ In addition, many studies have found ultrasound to be more sensitive in detecting fasciculations than EMG or physical examination alone (88% vs 98%).¹⁷ By prescreening patients with amyotrophic lateral sclerosis in the electrodiagnostic laboratory with ultrasound, muscles with fasciculations can be readily

Figure 5 Imaging of flexor carpi ulnaris and flexor digitorum profundus

(A) Normal flexor carpi ulnaris and flexor digitorum profundus demonstrating normal muscle architecture and echogenicity. This image was obtained with a 15 MHz linear array transducer GE Logiq 7 (GE Healthcare, Madison, WI). (B) Comparison image demonstrating an abnormally hyperechoic flexor digitorum profundus with loss of heterogeneity and a relatively normal-appearing flexor carpi ulnaris. This particular pattern is diagnostically sensitive for inclusion body myositis.

identified, thus considerably reducing the number of muscles needed to be studied by to validate the diagnosis. Further, diaphragmatic ultrasound is evolving as a potential marker of disease progression. This specific type of study can demonstrate decreased diaphragm movement and thickening with inspiration (figure 4).⁸ Recently, a correlation between ultrasound

Table Common uses and associated clinical findings in neuromuscular ultrasound

Focal entrapments (median, ulnar, peroneal)	Enlarged cross-sectional area at entrapment site
	Hypoechoogenicity
	Enlarged fascicles
	Increased vascularity of nerve
Inflammatory neuropathies (acute inflammatory demyelinating polyradiculoneuropathy, chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy)	Enlarged cross-sectional areas at nonentrapment sites
	Hypoechoogenicity
	Enlarged fascicles
	Increased vascularity of nerve
Hereditary demyelinating neuropathies (Charcot-Marie-Tooth)	Enlarged cross-sectional area throughout the course of the nerve in a distal to proximal gradient
	Hypoechoogenicity
	Enlarged fascicles
Amyotrophic lateral sclerosis	Fasciculations seen in muscle bodies in real time
Myopathies	Hyperechogenicity in muscle bodies
	Decreased muscle thickness
Brachial plexopathy/plexitis	Increased cross-sectional areas of trunks of plexus

Take-home points

- *Ultrasound applications in the electrodiagnostic laboratory are rapidly expanding.*
- *Ultrasound is noninvasive, inexpensive, and readily available.*
- *Ultrasound can characterize nerve entrapments, neuropathies, and myopathies in ways that classical electrodiagnostic testing cannot.*

thickness of the diaphragm and an electrodiagnostic estimate of residual motor units has been demonstrated.¹⁸

Myopathies

Ultrasound findings in muscle disease typically reveal atrophy and increased echogenicity.⁴ The distribution of ultrasound abnormalities can help identify specific disorders. In inclusion body myositis, increased echogenicity of the flexor digitorum profundus in relation to the flexor carpi ulnaris is a highly sensitive indicator of this disease (figure 5).¹⁹ A relatively normal echogenicity of the rectus femoris compared to the other quadriceps muscles is seen in acid maltase disease.⁴ Ultrasound has also been used as a marker for response to therapy in dermatomyositis. Initially, after initiation of immunosuppression, ultrasound paradoxically has shown increased muscle echogenicity.

After the first 3 months, muscle echogenicity was shown to normalize in patients responding to treatment.⁴

CONCLUSION

While ultrasound has not replaced the need for electrodiagnostic studies, it has become a useful accompaniment (table). The applications of neuromuscular ultrasound have rapidly expanded over the last several years, and based on its underlying technology, it is likely to continue to improve in terms of resolution and availability. The integration of noninvasive imaging with electrophysiology promises to expand the diagnostic abilities and acumen of neurologists and to increase the yield of clinical evaluation in diagnostic laboratories.

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A.L. Hommel conducted review of concept and design and acquisition of review data. M.S. Cartwright and F.O. Walker conducted critical revision of manuscript for intellectual content.

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