Original Article

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Spectrum of High Resolution Ultrasonography and Color Doppler Findings in Peripheral Neuropathy

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Abstract

Background: Available diagnostic modalities for peripheral neuropathies e.g clinical assessment, electrodiagnostics, skin and nerve biopsy has certain limitations. The role of imaging is very limited. Purpose of this study is to evaluate findings in various peripheral neuropathies on ultrasonography and color Doppler. **Subjects and Methods:** Fifty adult patients of either sex with already diagnosed peripheral neuropathies were evaluated with high resolution ultrasound and color doppler of the relevant peripheral nerves and were compared with age and sex matched fifty healthy adult controls. **Results:** The study included patients with various peripheral neuropathies (carpal tunnel syndrome, diabetic peripheral neuropathy, leprosy, chronic inflammatory demyelinating polyradiculoneuropathy, and peripheral nerve trauma). There was a significant increase in cross sectional area and change in echogenicity of median nerve at carpal tunnel in carpal tunnel syndrome ($p<0.05$). Multiple nerves in diabetic peripheral neuropathy and leprosy patients showed increased cross sectional area and altered echogenicity as compared to controls ($P < 0.05$). Patients with CIDP showed diffusely hyperechoic peripheral nerves. Sonography in peripheral nerve trauma showed significant hyperechogenicity and increased vascularity on doppler at site of trauma with precise localization. **Conclusion:** High resolution ultrasonography with color doppler showed greater extent of quantitative and qualitative alterations in peripheral nerves in various peripheral neuropathies. USG has the potential to complement other diagnostic investigations such as the nerve conduction study in polyneuropathies and can objectively measure nerve damage in some focal neuropathies. It is easily available and has the potential to become the first modality for screening or evaluation of peripheral neuropathies.

Keywords: Color Doppler, Peripheral Neuropathy, Ultrasonography.

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Introduction

History, physical examination, laboratory studies, electrodiagnostic studies (EDx), CSF examination, nerve and skin biopsy are already available diagnostic modalities for evaluation of peripheral neuropathy. But these are not free of limitations. There is no reliable means of studying proximal sensory nerves. Nerve conduction study results can be normal in patients with small-fiber neuropathies. Lower extremity sensory responses can be absent in normal elderly patients which may confound the results. EDx are not substitutes for a good clinical examination and do not provide information regarding the cause of neuropathy. Nerve biopsy, skin biopsy and CSF are invasive procedures. Clinical examination may suffer because of subjective errors like examination of thickened peripheral nerves.[1] This persued us to explore other modality of diagnostic method which may complement or supplement present methods.

Ultrasonography (USG) and magnetic resonance imaging (MRI) provide high-resolution assessment of peripheral nerves and permits direct assessment of pathological changes in nerve structure and/or in the adjacent tissue, as well. These enhance the information by illuminating the morphological aspects and etiology of peripheral nerve pathology. USG is more assessable, provides dynamic images, assesses long nerve segments in a short time, has easy bed-side-availability, benefit of non-invasivity, reasonably priced and has good resolution. So it is easy for use in everyday neurological practice. MRI on the other hand is appropriate for assessment of deep lying structures hindered by bone.[2]

All major nerves of the extremities, e.g. the median, ulnar, radial, sciatic, tibial and peroneal nerves, in their entire course can be evaluated by USG including smaller nerves, e.g. the posterior interosseus, superficial radial nerve, saphenous, sural and superficial peroneal nerves. Spinal nerves C4-C8, the supraclavicular brachial plexus, and cranial nerves like the vagal and accessory nerves can be seen on USG.[3]

There are certain limitations of ultrasonographic technique. For sonography of the peripheral nerves a high image quality and resolution are critical. For an optimal resolution

a high-end ultrasound unit equipped with a high-resolution broadband linear-array probe (e.g. 5—17 MHz) and corresponding soft-tissue software are necessary. In our hospital setting 5-12 MHz machines are available. The application of color doppler allows assessing the vascular situation of the nerves and their surroundings. This is particularly useful in inflammatory conditions, nerve tumors or compressive neuropathies.[4]

On transverse sections, the nerves appear as round to oval hyperechoic structures surrounded by an echogenic rim representing the epifascicular epineurium and the perineurial fatty tissue giving a honeycomb pattern. The rounded hypoechoic areas correspond histologically to the nerve fascicles, and the echogenic septa to the interfascicular epineurium [Figure 1]. In longitudinal views, the fascicular structure of the nerve is depicted as parallel echogenic lines within two bold hyperechoic (white) lines, the epineurium [Figure 2]. Nerve pathology is depicted as either an increase in cross sectional area (CSA) or diameter, fascicular discontinuity or a change in echotexture. Additional use of Doppler allows the assessment of blood flow to the nerve and the surrounding tissues.[5]

The purpose of the study is to assess the spectrum of appearance of peripheral nerves in various peripheral neuropathies.

Subjects and Methods

This is a hospital based observational study from December 2016 to September 2018. Fifty already diagnosed patients of peripheral neuropathy admitted or attended OPD in Department of Neurology, SMS hospital, Jaipur were enrolled as study population. Fifty age and sex matched healthy adult volunteers were selected from the patient's relatives, hospital employees or colleagues.

Clinical findings and investigation details including the nerve conduction study were charted. A detailed sonographic examination of the relevant peripheral nerves was done using 5–12 MHz compact linear array transducer. Nerve was screened throughout its course for suspected focal lesion. In suspected diffuse involvement, nerves were examined both in the axial and longitudinal sections at following levels:

1. Median nerve at carpal tunnel and 10 cm proximal to wrist in forearm.
2. Ulnar nerve at guyon's canal and behind medial epicondyle
3. Tibial nerve 3 cm above medial malleolus
4. Peroneal nerve 5 cm distal to head of fibula

Nerves were screened for thickness of the nerve (cross sectional area in mm2), echopattern, vascularity of the nerve (assessed with doppler), perineural soft tissue, or any focal /mass lesion. Similar parameters were recorded for the 50 healthy adult volunteers.

Statistical analysis:

The descriptive statistics included means and standard deviations calculated for each variable. The groups for categorical variables were analyzed using chi-square test and student's t-test was used for continuous variables. The level of significance was set at $p \leq 0.05$. For the statistical analysis, Statistical Package for the Social Sciences (SPSS), version 17.0 was used.

Ethics: Present study has been approved by institutional ethics committee and informed consent has been taken from subjects before enrolling them in study.

Results

Fifty patients of peripheral neuropathy included 15 patients of carpal tunnel syndrome (CTS), 15 patients of diabetic peripheral neuropathy (DPN), 10 patients of leprosy, 6 patients of chronic inflammatory demyelinating peripheral neuropathy (CIDP) and 4 patients of peripheral nerve trauma.

Fifteen cases of CTS had mean age of 39.21±2.39 yrs and 86% of the patients were females and compared with age and sex-matched controls ($p>0.05$). The mean CSA of the median nerve at the carpal tunnel in patient group was 13.44± 1.96 mm2 whereas that of matched controls was 6.43±0.76 mm2, and this difference in CSA was statistically significant ($P < 0.0001$). The mean CSA of median nerve at the forearm was also more than that of age-matched controls (6.41±0.89 vs 5.76±1.02) but the difference was not statistically significant ($p=0.07$). There was a significant difference in the wrist-forearm ratio (which is the ratio of the CSA of the median nerve at the carpal tunnel with that in the forearm) between the patients with carpal tunnel syndrome and matched controls(2.56± 0.32 vs 1.23 ± 0.56) ($p< 0.0001$). 86% of patients showed hypoechogeneicity and 40% patients showed intraneural vascularity. One patient showed evidence of tenosynovitis in carpal tunnel [Figure 3, Table1].

Tibial and median nerves were studied in 15 patients of diabetic peripheral neuropathy with a mean age of 60.4 years and compared with age and sex-matched controls ($p>0.05$). On high-resolution sonography, the mean CSA (mm2) of median nerve(10.64±1.45 vs 6.21 ± 1.23) and tibial nerve (16.90± 2.01 vs 7.32± 1.11) was more than in control which was statistically significant ($p<0.0001$). On color doppler increased vascularity was noted in 88% of cases. [Figure 4, Table2].

10 cases of leprosy with mean age of 38.25 years were studied and compared with age and sex-matched controls (p value> 0.05). On sonography, median nerve means CSA (mm2) at carpal tunnel was 11.92± 2.32 vs 5.87± 1.53 in controls. The difference was statistically significant ($p<0.0001$). Similarly the mean CSA(mm2) in leprosy patients of ulnar nerve at guyon's canal, peroneal and tibila nerves in leg was more than control group ($p<0.0001$). Hypoechoic nerves were seen in 8 out of 10 patients [Figure 5a] and increased vascularity was seen in 3 patients [Figure 5b], [Table 3].

In CIDP, unilateral median, ulnar, tibial and peroneal nerves were screened in six patients. The absolute values of CSA (mm2) were found increased in four out of six patients with

altered echogenicity in all four nerves. Increased vascularity was not seen in any of the patient. But because of small number of cases, results were not statistically significant [Figure 6].

Table 1: Comparison of ultrasonographic and color doppler parameters in carpal tunnel syndrome patients and control group.

	Cases (Mean ± SD)	Controls (Mean ± SD)	P- value
Age (years)	39.21 ± 2.39	37.32 ± 3.12	0.07
Female gender, n(%)	13(86)	14(93%)	0.53
Mean CSA(mm2)-carpal tunnel	13.44 ± 1.96	6.43 ± 0.76	<0.0001*
Mean CSA(mm2)-forearm	6.41 ± 0.89	5.76 ± 1.02	0.07
Mean CSA wrist-forearm ratio	2.56 ± 0.32	1.23 ± 0.56	<0.0001*
Altered echogenicity, n(%)	13(86)	0(0)	<0.0001*
Increased vascularity, n(%)	6(40)	0(0)	0.007*
Perineural soft tissue alteration, n(%)	1(6.6)	0(0)	0.31
CSA- Cross sectional area, n-number of subjects, SD- standard deviation, * statistically significant P value(<0.05)			

Table 2: Comparison of ultrasonographic and color doppler parameters in diabetic peripheral neuropathy patients and control group.

	Cases (Mean ± SD)	Controls (Mean ± SD)	P value (Mean ± SD)
Age (years)	60.39 ± 2.12	58.21 ± 4.27	0.08
Female gender, n(%)	9(60)	10(66)	0.73
Median Nerve Mean CSA(mm2)-carpal tunnel	10.64 ± 1.45	6.21 ± 1.23	<0.0001*
Tibial Nerve Mean CSA(mm2)	16.90 ± 2.01	7.32 ± 1.11	<0.0001*
Altered echogenicity, n(%)	13(88)	0(0)	<0.0001*
Increased vascularity, n(%)	13(88)	0(0)	<0.0001*
Perineural soft tissue alteration, n(%)	0(0)	0(0)	1.00
CSA- Cross sectional area, n-number of subjects, SD- standard deviation, * statistically significant P value(<0.05)			

Four cases of peripheral nerve trauma were enrolled in the study. Two cases were of post intramuscular injection foot drop out of whom one patient showed hypoechoic lesion in sciatic nerve in gluteal area and the other had hypoechoic common peroneal nerve throughout its length, without any evidence of any lesion above in sciatic nerve. One patient had foot drop post knee injury in which hypoechoic common peroneal nerve was seen. One patient was of radial nerve palsy post humerous fracture. On USG, radial nerve was found hypoechoic and impinged between fractured humerous fragments in arm. Vascularity was not found altered in any of the case on color doppler[Figure 7].

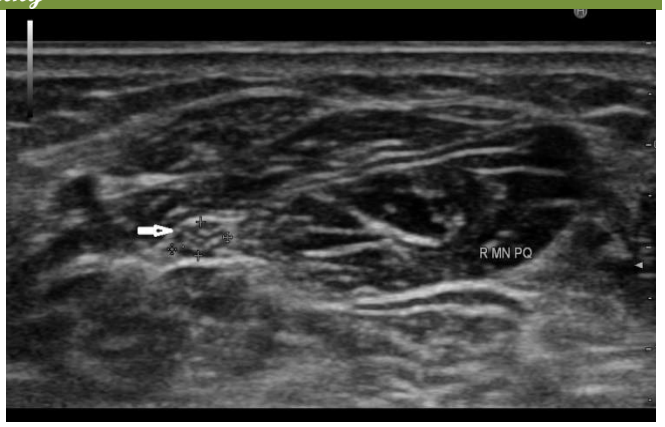

Figure 1: High resolution ultrasonography image of normal median nerve: Transverse scan in the forearm (arrow). Normal honeycomb appearance of the nerve is appreciated with hypoechoic fascicles embedded within a hyperechoic background.

Table 3: Comparison of ultrasonographic and color doppler parameters in leprosy patients and control group.

	Cases (Mean ± SD)	Controls (Mean ± SD)	P value
Age (years)	38.25±4.21	40.26±3.21	0.24
Female gender, n(%)	8(80)	8(80)	1.00
Median Nerve Mean CSA (mm2)-carpal tunnel	11.92 ± 2.32	5.87 ± 1.53	<0.0001*
Ulnar nerve Mean CSA (mm2)-guyon's canal	7.45 ± 1.02	4.87 ± 0.79	<0.0001*
Peroneal nerve Mean CSA (mm2)	17.10 ± 2.10	7.10 ± 1.41	<0.0001*
Tibial Nerve Mean CSA (mm2)	16.90 ± 2.34	7.32 ± 1.01	<0.0001*
Altered echogenicity, n(%)	8(80)	0%	0.0004*
Increased Vascularity, n(%)	3(30)	0%	0.06
Perineural soft tissue, n(%)	Normal	Normal	
CSA- Cross sectional area, n-number of subjects, SD- standard deviation, * statistically significant P value(<0.05)			

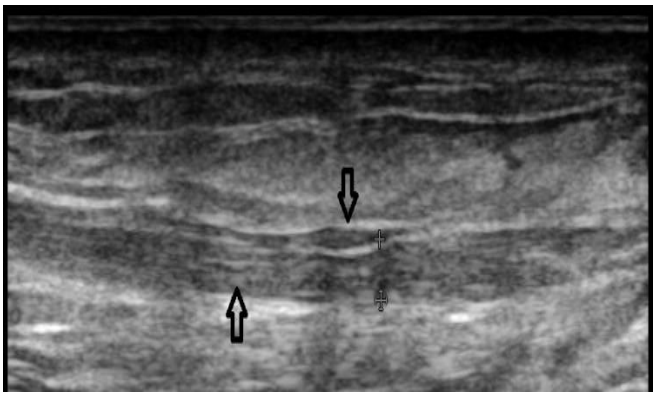

Figure 2: High resolution sonography image of normal median nerve: longitudinal scan in the forearm showing several parallel hyperechogenic lines (arrow) in a linear patternappearing as bundles of straw within two bold echogenic lines, which represent the epineurium.

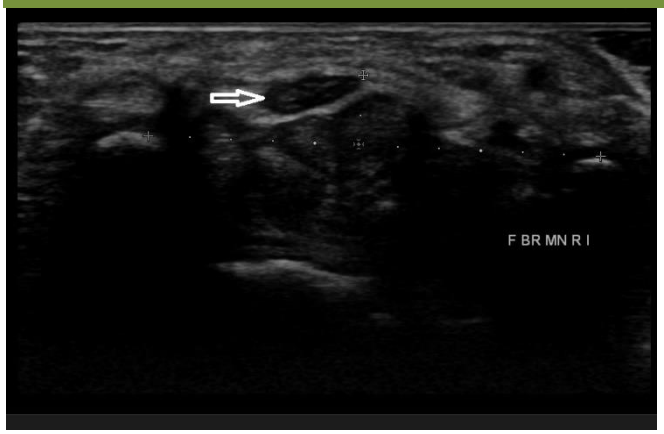

Figure 3: High resolution ultrasonography image of median nerve in the carpal tunnel showing increase in cross sectional area of the median nerve in the carpal tunnel with loss of normalechotexture (arrow).

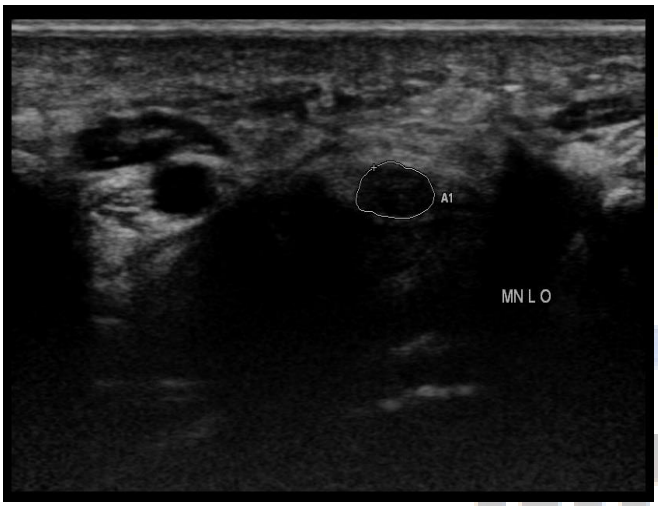

Figure 4: High resolution ultrasonography image of median nerve in the carpal tunnel in DPN patients: Nerve appears hypoechoeic and thickened with increase in cross sectional area (circled).

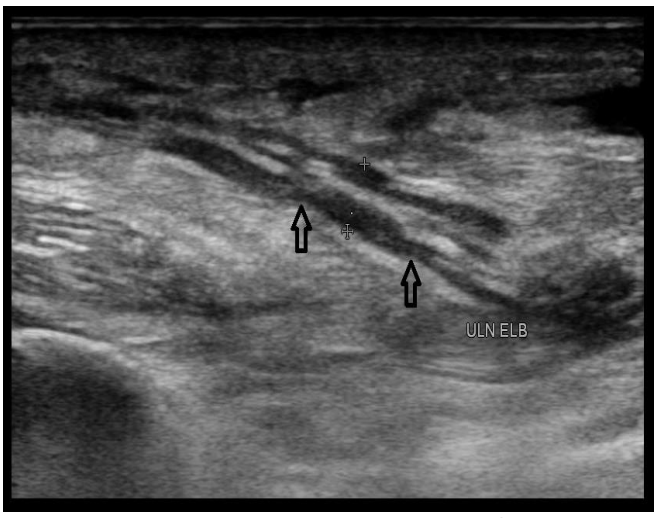

Figure 5(a): High resolution USG image of ulnar nerve (arrow) behind medial epicondyle in leprosy showing an abnormal echopattern in longitudinal scan.

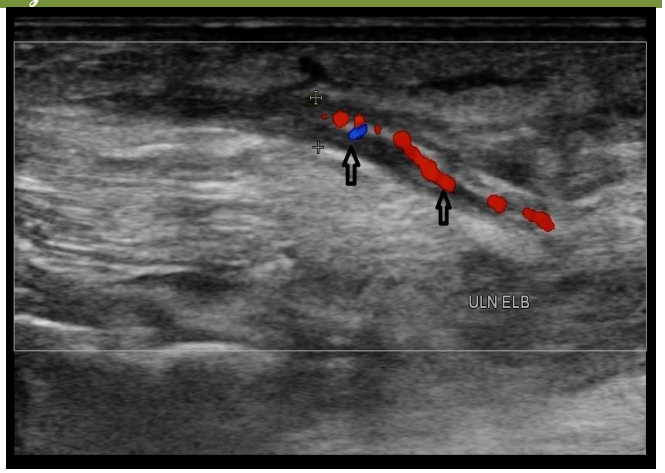

Figure 5(b): Colourdoppler of ulnar nerve behind medial epicondyle in leprosy showing incresedintraneural vascularity (arrow head).

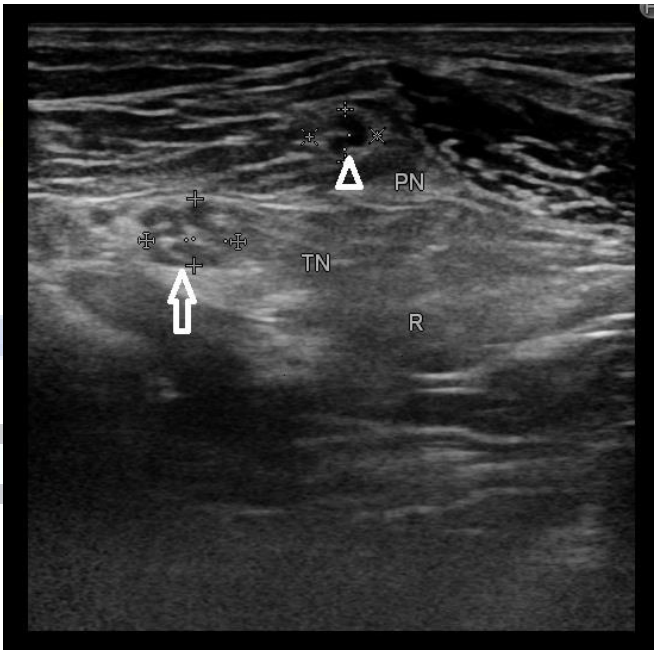

Figure 6: High resolution USG image of peroneal and tibial nerve in CIDP: showing thickened tibial (arrow) and peroneal nerve (arrowhead) with altered echotexture of peroneal nerve

Discussion

Present study showed showed significant difference in mean CSA and echogenecity in CTS vs control group. A number of studies have examined the parameters of the median nerve that are most useful in diagnosing CTS. It has been shown that the cross-sectional area (CSA) of the median nerve is significantly greater in those with CTS compared with healthy controls.[6-9] The compression of the median nerve in carpal tunnel leads to edema and the proliferation of the fibrous tissue proximal to the compression site, which in turns results in swelling of the nerve and increased cross-sectional area (CSA) in 2D image.[10] The most important parameters of median nerve ultrasonography predicting

CTS are CSA greater than 10 mm2, longitudinal noched or waistline appearance of the median nerve and higher intraneural vascularity.[11,12]

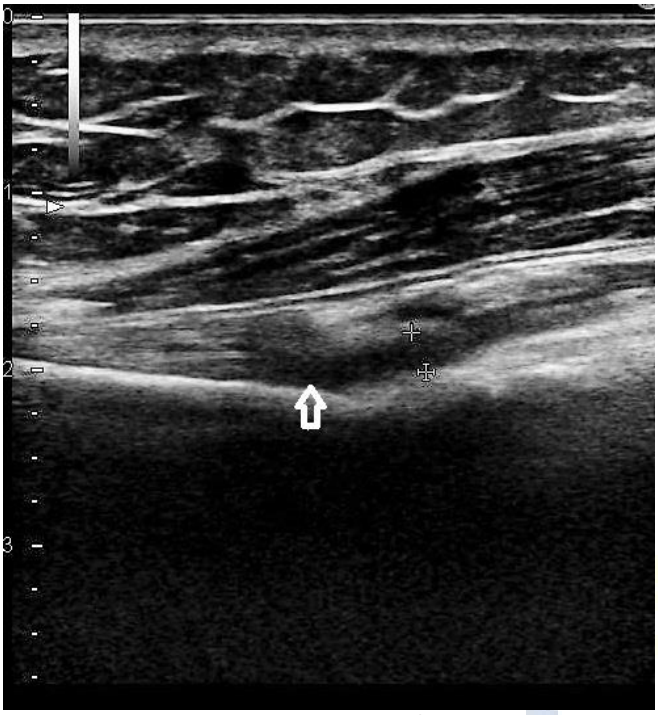

Figure 7: High resolution USG image of radial nerve at spiral groove showing entrapment of nerve in fractured humerus bone leading to hypoechoicechotexture of the nerve (arrow).

15 patients of diabetes showed significant difference in mean CSA and echogenecity. Singh K et al 2017 compared 75 patients with type 2 diabetes mellitus clinically diagnosed with diabetic peripheral neuropathy with 58 diabetic patients with no clinical suspicion of diabetic peripheral neuropathy and 75 healthy non-diabetic subjects were taken as controls. The cross sectional area and maximum thickness of nerve fascicles of the tibial nerves were calculated 3 cm cranial to the medial malleolus in both lower limbs. The cross sectional area and maximum thickness of nerve fascicles of the tibial nerve was larger in diabetic patients with or without peripheral neuropathy than in healthy control subjects, and concluded that ultrasonography can be used as a good screening tool in these patients.[13]FukashiIshibashi et al via USG stated that the morphological changes in peripheral nerves of type 2 diabetic patients were seen even prior to the clinical onset of neuropathy.[14]

Leprosy group showed increase in mean CSA and altered echopattern. It was consistent with study by Jain S et al 2009 on 20 leprosy patients which concluded that clinical examination of enlarged nerves in leprosy patients is subjective and inaccurate, whereas sonography provides an objective measure of nerve damage by showing increased vascularity, distorted echotexture and enlargement. This damage is sonographically more extensive and includes more nerves than clinically expected.[15]

Present study showed increased CSA and change in echogenicity in CIDP patients though limited by less number of subjects. Merola A et al 2016 studied 22 CIDP, 10 MMN patients and a group of 70 healthy controls who were evaluated with an ultrasound scan of the median, ulnar, peroneal, tibial, and sural nerves. Greater extent of quantitative and qualitative US alterations was observed in patients at intermediate versus higher functional disability and in nerves with demyelinating versus axonal damage. CIDP and MMN showed differential USG aspects, with greater side-to-side intranerve variability in MMN and higher cross-sectional areas in CIDP.[16] Tan CY et al 2018 used USG to differentiate between CIDP and diabetic peripheral neuropathy. In comparison to D-DSP, CIDP patients had markedly larger nerves at the proximal and non-entrapment sites of the upper limbs, suggesting that nerve ultrasound is useful in differentiating the two neuropathies.[17] USG may be helpful in differentiating DPN with CIDP, as increased vascularity was noted in 88% of subjects but in none of CIDP patients. This may be attributed to neovascularisation in DPN. Thus USG may provide insight into etiological aspects of neuropathy.

In traumatic neuropathy, USG showed area of focal hypogenecity at site of lesion or showed changes in nerves CSA and echopattern distally. Peer et al 2001 conducted study on 18 patients of peripheral nerve trauma and concluded that USG was successful in showing nerve axonal swelling, scar tissue or surgical implant compromising the nerve, neuroma and insufficient surgical repair.[18] Zhu et al 2011 conducted a prospective study on 202 patients with history of traumatic peripheral nerve injury. USG was helpful in evaluating the type of traumatic injuries and to monitor the morphological changes in injured nerve, particularly the inner part.[19]Bodner et al 2011 studied 11 patients with history of radial nerve palsy following fractured humerus. USG confirmed radial nerve injury, and showed nerve entrapment between bony fragments, complete nerve dissection, nerve laceration, nerve riding on the edges of bony fragments and nerve buried in callus.[20]

Out of the present available methods of diagnosis in peripheral neuropathy, USG has an upper edge because of low cost, higher sensitivity, easy availability and capacity to provide insight into etiology of peripheral neuropathy.

Conclusion

High resolution ultrasonography with colourdoppler showed greater extent of quantitative and qualitative alterations in peripheral nerves in various peripheral neuropathies. USG has the potential to complement other diagnostic investigations such as the nerve conduction study in polyneuropathies and can objectively measure nerve damage in some focal neuropathies. It is easily available and has the potential to become the first modality for screening or evaluation of peripheral neuropathies.

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