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Role of superficial peroneal sensory potential and high-resolution ultrasonography in confirmation of common peroneal mononeuropathy at the fibular neck

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Abstract

Background: Common peroneal mononeuropathy at the fibular neck (CPN) is one of the most frequent neuropathies of the lower extremities. Nerve conduction studies (NCS) have been used to confirm the diagnosis of CPN and localize common peroneal nerve abnormalities. High-resolution ultrasonography (HRUS) can aid in assessing the size of the common peroneal nerve.

Aim: Was to evaluate the superficial peroneal sensory potential (SPSP) and HRUS role in the confirmation of CPN.

Methods: This study was conducted on 70 patients presented with clinical and motor electrophysiological evidence of common peroneal neuropathy at the fibular neck and 70 controls. Clinical assessment, electrophysiological evaluations, and HRUS at the fibular neck were done.

Results: All the patients were electrophysiologically proven to have common peroneal motor neuropathy at the fibular neck, and seven of them showed abnormalities in nerve conduction studies only. The patients showed smaller common peroneal nerve motor and sensory responses and much larger cross-sectional area (CSA) of the common peroneal nerve at the fibular neck when compared with the controls. NCS and EMG positive findings are the most significant factor related to the increased HRUS CSA. Affected SPSP is significantly detected in patients with axonal affection. CSA of common peroneal nerve at the fibular neck showed a significant positive correlation with body mass index, motor, and sensory latencies. Also, it showed a significant negative correlation with motor and sensory amplitudes. HRUS CSA localized the lesion at the fibular neck with sensitivity and specificity 83% and 53% respectively. CSA plus SPSP affection sensitivity and specificity in confirming CPN were 91.9% and 89%.

Conclusion: HRUS CSA plus affected SPSP improve the diagnosis of CPN compared to standard electrophysiological criteria.

Recommendation: Further studies on a wider scale for detection of their role in the prediction of prognosis in CPN.

Trial registration: ClinicalTrials.gov [NCT03753178](https://clinicaltrials.gov/ct2/show/study/NCT03753178) (26-11-2018)

Keywords: High-resolution ultrasonography, Common peroneal electrophysiological evaluations, Common peroneal neuropathy

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Background

Common peroneal mononeuropathy at the fibular neck (CPN) is one of the most frequent mononeuropathies of the lower extremities. CPN is frequently caused by trauma (laceration, gunshot wounds, or traction), surgery, or compression. Risk factors for compression of the common peroneal nerve at the fibular neck are repetitive trauma, habitual prolonged leg crossing, patients at bed rest, poor positioning during surgery, marked weight loss, diabetes mellitus, high ankle sprain, fracture of the proximal fibula, and anatomic variants. Peroneal nerve palsies may also be caused by structural lesions such as ganglion cyst arising from the proximal tibiofibular joint [1]. In patients presenting with paresis or paralysis of foot dorsiflexors, 31% had weakness related to a common peroneal nerve lesion, 30% had L5 radiculopathy, and 18% due to a polyneuropathy [2].

The common peroneal nerve sub serves sensation to the dorsum of the foot and toes [3]. CPN motor fibers of the deep peroneal nerve (DPN) are more frequently affected than those of the superficial peroneal nerve (SPN). Fascicles of the deep branch of the common peroneal nerve are more anteriorly located and more vulnerable to injury than those of the superficial peroneal branch. The clinical and electrodiagnostic findings in CPN resemble the anatomical structure of the common peroneal nerve, and indeed, fibers for the deep peroneal nerve and the superficial peroneal nerve are bounded in separate fascicles along the course of the nerve [4].

Superficial peroneal nerve sensory potential (SPSP) should be performed to localize the site of injury [5]. Also, an evidence-based review conducted by the American Association of Neuromuscular and Electrodiagnostic Medicine concluded that there was class III evidence supporting the use of nerve conduction studies (NCS) for the diagnosis of peroneal neuropathy, specifically motor NCS of the peroneal nerve recording from the tibialis anterior and extensor digitorum brevis muscles (including conduction through the leg and across the fibular head), and orthodromic and antidromic superficial peroneal sensory NCS [6].

Electrodiagnostic testing is used widely to evaluate the function of the common peroneal nerve. SPSP have been examined in CPN with conflicting results. A loss in amplitude of this response implies some axonal loss affecting either the common peroneal nerve or its superficial branch [5]. Prominent axonal loss is the hallmark of most CPN lesions and suggested that abnormalities in sensory nerves mirror those in motor nerves [7].

Moreover, assessment of the structure of the common peroneal nerve is likely to improve the diagnostic yield “by using high-resolution ultrasonography (HRUS)” [8]. Ultrasound imaging is painless, does not expose the

patient to radiation, and has several advantages compared with magnetic resonance imaging in the laboratory setting, including reduced cost, accessibility, ability to image the entire length of the nerve in a single study, and the ability to image both statically and dynamically [9].

The aim of this study was to evaluate the superficial peroneal sensory potential and high-resolution ultrasonography role in the confirmation of common peroneal mononeuropathy at the fibular neck (CPN).

Materials and methods

The current study is a case-control study that was done in the period from January 2015 to January 2016. The study included 70 patients presented with clinical and electrophysiological evidence of common peroneal neuropathy at the fibular neck (CPN) attending to Zagazig University Hospitals (Neurology, Rheumatology and Rehabilitation, and Orthopedic departments) and insurance hospitals of Sharkia governorate (47 male and 23 female). Their age (mean \pm SD/years) was 40.4 ± 12.9 , and the duration between the onset of symptom and enrollment in the study ranged between 21 days to 6 months. Seventy (45 males and 25 females) apparently healthy volunteers were included as controls, and their age (mean \pm SD/ years) was 41.3 ± 11.8 . They were selected from the persons attending to blood bank for blood donation.

Ethical consideration

A written consent was taken from all of the participants. The study was approved from the institutional ethics committee of the faculty of medicine, Zagazig University (ZU-IRB#4729\ 24-6-2016).

Inclusion criteria

Patients were eligible for inclusion in the study if they had clinical and motor electrophysiological evidence suggesting CPN according to [3].

Clinical evidence of CPN

- Numbness of the anterolateral aspect of the lower limb from about midway between the knee and the ankle, most of the dorsal aspect of the foot and toes, and the web space between the first and second toes
- Weakness of the leg muscles innervated by the peroneal nerve. The strength of the tibialis anterior (TA), extensor hallucis longus (EHL), and peroneus longus muscles was tested using the [10]

Electrophysiological motor localizing evidence of CPN [3]

Peroneal motor nerve conduction velocity decrement ≥ 10 m/s across the fibular neck segment, or focal

conduction block, defined as compound motor action potential (CMAP) amplitude and area reduction $\geq 50\%$ across the fibular neck segment.

Exclusion criteria

Patients were excluded if any of the following was detected:

- Historical or clinical signs suggesting coexisting neurological conditions (e.g., polyneuropathy and motor neuropathy)
- Foot drop with symptoms, signs, or radiological findings of L5 radiculopathy in association with CPN
- Symptoms or signs suggesting systemic clinical illness like diabetes mellitus, renal failure, and hepatic failure
- Previous surgery for peroneal nerve

All patients included in the present study are subjected to:

- 1- Full history taking
- 2- Thorough clinical and neurological examination
- 3- Routine laboratories tests for exclusion of other systemic affection like diabetes mellitus, renal, or hepatic failure
- 4- Electrodiagnostic studies

All tests were done in the same room, at the time of clinical diagnosis using a Nicolet Viking Quest cart electrodiagnostic system. Lower extremity temperature was maintained at or above 30°C at the time of examination. The electrophysiological studies included the following:

A- Motor nerve conduction studies

Motor conduction study of the common peroneal nerve (ankle-fibular neck-popliteal fossa) and tibial motor nerve conduction study were performed with surface disc recording electrodes for the affected limb and the contralateral limb in all subjects. Evaluations of both upper limbs were added to exclude more wide lesions if suspected.

Common peroneal CMAPs were recorded over extensor digitorum brevis (EDB). If the common peroneal CMAP was not evoked with EDB recording, CMAP was recorded over tibialis anterior (TA).

We considered that the lesion is axonal via axonal loss estimation [3]:

Axonal loss of the motor branch of the common peroneal nerve was estimated by comparing the CMAP amplitude recorded from the EDB on the affected and contralateral sides.

An estimate of EDB axonal loss was obtained from the formula $(U - A)/U \times 100$

U: EDB response amplitude from the unaffected side.

A: (EDB response amplitude from the affected side.

Categorization based on the motor estimated axonal loss as follows:

No loss, $< 50\%$.

Mild to moderate loss, $50\text{--}75\%$

Severe loss, $> 75\%$

B- Sensory nerve conduction studies [11, 12]

Antidromic evaluation of the superficial peroneal nerve sensory potential (SPSP) at the ankle was studied with surface stimulating and recording electrodes on the affected limb and the contralateral limb in all subjects. The site of stimulation was just anterior to the edge of the shaft of the fibula and 14 cm proximal to the active ankle electrode. The active recording electrode was placed midway between the edge of the tibia and the tip of the lateral malleolus or 3 cm proximal to the bimalleolar line. The reference recording electrode was placed 3 cm distal to the active electrode.

SPSP was considered affected when any one of the following is detected [3]:

- No constant waveforms could be detected
- SPSP amplitudes $< 5 \mu\text{v}$ or $< 50\%$ of the contralateral side
- Increased peak latency $\geq 4.4 \text{ ms}$ (based on the standard distance of 14 cm)

C- Electromyographic study (EMG) was carried out using a concentric needle in the following muscles: extensor digitorum brevis (EDB), tibialis anterior, peroneus longus, tibialis posterior, extensor hallucis longus, short head of biceps femoris, vastus lateralis, medial head of gastrocnemius, iliopsoas, gluteus medius, tensor fascia lata, and paraspinal muscles. Concentric needle EMG was performed in all patients. Spontaneous and voluntary motor unit activity was assessed.

Radiological examination

A) Ultrasonographic assessment of patients and controls [13, 14]

Ultrasonographic examination by radiologist was conducted with a General Electric Logiq 7 Pro machine (GE Healthcare, Chalfont St Giles, England), using a 5- to 12-MHz linear array transducer. The cross-sectional area (CSA) of the common peroneal nerve was

determined within the echogenic rim surrounding the nerve at the level of the fibular neck with the probe perpendicular to the main nerve course in the transverse and longitudinal plane. The sonographic measurements were done on the same day or within 1 week after the electrodiagnostic studies.

The radiologist was blinded to the patients' electrophysiological study data. However, the radiologist was aware of the clinical and electrophysiological suspicion for common peroneal neuropathy.

Authors of the present study considered that common peroneal nerve is affected by the sonographic measurements if the value of CSA of the common peroneal nerve at the fibular neck was $> 11 \text{ mm}^2$ according to the study control group (Fig. 1).

- B) Plain radiographs were done to detect the underlying traumatic injuries, such as a proximal fibular head fracture or osseous tumors, or in assessing the severity of angular deformities about the knee. Lumbosacral plain X-ray or MRI was done only if needed to rule lumbosacral affection.

Statistical analysis

Descriptive statistical methods were used to calculate means and standard deviation (SD). For comparisons with the continuous variables, Student's *t* test was used. Comparison of categorical data was performed using the χ^2 test and the Fisher exact test. Logistic regression analysis was used to calculate odds ratios (OR) and 95% confidence intervals (CI) for risk estimation. A *p* value of less than 0.05 was considered statistically significant.

Intra-observer agreement was assessed using the kappa coefficient. Kappa value for intra-observer reproducibility was 0.73 indicating high reproducibility. From the measurements in our control group, we found the following cutoff value for an abnormally large peroneal nerve CSA at the fibular neck: 11 mm^2 . The sensitivity and specificity of sensory potentials and sonography were also assessed by a receiver operating characteristic (ROC) curve. Data were analyzed using statistical package of social science, version 14.0.0 software package (SPSS Inc., Chicago, Illinois, USA) [15].

Results

Seventy patients (23 males and 47 females) clinically and electrophysiologically proven to have common peroneal mononeuropathy at the fibular neck (CPN) besides the seventy (25 males and 45 females) controls were included in the present study. Their mean ages (\pm SD) were $40.4 (\pm 12.9)$ and $41.3 (\pm 11.8)$ years respectively. The duration between the onset of symptom and enrollment in the study ranged between 21 days to 6 months (20 ± 4 weeks). This study includes 33 (47%) patients presented with left side CPN and 37 (53%) patients presented with right side CPN.

There were no significant difference between patients and controls regarding age, gender, and body mass index, *p* values are equal to 0.667, 0.722, and 0.768 respectively. All the patients were electrophysiologically proven to have common peroneal motor neuropathy at the fibular neck, and seven of them showed abnormalities in the nerve conduction studies only (Table 1).

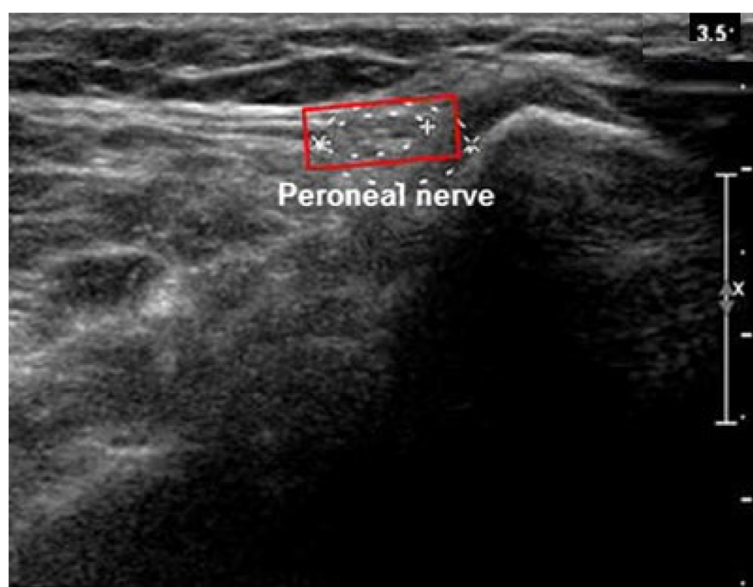


Fig. 1 Ultrasonographic findings of patients with common peroneal mononeuropathy at the fibular neck

Table 1 Demographic data and clinical findings of patients and controls included in the study

Variable	Patients (70)	Controls (70)	<i>p</i> value
Age (years)	40.4 ± 12.9	41.3 ± 11.8	0.667
Gender (female/male)	47 (67%)/23 (33%)	45 (64%)/25 (36%)	0.722
Body mass index	24 ± 2.1	23.9 ± 1.9	0.768
Duration/weeks	20 ± 4	–	
Side: left/right	33 (47%)/37 (53%)	–	
NCS and EMG positive findings	63 (90%)	–	–
NCS positive findings only	7 (10%)	–	–

NCS nerve conduction studies, EMG electromyography

Common peroneal NCS and ultrasonography results revealed a significant difference between the two groups regarding CMAP amplitude at popliteal fossa, CV across the fibular neck, and SNAP amplitude, as well as CSA at the fibular neck (Table 2).

Combined nerve conduction studies and EMG positive findings are the most significant risk factor related to increased HRUS CSA (*p* value = 0.000) (Table 3).

Affected SPSP was significantly detected in patients with axonal affection (*p* = 0.01) (Fig. 2).

Cross-sectional area of common peroneal nerve at the fibular neck showed a significant positive correlation with body mass index, motor, and sensory latencies (*r* = + 0.362, *p* = 0.023; *r* = + 0.172, *p* = 0.03; and + 0.351, *p* = 0.01, respectively). Also, an inverse correlation was seen between common peroneal nerve conduction velocity and cross-sectional area of common peroneal nerve at the fibular neck (*r* = − 0.231, *p* = 0.06) but it does not reach a significant level. Furthermore, it showed a significant negative correlation with motor and sensory amplitudes (*r* = − 0.131, *p* = 0.02 and *r* = − 0.112, *p* = 0.04, respectively) (Table 4).

The outcome measurement of increased HRUS CSA of the common peroneal nerve at the fibular neck (> 11 mm²) plus SPSP affection versus the electrophysiological motor evidence of CPN (test 1) sensitivity was 91.9% (95% CI = 0.83–0.99) and a specificity was 89% (95% CI = 0.55–0.83). The outcome measurement of increased HRUS CSA of the

common peroneal nerve at the fibular neck (> 11 mm²) only versus the electrophysiological motor evidence of CPN (test 2) sensitivity was 83% (95% CI = 0.55–0.83) and the specificity was 53% (95% CI = 0.70–0.80). Pairwise comparison of ROC curves showed that there was a significant difference between test 1 and test 2 (95% confidence interval = 0.07–0.40 and *p* value = 0.005) (Fig. 3).

Discussion

Sensory studies may be normal in some cases of common peroneal mononeuropathy at the fibular neck (CPN) despite abnormalities documented in motor nerve conduction studies. So, the aim of the present study was to evaluate the role of superficial peroneal sensory potential and high-resolution ultrasonography in confirmation of CPN.

In the present study, all the patients were electrophysiologically proven to have common peroneal motor neuropathy at the fibular neck; seven of them showed nerve conduction studies (NCS) abnormalities without concomitant abnormal EMG findings. Common peroneal nerve conduction studies and ultrasonography results revealed a significant difference between the two groups. The patients showed smaller common peroneal nerve motor and sensory responses when compared with the controls.

These findings met with the findings of [7], who reported that axonal loss and selective fascicular

Table 2 Comparing motor and sensory nerve conduction studies as well as ultrasonographic findings between patients and controls

Variable	Motor nerve conduction findings (deep peroneal nerve)				Sensory nerve conduction findings (superficial peroneal nerve)		Ultrasonography
	Distal CMAP amplitude (mv)	CMAP at popliteal fossa amplitude (mv)	CV across the FN (m/s)	Latency (ms)	Latency (ms)	SNAP amplitude (μv)	
Groups							
Patients (<i>n</i> = 70)	3.87 ± 1.14	2.9 ± 1.2	35.1 ± 3.7	6.18 ± 0.87	4.08 ± 1.94	3.18 ± 1.11	13 ± 1
Controls (<i>n</i> = 70)	3.78 ± 1.59	3.8 ± 1.4	44.46 ± 4.26	6.23 ± 0.75	4.04 ± 0.06	6.21 ± 0.01	9 ± 1
<i>p</i> value	0.701	0.000 ^a	0.000 ^a	0.716	0.863	0.000 ^a	0.000 ^a

CMAP compound motor action potential, CV conduction velocity, FN fibular neck, SNAP sensory nerve action potential, CSA cross-sectional area

^aSignificant

Table 3 Multiple regression analysis between electrophysiological findings and ultrasonography increased cross-sectional area $> 11\text{mm}^2$ of the patients included in the study

Electrophysiological findings	N (%)	HRUS CSA $> 11\text{mm}^2$ N (%)	95% C.I.	p value
Combined NCS and EMG positive findings	63 (90%)	38 (60%)	3.046–18.856	0.000 ^a
NCS positive findings alone	7 (10%)	3 (43%)	0.615–10.018	0.202
SPSP affection	46 (66%)	29 (63%)	1.365–5.378	0.004 ^a
Severe motor estimated axonal loss	42 (60%)	21 (50%)	1.738–7.048	0.000 ^a

NCS nerve conduction studies, EMG electromyography, SPSP superficial peroneal sensory potential, HRUS CSA high-resolution ultrasonography cross-sectional area of the common peroneal nerve

^aSignificant

involvement commonly occurs in common peroneal mononeuropathies. Specifically, deep peroneal nerve fibers are more commonly affected, and superficial peroneal sensory fibers are often spared in CPN with predominantly demyelinating lesions, whereas in axonal lesions, the impairment of both branches correlates more closely.

In the current study; the patient group showed much larger CSA of the common peroneal nerve at the fibular neck when compared with the control group. This met with the findings of [16], who found that the mean cross-sectional area (CSA) of the common peroneal nerve in common peroneal neuropathy patients was $13.2 \pm 1.4\text{mm}^2$. Moreover, [9] found that patients had a significantly larger CSA compared with patient controls and healthy controls ($p < 0.0001$ for all). The mean value of the CSA of the common peroneal nerve at the fibular head was 7.5mm^2 for controls and 12.7mm^2 for common peroneal neuropathy patients. Also, Seok et al. [14] found that the normal value of CSA of the common peroneal nerve at the fibular neck was $9.2 \pm 2.9\text{mm}^2$ in a healthy Korean population.

Authors of the present study found that combined nerve conduction studies and EMG positive findings are the most significant factor related to the increased

HRUS CSA. This is in parallel to [16] who found that HRUS CSA correlated with electrophysiological studies in confirming peroneal palsy at the fibular neck. Meylaerts et al. [13] also stated that HRUS may evaluate the nerve in its more superficial locations, such as around the fibular neck. However, it will not replace electrodiagnostic studies, because the former assesses morphology and the latter assess physiological function of the peripheral nerve. Also, another two previous studies [17, 16] concluded that HRUS CSA is of great value in diagnosis of nerve entrapment and compression syndromes caused by the mechanical or dynamic compression of a segment of a single nerve at a specific site as it passes through a narrow fibro-osseous tunnel or an opening in a fibrous or muscular structure.

In the present study, abnormal superficial peroneal sensory potential was significantly detected in patients with axonal affection ($p = 0.01$). This finding met with the finding of [7]. Also, this is in keeping with the observations by two other previous studies [18, 7]. They found that if the prominent hallmark of CPN lesion is an axonal loss, abnormalities in superficial peroneal sensory potential will mirror axonal affection in motor nerves.

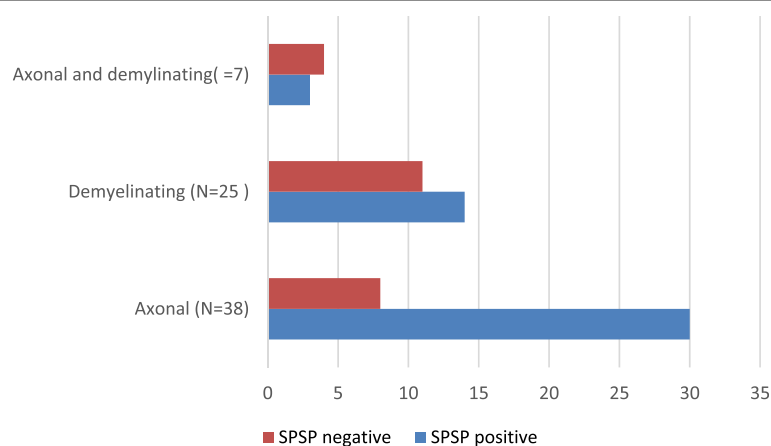
**Fig. 2** Relation between type of common peroneal nerve motor affection and superficial peroneal sensory nerve (SPSP) affection

Table 4 Correlation between cross-sectional area of the common peroneal nerve at the fibular neck and body mass index as well as common peroneal nerve conduction studies

Variable		Cross-sectional area at the fibular neck (mm ²)	
		<i>R</i>	<i>p</i>
Body mass index		+ 0.362	0.023 ^a
Common peroneal motor nerve (NCS)	Distal motor latency	+ 0.172	0.03 ^a
	Compound muscle action potentials amplitude	− 0.131	0.02 ^a
	Conduction velocity	− 0.231	0.06
Superficial peroneal sensory nerve (NCS)	Peak latency	+ 0.351	0.01 ^a
	Sensory nerve action potentials amplitude	− 0.112	0.04 ^a

NCS nerve conduction studies

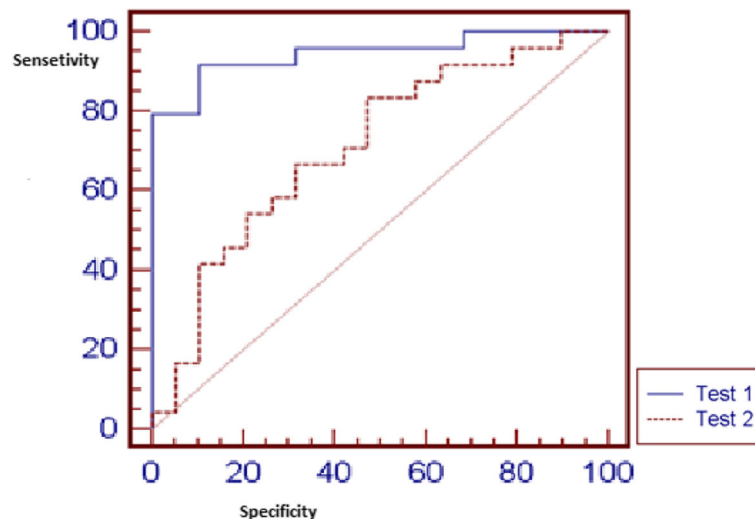
^aSignificant

Cross-sectional area of common peroneal nerve at the fibular neck showed a significant positive correlation with body mass index, motor, and sensory latencies. Also, an inverse correlation was seen between common peroneal nerve conduction velocity and cross-sectional area of common peroneal nerve at the fibular neck but it does not reach a significant level. Furthermore, cross-sectional area of common peroneal nerve at the fibular neck showed a significant negative correlation with motor and sensory amplitudes. This finding met with the findings of a previous study [14]. They found that nerve cross-sectional area was significantly and positively correlated with body mass index. Meylaerts et al. [13] also found that body mass index was positively correlated with common peroneal nerve CSA at the fibular head.

Also, this met with the findings of another study which agreed that high-resolution ultrasonographic cross-sectional area (HRUS CSA) correlated with electrophysiological studies in confirming peroneal palsy at fibular neck [13, 16].

Moreover, the outcome measurement of increased HRUS CSA of the common peroneal nerve at the fibular neck (> 11mm²) plus SPSP affection versus the electrophysiological motor evidence of CPN showed 91.9% sensitivity and 89% specificity, respectively. While the outcome measurement of increased HRUS CSA of the common peroneal nerve at the fibular neck (> 11mm²) versus the electrophysiological motor evidence of CPN showed 83% sensitivity for the common peroneal nerve affection and 53% specificity.

In the same line with our results, [9] found that measurement of the CSA of the common peroneal nerve of

**Fig. 3** Sensitivity and specificity of superficial peroneal sensory potential (SPSP) and high resolution ultrasonography in confirmation of common peroneal neuropathy at the fibular neck.

Test 1: Increased high-resolution ultrasonography cross-sectional area (HRUS- CSA) of the common peroneal nerve at the fibular neck (> 11mm²) plus superficial peroneal sensory nerve (SPSP) affection versus the electrophysiological evidence of common peroneal motor neuropathy at fibular the neck.

Test 2: Increased HRUS-CSA of the common peroneal nerve at the fibular neck (> 11mm²) versus the electrophysiological evidence of common peroneal motor neuropathy at the fibular neck

$> 8 \text{ mm}^2$ at the fibular head, also a cutoff value determined by the ROC curve, resulted in a sensitivity of 86% and a specificity of 73%. Combining the sonography with the standard criterion (clinical and electrodiagnostic findings) with assessment of the most thickened part of the nerve resulted in a cutoff value of $> 8 \text{ mm}^2$ (at the fibular head) with a somewhat higher sensitivity of 90% and a lower specificity of 69%.

Conclusion

HRUS CSA plus affected SPSP improve the diagnosis of CPN compared to standard electrophysiological criteria.

Recommendation

Further studies on wider scale for detection of their role in prediction of prognosis in CPN.

Abbreviations

CMAP: Compound motor action potential amplitude; CPN: Common peroneal mononeuropathy at fibular neck; CSA: Cross-sectional area; DPN: Deep peroneal nerve; EDB: Extensor digitorum brevis; EHL: Extensor hallucis longus muscles; EMG: Electromyography; HRUS: High-resolution ultrasonography; HRUS CSA: High-resolution ultrasonography cross-sectional area; MRC: Medical Research Council rating scale; NCS: Nerve conduction studies; ROC: Receiver operating characteristic curve; SPN: Superficial peroneal nerve; SPSP: Superficial peroneal sensory nerve potential; TA: Tibialis anterior muscles

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Availability of data and materials

Supporting the results of this article are included within the article (and its additional file(s)).

Authors' contributions

RN, WM, GN, EA, and TA carried out the work. RN wrote the manuscript, coordinated the research team, and reviewed the manuscript. RN, WM, and GN collected the patients, gathered clinical and electrophysiological data, and reviewed the manuscript. GN designed the study, coordinated the research team, had done the statistical analysis, and reviewed the manuscript. EA coordinated the research team and reviewed the manuscript. TA had done the imaging work in the present study and reviewed the manuscript. All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published.

Ethics approval and consent to participate

The study was approved from the institutional ethics committee of faculty of medicine, Zagazig University (ZU-IRB#4729\ 24-6-2016). A written consent was taken from all of the participants after explaining the details, benefits as well as risks to them.

Consent for publication

All participants had signed an informed consent to participate and for the data to be published.

Competing interests

The authors declare that they have no competing interests.

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