

Comparison of ultrasound findings in Guillain-Barre syndrome and chronic inflammatory demyelinating polyneuropathy for differential diagnosis

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Keivan Basiri^{1,2}, Mahsa Abdollahian¹, Majid Ghasemi^{1,2}

¹ Department of Neurology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

² Isfahan Neurosciences Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Keywords

Ultrasound Waves; Guillain-Barre Syndrome; Chronic Inflammatory Demyelinating; Polyneuropathies; Peripheral Nerves; Median Nerve; Ulnar Nerves

Abstract

Background: Peripheral nerve ultrasound (US) has been used as a promising diagnosing technique for peripheral nerve disorders. This study aimed to compare the US findings of Guillain-Barre syndrome (GBS) with chronic inflammatory demyelinating polyneuropathy (CIDP).

Methods: This case-control study was done on 25 patients with GBS at 3 weeks after onset of disease and 25 patients with CIDP. Demographic information and US results of median nerve at 2 points, ulnar nerve at 3 points, and tibial and peroneal nerves were collected.

Results: Left median nerve diameter in patients with CIDP with the mean of 0.141 ± 0.047 was more than GBS group with the mean of 0.095 ± 0.034 ($P < 0.001$). Both

sides of median nerve diameter in patients with CIDP were higher than patients with GBS ($P < 0.050$), but in the left side, it was more in patients with CIDP ($P = 0.003$).

Conclusion: The diameter and circumference of median, ulnar, and tibial nerves in forearm and elbow of patients with CIDP are more than patients with GBS; therefore, it may be possible to use US findings based on these differences in diagnosis and differentiation of the two diseases.

Introduction

Guillain-Barre syndrome (GBS) is a post-infectious immune-mediated neuropathy, classified into two subtypes of axonal and demyelinating and its

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diagnosis is based on clinical history, examination, cerebrospinal fluid (CSF) analysis supportive of albumin-cytological dissociation, and neurophysiological features of neuropathy.¹ Use of peripheral nerve ultrasound (US) has more recently risen in peripheral neuropathies investigation. Nerve conduction studies (NCS) are helpful in providing information on the nerves function as well as US to provide information on nerve morphology.² Recent technical improvement of sonography has rapidly achieved its clinical indications in neuromuscular diseases.³ In various peripheral neuropathies, it has been recognized that the altered size of peripheral nerves as the enlargement of a peripheral nerve shows demyelination in chronic inflammatory demyelinating polyneuropathy (CIDP), GBS, carpal tunnel syndrome (CTS), and other disorders, while in some diseases such as amyotrophic lateral sclerosis (ALS), smaller cross-sectional areas (CSAs) and diameters suggest axon loss.⁴ Van den Bergh and Rajabally used the criteria that defined CIDP as a relapsing or chronic progressive peripheral polyneuropathy.⁵ It is considered to be an acquired immune-mediated inflammatory disorder diagnosed clinically with NCS support and raised CSF protein without cells (approximately 75%-90% of cases) or a positive response to immunomodulatory treatment.⁶ A relatively new research area has been provided by peripheral nervous system (PNS) imaging with high-resolution US (HRUS). Nerve enlargement, increased hypoechogenicity, and intraneural vascularization are among the most pathological features that are prominently encountered.⁷ However, such distinction is not forthright because in conditions such as traumatic neurotmesis, axon damage due to compression and vasculitic neuropathy resulting to peripheral nerves enlargement may happen.⁸ To date, there are only a few reports on sonographic evaluation of GBS subtypes which are done on relatively small sample size.⁹⁻¹¹ Regarding that GBS occurs at all ages, especially adolescence and youth, and considering its complications and psychological effects and imposing significant financial burden on families, early detection of illness is one of the most important aspects of preventing more disadvantages. Considering the importance of the health, social, and economical aspects and in view of the para-clinical advances in diagnosis of GBS, and on the other hand, due to low costs of US and its accessibility and applicability, the identification

of this disease can be done by taking early treatment and its complications would be prevented to a great extent. Therefore, as a professional team of health providers will be more prepared for the treatment of these diseases in the case of early identification, and due to the lack of studies in relation to this subject, the present study compares GBS US findings with CIDP.

Materials and Methods

This case-control study was done with the aim of comparing the results of GBS US with CIDP. The study population consisted of 25 patients with GBS at 3 weeks after onset of disease and 25 patients with CIDP diagnosed by a neurologist. They were randomly selected among those admitted to neurology department of Al-Zahra Hospital in Isfahan during the years of 2016 to 2017. The inclusion criterion was willingness to participate in the study and exclusion criteria included GBS diagnosis after less than 3 weeks, having leprosy or Charcot-Marie-Tooth (CMT), and unwillingness at any phase. In addition, if the type of GBS was acute inflammatory demyelinating polyradiculoneuropathy (AIDP), the patients would be excluded.

Considering the confidence level of 95%, test power of 80%, error level of 0.17, and the results of previous studies³ reporting the standard deviation (SD) of median nerves in two groups ($SD_1 = 1.0$ and $SD_2 = 3.6$) and different mean of 2.1, 25 patients were considered to be in each group (total number of 50).

After receiving the code of ethics from the Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran (IR.MUI.MED.REC.1395.3.682) and written consent from patients, they were included in the study. Then they were asked about their demographic information including age, gender, and body mass index (BMI) and the data were recorded.

Then patients in both groups underwent US by neurologist using SonoSite device (SonoSite GmbH; Germany) in the supine position and arm adduction with hands and forearms maintained in neutral position. The room temperature was kept at 23 to 25 °C. The median nerve was measured at 2 points and the ulnar nerve at 3 points in both hands, so that the median nerve CSA was measured at the entrance to the carpal tunnel (retinaculum flexorum) (Figure 1) and the forearm (approximately 15 cm proximal to the retinaculum flexorum), and ulnar nerve CSA (Figure 2) was measured at the site of the Guyon's canal, the

forearm (approximately 15 cm proximal to Guyon's canal), and the elbow (between the inner epicondyle olecranon) (Figures 3 and 4).⁴



Figure 1. Ulnar nerve cross section in the wrist



Figure 2. Ulnar nerve cross section at 13 centimeters in the forearm

Tibial and peroneal nerve measurements were performed in the posterior internal ankle and in the anterior side of the ankle, respectively.



Figure 3. Median nerve cross section in the wrist

The collected data were analyzed using SPSS software (version 23, IBM Corporation, Armonk,

NY, USA). Quantitative variables were reported as the mean and SD and qualitative variables were demonstrated by frequency and percentage. Moreover, as the results of the Kolmogorov-Smirnov (KS) normality test indicated non-normal distribution of variables, Mann-Whitney and Fisher's exact tests were used. The significance level in all analyses was considered to be less than 0.05.



Figure 4. Median nerve cross section at 13 centimeters in the forearm

Results

In this study, out of 25 patients with CIDP, there were 21 (84%) men and 4 (16%) women with the mean age of 43.60 ± 11.87 years, and out of 25 patients with GBS, 16 (64%) cases were men and 9 (36%) cases were women with the mean age of 39.36 ± 10.64 years ($P > 0.05$) (Table 1).

Table 1. Determination and comparison of mean age and frequency distribution of patients in the two groups

Variable	CIDP (n = 25)	GBS (n = 25)	P
Sex [n (%)]			
Male	21 (84)	16 (64)	0.107
Female	4 (16)	9 (36)	
Age (year) (mean ± SD)	43.60 ± 11.87	39.36 ± 10.64	0.190
BMI (kg/m ²) (mean ± SD)	26.52 ± 6.34	25.13 ± 4.89	0.389

CIDP: Chronic inflammatory demyelinating polyneuropathy; GBS: Guillain-Barre syndrome; BMI: Body mass index; SD: Standard deviation

The results of median nerve US showed that the diameter of this nerve at the entrance to the carpal tunnel in the left hand of patients with CIDP with the mean of 0.141 ± 0.047 was more than GBS group with the mean of 0.095 ± 0.034 ($P < 0.001$).

Table 2. Determination and comparison of mean diameter and mean circumference of median nerve in the two groups

Median nerve	CIDP (n = 25) (mean ± SD)	GBS n = 25) (mean ± SD)	P
Median nerve diameter			
At the entrance to the carpal tunnel right hand	0.130 ± 0.046	0.136 ± 0.088	0.279
At the entrance to the carpal tunnel left hand	0.141 ± 0.047	0.095 ± 0.034	< 0.001
Right forearm	0.115 ± 0.168	0.104 ± 0.047	0.032
Left forearm	0.112 ± 0.042	0.074 ± 0.030	0.003
Median nerve circumference			
At the entrance to the carpal tunnel right hand	1.763 ± 0.518	1.722 ± 0.378	0.861
At the entrance to the carpal tunnel left hand	1.828 ± 0.422	1.439 ± 0.288	0.001
Right forearm	1.294 ± 0.264	1.123 ± 0.252	0.015
Left forearm	1.344 ± 0.303	1.064 ± 0.233	0.002

CIDP: Chronic inflammatory demyelinating polyneuropathy; GBS: Guillain-Barre syndrome; SD: Standard deviation

In addition, mean diameter of median nerve in the right and left forearms in patients with CIDP was higher than patients with GBS (left: 0.112 ± 0.042 vs. 0.074 ± 0.030 , $P = 0.003$; right: 0.115 ± 0.168 vs. 0.104 ± 0.047 , $P = 0.032$), while the mean diameter of the left hand medial nerve in patients with CIDP was more than patients with GBS (0.112 ± 0.042 vs. 0.074 ± 0.030 , $P = 0.003$). In addition, mean circumference of median nerve in the left hand and right and left forearm was significantly higher in patients with CIDP than patients with GBS ($P < 0.050$) (Table 2).

The findings of US of the ulnar nerve also showed that the nerve diameter in the forearm and elbow of the both hands was higher in patients with CIDP than patients with GBS ($P < 0.050$). In contrast, measuring the circumference of the nerve showed that left hand forearm and elbow of patients with CIDP with the mean of 1.144 ± 0.246 and 1.572 ± 0.374 , respectively, was higher than patients with GBS with the mean of 1.013 ± 0.221 and 1.364 ± 0.318 , respectively ($P < 0.050$) (Table 3).

The results of US of tibial and peroneal nerves showed that tibial nerve diameter in the left side

was significantly higher in patients with CIDP with the mean of 0.092 ± 0.036 than the patients with GBS with the mean of 0.068 ± 0.028 ($P = 0.010$). Moreover, the mean circumference of tibial nerve in the both sides of right and left was significantly higher in patients with CIDP than patients with GBS ($P < 0.050$) (Table 4).

On the other hand, the separate evaluation of US findings on gender of the patients in the two groups indicated that the differences were more in men than women, so that median nerve diameter and circumference in the distal, right, and left forearm in men with CIDP was significantly higher than the men with GBS ($P < 0.050$) (Table 5).

In addition, the mean diameter of the right forearm and right and left elbows in men with CIDP was significantly higher than the men with GBS ($P < 0.050$), and the mean circumference of ulnar nerve in the left hand forearm and elbow in men with CIDP was significantly higher than the men with GBS, while mean circumference of forearm right ulnar nerve in women with CIDP was significantly less than the women with GBS ($P < 0.050$) (Table 6).

Table 3. Determination and comparison of mean diameter and circumference of ulnar nerve in two groups

Ulnar nerve	CIDP (n = 25) (mean ± SD)	GBS (n = 25) (mean ± SD)	P
Ulnar nerve diameter			
At the entrance to the carpal tunnel right hand	0.139 ± 0.214	0.052 ± 0.018	0.409
At the entrance to the carpal tunnel left hand	0.052 ± 0.017	0.071 ± 0.073	0.351
Right forearm	0.079 ± 0.028	0.067 ± 0.025	0.048
Left forearm	0.132 ± 0.202	0.112 ± 0.178	0.037
Right elbow	0.095 ± 0.025	0.083 ± 0.040	0.017
Left elbow	0.139 ± 0.057	0.098 ± 0.041	0.009
Ulnar nerve circumference			
At the entrance to the carpal tunnel right hand	1.001 ± 0.293	0.941 ± 0.138	0.877
At the entrance to the carpal tunnel left hand	0.943 ± 0.206	0.934 ± 0.220	0.915
Right forearm	1.151 ± 0.251	1.094 ± 0.208	0.426
Left forearm	1.144 ± 0.246	1.013 ± 0.221	0.028
Right elbow	1.425 ± 0.310	1.300 ± 0.293	0.183
Left elbow	1.572 ± 0.374	1.364 ± 0.318	0.042

CIDP: Chronic inflammatory demyelinating polyneuropathy; GBS: Guillain-Barre syndrome; SD: Standard deviation

Table 4. Determination and comparison of mean diameter and circumference of tibial and peroneal nerves in the two groups

Nerve	CIDP (n = 25) (mean ± SD)	GBS (n = 25) (mean ± SD)	P
Tibial diameter			
Right foot	0.081 ± 0.029	0.066 ± 0.033	0.068
Left foot	0.092 ± 0.036	0.068 ± 0.028	0.010
Peroneal diameter			
Right foot	0.073 ± 0.129	0.051 ± 0.033	0.381
Left foot	0.069 ± 0.078	0.045 ± 0.026	0.058
Tibial circumference			
Right foot	1.096 ± 0.193	0.996 ± 0.257	0.043
Left foot	1.161 ± 0.255	1.013 ± 0.200	0.032
Peroneal circumference			
Right foot	0.832 ± 0.236	0.805 ± 0.175	0.773
Left foot	0.907 ± 0.181	0.824 ± 0.252	0.175

CIDP: Chronic inflammatory demyelinating polyneuropathy; GBS: Guillain-Barre syndrome; SD: Standard deviation

Discussion

Inflammatory peripheral nerve infiltrates are the pathological hallmarks of acute GBS, typically concentrated in the spinal roots and occurring with a lesser degree in the extremities peripheral nerve trunks.¹ Peripheral nerves involve in segmental demyelination and axonal degeneration depending on the subtype as the acute inflammation leading to involved tissue swelling suggests that nerve size can be a useful indicator of the disease severity as well as typical patterns recognition of nerve enlargement in different inflammatory nerve diseases.⁸ On the other hand, the typical CIDP happens in the ages of 30 to

60 years and is characterized by a progressive, symmetric, proximal, and distal muscle weakness, paresthesia, sensory dysfunction, and impaired balance, which may develop slowly over at least 2 months.^{9,10} Although CIDP symptoms do not usually reach the highest severity until at least 2 months from onset, a sub-acute onset with a monophasic course may occur in about 16% of the patients.⁹⁻¹¹

Nerve US can detect abnormalities in the majority of patients with CIDP. The increase of peripheral nerves and/or cervical nerve roots CSA and hypertrophy of the vagus nerve have been frequently reported in CIDP.¹²

Table 5. Determination and comparison of mean diameter and circumference of median nerve separately by gender in the two groups

Median nerve		CIDP (n = 25) (mean ± SD)	GBS (n = 25) (mean ± SD)	P
Median nerve diameter				
At the entrance to the carpal tunnel right hand	Male	0.136 ± 0.048	0.122 ± 0.045	0.308
	Female	0.100 ± 0.008	0.161 ± 0.137	0.940
At the entrance to the carpal tunnel left hand	Male	0.147 ± 0.048	0.097 ± 0.041	0.001
	Female	0.110 ± 0.034	0.090 ± 0.016	0.413
Right forearm	Male	0.112 ± 0.048	0.086 ± 0.045	0.009
	Female	0.167 ± 0.276	0.065 ± 0.010	0.825
Left forearm	Male	0.121 ± 0.039	0.077 ± 0.029	0.003
	Female	0.070 ± 0.033	0.069 ± 0.032	0.999
Median nerve circumference				
At the entrance to the carpal tunnel right hand	Male	1.829 ± 0.530	1.817 ± 0.402	0.964
	Female	1.412 ± 0.280	1.553 ± 0.273	0.503
At the entrance to the carpal tunnel left hand	Male	1.846 ± 0.379	1.481 ± 0.319	0.003
	Female	1.730 ± 0.674	1.364 ± 0.220	0.330
Right forearm	Male	1.342 ± 0.255	1.149 ± 0.241	0.012
	Female	1.040 ± 0.153	1.076 ± 0.280	0.604
Left forearm	Male	1.408 ± 0.276	1.084 ± 0.223	0.002
	Female	1.005 ± 0.221	1.027 ± 0.261	0.940

CIDP: Chronic inflammatory demyelinating polyneuropathy; GBS: Guillain-Barre syndrome; SD: Standard deviation

Table 6. Determination and comparison of the mean diameter and circumference of the ulnar nerve separately by gender in the two groups

Ulnar nerve		CIDP (n = 25) (mean ± SD)	GBS (n = 25) (mean ± SD)	P
Ulnar nerve diameter				
At the entrance to the carpal tunnel right hand	Male	0.156 ± 0.231	0.052 ± 0.018	0.370
	Female	0.052 ± 0.009	0.053 ± 0.019	0.940
At the entrance to the carpal tunnel left hand	Male	0.054 ± 0.018	0.066 ± 0.027	0.229
	Female	0.037 ± 0.009	0.081 ± 0.120	0.604
Right forearm	Male	0.084 ± 0.029	0.064 ± 0.023	0.010
	Female	0.073 ± 0.028	0.055 ± 0.010	0.260
Left forearm	Male	0.146 ± 0.218	0.142 ± 0.219	0.059
	Female	0.055 ± 0.019	0.058 ± 0.021	0.825
Right elbow	Male	0.100 ± 0.022	0.086 ± 0.047	0.005
	Female	0.070 ± 0.027	0.079 ± 0.024	0.710
Left elbow	Male	0.151 ± 0.054	0.099 ± 0.044	0.003
	Female	0.075 ± 0.017	0.096 ± 0.036	0.603
Ulnar nerve circumference				
At the entrance to the carpal tunnel right hand	Male	1.028 ± 0.312	0.947 ± 0.145	0.940
	Female	0.852 ± 0.076	0.930 ± 0.132	0.414
At the entrance to the carpal tunnel left hand	Male	0.969 ± 0.211	0.998 ± 0.223	0.575
	Female	0.802 ± 0.113	0.819 ± 0.170	0.998
Right forearm	Male	1.202 ± 0.238	1.085 ± 0.220	0.045
	Female	1.110 ± 0.196	0.882 ± 0.111	0.034
Left forearm	Male	1.181 ± 0.238	1.047 ± 0.244	0.047
	Female	0.942 ± 0.207	0.951 ± 0.171	0.940
Right elbow	Male	1.486 ± 0.294	1.343 ± 0.323	0.185
	Female	1.105 ± 0.168	1.223 ± 0.226	0.604
Left elbow	Male	1.662 ± 0.335	1.296 ± 0.328	0.001
	Female	1.097 ± 0.121	1.484 ± 0.276	0.203

CIDP: Chronic inflammatory demyelinating polyneuropathy; GBS: Guillain-Barre syndrome; SD: Standard deviation

The aim of the current study was to compare GBS US findings with CIDP. The present study was conducted on two groups of 25 patients with CIDP and GBS which most of them were men with the mean age of more than 30 years. Therefore, it can be said that the prevalence of this disease is more common in adult men of older than 30 years, which is in accordance with the above-mentioned studies. The US results of median nerve diameter and circumference evaluation showed that the diameter and circumference of this nerve at the entrance to the carpal tunnel in the left hand and in the both forearms of the CIDP group was significantly greater than the GBS group. In addition, a significant difference was seen between the diameter and circumference of the nerves in men of the both groups. In fact, men may be more likely to show changes in diameters and circumference of median nerve because of their different anatomy from women, so that they have median nerve with larger diameter and circumference.

Presently, there are few studies on the US findings in patients with GBS as well as comparing

the results with CIDP. In 47%-83% of patients with early GBS, nerve enlargement has been reported and it may be present in peripheral nerves and/or cervical nerve roots. The distribution of nerve changes may be patchy within an individual and it may be observed early before neurophysiological changes development.¹³

Zaidman et al. examined 17 patients with acute GBS and it was reported that 47% had statistical significant enlargement of median or ulnar nerves and 38% of subjects undergoing US during the 4 weeks after the onset of the symptoms had enlarged nerves. Although the study was not aimed to follow the changes of nerve size over time, changes were noted as early as 5 days of the disease or persisted as late as 15 years.¹⁴ In CIDP, variations of US findings may reflect different pathophysiological phases, although further histopathological correlation is needed. Regarding that CIDP is a chronic, segmental disorder often with a relapsing course, coexistence of different classes of nerve changes is expected in some patients.¹⁵

As it is assessed with Doppler US studies,

increase of nerve vascularity may also be seen in CIDP. Nerve blood flow strongly correlates with CSF protein and increases the number of enlarged nerves, suggesting the nerve vascularity and it may reflect disease activity. Grimm et al. evaluated the changes of the nerve size in 18 subjects with acute GBS during the first 1-3 days after onset.¹⁶ In the forearm segment of the median nerve, the most prominent increase of nerve size was reported. The C6 cervical roots were enlarged to a lesser degree and sural and ulnar nerve enlargement had no statistical significance. Kerasnoudis et al. developed the "Bochum ultrasound score" (BUS) to distinguish CIDP from AIDP and from multifocal motor neuropathy (MMN)/multifocal acquired demyelinating sensory and motor neuropathy (MADSAM). In this score, ulnar nerve CSA at Guyon's canal and arm, the radial nerve at spinal groove, and the sural nerve at the level of gastrocnemius muscle were determined to calculate the probability of CIDP.¹⁷

Padua et al. suggested an interesting classification of sonographic abnormalities in CIDP not only based on nerve CSA but also on features such as fascicle size and echogenicity. It seems that different class of abnormalities in the patients is associated with different disease duration and may have a different prognosis. For instance, patients with normal nerves CSA, but hypo-echogenic appearance, may have a worse prognosis in comparison to patients with slightly-enlarged nerves and normal echogenicity.¹⁸

As the results of the present study showed, the ulnar nerve diameter in the forearm and elbow was significantly larger in patients with CIDP than patients with GBS; also, the circumference of this nerve on the forearm and elbow of the left hand of patients with CIDP was more than patients with GBS. Finally, the left tibial nerve diameter and its circumference in both sides were greater in patients with CIDP than patients with GBS. There was no significant difference between the two groups in terms of diameter and peroneal nerve circumference.

In order to distinguish acute monophasic

illnesses such as acute GBS from chronic nerve conditions like CIDP, the parameters about the time sequence of enlargement and reversal were useful. Data about the mean of nerve size showed that the nerves enlarged at the admission time and had no further enlargement at 3 weeks later; at the subsequent measurement between the 3rd and 8th weeks and after that time, the swollen nerves gradually continued to slimming.

Conclusion

According to the results of this study, there was no significant difference in diameter and circumference of peroneal nerve between the two groups of patients with CIDP and patients with GBS. The results of this study showed that median nerve diameter and circumference at the entrance to the left hand carpal tunnel and the both forearms were significantly higher in patients with CIDP as well as the left hand tibial nerve diameter and its circumference in both hands. The diameter of the ulnar nerve in the both forearms and elbows and its circumference in the left forearm and elbow were also significantly higher in patients with CIDP. In general, it seems that the diameter and circumference of these three nerves in forearm and elbow of patients with CIDP are more than patients with GBS; therefore, it may be possible to use US findings based on these differences in diameter and circumference of median, ulnar, and tibial nerves in diagnosis and differentiation of the two diseases, but we can say that the peroneal nerve does not have this diagnostic value. In order to reach more reliable conclusion, it is suggested to do further studies.

Conflict of Interests

The authors declare no conflict of interest in this study.

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