ORIGINAL RESEARCH

Application and Value of Limbs Peripheral Nerve Ultrasound in Guillain-Barre Syndrome

Shan He, MM, Yuchan Lin, MD

ABSTRACT

Background • At present, some Guillain-Barre syndrome (GBS) patients have a relatively poor prognosis due to the lack of timely diagnosis, and the risk of death is difficult to reduce. At present, the level of clinical diagnosis of GBS is not ideal, and the time of clinical examination and diagnosis is relatively long. How to improve the level of clinical diagnosis, clinical treatment and prognosis of GBS has always been the focus of clinical research of GBS. This study mainly analyzes the application efficacy of limb peripheral nerve ultrasound in the diagnosis, classification and disease assessment of GBS, hoping to supplement the application research of limb peripheral nerve ultrasound in the diagnosis of GBS and provide some reference for the development of clinical diagnosis of GBS.

Objective • To explore the application and value of limb peripheral nerve ultrasound in Guillain-Barre syndrome (GBS).

Methods • In this case-control study, 35 GBS patients (GBS group) and 20 healthy volunteers (normal group) were enrolled, the ultrasound features of GBS, NCSA dimensions of limbs, NCSA sizes of limbs in patients with different types of GBS, and NCSA sizes of vagus nerves in patients with different conditions of GBS were clinically detected and collected.Pearson correlation coefficient was used to evaluate the correlation between limb nerve cross-sectional areas (NCSAs) and nerve electrophysiology indexes in GBS patients. The receiver operating characteristic curve (ROC) was adopted to analyze the value of limb NCSAs for diagnosing GBS.

Results • Compared with the normal group, NCSAs of multiple limbs neurodes in the GBS group increased significantly ($P < .05$). Patients with different GBS classifications had significantly different limb NCSAs in the proximal or distal nerve ($P < .05$). Compared with patients without autonomic nervous dysfunction, patients combined with autonomic nervous dysfunction had significantly expanded NCSA of the vagus nerve ($P < .05$). NCSAs of the median nerve and ulnar nerve were negatively correlated with motor nerve conduction velocity (MCV) and positively correlated with compound muscle action potential (CMAP) latency (both $P < .05$); NCSA of the median nerve showed a negative correlation with sensory nerve conduction velocity (SCV) ($P < .05$).The ROC curve showed that the auc of ncsa of median nerve (median), ulnar nerve (proximal), vagus nerve, brachial plexus, and common peroneal nerve in the diagnosis of GBS were 0.851, 0.813, 0.783, 0.774, and 0.670, respectively ($P < .05$), which had diagnostic efficacy. The sensitivity were 85.36%, 80.08%, 78.85%, 76.93% and 70.88%, respectively. The specificity were 68.29%, 73.65%, 78.86%, 80.29% and 83.56%, respectively.

Conclusion • Limbs peripheral nerve ultrasound can effectively assist the early diagnosis, classification, and assessment of the severity of illness of GBS, it has a good diagnostic effect on multi-limb ganglion NCSA and vagus nerve NCSA.In the future, the application of limb peripheral nerve ultrasound in the early diagnosis, classification and severity assessment of GBS can improve the efficacy of clinical diagnosis of GBS and provide a good basis for the improvement of prognosis of GBS. (*Altern Ther Health Med.* 2024;30(10):416-421).

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INTRODUCTION

Guillain-Barre syndrome (GBS) is an acute inflammatory peripheral neuropathy that most often occurs in males and is essentially an autoimmune disease.[1] Many patients suffer acute onset, and manifestations are featured by acute areflexia acroparalysis. Moreover, the patient's condition is aggravated progressively, but the disease is self-limited. GBS has become the most common cause of flaccid paraplegia besides poliomyelitis and is considered to be a type of severe acute clinical nerve system disease. GBS has a low incidence rate of about 0.6-4 people per 0.1 million people worldwide and 1-2 people per 0.1 million people in China.[2-5] However, the prognosis of GBS is unsatisfactory, and over 20% of patients still experience severe disability after active immunotherapy, with a mortality rate of about 5%.[6] Studies have revealed that the prognosis of GBS patients is correlated with accurate classification and the time of treatment.[7,8]

Current clinical examinations for GBS diagnosis include cerebrospinal fluid, serological, nerve electrophysiology examinations, and nerve biopsy, among which nerve electrophysiology examination is the main method for classifying GBS.[7] Nevertheless, these examinations often have hysteresis and do not possess the monitoring efficacy of immediacy, quickness, and dynamics. Ultrasonic technique has been developed rapidly in recent years, with remarkable superiority, such as non-invasion, rapid detection, and immediacy.[9] Furthermore, nerve ultrasound inspection equipment and techniques play a huge role in the clinical diagnosis and treatment of nerve injury and rupture, nerve block, diabetic peripheral neuropathy, and other nerve

diseases.[10,11] The detection time of nerve ultrasound is short, and doctors can quickly evaluate the patient's condition according to the test results. Compared with cerebrospinal fluid and other detection methods, neural ultrasound can track the changes of the patient's condition, quickly detect the changes of the patient's lesion, and avoid the problem of missing the best treatment time due to too long detection time. However, few studies have analyzed the specific changes in the limb nerves of GBS patients under nerve ultrasound, especially the differences in different GBS classifications and conditions under ultrasound. In addition, there are no reports on the diagnosis of GBS by nerve ultrasound quantitative parameters. In this study, quantitative parameters of nerve ultrasound were used to detect GBS patients and normal people, and the gap between the two was compared and analyzed. The efficacy of quantitative parameters of nerve ultrasound in the diagnosis of GBS patients was analyzed to fill the gap of quantitative parameters of nerve ultrasound in the diagnosis of GBS patients, and to provide new diagnostic ideas for clinical diagnosis of GBS patients. In this study, we retrospectively analyzed the clinical data of nerve ultrasound and nerve electrophysiology examinations in 35 GBS patients. We compared them with the data of 20 healthy volunteers and subgroups to explore the effect of limbs peripheral nerve ultrasound in the diagnosis, classification, and condition evaluation of GBS. We hope to provide a relevant reference for clinical practice.

MATERIALS AND METHODS

Patients

This study was approved by the Ethics Committee of The Affiliated Hospital of Guizhou Medical University. Thirty-five GBS patients who admitted to The Affiliated Hospital of Guizhou Medical University from January 2019 to June 2020 were enrolled (GBS group). Inclusion criteria: 1) Patients had a definite diagnosis of GBS[12] accompanied by a history of prodromic infection, with acute and early onset (course of disease <4 weeks); manifestations of symmetrical limb and facial muscles weakness, reduced or absent limbs tendon reflexes, and even dyspnea in a severe one; albuminocytological dissociation in the cerebrospinal fluid; slowed distal motor nerve conduction velocity (MCV) and prolonged latency by nerve electrophysiology examination; self-limited course of the disease. 2) Classifications were acute inflammatory demyelinative polyradiculoneuropathy (AIDP) and acute motor axonal neuropathy (AMAN) by nerve electrophysiology examination. Exclusion criteria: Patients with a diagnosis of recurrent GBS; patients with GBS variants and other classifications; patients with nerve injury and rupture, nerve block, diabetic peripheral neuropathy, myelitis, poliomyelitis, polymyositis, periodic paralysis, myasthenia gravis, and toxic peripheral neuropathy. Twenty physically healthy volunteers at the same time were selected in the normal group. GBS patients were classified by nerve electrophysiology examination as 15 AIDP patients and 20 AMAN patients and by the presence or absence of autonomic nerve dysfunction as 8 patients with autonomic nerve dysfunction and 27 patients without autonomic nerve dysfunction.

Nerve ultrasound examination

Philips EPIQ 7 color Doppler ultrasonic diagnosis apparatus was purchased from the Philips Ultrasound (Shanghai) Co. Ltd. The high-frequency linear array probe was an L5-12 probe at a frequency of 5-12MHz. All patients received examinations within 4 weeks after onset.

Superficial nerves (at a distance to the body surface of <2cm), such as the forearm ulnar nerve and median nerve, were detected by a probe at 12MHz, and the water cushion was used cooperatively if necessary. A probe at 5-7.5MHz was used to detect deep nerves, such as the hip sciatic nerve. Specific operations: The patient took a lying position with forearm pronation and limb abduction and fully exposed examination regions on the limbs. The probe was held vertically to the nerve. Continuous scanning was carried out along the nerve path. Then, the clearest and largest ultrasound image was selected to measure nerve cross-sectional areas (NCSAs), and measurement was performed again at the junction of hyperecho and hypoecho.[13] NCSAs of bilateral proximal (near to the armpit), middle (elbow), and distal (near to the wrist) median nerves, proximal (near to the armpit), middle (elbow), and distal (near to the wrist) ulnar nerves, radial nerve (radial groove), posterior tibial nerve at the malleolus medialis, and common peroneal nerve at the fibular head were measured in all patients. The range of measurement point of the nerve was 3cm at proximal and distal segments, except that the measurement range of the ulnar nerve at the elbow was 1cm from top to bottom. Each part of the nerve was measured thrice, separately, and the mean value was calculated. Force should be moderate during the measurement to avoid squeezing by the probe, which would cause a change of anatomical structure and nerve deformation.

Nerve electrophysiology examination

Nerve electrophysiology examination was performed for GBS patients 2-3 weeks after onset using Keypoint 4-channel electromyograph (Dantec Corporation, Denmark).

Specific operations: The examination was conducted in a quiet, shielded room at a room temperature of 21°C-25°C. The patient took a lying position and was instructed to be completely relaxed. Examination items included the sensory nerve conduction velocity (SCV), the amplitude and latency of sensory nerve action potential (SNAP) of the median nerve and ulnar nerve, as well as the MCV, the amplitude, and latency of compound muscle action potential (CMAP) of the median nerve, ulnar nerve, and common peroneal nerve. Motor nerve stimulation points of the median nerve included the wrist and elbow, and recording electrodes were all placed in the abductor pollicis brevis muscle. The ulnar nerve had the same motor nerve stimulation points as the median nerve, and recording electrodes were all placed in abductor digiti minimi. Motor nerve stimulation points of the common peroneal nerve were at 1cm outside the central back of the

ankle, under the fibular head beside the popliteal fossa, and outside of the popliteal fossa, and recording electrodes were placed under 1cm at the front of distal lateral malleolus in the dorsum of the foot. The sensory nerve recording electrode of the median nerve was placed on the index finger, and the stimulation point was 13cm next to the recording electrode on the wrist's median nerve. The sensory nerve recording electrode of the ulnar nerve was placed on the little finger, and the stimulation point was 11cm next to the recording electrode on the ulnar nerve of the wrist.

Evaluation criteria

For the evaluation of nerve electrophysiology examination results, the normal value of electromyography from the laboratory of Johns Hopkins Hospital, USA, was used as the determination standard.[14]

Electrophysiological GBS classification criteria: AIDP classification criteria:[15] The results of two nerve electrophysiology examinations indicated that two or more motor nerves had one of the following conditions: 1) MCV <90% of the lower limit of normal (LLN); if the distal compound muscle action potential (dCMAP) <50% LLN, MCV < 85% LLN. 2) Distal motor latency (DML) >110% of the upper limit of normal (ULN); if dCMAP <100% LLN, DML >120% ULN. 3) Discretized waveform. 4) F wave latency >120% ULN.

AMAN classification criteria:[15] The results of two nerve electrophysiology examinations indicated: 1) no demyelination mentioned above; 2) two or more motor nerves or dCMAP < 80% LLN, or the results of first examination conforming to AIDP diagnostic criteria while the results of second examination showing decreased amplitude of two or more motor nerves-conducted CMAP, normal distal latency and/or partial middle nerve conduction block (proximal amplitude / distal amplitude <0.5), and no reversible conduction block. Autonomic nerve dysfunction was diagnosed using the diagnostic criteria for autonomic nerve dysfunction in the International Classification of Diseases (ICD-10).[16]

Outcome measures

The NCSA with statistically significant difference between the GBS group and the normal group was selected for analysis, and the ganglion NCSA with the smallest difference (ratio) between the GBS group and the normal group was selected as the median nerve and ulnar nerve of NCSA. The receiver operating characteristic curve (ROC) of each NCSA was drawn, and the area under the curve (AUC), sensitivity and specificity were observed.

The secondary outcomes included the ultrasonographic characteristics of limb nerves and the size of NCSA. The size of NCSA in the extremities of GBS patients with different pathological types and conditions; The correlation between NCSA and the electrophysiological indexes of the median nerve, ulnar nerve and common peroneal nerve in the limbs of patients with GBS was detected. The nerve NCSA with the largest difference (ratio) between the GBS group and the normal group was selected as the NCSA of the median nerve and ulnar nerve for correlation analysis.

Table 1. General data (n, %, $\bar{x} \pm$ sd)

	GBS group (n = 35)	Normal group (n = 20)	t/χ^2	*P* value
Gender (n, %)			0.180	.672
Male	23 (65.71)	12 (60.00)		
Female	12 (34.29)	8 (40.00)		
Age (years)	40.35±19.95	42.06±15.55	0.353	.726
Height (cm)	162.83±11.82	167.98±12.35	1.511	.139
Weight (kg)	56.68±16.98	60.26±10.05	0.982	.331
Course of disease (days)	14.82±5.66			
Total scores of MRC <40 scores (n, %)	17 (48.57)			

Abbreviations: GBS, Guillain-Barre syndrome; MRC, Medical Research Council.

Table 2. Nerve ultrasound image features of GBS patients (n, %)

Group	Reduced internal echo	Disappeared mesh structure	Thickened outer membrane	Obscure boundary
GBS (n = 35)	204 (52.99)	250 (64.94)	146 (37.92)	296 (76.88)
Normal (n = 20)	18 (8.18)	30 (13.64)	14 (6.36)	35 (15.91)
χ^2	120.988	148.187	71.679	210.063
P value	.022	.013	.031	.014

Abbreviations: GBS: Guillain-Barre syndrome.

Statistical analysis

The statistical analysis of data was carried out by using SPSS 23.0. The enumeration data were expressed as the number of patients (percentage) (n, %) and analyzed by the chi-square test with bilateral α=0.05 as the significant level. Patients' age, height, weight, course of disease, and NCSA followed the normal distribution and were expressed as mean ± standard deviation ($\bar{x} \pm$ sd); comparison between groups was performed by using independent-samples *t* test, with bilateral α=0.05 as the significant level. The correlation between limb NCSAs and nerve electrophysiology indexes was evaluated by the Pearson correlation coefficient. The diagnostic value of limbs NCSAs for GBS was analyzed by ROC. $P < .05$ indicated a significant difference.

RESULTS

General data

There were no significant differences in gender, age, height, and weight between the GBS group and the normal group ($P > .05$). The mean course of disease in the GBS group was 14.82±5.66 days, and there were 17 patients with total scores of Medical Research Council (MRC) of < 40 scores. See Table 1 for details.

Nerve ultrasound image features of GBS

Under nerve ultrasound, compared with the normal group, the limb nerves in the GBS group showed more reduced internal echo (52.99% vs. 8.18%), disappeared mesh structure (64.94% vs. 13.64%), obscure boundary (76.88% vs. 15.91%) and thickened outer membrane (37.92% vs. 6.36%) (all $P < .001$). See Table 2 for details.

Comparison of limbs NCSA sizes

Compared with the normal group, NCSAs of the brachial plexus, vagus nerve, median nerve (proximal, middle, and distal

Table 3. Comparison of limbs NCSA sizes ($\bar{x}$ ± sd, mm^2)

NCSA	GBS group (n=35)	Normal group (n=20)	*t*	*P* value
Brachial plexus	48.26±9.43	30.24±4.66	9.463	.002
Vagus nerve	4.42±0.98	2.35±1.12	6.894	.016
Median nerve				
Proximal	13.34±4.42	8.45±2.93	4.921	.021
Middle	15.92±4.03	7.92±1.52	10.509	.000
Distal	7.92±2.35	5.29±2.05	4.336	.025
Ulnar nerve				
Proximal	14.93±4.95	5.92±1.27	10.197	.000
Middle	55.83±13.84	42.23±8.26	4.563	.022
Distal	9.22±3.92	3.99±1.02	7.463	.013
Radial nerve	5.35±1.22	4.86±1.63	1.170	.251
Tibial nerve (ankle)	15.98±5.92	15.62±4.93	0.242	.810
Common peroneal nerve	17.17±3.78	11.06±2.67	6.987	.014

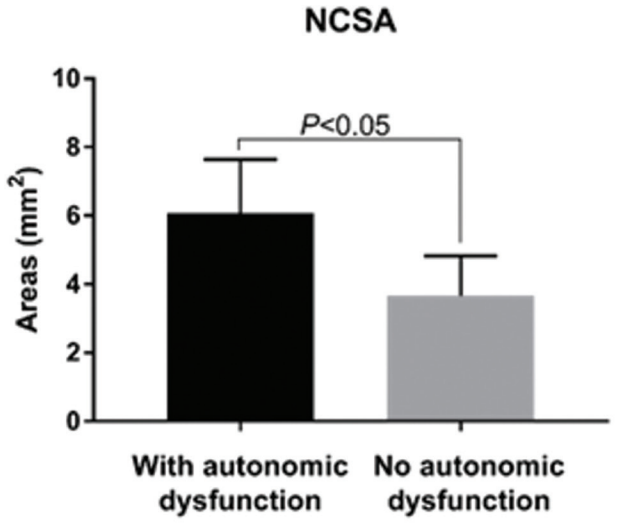
Abbreviations: GBS, Guillain-Barre syndrome; NCSA, nerve cross-sectional area.

Table 4. Comparison of limbs NCSA sizes in GBS patients with different classifications ($\bar{x}$ ± sd, mm^2)

NCSA	AIDP (n = 15)	AMAN (n = 20)	*t*	*P* value
Brachial plexus	49.54±9.03	47.76±8.87	0.582	.000
Vagus nerve	4.48±1.02	4.35±0.95	0.384	.704
Median nerve				
Proximal	18.34±4.42	10.45±2.93	5.996	.000
Middle	15.59±3.98	16.48±1.60	0.818	.425
Distal	6.25±1.92	9.09±2.33	3.949	.000
Ulnar nerve				
Proximal	15.42±4.88	14.78±4.17	0.408	.686
Middle	55.64±13.75	56.35±14.26	0.149	.883
Distal	6.59±2.82	11.16±4.37	3.750	.001
Radial nerve	5.30±1.20	5.36±1.65	0.125	.902
Tibial nerve (ankle)	15.48±4.90	16.22±5.92	0.404	.689
Common peroneal nerve	19.86±3.88	14.26±2.85	4.717	.000

Abbreviations: GBS, Guillain-Barre syndrome; NCSA, nerve cross-sectional area; AIDP, acute inflammatory demyelinative polyradiculoneuropathy; AMAN, acute motor axonal neuropathy.

Figure 1. NCSA size of the vagus nerve in GBS patients with different conditions



Abbreviations: GBS, Guillain-Barre syndrome; NCSA, nerve cross-sectional area.

segments), ulnar nerve (proximal, middle, and distal segments), and common peroneal nerve in the GBS group increased significantly (P < .001). There were no significant differences in NCSAs of the radial nerve and tibial nerve (ankle) between the two groups (P > .05). From the results of the NCSA size study of the limbs in the normal group and the GBS group, it can be seen that compared with the healthy people, the number of ncsa in the brachial plexus, vagus nerve, median nerve (proximal, middle and distal), ulnar nerve (proximal, middle and distal) and common peroneal nerve in GBS patients was significantly higher. The results of this study suggest that when a large number of ncsa in the brachial plexus, vagus nerve, median nerve (proximal, middle and distal segments), ulnar nerve (proximal, middle and distal segments) and common peroneal nerve are found in patients, further testing can be recommended to exclude the risk of GBS or make an early diagnosis. See Table 3 for details.

Comparison of limbs NCSA sizes in GBS patients with different classifications

AIDP patients had significantly larger NCSAs of the proximal median nerve and common peroneal nerve (P < .001) and smaller NCSAs of the distal median nerve and distal ulnar nerve (P < .01) than AMAN patients. There were no significant differences in NCSAs of the brachial plexus, vagus nerve, median nerve (middle), ulnar nerve (middle), radial nerve, and tibial nerve (ankle) between AIDP patients and AMAN patients (P > .05). See Table 4 for details.

Comparison of NCSA size of the vagus nerve in GBS patients with different conditions

Compared with patients without autonomic nervous dysfunction, patients combined with autonomic nervous dysfunction had significantly increased NCSA of the vagus nerve (P < .05), with a difference of approximately 1 time (Figure 1).

Correlations of NCSAs of the median nerve, ulnar nerve, and common peroneal nerve with nerve electrophysiology examination results in GBS patients

Correlation analysis of NCSAs of the median nerve (middle), ulnar nerve (proximal), and common peroneal nerve with nerve electrophysiology indexes showed a negative correlation between NCSAs of the median nerve (r=-0.329) and ulnar nerve (r=-0.245) and MCV (P < .05), a positive correlation between NCSAs of the median nerve (r=0.235) and ulnar nerve (r=0.188) and CMAP latency (P < .05), and a negative correlation between NCSA of the median nerve (r=-0.203) and SCV (P < .05) The ncsa area of the proximal median nerve and the common peroneal nerve should be paid attention to in the clinical diagnosis of GBS. If the NCSA area is too large or too small, the patient is at risk of GBS, and further detection is recommended. (Table 5).

ROC of limbs NCSA in the diagnosis of GBS

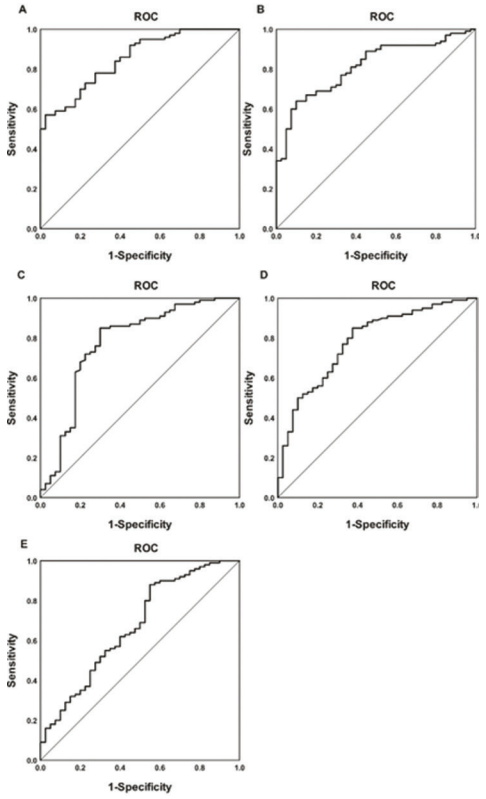
ROC revealed that AUCs of NCSAs of the median nerve (middle), ulnar nerve (proximal), vagus nerve, brachial plexus, and common peroneal nerve in the diagnosis of GBS were 0.851, 0.813, 0.783, 0.774 and 0.670, respectively (P < .05), showing a diagnostic efficiency; the sensitivities were 85.36%, 80.08%, 78.85%, 76.93% and 70.88%, respectively; the specificities were 68.29%, 73.65%, 78.86%, 80.29% and 83.56%, respectively (Figure 2).

Table 5. Correlations of NCSA with nerve electrophysiology examination results in GBS patients (n=35)

	Median nerve		Ulnar nerve		Common peroneal nerve	
	r	*P* value	r	*P* value	r	*P* value
Sensory nerve						
SCV	-0.203	0.044	-0.093	0.083	0.104	0.094
SNAP amplitude	0.090	0.292	0.132	0.203	0.126	0.230
SNAP latency	0.189	0.039	0.115	0.632	0.099	0.083
Motor nerve						
MCV	-0.329	0.029	-0.245	0.013		
CMAP amplitude	0.102	0.139	0.083	0.103		
CMAP latency	0.235	0.032	0.188	0.039		

Abbreviations: GBS: Guillain-Barre syndrome; NCSA, nerve cross-sectional area; SCV, sensory nerve conduction velocity; SNAP, sensory nerve action potential; MCV, motor nerve conduction velocity; CMAP, compound muscle action potential.

Figure 2. ROC of limbs NCSA in the diagnosis of GBS. A: Median nerve: AUC=0.851 (95%CI: 0.787-0.915); B: Ulnar nerve: AUC=0.813 (95%CI: 0.741-0.885); C: Vagus nerve: AUC=0.783 (95%CI: 0.699-0.867); D: Brachial plexus: AUC=0.774 (95%CI: 0.677-0.870); E: Common peroneal nerve: AUC=0.670 (95%CI: 0.568-0.772).



Abbreviations: GBS, Guillain-Barre syndrome; NCSA, nerve cross-sectional area; ROC, receiver operating characteristic curve; AUC, area under the curve; CI, confidence interval.

DISCUSSION

The onset of GBS is mainly caused by the misidentification of the body's immune system, which generates an immune response to autologous peripheral nerve components, resulting in pathological changes in limb nerves, such as edema, hyperemia, local perivascular lymphocyte and mononuclear macrophage infiltration, and segmental demyelination of nerve fibers.[1] In this study, under nerve ultrasound, the limb nerves of GBS patients showed reduced internal echo and thickened mesh with vague structure and obscure boundary, which were consistent with the pathological changes of GBS. Compared with healthy people, NCSAs of all examined nerves in GBS patients increased significantly except for the radial nerve and tibial nerve (ankle), which was similar to the results of previous studies.[17,18] It might be caused by Wallerian degeneration after nerve inflammatory edema, remyelination, or axonal injury in GBS patients.[17,18] ROC of NCSAs of limb nerves with differences between the two groups revealed that NCSAs of limb nerves played a diagnostic value for GBS, and the median nerve had the highest diagnostic efficiency with AUC of 0.851(95%CI: 0.787-0.915), sensitivity of 85.36% but a low specificity of 68.29%. Quantitative analysis of ROC suggested that NCSAs of limb nerves (especially the median nerve) in GBS patients were able to assist in the early diagnosis of GBS, improving the diagnosis accuracy. In addition, ROC showed that the AUCs of NCSA for the diagnosis of GBS of the median nerve (middle), ulnar nerve (near), vagus nerve, brachial plexus, and common peroneal nerve were 0.851, 0.813, 0.783, 0.774 and 0.670, respectively. The sensitivity was decreasing, suggesting that Choosing different diagnostic sites may lead to deviations in the final results. In order to improve the diagnostic efficiency of GBS, the appropriate NCSA type should be selected according to the patient's clinical conditions and imaging characteristics to improve the diagnostic efficiency.[16,18]

Clinical classifying of GBS is mainly carried out by nerve electrophysiology examination at present, and AIDP and AMAN are the two most common classifications of GBS.[19,20] The two classifications have similar manifestations but great differences in mortality and prognosis. The main manifestations of AIDP include decreased distal motor nerve conduction velocity, prolonged latency, abnormal discretized waveform, abnormal F wave, and conduction block.[20,21] AMAN is mainly manifested as the decreased CMAP amplitude and has higher mortality and poorer prognosis than AIDP.[8] The disadvantage of classifying by nerve electrophysiology is that it is difficult to classify the disease in early onset, and a second nerve electrophysiology examination after about 2-3-week disease progression is usually required to determine the specific classification.[7,22,23] Ultrasound is able to measure or continuously scan local peripheral nerves or multiple parts of the whole nerve, providing morphological changes and distribution characteristics of pathological changes along the nerve.[19,24] Therefore, ultrasound differences between different GBS subtypes may be a helpful supplement to electromyography examination and prospectively become a new basis for GBS classification. In this study, a comparison in limbs NCSAs between AIDP patients and AMAN patients showed that AIDP tended to thicken the proximal nerve, especially the median nerve, and the mean value of NCSA difference between the two groups was approximately 8mm^2. AMAN showed more significant distal nerve thickening. Similar results were obtained in the study by Mori et al., but the difference was that there was a larger sample size and different nerves analyzed in our study.[13] For example, we also found a difference in NCSAs of the common peroneal

nerves between AIDP and AMAN patients. In this study, nerve ultrasound examination was potentially useful in assisting GBS classification. However, previous studies showed no significant difference between NCSAs in the early onset of AIDP and AMAN.[8,25] In our study, patients were not classified according to the early NCSA data, so whether nerve ultrasound could classify GBS in the early stage needed to be further investigated. In addition, correlation analysis between limbs NCSAs and nerve electrophysiology indexes in GBS patients showed a negative correlation between NCSAs of the median nerve and ulnar nerve and MCV, a positive correlation between NCSAs of the median nerve and ulnar nerve and CMAP latency, and a negative correlation between NCSA of the median nerve and SCV. It corresponded to pathophysiological changes of GBS, suggesting that the more thickened the limb nerves were, the slower the MCV and the more prolonged the latency became, without significant effect on amplitude. However, there was no correlation between limb NCSAs and changes in the sensory nerve in GBS patients, which differed from the negative correlation between limb NCSAs and SCV in other peripheral nerve diseases such as diabetic peripheral neuropathy.[26] Thus, we considered that it might be related to the different pathogenesis and onset times of the two diseases (most GBS of acute onset).

Autonomic nervous dysfunction can affect the normal function of the cardiovascular system, respiratory system, digestive system, endocrine system, and other systemic systems, especially the cardiovascular system, such as elevation of blood pressure and increased heart rate, and even lead to death in severe cases. Studies have proved that autonomic nervous dysfunction in GBS is often a predictor of more severe conditions, and about 3%-14% of GBS patients die from recurrent cardiovascular dysfunction.[27,28] Therefore, it is essential to distinguish these patients in time to improve treatment and prognosis. In this study, GBS patients with autonomic nervous dysfunction had significantly increased NCSA of the vagus nerve compared with patients without autonomic nervous dysfunction, with a difference of approximately 1 time. It indicated that in clinical practice NCSA of the vagus nerve was able to be used to distinguish patients with autonomic nervous dysfunction, and corresponding treatment measures were implemented to improve the prognosis of patients.

There were some shortcomings in this study. In this retrospective study, some of the baseline characteristics of patients were limited, such as a large range of patients' age and the possible effect of the level of examining physicians on relevant examinations so the selection bias might exist. In the future, matching methods of gender, age, and others should be adopted to select appropriate controls to improve the study design further. However, there were some advantages in this study. First, compared with the previous study by Mori et al. (a total of 14 patients), the sample size was larger in our study, which made the results more representative. Second, the diagnostic efficiency of a quantitative parameter (NCSA) of ultrasound examination for GBS was analyzed in GBS patients, which provided more reference data for the clinical diagnosis of GBS. Furthermore, the results showed that limbs NCSAs of GBS patients might exert a potential value in GBS classification and condition evaluation.

In conclusion, limb peripheral nerve ultrasound plays a significant application value in GBS. Limbs NCSAs can effectively assist in the diagnosis, classification, and condition evaluation of GBS.

DECLARATION OF CONFLICT OF INTEREST

None.

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REFERENCES

1. Leonhard SE, Mandarakas MR, Gondim FAA, et al. Diagnosis and management of Guillain-Barré syndrome in ten steps. *Nat Rev Neurol*. 2019;15(11):671-683. doi:10.1038/s41582-019-0250-9
2. Foubert-Samier A, Penchet G, Yekhlef F, Lemasson G, Sibon I. [Guillain-Barré syndrome secondary to cranial surgery: direct or fortuitous relationship?]. *Neurochirurgie*. 2005;51(6):604-606. doi:10.1016/S0028-3770(05)83637-9
3. Hafsteinsdóttir B, Ólafsson E, Jakobsson F. Incidence and outcome of Guillain-Barré syndrome in Iceland: A population-based study. *Acta Neurol Scand*. 2018;138(5):454-458. doi:10.1111/ane.13000
4. Zhou RM, Shao B, Luo C, et al. [Analysis of differences in epidemiology and clinical features of Guillain-Barré syndrome between rural and urban areas of southern China]. *Zhonghua Yi Xue Za Zhi*. 2019;99(43):3432-3436.
5. Tian J, Cao C, Li T, et al. Electrophysiological subtypes and prognostic factors of guillain-barre syndrome in northern China. *Front Neurol*. 2019;10:714. doi:10.3389/fneur.2019.00714
6. Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barré syndrome. *Cochrane Database Syst Rev*. 2014;2014(9):CD002063.
7. Gómez Á, Díaz A, Carrión-Penagos J, Reyes J, Reyes S. Clinical and electrophysiological characteristics of Guillain-Barré syndrome in Colombia. *J Peripher Nerv Syst*. 2019;24(3):268-271. doi:10.1111/jns.12340
8. Gupta J, Jauhari P. How important it is to differentiate AMAN from AIDP in childhood GBS? A clinician's perspective. *Indian J Pediatr*. 2019;86(4):321-322. doi:10.1007/s12098-019-02918-3
9. Di Mascio D, Sileo FG, Khalil A, et al. Role of magnetic resonance imaging in fetuses with mild or moderate ventriculomegaly in the era of fetal neurosonography: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2019;54(2):164-171. doi:10.1002/uog.20197
10. Zeidenberg J, Burks SS, Jose J, Subhawong TK, Levi AD. The utility of ultrasound in the assessment of traumatic peripheral nerve lesions: report of 4 cases. *Neurosurg Focus*. 2015;39(3):E3. doi:10.3171/2015.6.FOCUS15214
11. Heinen C, Dömer P, Schmidt T, Kewitz B, Janssen-Bienhold U, Kretschmer T. Fascicular ratio pilot study: high-resolution neurosonography-a possible tool for quantitative assessment of traumatic peripheral nerve lesions before and after nerve surgery. *Neurosurgery*. 2019;85(3):415-422. doi:10.1093/neuros/nyy355
12. Wakerley BR, Uncini A, Yuki N; GBS Classification Group; GBS Classification Group. Guillain-Barré and Miller Fisher syndromes--new diagnostic classification. *Nat Rev Neurol*. 2014;10(9):537-544. doi:10.1038/nrneurol.2014.138
13. Mori A, Nodera H, Takamatsu N, et al. Sonographic evaluation of peripheral nerves in subtypes of Guillain-Barré syndrome. *J Neurol Sci*. 2016;364:154-159. doi:10.1016/j.jns.2016.03.042
14. Ibrahim J, Grapperon AM, Manfredonia F, van den Bergh PY, Attarian S, Rajabally YA. Serial electrophysiology in Guillain-Barré syndrome: A retrospective cohort and case-by-case multicentre analysis. *Acta Neurol Scand*. 2018;137(3):335-340. doi:10.1111/ane.12872
15. Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. *Lancet*. 2016;388(10045):717-727. doi:10.1016/S0140-6736(16)00339-1
16. Anandan C, Khuder SA, Koffman BM. Prevalence of autonomic dysfunction in hospitalized patients with Guillain-Barré syndrome. *Muscle Nerve*. 2017;56(2):331-333. doi:10.1002/mus.25551
17. Coras R, Korn K, Kuerten S, Huttner HB, Ensser A. Severe bornavirus-encephalitis presenting as Guillain-Barré-syndrome. *Acta Neuropathol*. 2019;137(6):1017-1019. doi:10.1007/s00401-019-02005-z
18. Ebrahim Soltani Z, Rahmani F, Rezaei N. Autoimmunity and cytokines in Guillain-Barré syndrome revisited: review of pathomechanisms with an eye on therapeutic options. *Eur Cytokine Netw*. 2019;30(1):1-14. doi:10.1684/ecn.2019.0424
19. Grimm A, Décard BF, Schramm A, et al. Ultrasound and electrophysiologic findings in patients with Guillain-Barré syndrome at disease onset and over a period of six months. *Clin Neurophysiol*. 2016;127(2):1657-1663. doi:10.1016/j.clinph.2015.06.032
20. Razali SNO, Arumugam T, Yuki N, Rozalli FI, Goh KJ, Shahrizaila N. Serial peripheral nerve ultrasound in Guillain-Barré syndrome. *Clin Neurophysiol*. 2016;127(2):1652-1656. doi:10.1016/j.clinph.2015.06.030
21. Wang T, Wang Z, Guo Z. Headache and intracranial hypertension in Guillain-Barré syndrome: a case report and literature review. *Int J Neurosci*. 2019;129(12):1179-1182. doi:10.1080/00207454.2019.1645139
22. Grapperon AM, Berro M, Salort-Campana E, Verschueren A, Delmont E, Attarian S. Guillain-Barré syndrome subtypes: A clinical electrophysiological study of 100 patients. *Rev Neurol (Paris)*. 2019;175(1-2):73-80. doi:10.1016/j.neurol.2018.01.379
23. Munayco CV, Soto Cabezas MG, Reyes MF, Arica Gutiérrez JA, Napanga Saldaña O. [Epidemiology of guillain-barré syndrome in Peru]. *Rev Peru Med Exp Salud Publica*. 2019;36(1):10-16. doi:10.17843/rpmesp.2019.361.3729
24. Sharma K, Tengsupakul S, Sanchez O, Phaltas R and Maertens P. Guillain-Barré syndrome with unilateral peripheral facial and bulbar palsy in a child: A case report. SAGE Open Med Case Rep 2019; 7: 2050313x19838750. doi:10.1177/2050313X19838750
25. Kuwahara M, Kusunoki S. Complement-mediated mechanism and complement inhibitors in Guillain-Barré Syndrome. *Brain Nerve*. 2019;71(6):581-587.
26. Pelosi L, Mulroy E. Diagnostic sensitivity of electrophysiology and ultrasonography in ulnar neuropathies of different severity. *Clin Neurophysiol*. 2019;130(2):297-302. doi:10.1016/j.clinph.2018.11.018
27. Verboon C, Doets AY, Galassi G, et al; IGOS Consortium. Current treatment practice of Guillain-Barré syndrome. *Neurology*. 2019;93(1):e59-e76. doi:10.1212/WNL.0000000000007719
28. Wachira VK, Peixoto HM, de Oliveira MRF. Systematic review of factors associated with the development of Guillain-Barré syndrome 2007-2017: what has changed? *Trop Med Int Health*. 2019;24(2):132-142. doi:10.1111/tmi.13181