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Application Value of Electromyography Combined With Heart Rate Variability in the Diagnosis of Diabetic Peripheral Neuropathy

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Abstract: Purpose: To explore the clinical value of Electromyography (EMG) and Heart Rate Variability (HRV) in the diagnosis of early DPN and provide the basis for early diagnosis, treatment, and prevention of DPN. **Methods:** 105 patients with type 2 diabetes mellitus (T2DM) in the Changji People's Hospital were treated from January 2023 to December 2023. They were stratified into DPN-symptomatic (DPN group, n=55) and DPN-asymptomatic (NDPN group, n=50) cohorts based on the presence or absence of clinically confirmed diabetic peripheral neuropathy. The clinical biochemical indicators, nerve electromyography, and HRV parameters were obtained from electronic medical records, and differences in detection results were compared between the two groups. Logistic regression was applied to analyze the influencing factors of DPN in diabetes patients. The receiver operating characteristic (ROC) curve was applied to analyze the diagnostic value of EMG combined with other parameters for DPN. **Results:** From the results of the general information, diabetes duration, glycosylated hemoglobin (HbA1c), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC) and FBG in the DPN group were significantly differences compared with the NDPN group ($p<0.05$). There were no statistically significant differences in gender, age years, uric acid, and other general data ($p>0.05$). Compared with the NDPN group, the motor nerve conduction velocity (MNCV), sensory nerve conduction velocity (SNCV) of the ulnar nerve, median nerve, and tibial nerve in the DPN group were statistically significant ($p>0.05$). The DPN group had higher average F wave latency and H wave latency in the tested nerve, with statistical significance ($p<0.05$). HRV parameters decreased significantly (SDNN, rMSSD, PNN50, and SDANN, all $p<0.05$). ROC analysis showed that the area under the ROC curve (AUC) of the combined diagnosis of DPN by duration of diabetes, HbA1c, EMG, and HRV was 0.897, the accuracy was 82.86%, the sensitivity was 78.00%, and the specificity was 87.27%. The AUC of the combined diagnosis of the four parameters for DPN was significantly higher than that of each alone ($p<0.05$). **Conclusion:** The combination of EMG and HRV has a high value in the assessment of DPN and can be used for early assessment of the extent of the lesion.

Keywords: Diabetes Peripheral Neuropathy; Electromyography; Heart Rate Variability; Diagnosis

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1.Introduction

With the development of the world economy and the gradual improvement of people's living standards and quality, diabetes has become a worldwide epidemic [1]. Diabetic peripheral neuropathy (DPN), one of the most prevalent chronic complications

of diabetes, imposes a substantial economic burden on healthcare systems due to its progressive nature and associated treatment costs [2,3]. The onset of diabetes peripheral neuropathy is insidious. When patients have obvious symptoms, they are often in the late stage of the disease, which often leads to irreversible nerve injury [4]. In the later stage, there will be serious consequences such as limb sensation and movement disorders, foot ulcers, and even death [5,6]. It not only resulted in a significant decline in the quality of life of patients but also placed a substantial financial burden on healthcare systems and society in general [7]. Therefore, for patients with diabetes peripheral neuropathy, early diagnosis and prevention are considered to be far more effective than treatment.

Electromyography is a simple and effective auxiliary method for diagnosing diabetic peripheral neuropathy, and can accurately reflect the degree of peripheral nerve damage in patients [8]. It evaluates the occurrence and development of DPN by detecting the velocity and amplitude of peripheral nerve conduction. Heart rate variability (HRV) is an important indicator for assessing diabetic peripheral neuropathy (DPN), especially valuable in early diagnosis and disease assessment. By monitoring HRV, the impaired autonomic function of diabetic patients can be detected at an early stage, so that timely interventions can be taken to reduce the occurrence of complications [9][10]. This study aims to investigate a novel diagnostic protocol integrating EMG and HRV analyses for enhancing the precision of DPN identification, with the ultimate goal of informing evidence-based therapeutic decision-making in diabetes care.

2.Materials and methods

2.1 Subjects

This study included 105 inpatients with type 2 diabetes mellitus (T2DM) who were enrolled between January 2023 and December 2023 at the Changji People's Hospital. They were divided into a DPN group (27 men, 28 women) and an NDPN group (28 men, 22 women) according to the presence or absence of peripheral neuropathy. The diagnosis criteria for T2DM were based on the 2023 Standards for the Medical Management of Diabetes by American Diabetes Association (ADA) [11] . The diagnostic criteria for DPN followed the 2025 Standards of care in Diabetes published by the ADA [12]. The inclusion criteria were as follows: (1) Compliance with type 2 diabetes; (2) Patients with neuropathy meeting the diagnostic criteria for DPN; (3) Age 18-80 years old; (4) Patients' medical records were complete. The Exclusion criteria were as follows: (1) Complicated with acute complications of diabetes mellitus; (2) Combined cardiovascular, pulmonary, hepatic, renal, hematopoietic system and other serious diseases not caused by diabetes; (3) Serious primary diseases and mental illnesses. (4) Peripheral neuropathy caused by other reasons. (5) Pregnant or lactating women. (6) Patients with incomplete clinical data.

2.2 Clinical data collection

The clinical data and medical histories of T2DM patients were obtained from electronic medical records. Baseline data on age, sex, and diabetes duration were collected. The following laboratory parameters were assessed: fasting blood glucose (FBG), glycated hemoglobin (HbA1c), total bilirubin (TBIL), triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), uric acid (UA), serum creatinine (Cr) and urinary microalbumin (mAlb) levels.

2.3 Nerve conduction studies (NCS)

All patients were examined using an electromyographic evoked potential meter (Viking Quest 4, America). Latency, amplitude, motor conduction velocity, and sensory conduction velocity of the bilateral median, ulnar, and tibial nerves were measured and recorded. In addition, the F-wave latency of all tested nerves and H-reflex of the tibial nerve were detected. These neurophysiological examinations were performed in a quiet environment and the temperature in the electrophysiology laboratory was maintained at 22-28℃ during tests. The abnormal judgment of NCS according to the NCS reference value of the Chinese population, and the abnormal H-reflex and F wave refer to the standard formulated [13,14].

2.4 Heart Rate Variability (HRV)

The time-domain parameters were measured and recorded using a 24-h Holter monitor (Zhongqi Biomedical Electronics Co., Ltd., Wuhan, China), which included the standard deviation of all normal to normal R-R intervals (SDNN, ms), standard deviation of 5-minute average NN intervals (SDANN, ms), square root of the mean of the squares of successive NN interval differences (rMSSD, ms) and the percentage of intervals>50 ms different from preceding interval (PNN50, %). HRV was

considered abnormal if at least two of the following six abnormal parameters were met: SDNN < 50 ms, SDANN < 40 ms, PNN50 < 0.75%, rMSSD < 15 ms [15,16].

2.5 Statistical analysis

Data were collected using SPSSAU (Beijing QingSi Technology Co., Ltd) and Z stats software (Hangzhou Mr. Zheng Statistical Technology Co., Ltd). The continuous variables were expressed as mean ± standard deviation, these not satisfying normal distribution were shown as M (25th-75th percentiles), and categorical variables were expressed as percentages (%). T-tests or Mann–Whitney U tests were carried out to compare the differences in these variables and the chi-square test for categorical variables between two groups. The significance level of tests in this study was considered as $p<0.05$.

3.Results

3.1 Comparison of clinical characteristics between two groups

A total of 105 patients (mean age = 57.19 ± 10.43 years) were enrolled in this work, which consists of 47 (44.77%) males and 58 (55.24%) females. The baseline clinical characteristics (gender, age, and clinical biochemical indicators) of patients are given in Table 1. When comparing the general clinical data between the DPN group and the NDPN group, the results revealed that there were significant differences in age, duration of diabetes, HbA1c, FBG, TC, and LDL-C ($p < 0.05$). There was no significant difference in Sex, TBIL, HDL-C, UA, Cr and mAlb. HbA1c, FBG, TC, and LDL-C were significantly increased compared with the NDPN group.

Table 1. Comparison of the biochemical indicators between the NDPN and DPN groups.

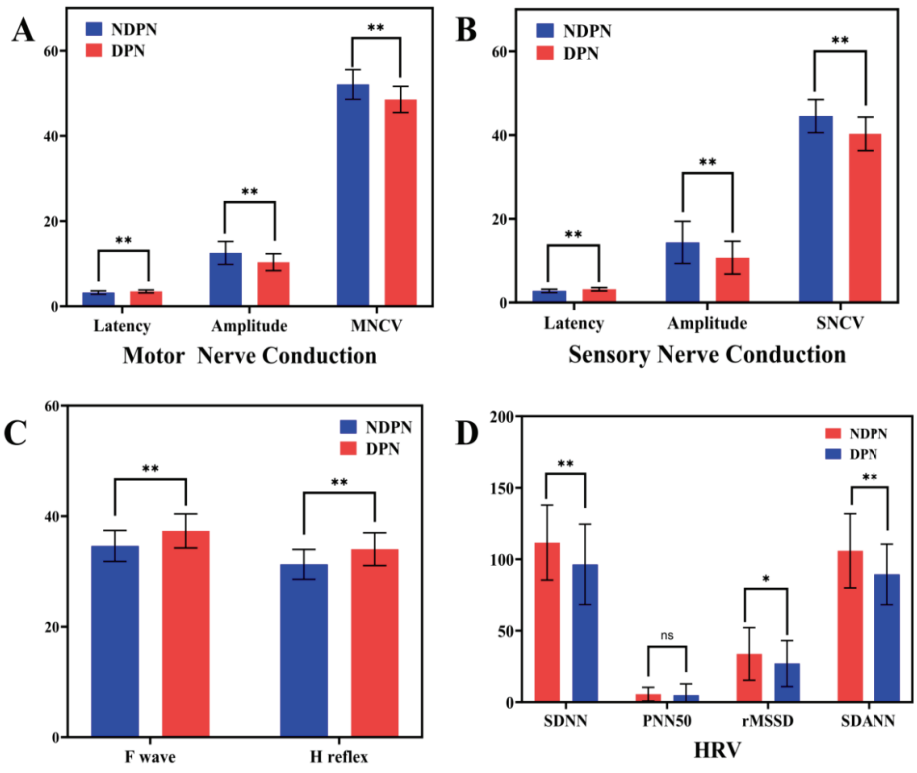
Group	DPN (n=55)	NDPN (n=50)	t/x^2/z	p
Sex (Male/Female)	25/30	22/28	0.022	0.881
Age (years)	60.05 ± 11.13	57.00 ± 6.32	1.750	0.084
Diabetes duration (years)	9.05 ± 5.42	4.60 ± 4.56	4.533	0.000 *
HbA1C (%)	10.29 ± 1.96	8.39 ± 1.94	4.971	0.000 *
TBIL	11.61 ± 3.29	11.15 ± 4.98	0.553	0.581
FBG (mmol/L)	9.59 ± 3.71	7.87 ± 3.16	2.554	0.012 *
TC (mmol/L)	4.62 ± 0.82	4.11 ± 0.93	3.018	0.003 *
HDL-C (mmol/L)	1.10 ± 0.32	1.12 ± 0.39	-0.326	0.745
LDL-C (mmol/L)	2.71 ± 0.76	2.30 ± 0.77	2.699	0.008 *
Cr (μmol/L)	58.48 ± 19.40	57.24 ± 10.13	0.416	0.679
UA (μmol/L)	235.00 (195.50, 306.00)	258.00 (211.25, 287.50)	-0.65	0.513
mAlb (mg/L)	8.50 (3.00, 21.05)	8.40 (3.87, 14.82)	-0.57	0.568

3.2 Neurophysiological examination results of patients

In this study, the latencies, amplitudes, motor and sensory conduction fiber velocity of the nerve were measured, and the difference in each parameter of the ulnar nerve, median nerve, and tibial nerve (Figure 1). For the comparison of motor nerve conduction detection parameters, as shown in Table S1, for the ulnar nerve and median nerve, the latency in the DPN group was significantly longer than that in the NDPN group and reached statistical significance. For the tibial nerve, latency was longer in the DPN group but did not reach statistical significance (4.02 ± 0.59 vs. 3.85 ± 0.62, p=0.095). Regarding the amplitude results, we found that amplitude significantly lowered in all tested nerves compared to the control group ($p < 0.05$). As

shown in Table S2, for the comparison of sensory nerve conduction detection parameters, we found that the latency of each nerve ($p < 0.05$) was significantly longer and the amplitude of the ulnar and median nerve was lower (13.65 ± 5.80 vs.16.33 ± 6.08, 16.30 ± 8.43 vs. 24.38 ± 10.17, $p < 0.05$) in DPN group than in NDPN group. Yet no statistical significance in the latency of the ulnar nerve and the amplitude of the tibial nerve. Table S3 shows that the motor nerve conduction velocity (MNCV) and sensory nerve conduction velocity (SNCV) were significantly reduced in the DPN group, compared with the NDPN group ($p < 0.05$).

Figure 1. Comparison of indicators of electromyography and HRV between the two groups. ($p < 0.05$, $p < 0.001$**)*



3.3 Comparison of F wave and H-reflex detection parameters between the two groups

As shown in Table S4, the average latency of the F wave of the tibial nerve, median nerve, and ulnar nerve in the DPN group was significantly longer than that in the NDPN group, and the difference was statistically significant ($p < 0.05$). The H-reflex minimum latency of the tibial nerve in the DPN group was significantly longer than that in the NDPN group ($p < 0.05$).

3.4 Comparison of the parameters of HRV detection between the two groups.

Statistically significant differences were found in SDNN, rMSSD, PNN50, and SDANN between DPN and NDPN groups ($p < 0.05$), as shown in Table 2.

Table 2. Time domain indicators of HRV comparisons between the two groups.

Group	DPN	NDPN	t / z	p
SDNN（ms）	96.35 ± 28.14	111.64 ± 26.23	-2.872	0.005*
PNN50（%）	1.00 (0.00, 5.50)	5.00 (2.00, 8.00)	-2.380	0.017*
rMSSD（ms）	23.00 (16.50, 34.50)	31.50 (20.25, 39.00)	-2.320	0.020*
SDANN（ms）	89.38 ± 21.23	105.86 ± 25.97	-3.573	0.001*

3.5 The risk factors of DPN were analyzed by binary logistic regression

As shown in Table 3, using DPN as the dependent variable, variables with statistical significance in univariate analysis and those that were professionally considered to have an impact on outcome were included in a binary logistic regression model,

which showed that duration of diabetes, HbA1c, LDL-C, and SDANN were independent factors influencing the occurrence of outcome ($p < 0.05$).

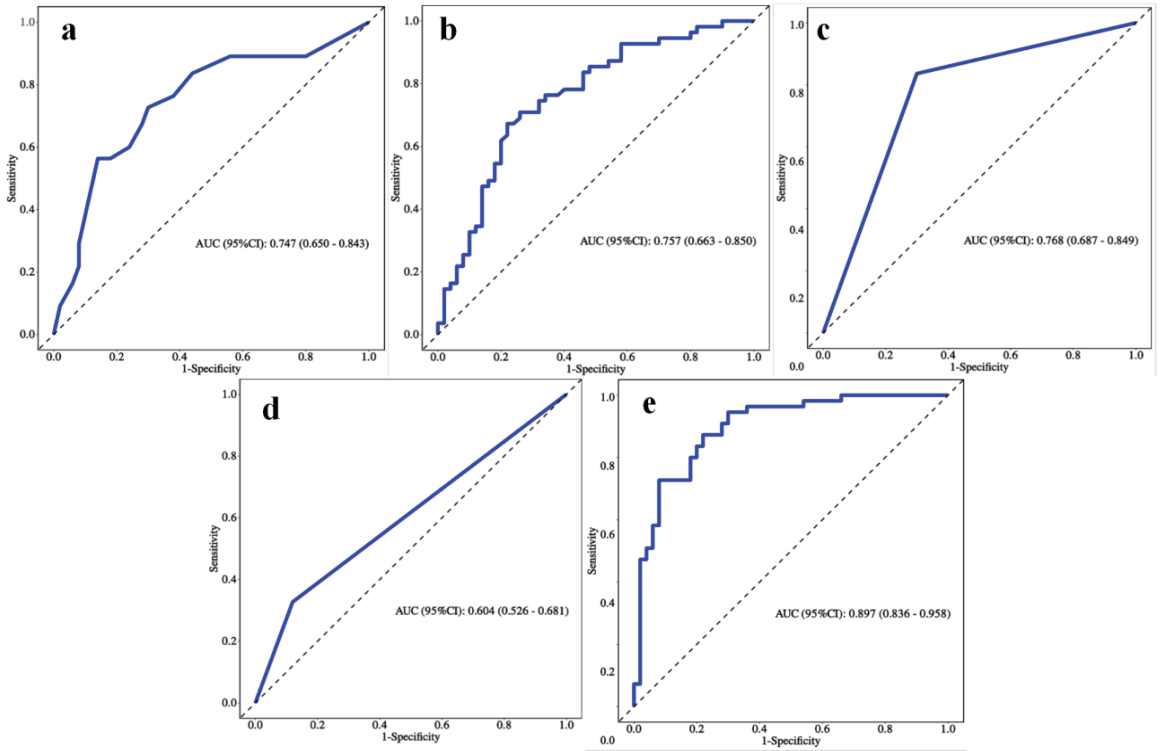
Table 3. Risk factors of DPN.

Variables	Single-factor logistic regression					Multinomial logistic regression				
	β	S.E	Z	P	OR (95%CI)	β	S.E	Z	P	OR (95%CI)
Duration of diabetes	0.181	0.047	3.866	<.001 *	1.199 (1.093 ~ 1.314)	0.221	0.058	3.830	<.001 *	1.247 (1.114 ~ 1.396)
HbA1c	0.483	0.116	4.178	<.001 *	1.621 (1.292 ~ 2.033)	0.516	0.138	3.735	<.001 *	1.675 (1.278 ~ 2.195)
LDL-C	0.693	0.271	2.560	0.010 *	1.999 (1.176 ~ 3.397)	0.951	0.379	2.514	0.012 *	2.589 (1.233 ~ 5.438)
SDANN	-0.029	0.009	-3.253	0.001 *	0.971 (0.954 ~ 0.988)	-0.023	0.012	-1.971	0.049 *	0.977 (0.955 ~ 0.999)
PNN50	-0.016	0.030	-0.520	0.603	0.984 (0.928 ~ 1.044)	0.026	0.046	0.557	0.577	1.026 (0.937 ~ 1.124)

3.6 The diagnostic efficacy of these duration of diabetes, HbA1c, EMG, HRV and their combination for DPN

ROC curve results showed that the AUC of the duration of diabetes, HbA1c, EMG, and HRV in diagnosing DPN were 0.747, 0.757, 0.768 and 0.604 respectively, and the AUC of the combination of the four was 0.897, significantly higher than that of each single index ($p < 0.05$), as shown in Figure 2 and Table S5.

Figure 2. The ROC curve (a) Duration of diabetes, (b) HbA1c, (c) EMG and (d) HRV and (e) their combined diagnosis of DPN.



4.Discussion

DPN is one of the main and common microvascular complications of diabetes mellitus, which can cause considerable morbidity in many patients [17,18]. The typical clinical manifestations are symmetrical numbness and motor and sensory disorders in the distal extremities [19, 20]. DPN is also an insidious disease and only a small number of patients have symptoms and signs in the early stage [21]. If the treatment is not timely, it may lead to gradual aggravation of nerve damage and serious

sequelae, such as diabetic foot, which may lead to non-traumatic amputation of patients [22]. Therefore, for diabetes patients, DPN is a risk factor for disability and death and it is very important to early screen and diagnose peripheral neuropathy of people with diabetes in the early stage and take effective target measures in the prevent the conditions, progression, and complications.

Regarding the clinical biochemical indicators, our data suggested that the HbA1c, TC, LDL-C, and Cr levels were higher in DPN group than in NDPN group. HbA1c level can reflect the blood glucose levels in patients with diabetes mellitus (for 8-12 weeks) [23]. It was also an independent risk factor for DPN in the multivariate analysis of this population [24]. Meanwhile, the results of the present study demonstrated that with the extension of the duration of diabetes and unqualified glycemic control, the prevalence of DPN increases significantly, which is consistent with the results of Hu et al [6]. Abnormal blood lipid metabolism is also a risk factor for DPN [25]. Based on our study, the results suggested that patients with DPN have higher peripheral blood TG, TC content, and lower HDL-C levels.

Electromyography has a high detection rate for minor neurologic lesions and can assist in the clinical screening and diagnosis of DPN. The results of the electromyography examination, showed that there were significant differences in the sensory latency, amplitude, MNCV and SNCV of all the examined nerves between the two groups ($p< 0.05$), and the sensory amplitude of the DPN group was significantly lower than that the NDPN group, which suggests that diabetic patients with neurological symptoms had peripheral nerve sensory and motor dysfunction, and the electromyography results were consistent with clinical symptoms. Diabetes mellitus patients' bodies are in a state of hyperglycemia, neurons can not synthesize nutrients, resulting in axonal damage, inducing nutritional disorders of nerve endings, leading to damage to distal nerves, and with the prolongation of the disease, the more serious the impact of the nerve fibers by the metabolism of glucose, which contributes to the body's lack of compensatory function, aggravating nerve damage [26]. Significant oxidative stress exists in patients with diabetes mellitus complicated by peripheral neuropathy, which contributes to the decline in neuron number and slowing of nerve conduction velocity due to oxidative stress in cells, and the oxidative stress worsens with the increase in diabetes duration, further decreasing the nerve conduction velocity [27]. As a result, there is a significant difference between motor and sensory nerve conduction in electromyography. The single NCS detection often reduces the detection rate. The NCS detection is combined with F wave and H-reflex detection to make up for the shortcomings of traditional techniques avoid missed diagnosis and misdiagnosis and improve the diagnostic value of DPN. For all tested nerves, the average latency of the F wave in DPN group was significantly longer than that in the NDPN group. Meanwhile, the H-reflex of the tibial nerve was explored and the H-wave minimum latency of tibial nerve in DPN group was significantly longer than that in NDPN group ($p< 0.05$), indicating that the detection of H-reflex was helpful for early diagnosis of DPN. DPN patients are prone to prolonged terminal motor latencies and slowed nerve conduction velocities, while F-wave latencies can reflect proximal neuropathy [28]. The H-reflex detects motor neuron excitability, and any lesion in the nerve reflex arcs can cause abnormalities of the H-reflex, which can be revealed even in diabetic patients with minor nerve injuries, which further demonstrates the value of neurography in the assessment of DPN [29][30].

Heart rate variability is an important indicator for assessing DPN, especially valuable in early diagnosis and disease assessment. By monitoring HRV, the impaired autonomic function of diabetic patients can be detected at an early stage, so that timely interventions can be taken to reduce the occurrence of complications. Decreased HRV in DPN patients suggests that the cardiac autonomic nervous system was impaired and that the vagus nerve was more likely to be impaired before the sympathetic nerve or that the vagus nerve was more severely impaired than the sympathetic nerve [31][32]. It has been reported in the literature that the correlation between patients with type 2 diabetes mellitus with peripheral neuropathy and their cardiac autonomic function analyzed by HRV shows that the duration of diabetes is closely related to the decline in HRV, and the most significant decline in HRV is in the first 5-10 years of the disease, so it is important to strengthen the strict control of blood glucose and early intervention therapy to slow down the development of the time of diabetic complications [33]. Tarvainen et al. reported that cardiac autonomic regulation is reduced in hyperglycemia without significant changes in sympathetic-vagal balance, that hyperglycemia is associated with a decrease in mean and heart rate, and that sustained high levels of blood glucose are an underlying factor contributing to the development of DPN in diabetic patients [34]. In this study,

the results showed that heart rate variability indices (SDNN, rMSSD, SDANN) were significantly lower in the DPN group than in the NDPN group ($p< 0.05$), which further confirms the diagnostic value of heart rate variability in diabetic peripheral neuropathy. We also analyzed the independent risk factors for DPN using binary logistic regression analysis, which showed that duration of diabetes, HbA1c, LDL-C, and SDANN were independent risk factors for DPN ($p< 0.05$). The diagnostic efficacy of diabetes duration, HbA1c, EMG, and HRV for DPN was analyzed using ROC curves, and the results showed that the AUC of combining the four indicators was 0.90, the sensitivity was 87%, the specificity was 85%, which was significantly higher than that of each of the individual indicators ($p < 0.05$). These results suggest that EMG combined with heart rate variability is valuable for early diagnosis and assessment of diabetic peripheral neuropathy.

5.Conclusion

In conclusion, our findings show that the pathological and physiological changes of the peripheral nerves in T2DM patients have already appeared in the early stage without symptoms of neurological damage, not only in the distal nerve, but also in the proximal nerve, and the proximal end is damaged earlier and more significantly than the distal end. Electromyography and heart rate variability tests are valuable in the early diagnosis and assessment of diabetic peripheral neuropathy. Electromyography is mainly used to assess nerve damage by detecting nerve conduction velocity and wave amplitude, while HRV reflects the degree of the lesion by evaluating cardiac autonomic function. The combination of the two can provide a more comprehensive assessment of the severity of diabetic peripheral neuropathy, and provide a more accurate basis for clinical prevention, early treatment and prognostic assessment.

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Conflict of Interests

The author(s)declare(s) that there is no conflict of interest regarding the publication of this paper.

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