RESEARCH ARTICLE

Utility of single fibre electromyography (SFEMG)and motor unit number estimation technique (MUNE) in the diagnosis and differentiation of polyneuropathies of different aetiology

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Abstract

Objective: To determine whether single fibre electromyography and motor unit number index can distinguish between axonal and myelin lesions in polyneuropathies.

Method: This case-control study was conducted at the Department of Medical Physiology, School of Medicine, University of Duhok, Iraq, and the Neurophysiology Department, Hawler Teaching Hospital, Erbil, Iraq, from January 2021 to March 2022. Group A had patients diagnosed with polyneuropathy regardless of the aetiology, while group B had age-matched healthy controls. Both groups were subjected to single fibre electromyography and motor unit number index as well as conventional nerve conduction study and concentric needle electromyography. Data was analysed using SPSS 26.

Results: Of the 140 subjects, 60(43%) were patients in group A; 40(67%) males and 20(33%) females with mean age 55.3±7.2 years. There were 80(57%) controls in group B; 43(54%) females and 37(46%) males with mean age 53.81±7.15. Group A had significantly higher single fibre electromyography jitter, and mean consecutive difference (MCD) values than group B ($p<0.05$). Group A patients with axonal polyneuropathy had a higher mean jitter (MCD) value (36.476.7ms) than those with demyelinating polyneuropathy (23.262.31 ms) ($P <0.05$). Patients in group A had a motor unit number index value with a significantly lower mean value ($p<0.05$) when compared to the controls. Axonal polyneuropathy patients had a lower MUNIX value (99.612.8) than demyelinating polyneuropathy patients (149.845.7) ($P< 0.05$).

Conclusions: Single fibre electromyography and motor unit number index could help differentiate between the pathophysiology of axonal and demyelinating polyneuropathy.

Key Words: Single fibre electromyography, Motor unit number index, Polyneuropathy classification, Nerve conduction studies.

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Introduction

While symptoms and objective evidence suggest polyneuropathy (PNP), like muscular power (weakness), muscular bulk (atrophy), altered sensation (numbness, paraesthesia, dysesthesia and altered deep tendon reflexes), a nerve conduction study (NCS) is usually required to confirm the diagnosis. The most significant objective of the electrophysiological examination in the evaluation of PNP is to identify the primary pathophysiology underlying the neuropathy as either axonal or demyelinating. This is required not only for diagnostic aetiology but also for prognosis and optimal PNP therapy.[1-6] Electrodiagnostic testing is also crucial for differential diagnosis, particularly for mononeuropathies (MNPs) and radiculopathies that match PNP symptoms[3, 4].

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Conventional CNS parameters do not reflect changes in microstructure and are limited in showing evidence of nerve recovery. In addition, only large fibres are tested in nerve conduction velocity studies, and, thus, the procedure is limited in detecting small-degree changes[7]. Motor unit number estimation (MUNE) is a quantitative electrophysiological approach that gives the number of functioning lower motor neurons (LMNs) in a muscle. Recent studies have demonstrated good test-retest reliability in healthy subjects and amyotrophic lateral sclerosis (ALS) patients, and its capability to track the loss of functional LMNs over time[8-12].

The single fibre electromyographic (SFEMG) technique extends information gained from conventional NCS by providing insights into the microstructure of muscle, specifically the nerve regeneration, or reinnervation, process[7,13]. SFEMG with concentric needle electrode (CNE) jitter measurement analysis is the most sensitive clinically used electrophysiological test in vivo for identifying postsynaptic neuromuscular junction dysfunction, called myasthenia gravis (MG)[14, 15].

The current study was planned to determine whether SFEMG and motor unit number index (MUNIX) could distinguish between axonal and myelin lesions in polyneuropathies and to look at the efficacy of SFEMG and MUNIX in identifying motor unit (MU) loss in PNPs as well their reinnervation characteristics.

Patients and Methods

This case-control study was conducted at the Department of Medical Physiology, School of Medicine, University of Duhok, Iraq, and the Neurophysiology Department, Hawler Teaching Hospital, Erbil, Iraq, from January 2021 to March 2022. After approval from the ethics review board of the Directorate of Health, Duhok, the sample was raised from Hawler Teaching Hospital and Rizgary Teaching Hospital, Erbil. Samples were collected at random in accordance with the disease population, those included were patients with reduced motor/sensory conduction velocities in at least two motor nerves in line with literature[15, 16]. Those with a severe degree of paresis or plegia, clear evidence of demyelinating or axonal loss, and those acquired or inherited PNPs were excluded[3]. No patient had conduction block or abnormal temporal dispersion, according to the European Standardised Telematic Tool to Evaluate Electrodiagnostic Methods (ESTEEM) criteria[3]. All those included were placed in group A, while age-matched healthy volunteers formed control group B.

Patients in group A were diagnosed as having PNP regardless of the aetiology and were diagnosed by consultant neurologists based on signs and symptoms, such as pain, paraesthesia, reduced deep tendon reflexes, decreased muscular force, and muscular atrophy with mild or moderate degree of severity.

All patients underwent electrophysiological evaluation, and motor and sensory conduction velocity was measured in three or more peripheral nerves in the lower and upper limbs (posterior tibial, common peroneal, sural, median (motor and sensory) and ulnar (motor and sensory nerves). Conventional electromyography (EMG) with disposable CNE was carried out in the tibialis anterior (TA) muscle and the first dorsal interosseous (FDI) muscle as distal muscles for the evidence of denervation and reinnervation evidence. The patients were then subjected to a motor unit number index (MUNIX) test, followed by concentric needle electrode jitter analysis using SFEMG technique [17]. The electrodiagnostic methodology proposed by evidence-based guidelines for electrodiagnosis of PNP1 was employed for NCS.

NCS was carried out at room temperature 37^{o} for both groups. All studies were done using the same EMG equipment (Nihon Kohden X1 Neuropack, Japan, and Cadwell Sierra Summit, United States) with the same filter settings for NCS, EMG and concentric needle SFEMG. Body temperature was maintained at 32-36^{o} using a heating light. The findings were compared with laboratory control material, and values beyond ±2 standard deviation (SD) were regarded as abnormal.

For MUNE, the ulnar nerve innervated abductor digiti-mini (ADM) muscle of the right or left hand was explored, using the original MUNIX protocol[9, 12]. The MUNIX assessment on ADM muscle was preferred because the evaluation is reasonably straightforward to quantify and because ulnar nerves are usually implicated in moderate PNP. The abductor of the hallux and the extensor digitorum brevis of the foot were not included because their compound muscle action potential (CMAP) amplitude is generally low in moderate PNP while the MUNIX approach requires a CMAP >0.5mv to be accurate[9].

For SFEMG, the voluntary activation method[17] was used to evaluate jitter characteristics in the indicated muscle. Before SFEMG, a conventional EMG was done in the selected muscle First Dorsal Interosseous (FDI) muscle from the upper limb and Tibialis anterior (TA) muscle from the lower limb) to corroborate neurogenic anomalies. The more distant one was studied from the common peroneal innervated TA muscle provided there was no plegia or severe paresis in voluntary activation and no evidence of radiculopathy. The measurement of jitter parameters by voluntary activation was done using disposable facial-size concentric needle electrodes (CNEs) (Ambu Neuroline Concentric, 25mm x 0.30mm [30G], recording area 0.02 mm2, Ambu A/S, Dk-2750 Ballerup-Denmark's; and Natus Technomed DCN, 25mm x 0.30mm [30G], recording area 0.02 mm^2, Technomed Europe, The Netherlands). EMG machine for concentric needle jitter measurement recording comprised a high-pass filter setting of 1kHz and 10kHz low-pass filter, as recommended[18].

Data was analysed using SPSS 26. Independent samples t-test and Pearson's linear correlation coefficient were used as appropriate. $P<0.05$ was considered significant.

Results

Of the 140 subjects, 60(43%) were patients in group A; 40(67%) males and 20(33%) females with mean age 55.3±7.2 years. There were 80(57%) controls in group B; 43(54%) females and 37(46%) males with mean age 53.81±7.15. Group A patients had duration of the disease or signs and symptoms ranging from 3 to 6 months.

There was a significant difference between the groups

(p<0.05) and also between the axonal and demyelinating subgroups concerning sensory latency, sensory nerve action potential (SNAP) amplitude and conduction velocity (p<0.05) (Table 1).

There was a significant difference in the mean values of peroneal, tibial, median and ulnar nerves distal motor latencies among patients with demyelinating PNP (4.3±0.7ms) and axonal PNP (4.1±0.6 ms) when compared to the controls (3.5±0.7ms) (p<0.05). There was a significant difference in CMAP amplitudes in axonal PNP (2.2±0.7mv) and demyelinating PNP (2.9±1.0mv) subgroups compared to the controls (4.5±1.5) (p<0.05) (Table 2).

The mean motor unit action potential (MUAP) duration was substantially longer in group A compared to group B (p<0.05) (Table 3).

SFEMG showed significantly greater jitter, MCD and MSD (mean sorted differences) values in patients with axonal PNP (36.4±6.71) compared to the controls (24.5±4.26) (p<0.05), This difference between the controls (24.5±4.26) was not significant when compared to patients with demyelinating PNP (23.2±2.30) (p>0.05). Mean jitter (MCD) value statistically more in individuals with axonal polyneuropathy (36.47±6.7ms) as compared to demyelinating polyneuropathy (23.26±2.31 ms) (P < 0.001). The mean CMAP amplitude and MUNIX values for all parameters were noted in detail (Table 4). A substantially lower MUNIX value was obtained from the axonal polyneuropathy patient group (99.6±12.8) compared to demyelinating polyneuropathic group (149.8±45.7) (P=0.017, P<

Table-1: Comparison of sensory conduction parameters among study groups and subgroups.

Mean±SD	Control	axonal PNP	P-Value	demyelinating PNP	P-Value	Axonal vs demyelinating PNP P-value
Sural latency(ms)	2.7±0.34	3.8±0.33	<0.005	4.0±0.3747	<0.005	>0.05
Sural amplitude(µv)	11.4±3.41	3.7±1.15	<0.005	4.8±0.3796	<0.005	<0.05
Sural velocity(m/s)	52.6±6.78	35.82±2.9	<0.005	35.2±3.05	<0.005	>0.05
Median sensory latency(ms)	2.6±0.24	4.2±=0.8	<0.05	3.7±0.5	<0.05	<0.05
Median sensory Amplitude(µv)	26.2±5.6	11.4±4.8	<0.05	16.1±5.0	<0.05	<0.05
Median sensory Velocity(m/s)	54.4±5.5	34.6±7.9	<0.05	37.9±4.7	<0.05	>0.05
Ulnar sensory latency(ms).	2.3±0.3	3.2±0.5	<0.05	3.1±0.5	<0.05	>0.05
Ulnar sensory amplitude(µv)	25.7±5.2	12.5±5.4	<0.05	15.4±5.0	<0.05	>0.05
Ulnar sensory velocity(m/s)	60.5±7.0	44.2±7.3	<0.05	45.9±7.5	<0.05	>0.05

PNP: Polyneuropathy, SD: Standard deviation.

Table-2: Comparison of lower limb motor nerve conduction results in study groups and subgroups.

Lower/Upper limb motor nerve conduction parameters	Control	axonal PNP	P-Value	demyelinating PNP	P-Value	Axonal vs demyelinating PNP P-value
peroneal distal latency(ms)	3.5±0.7	4.1±0.6	<0.05	4.3±0.7	<0.05	>0.05
peroneal amplitude(mv)	4.5±1.5	2.2±0.7	<0.05	2.9±1.0	<0.05	<0.005
peroneal velocity(m/s)	49.4±5.8	34.5±3.3	<0.05	34.1±3.1	<0.05	>0.05
tibial distal latency(ms)	3.9±0.8	4.7±0.6	<0.05	4.4±0.8	<0.05	>0.05
tibial amplitude(mv)	8.9±2.8	4.6±1.4	<0.05	7.1±2.7	<0.05	<0.005
Tibial velocity(m/s)	49.9±6.0	35.2±4.4	<0.05	34.3±4.2	<0.05	>0.05
tibial F-wave (ms)	45.8±5.6	57.7±4.9	<0.05	62.4±5.4	<0.05	<0.005
median distal latency(ms)	3.4±0.4	4.3±0.7	<0.05	4.4±0.8	<0.05	>0.05
median amplitude(mv)	7.6±1.6	6.4±1.6	<0.05	7.6±2.2	>0.05	<0.05
median velocity(m/s)	57.1±4.9	46.4±4.5	<0.05	48.2±5.6	<0.05	>0.05
ulnar distal latency(ms)	2.6±0.32	3.1±0.37	<0.05	3.1±0.57	<0.05	>0.05
ulnar amplitude(mv)	8.9±1.9	7.0±1.5	<0.05	8.4±1.8	>0.05	<0.05
ulnar velocity(m/s)	60.8±5.3	50.1±7.9	<0.05	48.5±7.7	<0.05	>0.05
ulnar F-wave latency(ms)	25.5±1.1	30.7±4.0	<0.05	30.8±4.6	<0.05	>0.05

PNP: Polyneuropathy, ms: Millisecond, mv: Millivolt, m/s: Meter/second.

Table-3: Comparison of mean potential motor unit findings among study groups and subgroups.

MUAP parameters	Control	axonal PNP	P-Value	demyelinating PNP	P-Value	Axonal vs demyelinating PNP P-value
MUAP-Duration(ms) TA	7.65±1.83	12.68±1.63	<0.05	9.97±1.51	<0.05	<0.005
MUAP-Phases TA	3.08± 0.23	4.0±0.3	<0.05	3.3±0.3	<0.05	<0.005
MUAP-Amplitude-TA-(µv)	777.4 ±188.4	1371.7±193.2	<0.05	1078.1±148.7	<0.05	<0.005
MUAP-Duration(ms) (FDI)	7.24±1.85	11.12±1.97	<0.05	9.2±1.19	<0.05	<0.005
MUAP-Phases (FDI)	3.03±0.1	3.5±0.3	<0.05	3.1±0.2	>0.05	<0.005
MUAP-Amplitude (µv) (FDI)	789.13±175.7	1249.9±236.6	<0.05	1053.14±72.6	<0.05	<0.005

PNP: Polyneuropathy, MUAP: Motor unit action potential, TA: Tibialis anterior, FDI: First dorsal interosseous.

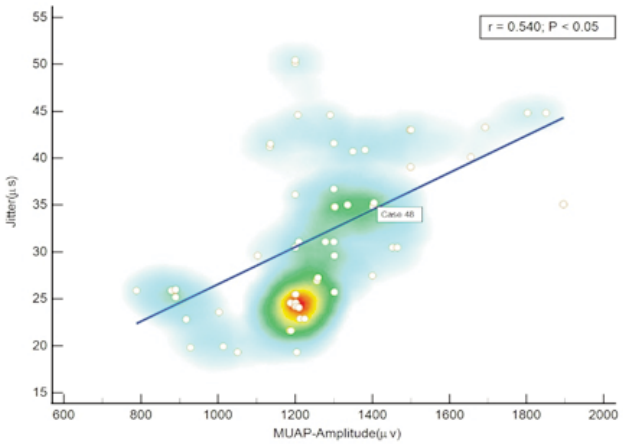

Figure:1 Scatter plot with fitted regression line showing the correlation between mean motor unit action potential (MUAP) amplitude and jitter value in patients with polyneuropathy (PNP)..

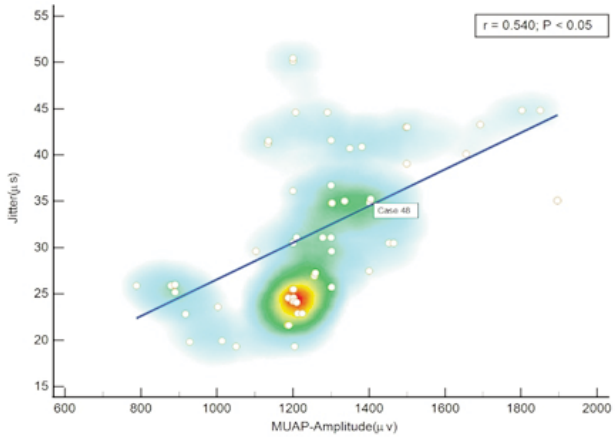

Figure:2 Scatter plot with fitted regression line showing the correlation between mean motor unit action potential (MUAP) duration and jitter value in patients with polyneuropathy (PNP)..

0.05). This difference between controls (175.4±55.04) and patients with demyelinating PNP (149.8±45.7) was not significant (p>0.05).

A significant positive correlation of jitter value was found with MUAP amplitude (r=0.540, p=0.05), and MUAP duration (r=0.442, p=0.05) (Figures 1,2). Although there was no significant link between the duration of the disease and the mean jitter values (r=0.017, p>0.05), a substantial negative link between the jitter value and the peroneal motor nerve CMAP amplitude (r=- 0.282, p=0.05) and conduction velocity (r=0.261, p=0.05) was noted. Additionally, there was a strong positive correlation between the jitter value and the patient's age (r=0.236, p=0.05).

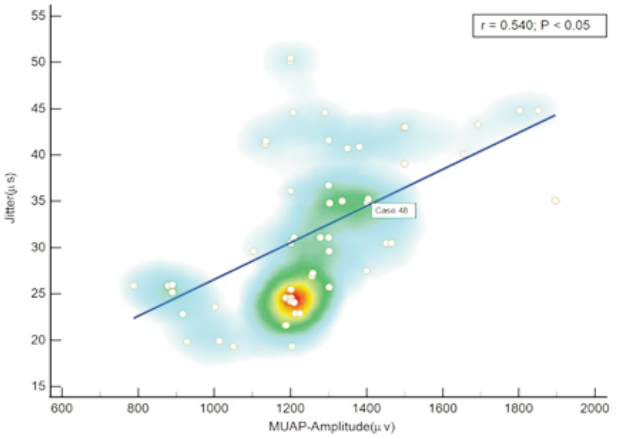

Figure-3: Scatter plot with fitted regression line showing the correlation between motor unit number index (MUNIX) value and ulnar motor compound muscle action potential (CMAP) amplitude in patients with polyneuropathy (PNP).

MUNIX and ulnar CMAP amplitude had a significant positive correlation (r=-0.959, p=0.05) (Figure 3). The jitter value positively correlated with both muscle atrophy and reduced muscle strength (r=0.442, p=0.05). Additionally, there was a positive connection (r=0.603, p=0.05) between the jitter value and muscular weakness. The age of the patient and mean MUNIX values had a significant negative correlation (r=0.640, p=0.05). There was a significant negative association between MUNIX levels and disease duration (r=0.636, p=0.05). MUNIX value and muscular atrophy also showed a significant negative connection (r=- 0.782, p=0.05). Finally, MUNIX had no significant association with decreased muscular strength and weakness (p>0.05).

Discussion

The main reason for the difficulty in distinguishing demyelinating PNP from axonal loss PNP is that conduction slowing "can be caused by secondary loss of fast-conducting, large-diameter fibres in axonal neuropathy, in addition to the involvement of myelin or Schwann cells in demyelinating" neuropathy[4, 19]. Unfortunately, PNP classification is far from consistent [20-22]. The majority of electrophysiological testing techniques for PNP demand testing motor and sensory nerves in two or more limbs[23].

Nerve conduction velocity (motor/sensory) and distal motor latencies (DMLs) are nearly similar in both types of PNP for all the nerves tested in earlier studies. However, for SNAP/CMAP amplitude, the SNAP amplitude was more significantly decreased in axonal compared to demyelinating PNPs in the sural and median nerve segments, while there was no significant difference for

the ulnar sensory nerve. The median nerve showed evidence of demyelination in the majority of the individuals with axonal PNP, but CMAP amplitudes were lower in the same patients[24, 25].

To differentiate between axonal and demyelinating PNPs, however, needle EMG may have limited value. There are very few publications on EMG usage in PNP diagnosis and categorisation, but FPs and positive sharp wave (PSWs) in the muscle were frequently interpreted as signs of axonal PNP, where only 6 (11.9%) patients with axonal PNP had increased insertional activity, and abnormal spontaneous activity of PSWs and FPs, which were taken as signs of active partial denervation and axon loss[4].

The current study provided evidence of neuromuscular remodelling and collateral reinnervation via significantly altered motor unit potential (MUP) morphology in terms of duration and percentage of polyphasic motor units. The cases of PNP appeared to be of the demyelinating pattern, since no denervation had taken place, there was no axonal damage. The finding was supported by the concentric needle EMG's lack of abnormal spontaneous activity and MUAP morphology that was within normal limits.

CNE jitter and MUNIX methods revealed the presence and degree of axonal loss or loss of functioning axons and reinnervation in patients with axonal and demyelinating PNPs to differentiate between the two pathophysiologies as the aetiology of PNP.

A previous study used a single fibre needle to test carpal tunnel syndrome (CTS) using SFEMG stimulated method[26], and it revealed increased jitter of the Abductor Pollicis Brevis (APB) muscle. A SFEMG study in the early stages of Guillian-Barre syndrome (GBS), showed that the patients had elevated jitter of varying degrees. Similarly, 74% of patients with chronic inflammatory demyelinating PNP (CIDP) had minimally abnormal jitter[27]. Another study[28] used SFEMG in PNPs with three distinct aetiologies, diabetes mellitus, uraemic and alcoholic PNP, and found varying degrees of elevated jitter in the subgroups.

The current study found that chronically reinnervated muscles had an increased jitter value. These changes were more pronounced in patients with axonal PNP than in patients with demyelinating PNP, which was shown in a prior study[26] as a sign that there was no motor axon loss in patients with demyelinating PNP. The results in the axonal PNP group of patients are considered evidence of reinnervation following prior denervation[14].

A study on chronic inflammatory demyelinating polyneuropathy (CIDP) patients[26] found decreased MUNIX values as a sign of axonal loss and an increase in average motor unit size index (MUSIX) values as a compensatory mechanism that demyelination caused axonal loss in these patients. This is consistent with the finding that axonal PNP patients had lower MUNIX values as a possible sign of axonal loss or loss of functioning axons and a higher average MUSIX value[26].

The motor unit size of patients with demyelinating PNP was not substantially different compared to the controls, and no potential compensatory reinnervation effects could be found. No reinnervation, as would be anticipated in demyelinating PNP patients, was shown by normal MUNIX and MUSIX.

The current study discovered a positive correlation between MUNIX and the highest CMAP amplitude of the tested nerve in control participants, which was consistent with the inclusion of CMAP amplitude in the MUNIX calculation. In line with a study[29], the current results showed a negative linear relationship between MUSIX and MUNIX in the patient group, which was comparable to previous studies[8, 9]. A negative correlation was also found between MUSIX and MUNIX in the control group, but no correlation of MUNIX with other parameters was discovered in the patient group.

Concentric jitter analysis revealed that PNP had a greater impact on the neuromuscular characteristics of the TA muscle in terms of the degree of MU loss and MU remodelling than the FDI muscle. In the PNP group, there was a strong positive correlation between the number of MUs in TA and FDI muscles, and motor weakness and muscular atrophy.

All axonal-type PNP patients in the current study had SFEMG evidence of reinnervation. Demyelinating PNP patients primarily complained of muscular weakness and diminished muscle power without muscular atrophy. Muscular atrophies, typically mild in the current cases, were common in axonal PNP, as was shown by a significant positive correlation between jitter value and diminished muscle power and muscle atrophy. Additionally, jitter value and muscle weakness have a positive link, and this correlation was also present. A study [30] showed that abnormal jitter values were lower in muscles that had not been denervated than in muscles that had been chronically reinnervated. The jitter value was significantly positively correlated with MUAP amplitude. The previous study[30] found no link between abnormal jitter value and MUAP amplitude, but the current study discovered a link between the two.

In contrast to a study[26], the duration of diseases in PNP patients and MUNIX were found to have a negative relationship in the current study. According to a previous study[29], there is no link between MUNIX and the duration of the disease in CIDP patients, or between MUNEs and the duration of the disease or the severity of the disease. Furthermore, no significant relationship existed between MUNIX and decreased muscular strength or weakness.

The current study has its limitations, including the lack of age adjustment in the correlation analysis. Due to the failure to account for the potential confounding effect of age, the current results may be susceptible to bias. Besides, patients experienced discomfort with the SFEMG needle examination compared to standard NCS and EMG examinations.

Conclusion

SFEMG jitter measurement and MUNIX could help differentiate between the pathophysiology of axonal and demyelinating polyneuropathy.

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Ethical approval: The study was authorized by the local research ethics board of the Director of Duhok Health. Informed verbal permission was acquired from all individuals before testing.

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Conflict of Interest: None.

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TMQ: Conception, design, acquisition, analysis, interpretation of data, drafting, revising it critically, final approval.
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