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Research Article

Gait Assessment in Chronic Inflammatory Demyelinating Polyradiculoneuropathy

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Background and Aims. Gait impairment is a common manifestation of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). However, clinicians lack an effective monitoring tool, as no gait test has been validated for CIDP. The aim of this study was to determine the usefulness of three tests in monitoring the clinical course of patients with CIDP: Timed Up and Go (TUG), 10-Meter Walk Test (10MWT), and 30-Second Chair Stand (30SCS). *Methods*. This is a prospective, single-center observational study. We included newly diagnosed CIDP patients starting treatment or relapsed CIDP patients requiring new treatment. We monitored the clinical course using CIDP-validated clinical scales and correlated changes in clinical status with the results of the gait tests. A ROC curve was developed, and we chose the cut-off point on each scale with the best specificity and sensitivity to detect change in clinical status. *Results*. A total of 20 patients have been recruited. The 3 tests show a statistical correlation with objective clinical improvement. In patients who have showed clinical improvement during the follow-up examination, a mean reduction of 4.8 seconds in TUG and 2.6 in 10MWT and a gain of 3 repetitions in 30SCS have been observed. The optimal cut-off points for each test were TUG ≤ 1 seconds, 10MWT ≤ 1 seconds, and 30SCS ≥ 1 repetition. The TUG test has the highest sensitivity (82.6%), and the 30SCS test has the highest specificity (100%) for detecting clinical improvement. *Conclusions*. The study found that the TUG and 30SCS tests could become effective tools for monitoring treatment response in CIDP patients.

1. Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a clinical entity with considerable phenotypic variability in both onset and course, and the response to treatment is disparate [1, 2]. During treatment, monitoring of the clinical course must be based on objective biomarkers that enable dose adjustment, assessment of treatment withdrawal in the event of a sustained response, and intensification or switching of treatment in the absence of a response [3, 4].

Several useful and widely validated biometric tests have been developed to monitor CIDP. These include disability assessment scales, such as the Inflammatory Neuropathy Cause and Treatment (INCAT) scale [5] and the Inflammatory Rasch-Built Overall Disability Scale (I-RODS) [6], and tools for the assessment of grip strength [7–9] and manual muscle strength according to the Medical Research Council sum score (MRC-SS) [10].

Gait impairment is a common manifestation in CIDP and can become the most disabling factor for patients. Therefore, having validated tools for monitoring gait impairment is

essential. However, we lack an effective measurement tool, as no gait test has been validated for CIDP. The main scales that have been used in clinical trials include Timed Up and Go (TUG) [11], the 10-Meter Walk Test (10MWT) [12], and the Six-Minute Walk Test (6MWT) [13], although none of these tests has been validated. Another objective indirect measure of lower limb strength and stability is the 30-Second Chair Stand (30SCS), which has been shown to be effective in other neurological diseases [14].

We consider the TUG, TMWT, and 30SCS to be easily applicable in clinical practice as they can be performed quickly and reproducible. Additionally, they do not require much space for their execution.

The aim of this study was to determine the usefulness of these 3 tests (TUG, TMWT, and 30SCS) in monitoring the clinical course of patients with CIDP starting immunomodulatory treatment.

2. Materials and Methods

2.1. Design and Study Participants. This is a prospective, single-center observational study, with patient recruitment starting in July 2021 and ending in July 2023.

Inclusion criteria for the study were as follows:

(1) Diagnosed with probable or definite CIDP according to criteria of the European Academy of Neurology/Peripheral Nerve Society (EAN/PNS 2021 criteria) criteria [4]

(2) Induction treatment cohort: newly diagnosed CIDP patients starting treatment or relapsed CIDP patients warranting new treatment (CIDP Disease Activity Status (CDAS) 5)

Exclusion criteria were as follows:

(i) Sensory and focal CIDP variants, due to the difficulty in monitoring response using clinical scales

(ii) Patients not classified as CIDP in the EAN/PNS 2021 guide: autoimmune nodopathies and chronic immune sensory polyradiculopathies (CISP)

Regarding the immunomodulatory treatment, the first-line induction treatment regimen was intravenous immunoglobulin (IVIg) or corticosteroids, depending on the specific clinical features of each patient. The treatment dose regimen is specified in Table 1. Clinical follow-up was performed every 2 months, and clinical improvement was defined as both improvement reported by the patient, with the improvement in one or more clinical scales reaching the minimum clinically important difference (MCID) value. Follow-up was concluded when the patient achieved clinical improvement with normal or stable abnormal examination results for >4 months (CDAS 4 A or B). Refractoriness to treatment was defined as the absence of objective clinical improvement after 4 months. In patients who were refractory to the first-line treatment, a second-line treatment with immunoglobulins or corticosteroids, or vice versa, was given.

The following CIDP-validated clinical scales have been used for clinical monitoring: I-RODS (centile score), INCAT, MRC-SS, and handgrip strength of the right hand (using the Martin vigorimeter). The MCID for each scale is as follows: I-RODS 4 points, INCAT 1 point, MRC-SS 4 points, and handgrip 8 points [3]. Patient evaluations were consistently conducted between the first and third day of IVIg treatment during follow-up visits.

Additionally, the following procedures have been performed at all visits to evaluate gait:

(i) TUG: time taken by the patient to rise from a chair with armrests, walk 3 meters, turn around, walk back to the chair, and sit down

(ii) 10MWT: time taken by the patient to walk 10 meters starting from a standing position

(iii) 30SCS: an alternative test to measure leg strength and stability, consisting of counting how many times the patient can stand up and sit down from a chair with arms crossed in front of the chest in 30 seconds

The gait tests were repeated twice, and an average was obtained. The reproducibility of the different tests was validated before starting the study, confirming inter-rater and inter-rater reliability at different points in time.

For each assessment, the results of the validated CIDP scales (INCAT, IRODS, MRC-SS, and grip strength), the results of the three applied walking tests (TUG, 10MWT, and 30SCS), and the clinical status as improvement yes or no were collected.

Table 1 summarizes the protocol used for the study.

The baseline epidemiological and clinical variables were collected at the time of inclusion in the study.

2.2. Statistical Analysis. The statistical analysis was performed using IBM SPSS Statistics for Windows, version 26.0.

Categorical variables were reported as frequencies (percentages) and continuous variables as mean ± standard deviation (SD) or median (interquartile range (IQR)), as appropriate *QQ*-plots were performed to explore whether quantitative data followed a normal distribution.

To determine which scales were significantly associated with the change of clinical status, general linear models for repeated measurements were performed. In this model, the change in the scales is assessed from visit to visit. The outcome of the visit (clinical status) was defined as improvement yes/no.

The Spearman correlation analysis was applied to examine the correlation between the clinical scales and the gait tests used.

We have chosen the receiver operating characteristic (ROC) curve approach as a previously reported anchor-based approach to assess MCID following ACDF [15]. The concept of MCID, as defined by the ROC curve approach, refers to the change value that optimizes sensitivity and/or specificity for a positive response. It is the value that balances and maximizes both sensitivity and specificity equally. Thus,

Table 1: Study protocol, including the intervention performed, follow-up frequency, and definition of clinical status.

Target patients	Newly diagnosed CIDP patients starting treatment or relapsed CIDP patients warranting new treatment (CDAS 5)
Treatment applied	Induction treatment regimen (i) IVIg 0.4 gr/kg × 5 days every 3 weeks OR (ii) PDN (60 mg for 6 weeks with subsequent) or DXM 40 mg × 4 days every 4 weeks
Clinical control	Every 2 months
Scales	INCAT, IRODs, MRC-SS, grip strength, TUG, 10MWT, 30SCS
Clinical status	Improvement yes = 1 + 2 (1) Improvement reported by the patient (2) Improvement equal to or greater than MCID in ≥1 CIDP scales (I-RODS, INCAT, MRC-SS, grip strength)

IVIg: intravenous immunoglobulins; PDN: prednisone; DXM: dexamethasone; INCAT: Inflammatory Neuropathy Cause and Treatment; I-RODS: Inflammatory Rasch-Built Overall Disability Scale; MRC-SS: manual muscle strength according to the Medical Research Council sum score; TUG: Timed Up and Go; 10MWT: 10-Meter Walk Test; 30SCS: 30-Second Chair Stand; MCID: minimum clinically important difference.

a ROC curve was developed, and we chose the cut-off point on each scale with the best specificity and sensitivity to detect changes in clinical status.

A p value of less than 0.05 was considered statistically significant.

2.3. Standard Protocol Approvals, Registration, and Patient Consents. The study was approved by the bioethics committee of Vall d'Hebron University Hospital (CEIC VHIR PR(AG)429/2021).

All participants included in the study gave their written informed consent after a full explanation of the procedure.

2.4. Data Availability. Anonymized data from this study will be shared at the request of any qualified investigator.

3. Results

3.1. Description of the Sample. A total of 20 patients have been recruited. The median age at onset was 55.9 years (SD ± 13.6), and 75% was male patients. In total, 9 patients had a typical CIDP pattern.

Six patients did not respond to first-line treatment. Second-line treatment was given to 5 of them, 3 of whom responded. A single patient who had received first-line treatment with IVIg did not undergo second-line treatment due to previous intolerance to corticosteroids.

At baseline, gait test results were as follows (median): TUG 11.0 seconds (IQR 12.0), 10MWT 10.0 seconds (IQR 11.5), and 30SCS 5.0 repetitions (IQR 11.0).

16 treatment-naïve patients and 4 who had experienced relapse were included in the study. No statistically significant differences in treatment response or clinical outcomes were observed between the two subgroups at the beginning of the study.

Table 2 summarizes the demographic and clinical characteristics of the sample.

3.2. Usefulness of Gait Test in Clinical Monitoring of CIDP. Table 3 shows the statistical results of the repeated measure test used to analyze the variability of each scale over time, compared to the clinical status at each visit. Additionally, we show the difference between the pre- and postmean for each scale.

It is observed that all 3 tests show a statistical correlation with objective clinical improvement. In patients who have showed clinical improvement during the follow-up examination, a mean reduction of 4.8 seconds in TUG and 2.6 in 10MWT and a gain of 3 repetitions in 30SCS have been observed.

Table 4 shows the diagnostic yield of the three gait tests to detect improvement. To determine the MCID of the three gait tests in our sample of CIDP patients, we performed an ROC curve analysis (Supplementary Figure 1). We therefore defined the optimal cut-off point for each variable: TUG ≤ 1 second, 10MWT ≤ 1 second, and 30SCS ≥ 1 repetition. Subsequently, we defined the sensitivity and specificity for each test based on the cut-off point. We can observe that the TUG test has the highest sensitivity (82.6%) and the 30SCS test has the highest specificity (100%) for detecting clinical improvement. The 10MWT has the lowest sensitivity and specificity of them all.

Considering the subgroup of patients with a baseline TUG score of >15 seconds, for whom a one-second decrease may not be considered clinically significant, a new analysis was performed to assess the degree of improvement. Among patients who showed improvement, a much more notable improvement in TUG was observed (median 9.7 seconds, with a total range of 4 to 32 seconds). The percentage of improvement in TUG was calculated, ranging from 21% to 60% in this subgroup of patients.

A supplementary material (Supplementary Table 1) provides documentation of correlations between gait tests and clinical outcomes. This analysis underscores a statistically significant correlation between the TUG test and the 30SCS test with observed changes in clinical scales (I-RODS, grip strength, and MRC-SS).

4. Discussion

This study is the first to analyze and compare different gait tests used for clinical monitoring of patients with CIDP.

The present study showed that the three tests could become effective tools for assessing gait in CIDP patients, having demonstrated a statistical correlation with clinical improvement. Therefore, these tools on their own can assist

Table 2: Demographic and clinical characteristics of the sample.

Variables	CIDP patients
Age at onset (years) (mean ± SD)	55.9 (13.6)
Sex	
Male, *n* (%)	15 (75)
Female, *n* (%)	5 (5)
EFNS/PNS criteria (2021)	
CIDP, *n* (%)	19 (95)
Possible CIDP, *n* (%)	1 (5)
Clinical form	
Typical CIDP, *n* (%)	9 (45)
Multifocal CIDP, *n* (%)	4 (20)
Distal CIDP, *n* (%)	6 (30)
Sensory predominant CIDP, *n* (%)	1 (5)
Disease duration (years) (mean/IQR)	3.6 (6.7)
Response to first-line treatment	14/20 (70%)
IVIg	12/16 (75%)
Corticosteroids	2/4 (50%)
Response to second-line treatment	3/5 (60%)
IVIg	1/1 (100%)
Corticosteroids	2/4 (50%)
Baseline scales of CIDP	
INCAT total (mean/IQR)	3 (3)
IRODS centile (mean ± SD)	54.4 (16.3)
MRC-SS (mean/IQR)	57 (5)
Grip strength (kPa)—right hand (mean ± SD)	51.5 (28.1)
TUG (sec) (mean/IQR)	11 (12)
10MWT (sec) (mean/IQR)	10 (11.5)
30SCS (rep) (mean/IQR)	5 (11)

IVIg: intravenous immunoglobulins; INCAT: Inflammatory Neuropathy Cause and Treatment; I-RODS: Inflammatory Rasch-Built Overall Disability Scale; MRC-SS: manual muscle strength according to the Medical Research Council sum score; TUG: Timed Up and Go; 10MWT: 10-Meter Walk Test; 30SCS: 30-Second Chair Stand; sec: seconds; rep: repetitions.

Table 3: Variability of each scale over time (mean and standard error) differentiating for clinical status. Correlation (*p* value) between variability of each scales and clinical status using the intrasubject repeated measurement statistical method.

	Clinical improvement		*p* value
	No	Yes	
TUG (sec)	+1.5 (2.2)	-4.8 (7.3)	0.025
10MWT (sec)	+1.1 (3)	-2.6 (4.5)	0.039
30SCS (rep)	-1 (1.3)	+2.5 (2.8)	0.002

TUG: Timed Up and Go; 10MWT: 10-Meter Walk Test; 30SCS: 30-Second Chair Stand; sec: seconds; rep: repetitions.

neurologists in monitoring patients with CIDP, as they provide an objective and easily reproducible measure.

Additionally, using cut-off points of -1 seconds for the TUG and +1 repetition for the 30SCS test, we achieved a high diagnostic sensitivity and specificity for determining clinical improvement. Although 1 second may not seem clinically significant, there are two key factors to consider in understanding this value. Firstly, in less severe patients, we start from a baseline of 5-7 seconds as a result of the tests; and in these cases, an improvement of 1 second can represent a 20% improvement. Furthermore, it must be taken into account that patients who have not shown objective clinical improvement after the treatment have generally worsened their scores in gait tests. Therefore, even if the improvement is minimal, it indicates a progressive recovery. Moreover, patients exhibiting severely impaired baseline Timed Up and Go (TUG) test scores (>15 seconds) experienced notably larger improvements across all cases, with a minimum reduction of 4 seconds, equating to a 21% enhancement.

Table 4: Analysis of the sensitivity and specificity of the 3 tests studied in the CIDP-N patient group.

	Cut-off point	Sensitivity	Specificity
TUG	≤1 seconds	82.6%	87.5%
10MWT	≤1 seconds	52.2%	62.5%
30SCS	≥1 repetition	78.3%	100%

CIDP-N: CIDP-naïve; TUG: Timed Up and Go; 10MWT: 10-Meter Walk Test; 30SCS: 30-Second Chair Stand.

Regarding the TUG test and 10MWT, we consider that TUG test has been more sensitive and specific than the 10MWT as it evaluates the entirety of deficits given that it involves different actions such as standing up/sitting down on the chair, walking, and turning; and in CIDP, there may be a multifactorial cause of gait impairment. Additionally, we consider that the 30SCS has been sensitive and specific due to its easy reproducibility, and as it deals with absolute values, it is easier to monitor.

One of the main limitations of our study is the small sample size. As CIDP is a rare entity, conducting larger single-center studies is challenging. However, considering the limited sample size of our study, it is imperative to validate the findings in a larger multicenter cohort.

The study excluded sensory CIDP due to challenges in monitoring clinical improvement using validated scales, thus acknowledging the limitation of not including this patient subgroup. However, cases with sensory predominant and distal CIDP were included in the study, as it was believed that despite their milder motor symptoms, abnormalities in the strength tests utilized could still be detected at their onset.

5. Conclusions

In conclusion, we consider both TUG and 30SCS to be useful new tools for monitoring treatment response in CIDP patients. Since it is easy to use them in clinical practice, we would recommend their routine use in neuromuscular clinics.

Data Availability

Anonymized data from this study will be shared at the request of any qualified investigator.

Ethical Approval

We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Conflicts of Interest

None of the authors has any conflict of interest to disclose.

Supplementary Materials

Supplementary 1. Supplementary Table 1: correlation between changes in gait test and clinical outcomes: results expressed in correlation coefficients (p values).

Supplementary 2. Supplementary Figure 1: ROC curves of the 3 gait tests. ROC: receiver operating characteristic; AUC: area under the curve; CI: confidence interval.

References

[1] C. Bunschoten, B. C. Jacobs, P. Y. K. Van den Bergh, D. R. Cornblath, and P. A. van Doorn, "Progress in diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy," *The Lancet Neurology*, vol. 18, no. 8, pp. 784–794, 2019.

[2] H. C. Lehmann, D. Burke, and S. Kuwabara, "Chronic inflammatory demyelinating polyneuropathy: update on diagnosis, immunopathogenesis and treatment," *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 90, no. 9, pp. 981–987, 2019.

[3] J. A. Allen, F. Eftimov, and L. Querol, "Outcome measures and biomarkers in chronic inflammatory demyelinating polyradiculoneuropathy: from research to clinical practice," *Expert Review of Neurotherapeutics*, vol. 21, no. 7, pp. 805–816, 2021.

[4] P. Y. K. Van den Bergh, P. A. van Doorn, R. D. M. Hadden et al., "European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force-second revision," *European Journal of Neurology*, vol. 28, no. 11, pp. 3556–3583, 2021.

[5] R. Hughes, S. Bensa, H. Willison et al., "Randomized controlled trial of intravenous immunoglobulin versus oral prednisolone in chronic inflammatory demyelinating polyradiculoneuropathy," *Annals of Neurology*, vol. 50, no. 2, pp. 195–201, 2001.

[6] S. I. NesVan, E. K. Vanhoutte, P. A. Van Doorn et al., "Rasch-built overall disability scale (R-ODS) for immune-mediated peripheral neuropathies," *Neurology*, vol. 76, no. 4, pp. 337–345, 2011.

[7] T. H. P. Draak, M. H. J. Pruppers, S. I. van Nes et al., "Grip strength comparison in immune-mediated neuropathies: Vigorimeter vs. Jamar," *Journal of the Peripheral Nervous System*, vol. 20, no. 3, pp. 269–276, 2015.

[8] V. Mathiowetz, "Comparison of Rolyan and Jamar dynamometers for measuring grip strength," *Occupational Therapy International*, vol. 9, no. 3, pp. 201–209, 2002.

[9] E. K. Vanhoutte, N. Latov, C. Deng et al., "Vigorimeter grip strength in CIDP: a responsive tool that rapidly measures the effect of IVIG–the ICE study," *European Journal of Neurology*, vol. 20, no. 5, pp. 748–755, 2013.

[10] E. K. Vanhoutte, C. G. Faber, S. I. van Nes et al., "Modifying the Medical Research Council grading system through Rasch analyses," *Brain*, vol. 135, no. 5, pp. 1639–1649, 2012.

[11] D. Podsiadlo and S. Richardson, "The timed 'up & go': A test of basic functional mobility for frail elderly persons," *Journal of the American Geriatrics Society*, vol. 39, no. 2, pp. 142–148, 1991.

[12] R. W. Bohannon, "Comfortable and maximum walking speed of adults aged 20-79 years: reference values and determinants," *Age and Ageing*, vol. 26, no. 1, pp. 15–19, 1997.

[13] P. Agarwala and S. H. Salzman, "Six-minute walk test: clinical role, technique, coding, and reimbursement," *Chest*, vol. 157, no. 3, pp. 603–611, 2020.

[14] E. Westerberg, C. J. Molin, S. Spörndly Nees, J. Widenfalk, and A. R. Punga, "The impact of physical exercise on neuromuscular function in myasthenia gravis patients," *Medicine*, vol. 97, no. 31, p. e11510, 2018.

[15] A. G. Copay, B. R. Subach, S. D. Glassman, D. W. Polly Jr., and T. C. Schuler, "Understanding the minimum clinically important difference: a review of concepts and methods," *The Spine Journal*, vol. 7, no. 5, pp. 541–546, 2007.