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Validity and Responsiveness of Balance Measurements Using Posturography in Patients With Immune-Mediated Neuropathies

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Keywords: balance | CIDP | IgM-related polyneuropathy | posturography | responsiveness | validity

ABSTRACT

Background and Aims: Validated objective measures for balance in immune mediated neuropathies are lacking. In this study, we investigated the clinimetric properties of posturography using a force platform, a quantitative assessment of postural control.

Methods: We assessed patients with chronic inflammatory demyelinating polyneuropathy (CIDP) and IgM-related polyneuropathy (IgM-PNP) using sway parameters (path, area and amplitude) measured at multiple time points. Validity was investigated by assessing differences in sway path between patients with and without reported balance symptoms and by assessing correlations of sway path with (established) impairment measures related to balance, disability and quality of life (QoL). Responsiveness was assessed by means of an anchor-based approach, using a patient anchor and two disability scales.

Results: We included 52 CIDP and 13 IgM-PNP patients. In CIDP, sway path was 25% longer in patients reporting balance symptoms relative to patients without balance symptoms ($p = 0.03$). There was excellent reliability between consecutive measurements in both CIDP and IgM-PNP. Moderate to good correlations were observed between sway path and an ataxia scale (CIDP: Spearman's $\rho = 0.46$, 95% CI: 0.2–0.69; IgM-PNP: Spearman's $\rho = 0.72$, 95% CI: 0.28–0.96) while correlations with related disability measures and QoL were poor. Changes in sway parameters over time were not consistently associated with changes in other outcome measures.

Interpretation: Posturography measurements showed poor validity and responsiveness. Therefore, despite excellent reliability, using a force platform in clinical practice or trials for immune-mediated neuropathies cannot be recommended.

Milou R. Michael and Robin van Veen contributed equally to this article.

1 | Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) and IgM-related polyneuropathy are immune-mediated neuropathies with different aetiologies and clinical manifestations. Both neuropathies share that balance disturbances during stance and gait can be a substantial cause for disability [1, 2] and can lead to an increased risk of falling. In a study on symptom burden in CIDP, around 90% of patients reported having experienced disturbances in balance, and loss of balance was the symptom that was most bothersome to patients [3]. Moreover, gait performance has been shown to correlate to quality of life in patients with CIDP [4]. Hypotheses concerning the determinants of balance impairment involve deficits in somatosensory function, leading to increased postural sway and decreased ability to elicit corrective responses, weakness of ankle and hip muscles and/or disturbed coordination of the lower extremities [5–7].

Although balance during stance and/or gait is commonly affected in CIDP and IgM-related polyneuropathy, no outcome measures specific for balance have been clinimetrically evaluated. Currently, clinical assessment in CIDP relies on a combination of outcome measures, such as the Inflammatory Neuropathy Cause and Treatment Disability Scale (INCAT-DS) and the Inflammatory Rasch-Built Overall Disability Scale (I-RODS) [8–10], focusing on disability, and impairment measures including grip strength measurement and the Medical Research Council sum score (MRC-SS) for muscle strength [11–13]. The timed up and go (TUG) test is potentially valuable in gait assessment, but its validity and sensitivity to change in CIDP are unknown [14]. Consensus on outcome measures for IgM-related polyneuropathy is lacking. A recent study proposed posturography, using a force platform that measures postural sway, represented by excursions of the centre of pressure (CoP) over a support base, as a sensitive and objective measure of imbalance in patients with typical CIDP treated with intravenous immunoglobulins (IVIg) [15]. This study was limited by a short follow-up and did not include other treatment modalities, CIDP variants, different disease activity stages or other inflammatory neuropathies.

In this study, we investigated clinimetric aspects and focused on the validity and responsiveness of posturography by means of a force platform as a measure for balance in a diverse group of patients with CIDP and patients with IgM-related polyneuropathy.

2 | Materials and Methods

2.1 | Study Population

We recruited patients with CIDP and patients with IgM-related polyneuropathy as part of an ongoing prospective cohort study. Written informed consent was obtained from all participants prior to the study, and the study was approved by the local Medical Ethical Committee (METC 2019_105). Patients with CIDP were diagnosed according to the EFNS/PNS 2010 guidelines [16] and were eligible for inclusion if they fulfilled definite, probable or possible criteria and had either (1) active disease (defined as history of progression justifying start or change of treatment as determined by treating physician, group 1), or (2) stable disease after at least 3 months of treatment with IVIg and/or corticosteroids, starting treatment withdrawal or tapering (group 2). For participants with active disease at baseline (group 1), follow-up could be extended when treatment was tapered or discontinued after (maximal) improvement was reached (cross-over from group 1 to group 2). According to local protocol, first-line treatment consisted of IVIg, corticosteroids or a combination of both, mainly as participants in a double-blind randomized controlled trial comparing IVIg monotherapy to combination treatment with IVIg and corticosteroids [17].

Patients with IgM-related polyneuropathy were diagnosed by their treating physician based on the presence of monoclonal IgM in combination with either anti-MAG antibodies and/or a typical phenotype according to 2010 EFNS/PNS guidelines for paraproteinemic neuropathies [18].

Patients were included in the present study if they were able to complete a posturography measurement at least once, regardless of treatment status. Patients were excluded if they were unable to stand unsupported for the entire duration of follow-up, or if it was likely that balance problems were caused by another aetiology than the polyneuropathy.

2.2 | Follow-Up and Classification of Visits Based on Disease Activity

Patient demographics and treatment characteristics were collected at baseline. Patients with CIDP were evaluated at intervals of 6 or 12 weeks, and patients with IgM polyneuropathy were evaluated every 12 weeks. The latter was based on the generally accepted indolent course of the disease. Total follow-up duration was either 24 weeks for each group or 52 weeks in case of cross-over from group 1 to group 2. Additional visits were planned in case of patient-reported deterioration.

We classified each visit in three categories based on treatment changes due to disease activity (i.e., start of treatment, increase of treatment, switch of treatment or treatment added). The first category consisted of visits with 'active disease', that is, a treatment change was made during this visit due to progression of symptoms, impairment and/or functional deficits. The second category ('recent active disease') consisted of visits within 18 weeks following visits with 'active disease'. The third category consisted of visits with 'stable disease', that is, no changes were made in the 18 weeks prior to that specific visit.

2.3 | Posturography Measurements

Posturography measurements were performed using a Kistler force plate 9260AA (Kistler Group, Winterthur, Switzerland) and Kistler's Measurement, Analysis and Reporting Software (MARS v3.0.3.73). All patients were instructed to stand barefoot on the platform in four different conditions: feet apart, eyes open (FAEO), feet apart, eyes closed (FAEC), feet together, eyes open (FTEO) and feet together, eyes closed (FTEC), in a quiet stance

with the arms hanging passively alongside the body. Each condition was measured consecutively in the order described above and for a duration of 20 s. This cycle was repeated once without a resting phase. Recordings were made of postural sway parameters: total sway path (total trajectory travelled by center of pressure, CoP, in millimetres), total sway area (the area swept by the CoP trajectory relative to central point, in mm^2) and total sway amplitude (combined variable consisting of the CoP trajectory in the anteroposterior and mediolateral direction divided by the number of directional changes, in millimetres) (Figure S1). If patients were unable to perform a specific stance condition without support or at all, the measurement was not used for analysis. Two consecutive measurements were attempted for all visits. For patients with two successful measurements during a single visit, the mean for each stance condition was calculated for each parameter and used for analyses to reduce measurement error. For patients with only one successful measurement, this measurement was used for the analyses.

2.4 | Outcome Measures

The following outcome measures were recorded at each visit: the MRC-SS (range 0–60) [13], the Modified Inflammatory Neuropathy Cause and Treatment Sensory Score (mISS, range 0–33) [19, 20], the TUG (in seconds), the Inflammatory INCAT-DS (range 0–10) and an ataxia sum score (ataxia-SS, range 0–94) created for the IMAGiNe study [21], based on items originating from the Modified International Cooperative Ataxia Rating Scale (MICARS) and the Scale for the Assessment and Rating of Ataxia (SARA) [22, 23]. This is a preliminary ordinal scale and will be transformed into a linear scale using Rasch analyses in the context of the IMAGiNe study. In addition, we collected patient-reported outcome measures, including the I-RODS (range 0–100 centiles), EuroQol 5D thermometer (EQ-5D, range 0–100) for quality of life [24], patient global impression of change (PGIC, Likert scale ranging from 1 [very much improved] to 7 [very much deteriorated] compared to the start of the study and to the previous assessment), the 'current pain' item of the Pain Intensity Numeric Rating Scale (PI-NRS, range 0–10) [25], the Rasch Fatigue Severity Scale (R-FSS, range 0–21) [26] and the Hospital Anxiety and Depression Scale (HADS, total score consisting of a summation of the subscales for anxiety and depression, ranging from 0 to 42) [27]. Additionally, patients were asked to report on the presence of balance symptoms (yes or no).

2.5 | Outcomes

In addition to commonly used outcome scores based on abovementioned outcome measures, we created separate lower extremity scores for the MRC, mISS and INCAT-DS (i.e., MRC-SS-LE ranging from 0 to 30, mISS-LE ranging from 0 to 16 and INCAT-DS-LE ranging from 0 to 5), as balance is likely largely related to impairment and disability in the legs and not the arms. We also specifically focused on the ataxia-SS item reflecting gait (item 1) and created a composite ataxia score reflecting stance by summing the scores from ataxia-SS items 2–5 (standing capacities with eyes open; spread of feet in natural position without support, eyes open; body sway with feet together and eyes open; body sway with feet together and eyes closed).

We used sway path as the primary outcome as this is the most used variable in literature and the most feasible stance for patients yielding the most data points. Other posturography parameters were used as secondary outcomes for validity analyses. For responsiveness analyses, we used the two parameter/stance combinations that met the highest number of hypotheses for feasibility and validity combined (see below, hypotheses of clinimetric properties).

2.6 | Hypotheses of Clinimetric Properties

To investigate clinimetric properties of sway parameters, we first developed a conceptual framework for the construct of balance in immune-mediated neuropathies and the underlying expected associations between gait, stance, impairment measures, disability and quality of life and their corresponding scores (Figure 1). We defined hypotheses regarding the feasibility, reliability, validity and responsiveness of the posturography measurements based on the best available evidence (Table S1). We considered the clinimetric quality sufficient when the measurement was feasible, reliable and at least 7/11 validity and 6/9 responsiveness hypotheses were satisfied. We chose a somewhat less strict cutoff for our hypotheses of sufficient quality compared to the 75% recommended in the literature [28] because our hypotheses were based on relatively low-quality evidence.

2.7 | Analyses

Statistical analyses were performed using R Statistical Software version 4.3.1 [29]. Patients with CIDP and IgM-related polyneuropathy were analysed separately, as we hypothesized that the strength of the correlations of impairment measures and balance might differ based on different polyneuropathy phenotypes (e.g., IgM-related polyneuropathy typically presents with predominantly sensory symptoms, and with less pronounced motor deficits [30]). We compared demographics and distributions of outcome measure scores, including posturography parameters (sway path, sway area and sway amplitude) between patients with CIDP and IgM-related polyneuropathy. Associations between two ordinal variables, or one continuous and one ordinal variable, were tested using Spearman's Rank correlations. Also, we used Spearman's Rank correlations (instead of Pearson correlation coefficient) for associations between two continuous variables based on the (nonnormal) distribution and outliers. Associations between one continuous variable and a binary or categorical variable were tested using Mann–Whitney U or Kruskal–Wallis tests as appropriate. We did not remove outliers from the primary dataset in order to capture the broadest spectrum of balance impairment in our data. Due to the exploratory nature of this study, we did not correct for multiple comparisons.

2.7.1 | Feasibility

Feasibility of measurements was assessed by recording the ability to adequately perform the four stance conditions (FAEO,

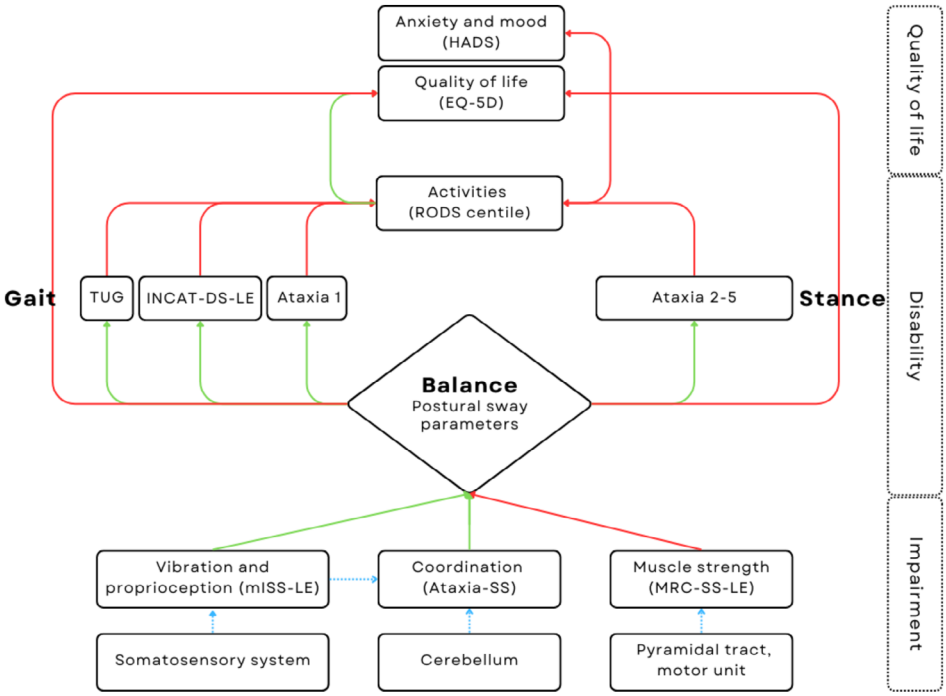

FIGURE 1 | Conceptual framework for the construct of balance in patients with CIDP and IgM-related polyneuropathy. Expected positive correlations between scores are represented by green arrows, expected negative correlations between scores are represented by red arrows. Ataxia 1 reflects an item assessing gait. Ataxia 2–5 reflects items assessing stance. Ataxia SS, ataxia sum score; CIDP, chronic inflammatory demyelinating polyneuropathy; EQ-5D, EuroQol 5D, quality of life; HADS, Hospital Anxiety and Depression Scale; INCAT-DS-LE, Inflammatory Neuropathy Cause and Treatment Disability Score, lower extremities; mISS-LE, modified Inflammatory Neuropathy Cause and Treatment Sensory Score, lower extremities; MRC-SS-LE, Medical Research Council sum score, lower extremities; RODS, Rasch-built overall disability scale; TUG, timed up and go.

FAEC, FTEO and FTEC) for all patients for all available visits with posturography measurements.

2.7.2 | Reliability

To assess test–retest reliability, we used two consecutive measurements performed on the first visit for CIDP and IgM-related polyneuropathy separately. We then employed a two-way mixed effects model for calculation of the intraclass correlation coefficient for agreement ($ICC_{agreement}$).

2.7.3 | Validity

We used multiple approaches to investigate validity. First, we assessed the effect of the presence of patient-reported balance symptoms (yes or no) during any visit on posturography parameters using mixed effects modelling (nlme package) [31]. Second, using the first visit of all patients, we assessed correlations of posturography parameters with other outcome measures (I-RODS, MRC-SS and MRC-SS-LE, INCAT-DS and INCAT-DS-LE, mISS and mISS-LE, ataxia scores [ataxia-SS, ataxia score for stance and ataxia gait item], TUG, EQ-5D, HADS, R-FSS and PI-NRS). As subgroup analysis (only conducted for our primary outcome), we examined correlations during visits of CIDP patients with either active or stable disease (allowing only the first visit labelled as such) separately. Visits with 'recent active disease' were not used to assess validity because we expected those to be heterogenous with regard to disease activity. We obtained 95% confidence intervals for the correlation coefficients by means of bootstrapping (R package RVAideMemoire) [32].

2.7.4 | Responsiveness

For responsiveness, only CIDP patients were analyzed, as IgM polyneuropathy patients were expected to remain stable during follow-up. All patients with two or more visits with posturography measurements were selected. Because there is no consensus on the best method to assess responsiveness, we used multiple approaches. We used an anchor-based method for relevant improvement or deterioration as our main responsiveness analysis.

For each patient, change scores between pairs of subsequent visits were calculated for the posturography parameter, the I-RODS, and INCAT-DS-LE. Because a gold standard for change in balance is lacking, we used three outcome measures as anchors: one patient anchor, the PGIC, and two disability anchors: the I-RODS and INCAT-DS-LE. Cut-offs for relevant improvement and deterioration can be found in the Supporting Information Methods S1. We employed mixed effects modelling (nlme package) to assess the relation between improvement or deterioration on these outcome measures and changes in posturography parameters, using 'stable' as a reference category. We performed additional responsiveness analyses using correlations between change scores of posturography parameters and other outcome measures, the

TABLE 1 | Demographics at first visit.

	CIDP ($n=52$)	IgM-PNP ($n=13$)
Age, median (IQR)	62.5 (53.0, 69.0)	70.0 (63.0, 73.0)
Gender: male (*n*, %)	39 (75.0%)	7 (53.8%)
Disease activity classification (*n*, %)	17 (32.7%)	NA
– Active disease	11 (21.2%)	
– Recent active disease	24 (46.2%)	
– Stable disease		
CIDP subtype (*n*, %)	34 (65.4%)	NA
– Typical	12 (23.1%)	
– Multifocal	3 (5.8%)	
– Distal	3 (5.8%)	
– Motor predominant		
Disease duration (*n*, %)	26 (50.0%)	7 (53.8%)
– < 1 year	15 (28.8%)	5 (38.5%)
– 1–5 years	11 (21.2%)	1 (7.7%)
– > 5 years		
Currently treated (*n*, %)	32 (61.5%)	2 (15.4%)
– Immunoglobulins	24 (46.2%)	0 (0%)
– IVIg + corticosteroids	6 (11.5%)	0 (0%)
– Rituximab	1 (1.9%)	2 (15.4%)
– Dexamethasone + mycophenolate mofetil	1 (1.9%)	0 (0%)
PROMS, median (IQR)	65 (51, 80)[b]	67 (53, 75)[b]
– EQ-5D thermometer	9 (3, 15)[c]	11 (6, 14)
– HADS	1 (0, 4)[a]	1 (0, 4)[a]
– PI-NRS (current)	13 (7, 19)[c]	17 (10, 20)[b]
– R-FSS		

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; EQ-5D, EuroQol 5D thermometer; HADS, hospital anxiety and depression scale; IgM-PNP, IgM-related polyneuropathy; IVIg, intravenous immunoglobulins; PI-NRS, Pain Intensity Numeric Rating Scale; PROMS, Patient Reported Outcome Measures; R-FSS, Rasch Fatigue Severity Scale.
[a]1 missing.
[b]2 missing.
[c]3 missing.

detailed methods of which can be found in the Supporting Information Methods S1.

3 | Results

Posturography measurements were available for a total of 67 patients (54 patients with CIDP and 13 patients with IgM-related polyneuropathy). Two CIDP patients were excluded from the study: one patient with Parkinson's disease as balance impairment could not with certainty be attributed to polyneuropathy; and one patient with severe tremor, which introduced measurement artifacts. Both conditions led to extreme outliers. Demographics are displayed in Table 1. For 54 patients, two or more visits with measurements were performed during follow-up (41 patients with CIDP and 13 patients with IgM-related polyneuropathy). In total, 154 visits with posturography measurements were available (CIDP $n=127$ and IgM $n=27$).

Postural sway parameters did not differ between patients with CIDP and IgM-related polyneuropathy on the first visit (data not shown). Distributions of disability and impairment measure scores at the first visit are depicted in Figure 2. In CIDP, several parameters differed between males and females (sway path and area in the FTEO and FTEC stance conditions). There were no relevant correlations (defined as $\rho > 0.4$) between postural sway parameters and age (all patients) and no differences between CIDP variants, although these groups were small (data not shown).

3.1 | Feasibility

Feasibility differed widely between the different stance conditions, and for active compared to stable disease, with the FAEO being the only stance condition that every patient was able to perform (Table 2).

3.2 | Reliability

The ICC agreement for sway path in the FAEO stance condition tested was 0.91 (95% CI 0.57–1.75) in CIDP and 0.94 (95% CI 0.31–3.15) in IgM-related polyneuropathy, indicating excellent reliability. The ICC values for all sway parameters are presented in Table S2.

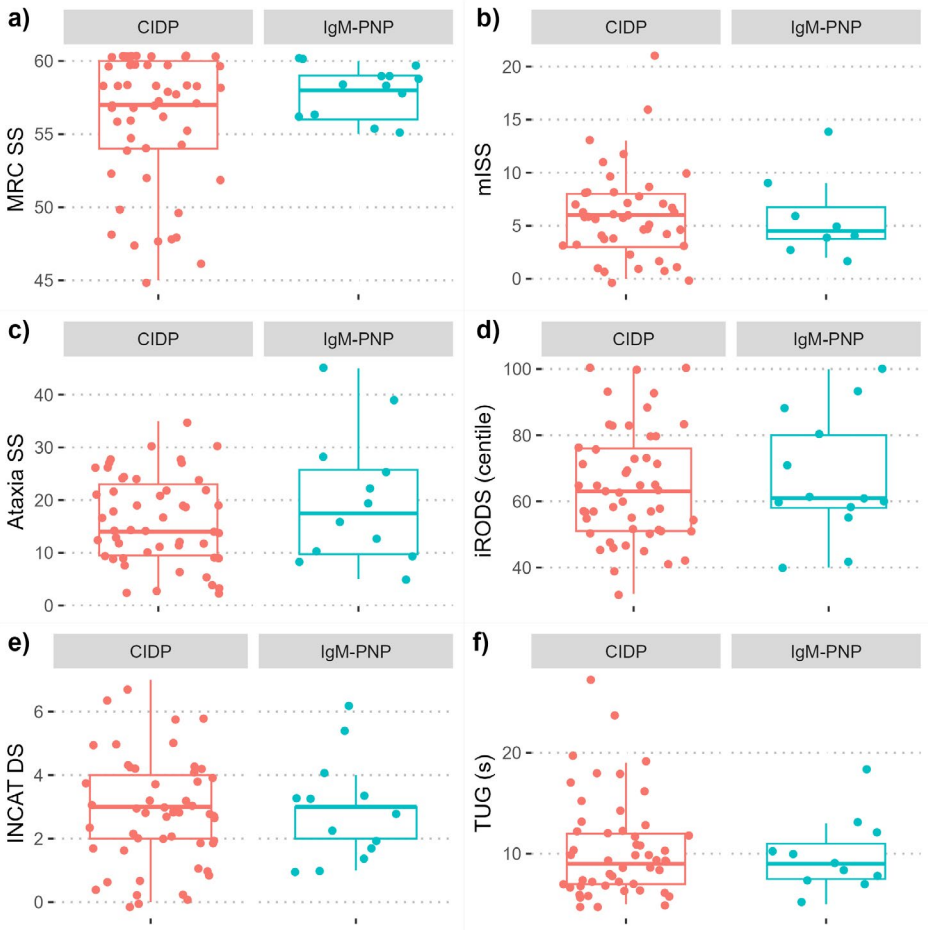

FIGURE 2 | Distributions of disability and impairment measure scores. Disability and impairment scores in patients with CIDP and patients with IgM-related polyneuropathy at first visit. Higher scores on the mISS, ataxia SS, INCAT-DS and TUG indicate more severe impairment/disability. Lower scores on the MRC-SS indicate more severe disability/impairment. Ataxia SS, ataxia sum score; CIDP, chronic inflammatory demyelinating polyneuropathy; IgM-PNP, IgM-related polyneuropathy; INCAT-DS, Inflammatory Neuropathy Cause and Treatment Disability Score; I-RODS, inflammatory Rasch-built overall disability scale; mISS-LE, modified Inflammatory Neuropathy Cause and Treatment Sensory Score; MRC-SS, Medical Research Council sum score; TUG, timed up and go.

TABLE 2 | Feasibility of measurements. Ability to stand unassisted in all four stance conditions at first measurement attempt, allowing multiple visits per patient per category.

	CIDP 127 visits of 52 patients			
Able to stand unassisted	**Active disease 29 visits of 25 patients**	**Recent active disease 36 visits of 28 patients**	**Stable disease 62 visits of 36 patients**	**IgM-PNP27 visits of 13 patients**
In all conditions (once)	62% (18/29)	81% (29/36)	87% (54/62)	69% (18/27)
In stance condition				
Feet apart eyes open (FAEO)	100% (29/29)	100% (36/36)	100% (62/62)	100% (27/27)
Feet apart eyes closed (FAEC)	83% (24/29)	94% (34/36)	100% (62/62)	85% (23/27)
Feet together eyes open (FTEO)	97% (28/29)	94% (34/36)	100% (62/62)	96% (26/27)
Feet together eyes closed (FTEC)	62% (18/29)	81% (29/36)	87% (54/62)	67% (18/27)

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; IgM-PNP, IgM-related polyneuropathy.

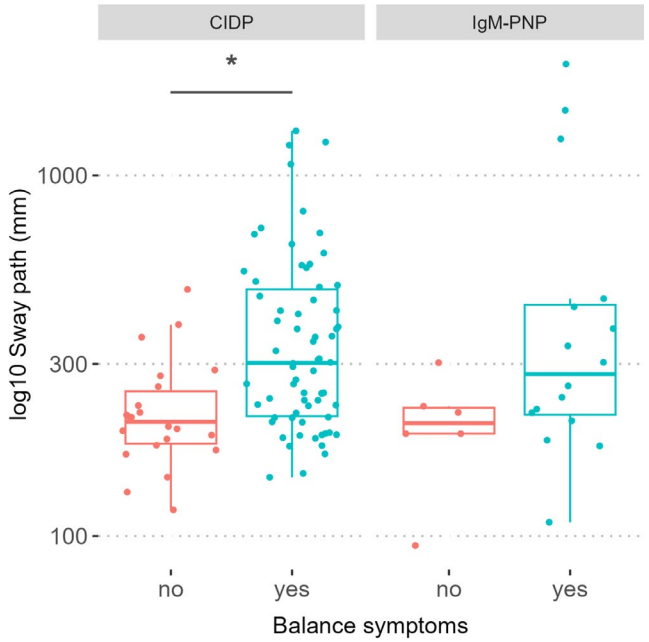

FIGURE 3 | Sway path differences between patients with and without balance symptoms Log10 Sway path (mm) in the FAEO stance condition for patients with and without self-reported balance symptoms, CIDP and IgM-related polyneuropathy separately. Sway path is the total trajectory travelled by the CoP in millimetres, with increased sway path suggesting increased balance impairment. CIDP, chronic inflammatory demyelinating polyneuropathy; CoP, center of pressure; FAEO, feet apart eyes open; IgM-PNP, IgM-related polyneuropathy.

3.3 | Validity

3.3.1 | Patients With CIDP

Posturography measurements were obtained from 52 patients with CIDP across 127 visits. For 40 patients and 88 of these visits, information about the presence of balance symptoms was recorded (balance symptoms: $n=66$, no balance symptoms: $n=22$). Patients reporting balance symptoms demonstrated a longer sway path (FAEO condition, 25% longer, $p=0.03$, Figure 3), which was even more pronounced when visual cues were removed (FAEC condition, 64% longer, $p<0.001$). Other posturography parameters also differed between patients with and without balance symptoms, except sway amplitude and area in the EO conditions (Table S3). Including gender as a covariate in our models did not significantly alter the results (data not shown).

The results of correlations of sway path in FAEO stance condition with scores of other outcome measures in patients with CIDP can be found in Figure 4a. Overall, the direction of all correlations was in line with our conceptual framework (Figure 1). However, correlations with the MRC-SS-LE (ρ: −0.34; 95% CI: −0.59 to −0.05), the INCAT-DS-LE (ρ: 0.33; 95% CI: 0.07–0.57) and the TUG (ρ: 0.33; 95% CI: 0.05–0.59) were insufficient to confirm our hypotheses. Sway path FAEO correlations with all ataxia measures: that is, the ataxia item for gait (ρ: 0.41; 95% CI: 0.11–0.65), the ataxia score for stance (ρ: 0.7; 95% CI: 0.51–0.83) and the ataxia-SS (ρ: 0.46; 95% CI: 0.2–0.69) did meet

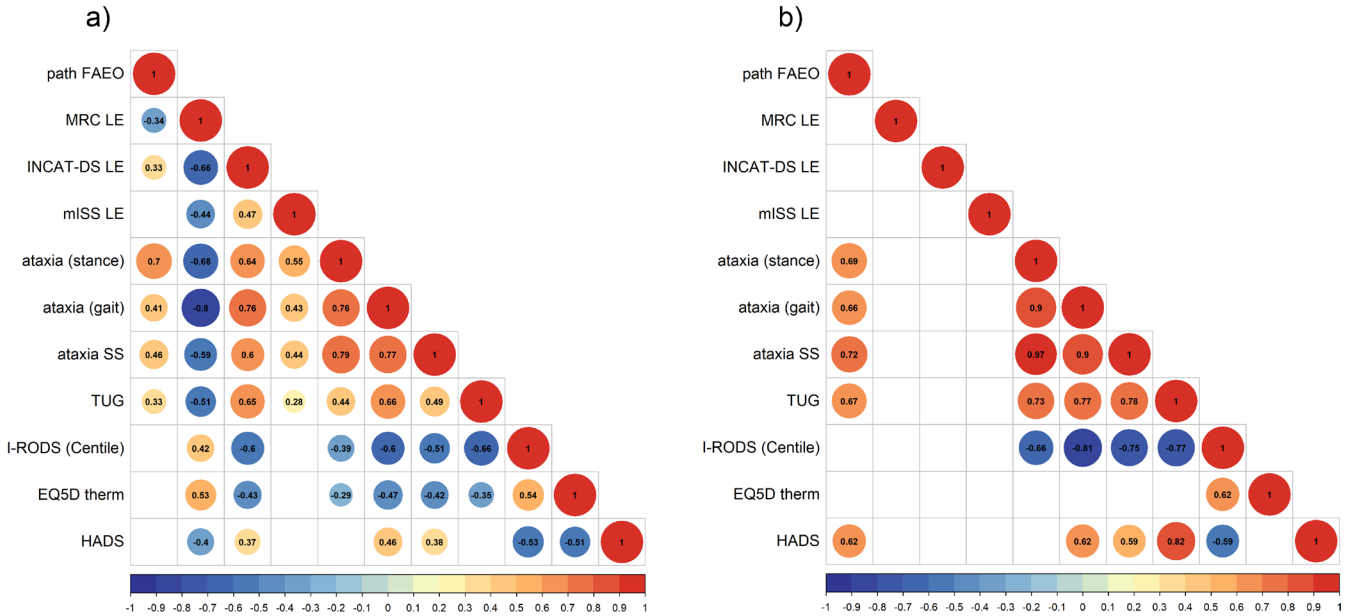

FIGURE 4 | Sway path correlations with other outcome measures. (a) Correlations of sway path in the FAEO stance condition with other outcome measures, for patients with CIDP. (b) Correlations of sway path in the FAEO stance condition with other outcome measures, for patients with IgM-related polyneuropathy. The first column represents correlations of sway path FAEO with other outcome measures, for example, in CIDP, sway path FAEO showed correlation of −0.34 with MRC-LE. Only correlations with 95% confidence interval excluding 0 are shown. Ataxia SS, ataxia sum score; CIDP, chronic inflammatory demyelinating polyneuropathy; EQ-5D, EuroQol 5D thermometer of quality of life; FAEO, feet apart eyes open; HADS, Hospital Anxiety and Depression Scale; I-RODS, inflammatory Rasch-built overall disability scale; INCAT-DS-LE, Inflammatory Neuropathy Cause and Treatment Disability Score, lower extremities; mISS LE, modified Inflammatory Neuropathy Cause and Treatment Sensory Score, lower extremities; MRC-SS LE, Medical Research Council sum score, lower extremities; TUG, timed up and go.

our hypotheses. No correlation was found with the I-RODS or other patient-reported outcomes (Figure 4a).

We additionally repeated these analyses for other stance conditions, for sway area and sway amplitude (Figure S2A), and separately for patients with active or stable CIDP (Table S4, Figures S3, S4), but did not find evidence of validity in these analyses (Table S3).

3.3.2 | Patients With IgM-Related Polyneuropathy

We found no difference in posturography parameters between patients with and without reported balance symptoms; however, group size was small (27 visits, balance symptoms: $n=16$; visits reporting no balance symptoms: $n=6$, missing: $n=5$, Figure 3 and Table S5).

The correlations of posturography parameters with scores of other outcome measures in patients with IgM-related polyneuropathy can be found in Figure 4b (primary outcome: sway path FAEO) and Figure S2B (all outcomes). Sway path in the FAEO stance condition showed moderate to good correlation with the ataxia item for gait (ρ: 0.66; 95% CI: 0.22–0.88), the composite ataxia score for stance (ρ: 0.69; 95% CI: 0.25–0.94) and the ataxia-SS (ρ: 0.72; 95% CI: 0.28–0.96), in line with our hypotheses. In addition, sway path FAEO correlated with the TUG (ρ: 0.67; 95% CI: 0.04–0.89). With the exception of the ataxia variables, only a few correlations between our secondary outcomes and other outcome measures met our hypotheses of validity (Table S5).

3.4 | Responsiveness

Sway path in the FAEO and FAEC stance met the highest number of hypotheses for feasibility and validity combined, and were used for the responsiveness analyses.

For 41 patients with CIDP, more than one posturography measurement was available. Figure 5 shows change scores in sway path in the FAEO stance condition for three anchors. We found a reduction of sway path in FAEO in patients who improved on the PGIC (−121 mm, $p=0.04$), but no increase in patients who deteriorated. Using the I-RODS as an anchor, no changes in sway path in FAEO were found between groups. Finally, for the INCAT-DS-LE, an increase for patients who deteriorated was observed (+163 mm, $p=0.03$) relative to patients who remained stable, but no decrease in patients who improved. Additional responsiveness analyses, exploring correlations and associations with change scores of other impairment measures, also did not show evidence of responsiveness (Figure S5 and Table S3). Similar results were observed for sway path in the FAEC stance condition (Table S3).

4 | Discussion

In this study, we explored clinimetric aspects of posturography using a force platform as a measure for balance in patients with CIDP and IgM-related polyneuropathy. Importantly, although the reliability of posturography measurements was excellent, feasibility in this patient population was limited, as only one stance condition could be performed by all patients. In CIDP patients, we found that the sway path differs between patients with and without reported balance symptoms. However, a consistent correlation was observed only for the ataxia scores and not consistently for other related disability measures, impairment measures and quality of life. In patients with IgM-related polyneuropathy, significant correlations were consistently observed for the sway path and the ataxia scores only, although the group size was small. These findings did not meet our criteria for good and clinically relevant validity of posturography measurements. Also, changes in posturography parameters were not consistently associated with changes in other outcomes such as the PGIC, I-RODS, and INCAT-DS-LE and did not meet our criteria for responsiveness.

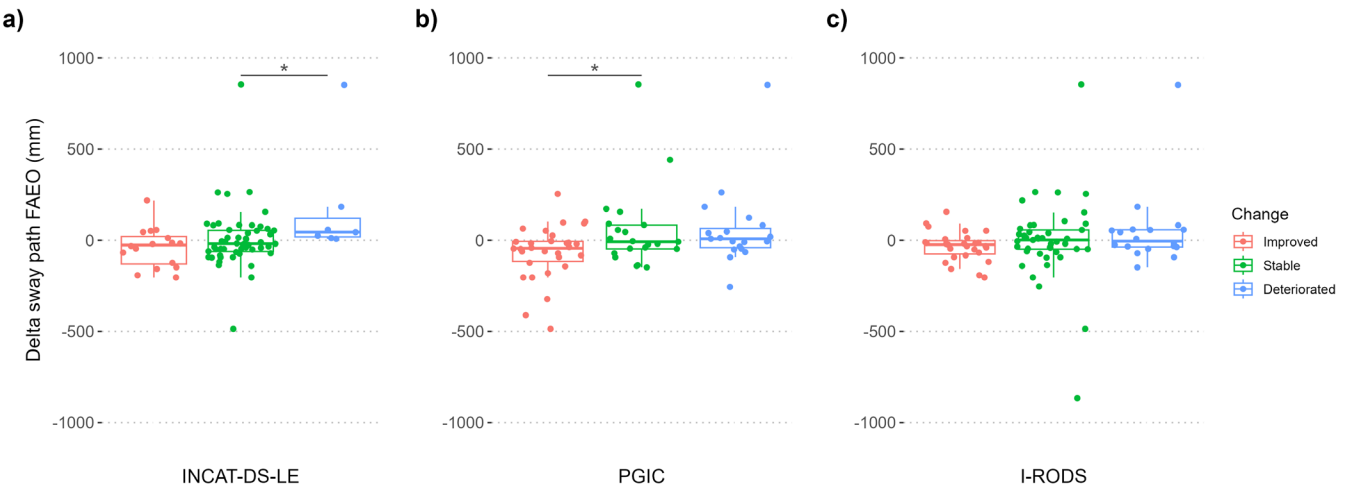

FIGURE 5 | Responsiveness in patients with CIDP. Distribution of sway path changes (mm) in FAEO stance condition (a) based on changes in leg disability represented by INCAT-DS-LE; (b) based on PGIC; (c) based on changes in I-RODS (centile) equal or larger than the MCID of four points. '*' represents a statistically significant difference. CIDP, chronic inflammatory demyelinating polyneuropathy; FAEO, feet apart eyes open; I-RODS, inflammatory Rasch-Built Overall Disability Scale; INCAT-DS-LE, INCAT disability score, lower extremities; MCID, minimal clinical important difference; PGIC, patient global impression of change.

Previous research proposed posturography measurements with a force platform as an objective marker of therapeutic effectiveness of IVIg in patients with CIDP [15]. This study showed a reduction in sway path concordant with subjective improvement in balance after IVIg infusion in an FTEC, and a tandem stance. Other outcome measures, including the I-RODS, MRC-SS, and INCAT sensory sum score (ISS), did not correlate with posturography measurements and showed no significant changes. This is consistent with our findings. It is unclear if small changes in postural sway parameters and subjective changes in balance are clinically meaningful. In our sample, most patients did show clinically relevant changes on other (validated) outcome measures.

In some patients, residual sensory or motor deficits that lead to balance impairment may be compensated over time by strategies or relying more on other determinants of balance [7]. Possibly, these compensatory mechanisms may limit the negative effects of balance impairments on disability and quality of life measures. Due to our sample size, we were not able to assess the difference between patients with new deficits compared to chronic residual deficits. However, in CIDP patients with active disease (of which 52% had disease duration of <1 year) we also did not find correlations between balance impairments and disability and quality of life.

Other electronic measurement instruments assessing balance and/or gait, such as walkways with pressure sensors (GAITRite), electromagnetic trackers, and gyroscopes, have only been studied in small samples of patients with inflammatory neuropathies, and their clinimetric properties have not yet been evaluated [7, 33]. Alternatively, patient-reported or more functional measurement instruments assessing (elements of) balance, such as a timed up-and-go test, could provide good validity and responsiveness.

This is the first study to evaluate posturography measurements in a diverse group of patients with inflammatory neuropathies in a longitudinal setting. There are several limitations to consider. First, as patients unable to stand unassisted were not included and many patients could not perform all stance conditions, analyses were restricted to selected groups of patients. This resulted in a skewed sample, which may not capture the variability or extremes necessary to fully reflect the relationship between the measurement and the construct. Second, our sample size for IgM-related neuropathy was small, which limits the reliability of the results in this population. Third, we used ordinal scales, such as the INCAT-DS, which do not assume equal distances between categories, for some of our analyses, complicating the interpretation of our results. To address these concerns, we examined validity and responsiveness from multiple angles by using different outcome measures, aiming to capture a more comprehensive picture despite the inherent limitations of ordinal scales. This led to multiple testing for many of the analyses, which increases the risk of a type 1 error. We did not correct as most correlations observed were already above the 0.05 threshold without correction. Fourth, we used an ataxia scale, the TUG, and subscales for the lower extremities for some analyses, the validity and responsiveness of which are unknown in immune-mediated neuropathies. For validity analyses, we also used a question regarding whether patients did or did not experience balance symptoms, although we did not explore what patients interpret as balance symptoms and how this relates to other impairments. Additionally, we included the PGIC, I-RODS and INCAT-DS-LE as external anchors for responsiveness analyses, which are not specific to balance. Nevertheless, we hypothesized that balance would change in concordance with changes on these outcomes, as all these measures are related to balance. Considering the continued need for a valid, linear and objective measure for postural stability in this population frequently affected by balance impairment, future endeavors should focus on other, for example, portable devices for posturography, such as an accelerometer, which enables dynamic assessment of natural movements and longer-term measurements of both stance and gait [34]. Longitudinal studies are needed to assess reliability and responsiveness of these measures.

In conclusion, although postural sway measurements using a force platform were reliable, the feasibility of the measurements was limited. Furthermore, the measurements did not meet our criteria for validity and responsiveness. Based on these findings, we cannot recommend routine use in clinical care or trials for CIDP or IgM-related polyneuropathy.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.