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Original Research

Goal Attainment: A Clinically Meaningful Measure of Success of Botulinum Toxin-A Treatment for Lower Limb Spasticity in Ambulatory Patients

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KEYWORDS
Botulinum toxins;
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Gait;
Goals;
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Muscle spasticity;
Rehabilitation;
Stroke

Abstract *Objectives:* The objectives of this study were to evaluate whether botulinum toxin type A (BoNT-A) treatment for lower limb spasticity leads to patient goal attainment and identify factors associated with positive goal attainment and to assess the effect of BoNT-A treatment on patients' gait.
Design: Retrospective cohort study between June 2014 and February 2019.
Setting: Public outpatient spasticity clinic in a tertiary hospital.
Participants: Thirty patients (N=30; 50% female; average age, 50.5y) with lower limb spasticity of heterogenous etiologies (96.7% cerebral±spinal origin and 3.3% isolated spinal origin); 73.3% (N=22) of patients had previously received BoNT-A treatment.
Interventions: BoNT-A injection to lower limb muscles.
Main Outcome Measures: The primary outcome measure was goal attainment measured using Goal Attainment Scaling. The Modified Ashworth Scale (MAS) was used to assess spasticity. Gait was characterized by spatiotemporal parameters.
Results: Fifty-six treatment episodes were analyzed and showed that BoNT-A treatment resulted in a significant reduction in spasticity (pretreatment MAS=3.18±0.73; posttreatment MAS=2.27±0.89; $P<.001$) with no associated change in gait parameters. Logistic regression revealed that most patients (74.1%) achieved all of their goals, with younger patients having a high likelihood

List of abbreviations: BoNT-A, botulinum toxin type A; CI, confidence interval; GAS, Goal Attainment Scaling; LPA, latent profile analysis; MAS, Modified Ashworth Scale; OR, odds ratio.

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of goal attainment regardless of their gait profile identified by latent profile analysis of the gait parameters. Patients considered to have a low functioning gait profile demonstrated a significantly greater likelihood of goal attainment than patients with the other gait profiles combined (odds ratio, 45.6; 95% confidence interval, 1.3-1602.1; *P*=.036). Chronic spasticity and pretreatment severity of spasticity (MAS) and its reduction were not associated with likelihood of goal attainment.

Conclusions: The success and efficacy of BoNT-A treatment in improving patient perceived gait quality and reducing the negative symptoms of spasticity were best measured using Goal Attainment Scaling. The study emphasizes the importance of measuring patient goals as a clinical outcome. Gait parameters were most informative when used collectively to classify patients based on their overall gait profile, which assisted in identifying differences between patients' likelihood of goal attainment after treatment.

Spasticity, a sequelae of numerous neurologic disorders, is characterized by a velocity-dependent increase in muscle tone that results in resistance to passive movement, involuntary muscle spasms, and contractions.[1,2] Lower limb spasticity can have disabling consequences, including pain, spasm, altered posture, deformity of the foot and ankle, and impairment of gait and mobility.[3,4] The effect on gait and mobility is associated with loss of function and independence; higher morbidity, including falls and fracture[3]; and premature residential aged care placement.[5-7] Prevention and management of lower limb spasticity and sequelae are therefore an important focus of neurologic rehabilitation.

Previous research has demonstrated the positive effects of focal injections of the neurotoxic protein botulinum toxin type A (BoNT-A) in treating spasticity, and it is now a widely accepted treatment modality.[8-18] Studies investigating the effect of BoNT-A on lower limb spasticity have concentrated on outcomes including gait, safe and independent mobility, and activities of daily living.[3,8-10,13-15,17,19-27] To date, the evidence regarding the benefit of BoNT-A mediated reduction in lower limb spasticity on functional outcomes remains inconsistent.[20]

In clinical practice the indications and objectives for BoNT-A treatment of lower limb spasticity are diverse and patient specific, as are the patient's priorities and expectations of the treatment. Rehabilitation-centered frameworks should therefore include a meaningful patient-focused purpose for BoNT-A treatment, beyond reducing spasticity itself,[28] by identifying patient needs, priorities, and goals and tailoring treatment toward addressing and achieving these.

Few previous studies examining BoNT-A treatment for lower limb spasticity have reported the nature of patient goals, examined goal attainment outcomes, or investigated factors associated with the likelihood of goal attainment.[15,25,29,30] A better understanding of such relationships is of clinical value, may guide patient selection, and help predict positive treatment outcomes. Hence, the primary aim of this study was to evaluate the attainment of patients' self-identified treatment goals and factors associated with the likelihood of patient goal attainment. A secondary aim was to assess the effect of BoNT-A treatment on the gait of patients with lower limb spasticity.

Methods

A retrospective pre-post intervention cohort study was conducted involving a review of clinical records from a hospital-based outpatient spasticity clinic between June 2014 and February 2019. The study was approved by the Southern Adelaide Local Health Network Human Research Ethics Commitee . Informed consent was waived because of the retrospective nature of the study. Patients were included if they had received injection of BoNT-A to at least 1 lower limb muscle for the treatment of spasticity, were able to independently mobilize barefoot (no orthoses) at least 10 m (±their usual gait aid), and had outcome measures recorded on the day of BoNT-A injection(s) (pretreatment) and at a review within 4-8 weeks of the BoNT-A injection(s) (post-treatment). Etiologies of spasticity included ischemic stroke, hemorrhagic stroke, multiple sclerosis, spinal cord injury, acquired brain injury, cerebral palsy, and other neurologic conditions. The data collected reflected real-world clinical practice with the physician clinically evaluating and selecting appropriate target muscles, BoNT-A product, dose, volume, and number of injections. The brand/formulations used included incobotulinumBoNT-A, abobotulinumBoNT-A, and onabotulinumBoNT-A.

Outcome measures

Muscle tone was measured using the Modified Ashworth Scale (MAS), a widely used reliable and validated tool for assessing spasticity.[31-34] For analyses purposes, 1+ was incremented to 2 and so on, resulting in grades of 0, 1, 2, 3, 4, and 5, consistent with previously reported methodologies.[20]

Gait was assessed using a GAITRite[a] sensorized walkway (4.3-m active area) positioned in the middle of a 10-m-long path. Patients completed 4 trials walking barefoot at their self-selected comfortable walking speed along the 10-m path and over the walkway while using their usual gait aid if needed. Gait was characterized by 10 spatiotemporal parameters: walking speed, cadence, stride length, step length, step length differential, step width, and the percentage of gait cycle in stance, swing, single-support, and double-support. Mean values of each parameter were

calculated using the last 3 walking trials of each pre- and posttreatment assessment.

Goal Attainment Scaling (GAS) is an established patient-centered method for defining individualized and quantifiable goals with a focus on improvement in function and participation.[35-37] GAS can be used to assess efficacy of treatments and appears to be a sensitive marker of patient-perceived improvement.[35-38] Before treatment, patients self-identified 1-3 treatment goals with support from the clinician to clarify, focus, and quantify these in line with the GAS method. The goals were not weighted by importance or difficulty. Content and themes of patient goals were examined by a descriptive analysis and goals were classed as either active or passive. We calculated GAS scores using the Kiresuk and Sherman method using −1 as a baseline.[36] Goal achievement was evaluated with respect to the expected level of achievement at the posttreatment review, with possible scores of +2 (much better than expected), +1 (better than expected), 0 (expected), −1 (partial or less than expected), or −2 (much less/worse than expected).[35,36,38] The GAS *T*-score formula was used to enable individual GAS scores to be normalized and compared.[35-38]

Power Analysis

The study had a 93.4% power to detect a 10% change in mean walking speed of 83.2 cm/s between pre- and posttreatment assessments. This was calculated based on 30 patients included in the analysis (average of 3.7 measures per patient, with an average of 2 treatment episodes with both a pretreatment and posttreatment measure), a within-patient correlation between measures of ρ=0.9 (based on the intraclass correlation coefficient for the mixed effects model), and a within-group standard deviation of 31.3 cm/s.

Statistical analysis

Descriptive statistics were used to describe the pretreatment characteristics of the patients using the mean and SD, median and interquartile range, or frequency (percentage) as appropriate. A multilevel model was used to determine the effect of BoNT-A treatment on each of the gait parameters. The fixed effects included in the model were assessment (pretreatment vs posttreatment), leg (injected vs noninjected), the treatment number for each treatment episode (between 1 and 6), and an Assessment × Leg interaction. Patient was included as a random intercept. As a sensitivity analysis, we also used analysis of variance to assess whether there were any treatment effects according to pretreatment walking speed tertile. For the purposes of analysis, the etiology variable was collapsed into 4 categories: stroke, acquired brain injury, cerebral palsy, and other.

The gait profile for each patient based on pretreatment gait parameters for the injected leg was determined using latent profile analysis (LPA). Models were estimated for between 2 and 6 latent (hidden) profiles to distinguish up to 6 different gait profiles in the cohort. Once the final model was selected, probabilities of profile membership were calculated for each subject and for each profile. The gait profile corresponding to the highest probability across all of the different profiles was used for determining the profile membership of each patient. Model fit was based on the lowest Akaike information criterion and the Bayesian information criterion. The final selected model was based on both model fit and parsimony with consideration to the size of each profile, with 5% of patients per profile considered a good rule of thumb for the minimum size.[39] Differences in means for each gait parameter across the profiles were determined using linear regression.

Univariate and multivariate logistic regression analyses were used to determine whether patient gait profile and other patient characteristics were predictors of goal attainment. The dependent variable was goal attainment and the independent variables included gait profile, age, sex, whether or not the upper limb was injected, GAS score, etiology (stroke or other vs acquired brain injury and cerebral palsy), and step length. Similarly, patient gait profile was assessed as a predictor of pretreatment MAS using linear regression analysis.

All analyses were performed using STATA.[b] LPA was performed using the STATA "gsem" command for generalized structural equation modeling. Effect estimates between pretreatment and posttreatment are reported as mean ± SE unless otherwise specified. A 2-sided type 1 error rate of α=.05 was considered statistically significant for the logistic regression analyses. A 2-sided type 1 error rate of *P*=.005 was considered significant when comparing the 10 gait parameters across profiles.

Results

A total of 30 patients completed at least 1 (median, 1; range, 1-6; interquartile range, 1) BoNT-A treatment episode with the posttreatment review at a mean ± SD of 52± 13.8 days after the BoNT-A injection(s). A total of 56 treatment episodes were identified, with gait measures available for all 56 episodes and GAS scores available for 54 episodes. Eight patients had missing posttreatment GAS scores, leaving 48 observations from 22 patients for inclusion in the logistic regression analyses of goal attainment.

Patient and treatment characteristics

Patient and treatment characteristics including age, etiology, duration of spasticity from diagnosis (excluding childhood conditions) to BoNT-A treatment, and previous BoNT-A exposure are summarized in table 1. The distribution and frequency of lower limb muscles injected are summarized in table 2.

Muscle tone

Muscle tone decreased after treatment (pretreatment MAS=3.18±0.73 vs posttreatment MAS=2.27±0.89; *P*<.001). The mean±SE post−BoNT-A MAS score declined significantly by −0.91±0.12 (*P*<.001) after adjusting for the number of treatments (using the 0-5 MAS grading for consistency of analysis).

Gait parameters

The mean ± SD pretreatment walking speed of the patients at their first treatment episode was 77.2±30.2 cm/s. Most

Table 1 Characteristics of the patient cohort and BoNT-A treatment

Patient Characteristics		%
Age (y), mean ± SD (range)	50.5±14.7 (18-79)	
Sex	Female	50
	Male	50
Etiology	Acquired brain injury	26.7
	Ischemic stroke	23.3
	Cerebral palsy	16.7
	Hemorrhagic stroke	10
	Multiple sclerosis	10
	Other (corticobasal degeneration, Sjögren-Larsson syndrome, hereditary spastic paraparesis)	10
	Spinal cord injury	3.3
Duration of spasticity (y), mean ± SD (range)	13.5±11.6 (<1-33)	
Level of independent ambulation	Unaided	53.3
	Single-point stick or quad stick	20.1
	Rollator frame or 4-wheeled walker	13.3
	Crutches	13.3
Treatment Characteristics		%
Leg injected	Left	48.2
	Right	46.4
	Bilateral	5.4
Upper limb injected	Concurrent upper limb injection	53.6
	No upper limb injection	46.3
Previous exposure to BoNT-A	Previous exposure documented	73.3
	No previous exposure documented	26.7
Follow-up rehabilitation	Physiotherapy, not specified	50
	Home exercise program/self-directed	30
	Intensive day rehabilitation program	20

patients walked at speeds considered suitable for community ambulation, with 46.7% (n=14) classified as community ambulators (>80 cm/s), 46.7% (n=14) as limited community ambulators (40-80 cm/s), and 6.6% (n=2) as household ambulators (<40 cm/s).[40] Multilevel modeling revealed no significant changes in any of the 10 gait parameters (fig 1). A subgroup analysis stratifying patients according to their pretreatment walking speed tertile (21-64 cm/s, 65-102 cm/s, and 103-146 cm/s) also did not find a significant change in any of the gait parameters for each tertile ($P>.005$).

Table 2 Distribution and frequency of lower limb muscle sites injected across the 56 BoNT-A treatment episodes

Muscles	Frequency	% Total Treatments
Gastrocnemius (medial, lateral)	38	67.9
Tibialis posterior	32	57.1
Soleus	28	50.0
Flexor digitorum longus	17	30.4
Flexor digitorum brevis	12	21.4
Flexor hallucis longus	11	19.6
Rectus femoris	6	10.7
Semitendinosus	6	10.7
Biceps femoris	5	8.9
Semimembranosus	5	8.9
Flexor hallucis brevis	4	7.1
Extensor hallucis longus	2	3.6
Adductors (longus, brevis, magnus)	1	1.8
Tibialis anterior	1	1.8

Patient treatment goals and goal attainment

A summary of the descriptive goals analysis is shown in figure 2. Of 106 individual goals, 62.3% (n=66) were considered active pertaining to improving gait quality and prerequisites of gait such as improving foot clearance and ankle stability, and the remaining 37.7% (n=40) were passive relating to reducing the negative symptoms of spasticity such as pain, spasm, and toe curling. Only 1 of 106 goals was to increase walking speed.

There was a statistically significant increase in GAS *T*-score after treatment (mean ± SD pretreatment GAS *T*-score=37.9±1.2 vs posttreatment GAS *T*-score=55.8±12.6; $P<.01$). There was no difference ($P=.98$) in the percentage of active goals (77.3%, n=51) and passive goals (77.5%, n=31) achieved. Most patients (74.1%) achieved all of their self-identified goals or did better than expected, with 55% of patients achieving the highest GAS outcome of doing "much better than expected." Less than a quarter (24.1%) of patients did "less well than expected," and only 1.9% of patients were "much worse than expected."

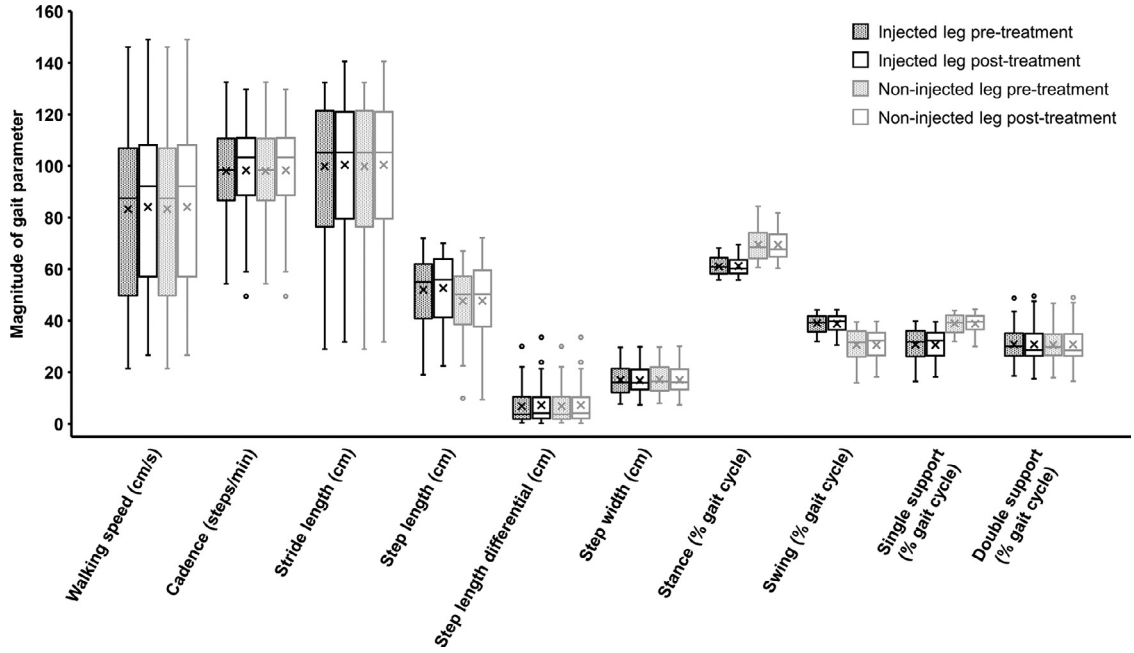

Fig 1 Box plots of the 10 spatiotemporal gait parameters for the injected leg and noninjected leg pre— and post—BoNT-A treatment for the 56 treatment episodes. There were no statistically significant pre- and posttreatment differences for any of the 10 gait parameters.

Patient gait profiles

All LPAs, based on the gait parameters, with 2, 3, 4, 5, and 6 specified latent profiles, converged successfully. Based on the lowest Bayesian information criterion, the optimal number of profiles was 5. Figure 3 illustrates radar plots of standardized (z scores) gait parameters representing the 5 different gait profiles identified by LPA. The mean probability of accurately assigned profile membership ranged from 0.965 for profile 2 to 0.999 for profile 1, indicating a high degree of certainty that each patient was assigned to the correct gait profile. There were 13, 13, 12, 10, and 8 patient records across the 56 treatments in profiles 1, 2, 3, 4, and 5, respectively. There were overall significant differences ($P<.005$) across the 5 profiles for 9 of the 10 gait parameters except for step length differential ($P=.28$). Profile 1 was considered characteristic of a patient who was low functioning exhibiting a slower walking speed, lower cadence, and shorter stride and step lengths compared with profile 4 of a patient with conversely higher functioning gait characteristics (see fig 3).

Predictors of goal attainment: gait profile, GAS *T*-score, and MAS

Univariate analysis showed there was no overall difference in odds of goal attainment across the 5 patient gait profiles ($P=.94$). Multivariate analysis, which included gait profile,

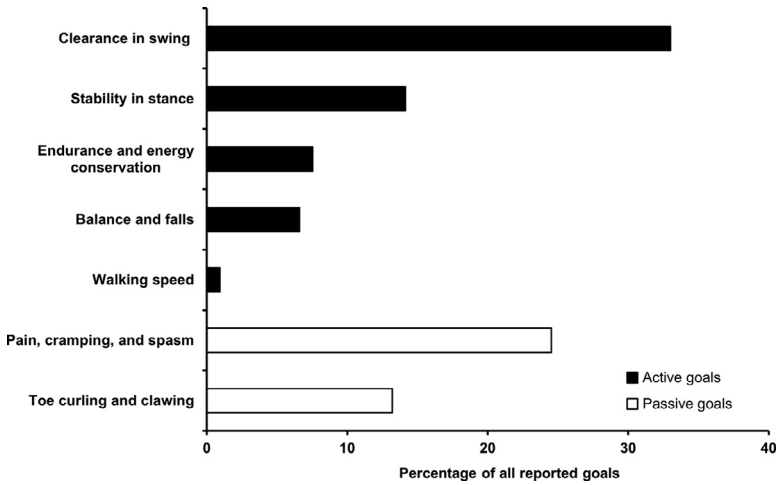

Fig 2 Descriptive analysis of the active (dark shade) and passive (light shade) treatment goals reported by patients across the 56 BoNT-A treatment episodes. Active goals related to improving the quality of gait and the ability to achieve the pre-requisites of gait and passive goals related to reducing negative symptoms of spasticity.

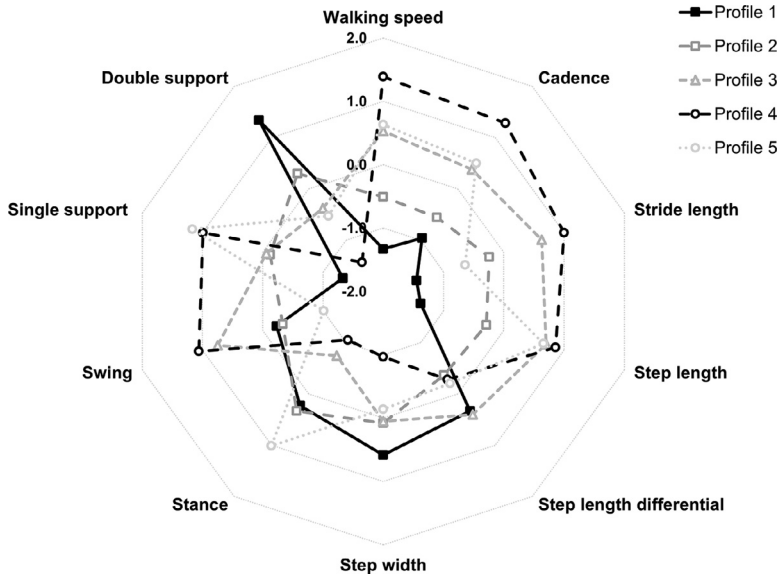

Fig 3 Radar plots of the 10 standardized (*z* scores) pre—BoNT-A treatment spatiotemporal gait parameters representing the 5 different gait profiles.

age, GAS score, etiology (stroke or other vs acquired brain injury and cerebral palsy), and step length, revealed that the odds of goal attainment was lower with older age (odds ratio [OR], 0.76; 95% confidence interval [CI], 0.58-0.98; *P*=.034), lower when fewer treatment goals were set (OR, 0.43; 95% CI, 0.19-0.98; *P*=.046), and nonsignificantly different across patient gait profiles (*P*=.15). When adjusting for the same variables, those with low functioning gait (profile 1) had a higher odds of goal attainment than the other 4 patient gait profiles combined (OR, 45.6; 95% CI, 1.3-1602.1; *P*=.036). Figure 4 illustrates that younger age was associated with a near 100% probability of goals being achieved irrespective of pretreatment patient gait profile. Univariate and multivariate analyses of pretreatment MAS revealed no overall difference between the 5 patient gait profiles (*P*=.58 and *P*=.60, respectively). Neither the pretreatment MAS score nor the magnitude of change in MAS after treatment was associated with the likelihood of achieving goals.

Discussion

The present study aimed to assess the effect of receiving BoNT-A injections for the treatment of lower limb spasticity on gait and goal attainment in a heterogenous outpatient cohort. BoNT-A treatment was efficacious in reducing tone and spasticity but was not associated with any discernible improvements in gait parameters, consistent with previous studies.[23,26] We report novel information on the nature of patients' treatment goals and levels of goal achievement

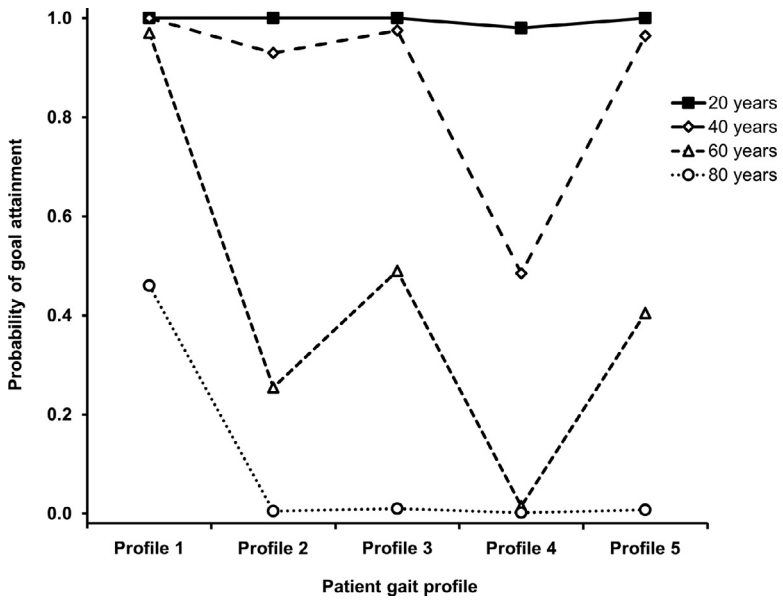

Fig 4 Probability of goal attainment based on patient gait profile and age.

and that patient age and gait profile were associated with goal attainment. Our results suggest that GAS scoring may be the key measure to assess improvements in both the patient's perceived gait quality and negative spasticity symptoms. Our findings were based on a diverse range of patients in an outpatient spasticity clinic and may therefore have generalizability to similar populations.

Although objective gait parameters, including walking speed, revealed no significant changes in gait, the majority of patients' treatment goals were active in nature, relating to improving gait quality, and most patients achieved their goals after treatment. The cohort of patients demonstrated a similar level of achievement of active and passive goals, in contrast to a previous study finding that passive goals were more likely to be achieved than active goals.[30] Walking speed itself was likely underrepresented as a patient goal because of the relatively high pretreatment walking speed of the cohort (mean, 77.2 cm/s).

The likelihood of patients in the present cohort achieving their treatment goals was strongly associated with age but not chronicity or severity of spasticity. Younger patients had almost 100% probability of goal attainment, regardless of their gait profile (see fig 4). This compares with findings by Mullins et al,[30] who reported that younger patients were more likely to achieve mobility and transfer goals after BoNT-A treatment. The average duration of spasticity in the present cohort was 13.5 years; however, this chronicity was not a barrier to goal achievement. Neither pretreatment MAS score nor its change were predictors of goal attainment, suggesting that successful goal attainment is unlikely to be limited to those with severe spasticity or those who demonstrate greater reduction in clinical measures of tone and spasticity.

Classifying patients into different gait profiles based on all of the gait parameters, which individually showed no significant changes, helped identify differences in the likelihood of goal attainment between specific patient gait profiles. Although there was no difference in the odds of goal attainment between the 5 patient profiles, when comparing profile 1, characterized by low functioning gait (in the context of the cohort's capacity for community ambulation), with the combination of profiles 2-5 with relatively higher functioning gait (see fig 3) it was revealed that the low-functioning patients' odds of goal attainment was 45 times higher. This finding may be explained by a higher ceiling effect of BoNT-A in the low-functioning patients. By classifying patients in terms of their gait function, as defined by their overall gait profiles rather than individual gait parameters, we were able to assess differences in the likelihood of goal attainment, potentially offering a more practical outcome for use by the treating clinician. It also helped demonstrate that lower functioning patients have high treatment success as measured by goal attainment and should not be excluded from treatment.

The lack of a significant change in overall gait function as measured by walking speed, despite adequate power to detect changes of 10% or more, may be explained by several factors. Only a small number of patients participated in intensive and structured rehabilitation, which may have reduced any beneficial effects of BoNT-A on gait because previous research has reported that combining both achieves the largest improvements in terms of gait quality, speed, and endurance.[38] The mostly chronic spasticity exhibited by this cohort may have limited improved outcomes in walking speed that generally occur with BoNT-A treatment of more recent onset spasticity.[21,27,39] Additionally, most patients (19 of 30) received only single episodes of BoNT-A treatment and improvements in walking speed often require repeated injections.[20] Finally, walking speed may not be a satisfactory standalone outcome measure because increases may be confounded by patients using maladaptive strategies.[41-43]

Study limitations

The study was primarily limited by its retrospective design, small cohort, and lack of a control group. The study cohort had heterogenous etiologies of spasticity and the duration between onset or diagnosis of spasticity and treatment was variable. We acknowledge that we were unable to determine whether the effects of BoNT-A were the same in patients who received only 1 treatment in the study compared with those who received multiple treatments, as well as the potential effect of any past treatments with BoNT-A because of the limited numbers of participants in these subgroups for further statistical analysis.

Despite these limitations, our study has several strengths, including a well-described cohort from a real-world outpatient spasticity clinic; a comprehensive set of validated outcomes including the MAS, instrumented gait assessments, and GAS; and a patient-centered approach to the analysis based on patient gait profiles.

Conclusions

The efficacy of BoNT-A treatment was characterized by reductions in spasticity (MAS) and positive goal attainment (GAS). Objective gait parameters on their own showed no change and did not reflect patient perceptions of successful treatment, which generally focused on ameliorating the pre-requisites of gait. This emphasizes that measuring patient-identified treatment goals is a meaningful and important clinical outcome. Classifying patient gait profiles on the basis of all of the gait parameters offered a more informative use of these data, which assisted in identifying differences in patient goal attainment and warrants further investigation. A combination of patient-centered, goal-oriented, and gait-sensitive outcomes is likely necessary to effectively assess the efficacy of BoNT-A treatment and likelihood of goal attainment after treatment for lower limb spasticity.

Suppliers

a. GAITRite Platinum Plus Classic walkway; CIR Systems, Inc.
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