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Original Article

Exploring the association between outcome measures to guide clinical management in patients with amyotrophic lateral sclerosis

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Abstract. [Purpose] The usefulness and limitations of outcome measures changes throughout functional decline of patients with Amyotrophic Lateral Sclerosis (ALS). This study aims to describe associations between outcome measures in patients with ALS over time. [Participants and Methods] Participant data was collected at a multidisciplinary ALS clinic during regular clinic visits, including gait velocity, Timed Up and Go, the ALS Functional Rating Scale-Revised, and it's Gross Motor Subscale. [Results] All gait velocity measures were <1.2 m/sec; average Timed Up and Go was >13.5 sec. There was strong internal consistency between ALS Functional Rating Scale-Revised and its functional mobility components and a strong, significant correlation between the Timed Up and Go and the Gross Motor Subscale. [Conclusion] Patients with ALS are not community ambulators and demonstrate risk for falls. We found concurrent validity between objective and self-reported measures. The strong association between the Gross Motor Subscale and the Timed Up and Go may allow PTs to utilize the self-reported Gross Motor Subscale to predict fall risk. Clinically, when the Timed Up and Go and gait velocity are no longer appropriate due to disease progression, the Gross Motor Subscale can provide insight into functional decline.

Key words: Amyotrophic Lateral Sclerosis (ALS), Outcome measures, Amyotrophic Lateral Sclerosis Functional Rating Scale Revised (ALSFRS-R)

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INTRODUCTION

Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease with progressive degeneration of upper and lower motor neurons leading to profound functional deficits. ALS results in progressive paralysis and death through destruction of the corticomotor neurons, possibly occurring through environmental or genetic triggers[1, 2)]. An estimated 1.5 to 2.7 per 100,000 people are diagnosed each year with this rapidly progressive disease[3–5)]. In patients with ALS (pALS), survival ranges vary greatly, with the majority of patients succumbing to respiratory failure within 3–5 years of symptom onset[6)], although more than 10% do survive greater than 10 years[7)]. ALS survival range has been found to be dependent upon "clinical presentation, rate of disease progression, early presence of respiratory failure, and the nutritional status of patients"[6)]. Factors that lead to a better prognosis and longer survival include: limb-onset, younger age, increased breathing capacity, stable weight, and a longer interval between new symptom onsets[2)].

The clinical hallmark of ALS is the presence of both upper motor neuron (UMN) and lower motor neuron (LMN) features[6)] yielding mixed clinical symptoms[2, 5, 8)]. The progressive loss of neurons leads to muscle paralysis and subsequent impaired swallowing, respiration, ambulation, and coordination[9)]. Persons can present with limb-onset (about 70%), bulbar-onset

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(about 25%), or other initial presentations, with progressive dispersion to other regions[6, 10]. Early symptoms of limb-onset ALS include weakness, fasciculations, fatigue, cramps, and muscular atrophy[10]. In conjunction with focal weakness, fatigue plays a role in symptom management; 83% of all patients with ALS can demonstrate fatigue[11]. Fatigue is multifactorial, owing to impaired muscular activation, generalized deconditioning from immobility, and depression[11, 12].

There are significant challenges in diagnosing ALS in the early stages when patients have few signs and symptoms. Initial symptoms are usually subtle, mimic other neurological diseases, and often lead to a delayed diagnosis. On average, it takes approximately a year for a patient to be diagnosed with ALS[13] and over 17 months to first receive care in a Multidisciplinary ALS Clinic[14]. This protracted delay can prevent the patient and family from receiving requisite interventions[8].

Multidisciplinary ALS Clinics (MDCs) have become an inveterate gold standard of care where experts and services are assembled to meet the needs of pALS[15]. Research citing the benefits of MDCs has been mixed; however, studies support the following advantages of these specialty clinics: improved quality of life, lengthened survival, fewer hospital admissions with decreased lengths of stay, and increased use of adaptive equipment[8–10, 14–18]. MDCs have the ability to create the opportunity to redefine best practice and improve standards of care for this specialized patient population. In the local MDC, functional performance is assessed using the timed up and go (TUG) and gait velocity (GV), among other measures. Attendees complete a widely utilized functional scale called the ALS Functional Rating Scale-Revised (ALSFRS-R)[19] to assess patient status and, theoretically, to guide treatment in MDCs[20, 21]. Mobility issues are specifically highlighted in the Gross Motor Subscale (GMS) of the ALSFRS-R.

Gait performance is a key assessment used to track functional decline among persons with ALS[22]. Various gait deficits are observed and can be related to the degree of disability, corticospinal degeneration, and neuromuscular impairment. Deviations include general unsteadiness, impaired initiation, and stride interval fluctuations[23, 24]. Cognitive and motor dual task activities can further alter gait performance[25]. Gait deficits can be exacerbated by extrapyramidal deficits in ALS, which increases both the variability and heterogeneity of motor symptoms[18, 24]. GV may vary according to presentation with limb- versus bulbar-onset disease manifestations[26]. Schell and colleagues noted a positive association between fall incidence and lower extremity weakness in persons with ALS. Regardless of onset type, ALS disease progression irrevocably impacts function, ambulation, balance, and risk for falls. The aggregate of symptoms among persons with ALS can heighten fall risk[27].

While studies of persons with ALS have focused on multidimensional physical performance, less is known about the relationship between self-reported measures, temporal gait degradation, and objective physical performance measures among pALS. The purpose of this study was to describe the association between objective measures, the TUG and GV, and the self-reported ALSFRS-R measures among pALS. Analyzing this performance could support concurrent validity of the measures and descriptive performance of the instruments over time.

PARTICIPANTS AND METHODS

All data was obtained throughout the course of normal tertiary outpatient care and incorporated data from multiple visits at the local MDC. The study was approved by both hospital- and university-based institutional review boards (Peninsula Regional Medical Center (now TidalHealth Peninsula Regional) Research Review Committee Approval No. P16-023; University of Maryland Eastern Shore, Institutional Review Board Approval No. P2015-011 and P2017-006). pALS were recruited voluntarily from a local MDC in a rural setting and written informed consent was obtained from live participants. Inclusion criteria for eligibility in the study comprised patients who (a) received tertiary care at a Multidisciplinary ALS Clinic in Salisbury, MD, USA; (b) were at least 18 years old at the time of care; and (c) had a diagnosis of probable, laboratory-supported probable or definite ALS. Exclusion criteria were (a) any clinical evidence or suspicion of any other neurological disease; (b) any experimental drug used within the term of care (excluding Rilutek/Riluzole); and (c) any surgical intervention(s) or comorbid disease(s) likely to have hastened the need for chronic assistive device use. In addition, retrospective chart reviews were utilized for deceased patients who had received care at the local MDC. Their medical records were canvassed for data in the same manner as actively consented participants.

Functional mobility was measured with the TUG test. The instrument demonstrates reliability, validity, and fall risk prediction[28]. Following the command "Go", participants stood from a standard arm chair, ambulated three meters at their self-selected natural pace, turned, and returned to seated position in the chair. Participants utilized their usual assistive walking device. A standard cut-off score for fall risk in community dwelling adults is 13.5 sec[29]; moreover, the test is both feasible and reliable[30]. Metrics of the TUG are supported by strong concurrent validity with the Berg Balance Scale, GV, and stair climbing[31]. Krieg and colleagues investigated postural control in persons with ALS and noted that both the TUG and GV detected motor deficits common among individuals with ALS[32].

GV was measured using the 10 meter (m) walk test and analyzed in meters per second (m/sec)[33]. Participants ambulated ten meters at their normal, self-selected speed. Areas were demarcated to allow acceleration and deceleration intervals before and after the 4 m timed segment. GV is a reliable, valid, sensitive, and specific measure of walking speed[34, 35]. Descriptive gait speed values have been reported by age, gender, and diagnosis[34, 36] including a cut-off of 1.2 m/sec for community ambulation[37]. Gait velocity is also a strong indicator for disability status and disease progression in patients with ALS[26].

For safety purposes during functional testing at the MDC, local participants' vital signs were monitored and measures were used to ensure safe mobility. A gait belt was utilized at all times with the PT guarding appropriately for safety. For the

TUG and GV, participants performed zero to three trials at each MDC visit. This study includes data from the first and second trials of these measures.

The ALSFRS-R is a self-reported functional rating scale specific to persons with ALS[19, 38], used to quantify function and monitor disability progression. It was developed by Cedarbaum and is included as Table 1 in his 1999 publication[38]. At the local MDC, the scale is routinely completed by persons with ALS or their caregivers. The ALSFRS-R includes 12 questions about ability in 12 specific functions, scored from zero to four points in each function for a maximum score of 48 points. The questions can be grouped into 4 domains, which are interpreted as subscales: gross motor, fine motor, bulbar, and respiratory. Each subscale includes 3 questions for a maximum of 12 points per subscale. We specifically utilized the GMS which includes the functions of turning in bed and adjusting bedclothes (GMS-Bed), walking (GMS-Walk), and climbing stairs (GMS-Stairs)[19, 38]. The ALSFRS-R has been shown to have good reliability and construct validity[38, 39], and is used to predict survivability in pALS[38, 40]. In research, it is used to relate function to measures such as falls[27], quality of life[38] and nutritional status[41]. Lee notes that, "The ALSFRS-R is the most commonly used functional rating instrument in clinical practice and clinical trials"[19]. Measures derived from the ALSFRS-R have been noted for potential usefulness for daily clinical work in MDCs[20, 21].

Statistical analyses included descriptive statistics (means and standard deviations), Pearson product moment parametric correlations and Spearman's rho nonparametric correlations. IBM SPSS Statistics (v. 28.0, Armonk, NY, USA) was used for most statistical analyses; Microsoft Excel (v. 2016, Redmond, WA, USA) was minimally used. $P<0.05$ was established for statistical significance; recognition of increased significance at the $p<0.01$ level was also discussed.

RESULTS

Participants (Table 1) included twenty-eight persons with ALS (15 males, 13 females) with an average age at first symptoms of 66 years, 3 months (range: 49 to 81 years). The average time from first signs/symptoms (S/S) to diagnosis was 14.1 months (range: 0.0 to 52.5 months). The delay between diagnosis and their first visit to the MDC was 4.6 months (range: −9.1 to 32.4 months), representing an average delay from first symptoms to first MDC visit of 18.7 months. Outcome measures (Table 2) show that at no time, over 33 sets of trials at the multidisciplinary ALS clinic, did pALS demonstrate a GV greater

Table 1. Participant characteristics

Number	Gender	Onset category	Age at 1st S/S
28	15 Males	16 Limbs	mean: 66 years, 3 months
	13 Females	12 Bulbars	range: 49–81 years
Time categories (months)	1st S/S to Diagnosis	Diagnosis to 1st MDC visit	1st S/S to 1st MDC visit
	14.1 ± 11.0, 0.0 to 52.5	4.6 ± 7.6, −9.1 to 32.4	18.7 ± 13.6, 3.9 to 55.8

Data in Time categories: Mean ± standard deviation, range. 1st S/S: First signs/symptoms of Amyotrophic Lateral Sclerosis (ALS); 1st MDC visit: 1st visit to multidisciplinary ALS clinic.

Table 2. Descriptive statistics of outcome measures

	n	Mean ± SD	Min	Max	Max points possible
Time categories (months)					
1st S/S to diagnosis	28	14.1 ± 11.0	0.0	52.5	n/a
Diagnosis to 1st MDC visit	28	4.6 ± 7.64	−9.1	32.4	n/a
1st S/S to 1st MDC visit	28	18.7 ± 13.6	3.9	55.8	n/a
Outcome measures					
TUG (sec)	39	18.9 ± 13.4	6.0	66.0	n/a
GV (m/sec)	33	0.426 ± 0.199	0.077	1.13	n/a
Total ALSFRS-R	92	29.4 ± 8.80	10	46	48
GMS	87	5.84 ± 3.46	0	12	12
GMS-Bed	87	2.38 ± 1.39	0	4	4
GMS-Walk	87	2.05 ± 1.14	0	4	4
GMS-Stair	87	1.41 ± 1.34	0	4	4

1st S/S: First signs/symptoms of Amyotrophic Lateral Sclerosis (ALS); Diagnosis: Diagnosis of ALS; 1st MDC visit: 1st visit to multi-disciplinary Amyotrophic Lateral Sclerosis (ALS) clinic; TUG: Timed Up and Go; GV: Gait velocity; ALSFRS-R: ALS functional rating scale-revised; GMS: Gross Motor Subscale of ALSFRS-R; GMS-Bed, GMS-Walk, GMS-Stairs: Individual functional components scored in the ALSFRS-R which total to create the GMS score.

than 1.2 m/sec (max=1.13 m/sec). The average GV was 0.43 m/sec (± 0.20; range 0.08 to 1.13). On average, pALS demonstrated TUG scores greater than a 13.5 sec cutoff (mean: 18.9 sec), with 56.2% of the TUG scores greater than 13.5 sec. Participants had an average total ALSFRS-R score of 29.4 of the 48 possible points. The GMS and all three of its components were scored by pALS from the low of zero to the maximum score. The average GMS score was 5.8 of 12 possible points.

Correlation studies (Table 3) showed a strong, significant negative relationship between TUG and GV performance (R=0.704; $p<0.01$). In addition, there was a significant correlation between the total ALSFRS-R score and TUG (R= −0.449; $p<0.05$), but not a significant correlation between total ALSFRS-R and GV ($p>0.05$). The GMS score was significantly correlated ($p<0.01$) with both the TUG (R= −0.816, a strong correlation) and GV (R=0.683, a moderate correlation).

The TUG demonstrated a significant moderate relationship with each GMS component: GMS-Bed (R= −0.597), GMS-Walk (R= −0.498), and GMS-Stair (R= −0.686) at the $p<0.01$ level. GV had a significant relationship with the GMS (R=0.683) at the $p<0.01$ level and with two of its components at the $p<0.05$ level (GMS-Walk R=0.534, GMS-Stair R=0.540). GV's relationships with the total ALSFRS-R and the GMS-Bed component were not significant.

All studied ALSFRS-R measures were significantly correlated with each other ($p<0.01$). The ALSFRS-R total score showed a strong positive correlation with the Gross Motor Subscale (R=0.754). When examining the relationship of the total ALSFRS-R with each of the 3 GMS components, a moderate positive correlation was found for all three, GMS-Bed (R=0.696), GMS-Walk (R=0.634), and GMS-Stair (R=0.693). The Gross Motor Subscale had a strong positive correlation with all 3 of its components, GMS-Bed (R=0.857), GMS-Walk (R=0.883), and GMS-Stair (R=0.944).

Of the 3 Time categories (Months since 1st signs/symptoms (S/S), Months since Diagnosis, and Months since 1st MDC visit), GV only correlated significantly with Months since Diagnosis (R=0.361), and only at the $p<0.05$ level. The positive correlation between all Time categories and gait velocity is of note. The TUG demonstrated no significant correlation with any of the three Time categories ($p>0.05$, $R< \pm 0.10$).

A longitudinal analysis of the ALSFRS-R, its GMS, and the three individual GMS components showed a significant negative correlation with all three Time categories ($p<0.01$). All correlations were of moderate strength (R range: −0.469 to −0.682).

Given the strong (R= −0.816) significant correlation between the TUG and the GMS, an equation of their relationship was developed with the GMS set as the independent variable and the TUG as the dependent variable. With the equation of y= −3.682x + 45.86, a TUG score of 13.5 sec related to a GMS score of 8.79 points (Fig. 1).

DISCUSSION

The PT's role in management of pALS in MDCs includes evaluating motor function and safety and assessing needs for DME[2]. The authors' objective was to investigate outcome measures in order to guide intentional selection of outcome measures throughout the progression of the disease. Selection of physical therapy outcome measures, evaluation of functional movement, and investigation of risk for falls in pALS in the early stage of ALS is documented by Sanjak and Russo[22, 42]. Both studies found the use of BERG, DGI, TUG, and Six min walk test to be valuable during the early stage of ALS. Similar to the recommendations reported by Lui and Byl, regarding exercise choices in pALS, PTs working with pALS should base outcome measure selection on observations of clinical progression and physical ability[43]. As pALS progress to later stages of the disease, there is a lack of information regarding outcome measures that are both appropriate and can accurately represent functional decline in mobility.

Table 3. Relationship of outcome measures and time categories

	Objective measures		ALSFRS-R, GMS & Components					Months since:		
	TUG	GV	Total ALSFRS-R	GMS	GMS-Bed	GMS-Walk	GMS-Stair	1st S/S	Dx	1st MDC Visit
TUG	---	−0.704**,1	−0.449*	−0.816**	−0.597**	−0.498**	−0.686**	−0.064	−0.072	0.094
GV	−0.704**,1	---	0.162	0.683**	0.440	0.534*	0.540*	0.317	0.361*	0.154
Total ALSFRS-R	−0.449*	0.162	---	0.754**	0.696**	0.634**	0.693**	−0.599**	−0.611**	−0.682**
GMS	−0.816**	0.683**	0.754**	---	0.857**	0.883**	0.944**	−0.586**	−0.542**	−0.526**
GMS-Bed	−0.597**	0.440	0.696**	0.857**	---	0.587**	0.700**	−0.498**	−0.497**	−0.469**
GMS-Walk	−0.498**	0.534*	0.634**	0.883**	0.587**	---	0.844**	−0.515**	−0.486**	−0.483**
GMS-Stair	−0.686**	0.540*	0.693**	0.944**	0.700**	0.844**	---	−0.606**	−0.542**	−0.490**

Data are Correlation coefficients (R), Spearman's rho. TUG: Timed Up and Go; GV: Gait velocity; ALSFRS-R: Amyotrophic Lateral Sclerosis (ALS) functional rating scale-revised; GMS: Gross motor subscale of ALSFRS-R; GMS-Bed, GMS-Walk, GMS-Stairs: Individual functional components scored in the ALSFRS-R which total to create the GMS score; 1st S/S: First Signs/Symptoms of ALS; Dx: Diagnosis of ALS; 1st MDC visit: 1st visit to multi-disciplinary ALS clinic.
**Correlation is significant at the 0.01 level (2-tailed), *Correlation is significant at the 0.05 level (2-tailed).
[1]Correlation coefficient is R, Pearson's product moment.

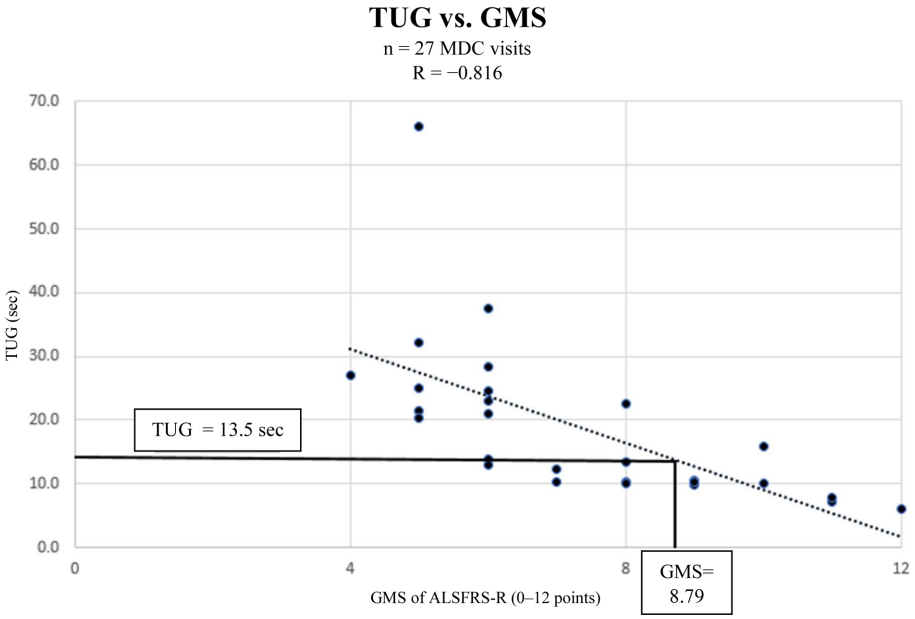

Fig. 1. Relationship of TUG and GMS. y=−3.682x + 45.86; TUG score of 13.5 sec relates to a GMS of 8.79 points.
TUG: Timed Up and Go; GMS: Gross Motor Subscale of the ALS Functional Rating Scale-Revised; MDC: Multi-disciplinary ALS Clinic; R: Spearman's rho correlation coefficient.

The local MDC data supports some expected information regarding pALS and the progression of the disease. Lengthy delays exist in diagnosing and treating ALS. From the time of 1st symptoms, it takes over a year to diagnose ALS (14.1 months) and over a year and a half to treat pALS in the local MDC clinic (18.7 months). Our study confirms what PTs working with pALS likely suspected: from the first time that persons with Amyotrophic Lateral Sclerosis perform GV at the MDC, they are not community ambulators. GV never reached the 1.2 m/sec level, the threshold indicating a community ambulator (max=1.13 sec). In addition, the average TUG score of 18.9 sec is greater than the 13.5 second cut-off for fall risk for community dwelling adults[29]. Out of all TUG scores, 56% were greater than and 44% were less than the 13.5 sec cut off. Based on the progressive nature of ALS, fall risk, prevention and intervention should be addressed routinely.

In our dataset, the GV and the TUG demonstrate a typical inverse relationship with a strong, significant correlation, although neither showed a significant decline over time. Scores for the ALSFRS-R, its GMS, and all three GMS components (GMS-Bed, GMS-Walk, GMS-Stair) decline over time. Significant positive correlations among all five of these measures demonstrate internal consistency among the ALSFRS-R and its functional mobility components. The GMS demonstrates moderate predictive ability with all three Time components (R^2 0.277–0.343), indicating its ability to more accurately reflect the functional decline in pALS.

As van Eijk reported, using the ALSFRS-R as a whole may dilute the power of the result by taking too many factors into account at once. The total score is limited by multidimensionality which prevents a direct comparison of status, disease stage, or prognosis between pALS with identical scores[44]. For example, two patients may have the same total ALSFRS-R score, however, one may have a high GMS, with a low respiratory subscale and the other may have a low GMS but a high respiratory subscale. The subscale scores highlight two very different presentations in patients with the same total ALSFRS-R. Supporting evidence suggests that using a subscale approach to analyze ALSFRS-R data allows for a greater empirical value for ALS research with increased confidence versus analyzing the total score alone[44–46]. In the MDC, each discipline may find value in a corresponding subscale. For PTs concerned with functional mobility, we found the Gross Motor Subscale of the ALSFRS-R to be a valuable outcome measure.

The present study demonstrates some information that requires further consideration regarding the relationships between standard objective measures of function and ALS-specific self-reported measures of function. GV is considered a useful measure to understand the functional mobility of many populations[37, 47], including pALS[26, 27]. The correlation for GV and total ALSFRS-R was positive, but weak and insignificant, perhaps limited by the multidimensionality of the total score, as discussed above. Mathematically, the relationship of GV with these nested components is interesting, but a full exploration may be of little use in understanding the function of pALS. The GMS-Walk component is a simple self-report measure that would seem to be directly related to GV. It offers a choice of 5 statements for pALS to describe their walking, and GV involves only walking. The GMS-Walk component, however, explains only 29% of GV. The GMS, on the other hand, explains nearly half of GV (47%), with a higher level of significance. This relationship demonstrates the benefit of utilizing the full GMS to consider functional mobility such as GV and ambulation.

Our findings echo Sukockienė's findings that total ALSFRS-R scores significantly and negatively correlate with the TUG[48], pALS were slower as their self-rated function decreased. We also found that the TUG score was significantly and negatively correlated with the GMS and its three components. As with GV, of the studied self-report measures, the 3-component GMS had the strongest and most significant relationship with the TUG, explaining 67% of the TUG score. This relationship highlights the potential usefulness of the GMS when performance of the TUG is not appropriate. Interestingly, of the 3 separate components of the GMS, the TUG demonstrated the strongest significant correlation ($R=-0.686$, $p<0.01$), with the GMS-Stair component. Both of these measures provide insight into a person's ability to lift their body weight for functional use. In contrast to gait velocity, which measures only the speed of sustained ambulation, the TUG also incorporates the motions of rising from a chair, turning, and the combination of turning and lowering into a chair, providing information beyond the numerical TUG score.

Current literature shows that slower TUG scores are correlated to higher fall risk for all populations[29, 49, 50]. When assessing the usefulness of the TUG, Barry et al. debates the validity of the TUG's predictive ability to prospectively determine risk for falls in community dwelling adults who have known deficits affecting balance and mobility[51]. We concur that in a general population, this outcome measure should not be used in isolation. However, the TUG continues to be used in clinical practice and the activities required for the TUG can add valuable information in the assessment of patient function[48, 52, 53]. Further investigation of the TUG, including larger studies that assess inter-rater and intra-rater reliability, how the inability to perform the TUG test relates to risk of falls, the influence of using ADs and braces, and the association of TUG scores with quality of life will help better define the role of the TUG test in the clinical care of pALS[27].

We found the GMS to have the expected relationship and significant correlations ($p<0.01$) with all studied measures of the ALSFRS-R. It demonstrates strong correlations with the TUG, the total ALSFRS-R and all GMS components, and moderate correlations with GV and all time components. The GMS appears to be a robust measure of functional mobility in pALS. As a paper-based self-report measure, it does not use the limited physical energy of pALS. With a possible score range of 0–12, the GMS provides insight into tangible changes in function. Despite being useful and appropriate, the GMS is under-utilized in guiding treatment decisions in pALS.

In 2005, Kaufman noted two benefits of validating the ALSFRS-R beyond clinical trials. First, clinicians may translate trial results to use for pALS outside of clinical trials, and second, clinicians may understand the usefulness of the ALSFRS-R for management of pALS[40]. Now more than 15 years later, we have learned that the subscales of the ALSFRS-R are more useful than the total ALSFRS-R for understanding the changing function of pALS[19, 46, 54]. Rather than limiting its value, this understanding of subscales can add value and usefulness to the outcome measure; subscales were identified as a potentially useful target in developing a prognostic model to support clinical decisions[55]. For PTs focused on functional mobility, a pALS's self-rated ability in Bed, Walk and Stair function, combined in the GMS, is a clear area of interest. The ALSFRS-R is widely collected for clinical trials and in MDCs[20, 54]. It can be easily and successfully administered[19, 40] and has been shown to be valid when administered by phone[56], videoconferencing[57], or online[58]. The literature does not, however, demonstrate significant utilization of the ALSFRS-R as a tool to guide treatment decisions by members of the interdisciplinary team for the management of individual pALS, as Kaufmann alluded to in 2005[40]. Although it is clear that the ALSFRS-R and its GMS are useful, they are not being utilized. The GMS deserves further study as a potential indicator of specific functional abilities, deficits, or DME needs in pALS.

The present study provides novel information relating the TUG and its cut-off values for fall risk with the ALS-specific GMS. Consistent with previous research[52], we found the TUG to have a significant, strong negative correlation with the total ALSFRS-R score. Further, we found the GMS of the ALSFRS-R to have a more significant and stronger correlation with the TUG than the total ALSFRS-R. The current study demonstrates that the GMS has the potential to be used as a proxy for the TUG to indicate risk of falls.

The relationship between the TUG and the GMS, as noted in Fig. 1, is predictive ($R^2=0.6658$), making it a safe abstraction for PTs to use the GMS as a component in fall risk assessment. This may be particularly useful to provide insight into fall risk when a PT negates the use of the TUG based on clinical reasoning. Given the line of best fit, a TUG score of 13.5 sec relates to a GMS score of 8.79 points. We postulate that a GMS score of 9 or less may be used to indicate an increased risk of falls in pALS and the need to participate in fall risk interventions.

Limitations of the study include the natural tolerance and endurance capacity of pALS during a single session. Also, due to the progressive nature of the disease, variability in the number and frequency of MDC visits and ensuing follow-up can occur throughout an episode of care. Physical performance measures and thresholds validated for pALS are limited. Finally, the local MDC may have unique features that limit the generalizability of this study to other clinics. Further studies should include participant onset phenotypes and disease stage comparisons with larger sample sizes. Analyses could assess the impact of caregiver burden with increased care responsibilities.

ALS is a progressive and fatal disease; the patients and caregivers benefit from PT management guided by appropriate use of outcome measures. Our study found pALS are not community ambulators and demonstrate risk for falls. When persons with ALS are no longer ambulatory or appropriate to perform standard, physical outcome measures, the usefulness of the GMS cannot be overemphasized. The GMS corroborates the risk for falls without actually having to perform objective measures at the MDC. To our knowledge, this was the first study to evaluate the relationship of the self-reported GMS over time and with objective functional gait measures in pALS. We found concurrent validity between the TUG, gait performance

(GV), the multidimensional ALSFRS-R, and its Gross Motor Subscale component. Based on its relationship with the TUG, a self-reported, three question GMS score ≤9 may be indicative of a fall risk. Clinically, when the TUG and GV are no longer appropriate in the MDC due to fatigue or overall progression of ALS, the GMS of the ALSFRS-R can provide insight into functional decline, specifically fall risk.

Conflict of interest

There are no conflicts of interest to disclose.

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