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Balance Confidence and Falls in Non-Demented Essential Tremor Patients: The Role of Cognition

Ashwini K. Rao, EdD, OTR, FAOTA*,

Department of Rehabilitation & Regenerative Medicine (Program in Physical Therapy) and G.H. Sergievsky Center, College of Physicians and Surgeons, Columbia University

Arthur Gilman, BS, G.H., and

Sergievsky Center, College of Physicians and Surgeons, Columbia University

Elan D. Louis, MD, MS

Department of Neurology, G.H. Sergievsky Center, and Taub Institute for Research on Alzheimer's Disease and the Aging Brain, College of Physicians and Surgeons, Department of Epidemiology, Mailman School of Public Health, Columbia University

Abstract

Objective—To examine 1) the effect of cognitive ability on balance confidence and falls, 2) the relationship of balance confidence and falls with quantitative measures of gait, and 3) measures that predict falls, in people with Essential Tremor (ET).

Design—Cross-sectional study. Setting: General community.

Participants—One-hundred-eighty participants (132 people with ET and 48 controls). People with ET were divided into two groups based on the median score on the modified Mini Mental State Exam: ET-LCS vs. ET-HCS.

Interventions—Not applicable.

Main Outcome Measures—Activities of Balance Confidence-6 (ABC) scale and falls in the previous year.

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*Corresponding Author Address: Ashwini K. Rao, 710 West 168th Street, 8th Floor, New York, NY 10032, akr7@cumc.columbia.edu.

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Author Roles

Ashwini K. Rao: Research project: conception, organization and execution; Statistical

Analysis: Design, execution, review and critique; Manuscript preparation: writing the first draft, review and critique

Arthur Gillman: Research project: organization, execution; Statistical Analysis: Review and critique; Manuscript Preparation: Review and critique

Elan D. Louis: Research project: conception, organization and execution; Statistical Analysis: Review and critique; Manuscript preparation: Review and critique

Results—ET-LCS had lower ABC-6 scores and a greater number of falls than ET-HCS ($p < 0.05$ for all measures) or controls ($p < 0.01$ for all measures). Quantitative gait measures were significantly correlated with ABC-6 score and falls. Gait speed ($p < 0.007$) and ABC-6 score ($p < 0.02$) were significant predictors of falls. Receiver Operating Characteristic curve analysis revealed that gait speed < 0.9 m/s and ABC-6 score $< 51\%$ were associated with moderate sensitivity and specificity in identifying fallers.

Conclusions—People with ET with low cognitive scores have impaired gait, and report lower balance confidence, and higher number of falls than their counterparts with higher cognitive scores, and controls. We have identified assessments that are easily administered (gait speed and ABC-6 scale), and are associated with falls in ET.

Keywords

Essential Tremor; gait; cognition; falls; balance confidence

Essential tremor (ET) is a highly prevalent neurological disorder with motor and non-motor impairments^{1–3}. Recent work indicates that people with ET demonstrate gait and balance impairments greater than that seen in age-matched controls^{4–9}. Balance impairment is evident on clinical assessment (tandem walk), in which people with ET demonstrate higher number of mis-steps (defined as steps taken in a direction away from a straight line)^{4, 6, 7}. Quantitative gait analysis demonstrates that people with ET have lower speed and cadence, decreased consistency of stepping (step time difference), and impaired dynamic balance (time spent in double support)⁹. The clinical features of ET can also include cognitive impairments in the domains of attention, executive function and memory^{10, 11}. Since functional ambulation often involves concurrent performance of motor and cognitive skills, impairments during dual-task performance may be predictive of falls, as is seen in the elderly^{12, 13}. Falls may cause injuries, and are associated with nursing home admission and increased mortality¹⁴.

We recently observed that gait impairments were worse in people with ET when performing a cognitive task during gait¹⁵. Performance decrement was most prominent in a subset of people with ET with lower scores on a cognitive test (ET-LCS). However, we do not know whether this sub-group (with lower cognitive scores) is at a greater risk of *functional* balance difficulty (i.e., lower balance confidence and more falls).

The purpose of this follow-up study was to 1) evaluate in an *a-priori* manner whether balance confidence is lower and falls are higher in ET-LCS than in people with ET who have higher cognitive test scores (ET-HCS) or in controls; 2) examine if balance confidence and falls are correlated with quantitative measures of gait; and 3) determine measures that predict falls. We collected new retrospective falls data on our cohort of 213 subjects, for whom we had previously only reported quantitative gait data^{9, 15}.

Methods

2.1 Subjects

Details about our cohort have been reported previously^{9, 15}. Briefly, participants were recruited as future brain donors to the Essential Tremor Centralized Brain Repository (ETCBBR). We enrolled people with ET and spousal controls living across the United States. A movement disorder specialist confirmed the diagnosis of ET using published diagnostic criteria (moderate or greater amplitude kinetic tremor during three or more activities, or a head tremor in the absence of Parkinson's disease (PD)). Spousal controls were included if they did not have a diagnosis of ET. We excluded people with ET with Modified Mini Mental State Examination (mMMSE) score <40, as this is often indicative of underlying dementia^{16–19}. Additional exclusion criteria for ET and control participants were presence of other neurological disorders (PD, dystonia or stroke), and orthopedic impairments that may have impaired walking. All enrolled participants (151 ET and 62 spousal controls, N = 213) signed an informed consent form, approved by the Institutional Review Board in accordance with the Declaration of Helsinki.

2.2 Assessment

Our original cohort (N=213) was tested at home. All participants underwent a clinical assessment that included collection of demographic and clinical data, a neurological examination, and quantitative gait analysis. People with ET were also administered the mMMSE (range = 0–57, higher scores indicate better function)²⁰. This valid and reliable test¹⁶ is an expanded version of the Folstein Mini Mental State Examination²¹. As an add-on telephone assessment, three to six months later, we obtained data on balance confidence and falls. We administered the 6-item Activities of Balance Confidence Scale (ABC-6) scale^{22, 23}. The scale asks participants to rate their confidence in performing functional activities without losing balance or becoming unsteady. Scores range from 0 (not confident at all) to 100 (completely confident). The 6-item version of the ABC scale has been validated against the parent ABC questionnaire, which consists of 16 items²². In addition, we asked patients to indicate how many falls they had during the past year. Falls were defined as “an event which results in a person coming to rest inadvertently on the ground or supporting surface, and other than as a consequence of a violent blow, loss of consciousness or sudden onset of paralysis”²⁴. A single experimenter made all telephone calls. The experimenter has more than five years of experience with administering telephonic interviews and was trained by the first author in administration of the ABC-6 scale. The experimenter was blinded to the study hypothesis, to avoid biases in the collection of information.

Quantitative gait data were collected with the Gaitrite[®] mat, a 4.6 meter long computerized mat that registers the location and timing of each footfall. The gait mat was placed in the middle of a quiet hallway in participants' homes. We had ascertained that each participant had sufficient space for collecting gait data and have reported the procedure in detail previously^{9, 15}. We analyzed the following gait measures that were sensitive in differentiating people with ET from controls¹⁵: speed, cadence, step length, step time

difference, and percent of gait cycle spent in double support. We also computed coefficient of variation of stride length and stride time.

2.3 Statistical Analysis

Analyses were carried out in IBM-SPSS (Version 21; Chicago, IL). We used the Kolmogorov-Smirnov test to examine normality of data distribution. For data that were normally distributed we used parametric statistics, and for data that were not normally distributed we used non-parametric statistics. Comparison of ABC-6 and falls across groups (ET-LCS, ET-HCS and control) was conducted with multivariate analysis of variance (ANOVA) with age as a covariate. To examine differences in the number of fallers per group (individuals who reported >2 falls in the previous year^{12, 25}), we used a non-parametric test, the Jonkheere-Terpstra Test of Ordered Alternatives²⁶. The Jonkheere-Terpstra test is useful when the alternate hypothesis includes *a-priori* ordering, as was the case in our study. We hypothesized that ET-LCS would have higher number of fallers than ET-HCS who, in turn, would have higher number of fallers than controls.

To examine associations between ABC-6 and falls with quantitative gait variables, we used Pearson's correlation coefficients. We also conducted linear regression analysis to examine if ABC-6 score and gait variables (independent variables in separate analyses) were associated with falls (dependent variable). Finally, we constructed Receiver Operating Characteristic (ROC) curves for ABC-6 and gait speed in order to determine their diagnostic performance. We chose these variables because they demonstrated significant correlation with falls, and are easy to administer in any clinical setting. The dependent variable was fallers, previously defined as individuals with more than 2 falls in the previous year^{12, 25}. We calculated the Area Under the Curve (AUC) with 95% confidence intervals, and cut-off values that produced optimal sensitivity and specificity.

3. Results

From the original sample of 213 people, we obtained balance confidence and falls data from 180 subjects (33 subjects were not available). There were no differences in age or gender between these 33 and the 180 who participated ($p>0.05$). People with ET were divided into two groups based on the median score (50) on the mMMSE: those below 50 were classified as non-demented ET-lower cognitive score (ET-LCS) and patients with a score ≥ 50 were classified as ET-higher cognitive score (ET-HCS). We used the median value of the mMMSE score for several reasons. First, it is mathematically derived and therefore less subject to bias and/or post-hoc manipulation. Second, it conveniently provides subgroups of equal value as well as subgroups of maximal possible size. Third, our previously published work demonstrates that the derived subgroups clearly demonstrate meaningful clinical differences¹⁵. The value 50, chosen mathematically, also has significant clinical relevance. This value is equivalent to a Folstein Mini-Mental State Examination²¹ score of 26, which in many studies has been used as a cut off for cognitive impairment^{27, 28}. Demographic and clinical data are presented in Table 1. Detailed examination of the mMMSE indicated that ET-LCS had lower scores across all domains of the mMMSE, compared with ET-HCS. Kruskal-Wallis ANOVA revealed an effect of age (chi-square= 20.79, $p<0.0001$): on

average, people with ET were older than controls. Since age was significantly different across groups, statistical analysis included age as a covariate. There was no difference in the age of tremor onset between the two ET subgroups.

3.1 Balance Confidence and Falls

We compared balance confidence between groups (ET-LCS, ET-HCS and controls) with an ANOVA, and included age as a covariate (Table 1). We found a main effect of group ($F=4.98$, $p=0.008$) - control subjects had higher scores on the ABC-6 than ET-HCS (not statistically significant, $p=0.07$), and higher scores than ET-LCS ($p<0.01$). ET-HCS had higher ABC-6 scores than ET-LCS ($p<0.04$). Thus, ET-LCS had lowest balance confidence. Age was also a significant factor, in addition to group, in explaining the difference between groups ($F=12.81$, $p<0.001$).

Average number of falls across three groups (controls, ET-HCS, ET-LCS) was analyzed with an ANOVA, with age as a covariate. We found a main effect of group ($F=6.46$, $p<0.01$): control participants had fewer falls than ET-HCS ($p<0.01$) and ET-LCS ($p<0.0001$). ET-HCS had fewer falls compared with ET-LCS ($p<0.05$). There was a progressive increase in the average number of falls from control participants to ET-HCS to ET-LCS. Age was not a significant factor, in the presence of group differences, for average number of falls ($F=0.39$, $p=0.53$). The percentage of fallers was highest in ET-LCS (58.7%), lower in ET-HCS (50.7%) and lowest in controls (31.2%), as seen in Table 1. Results of the Jonckheere-Terpstra test indicated a significant effect of group (Test statistic= 2.31, $p<0.02$).

3.2 Association of Balance Confidence and Falls with Gait Measures

Overall, quantitative gait measures were associated with balance confidence and falls (Table 2). In particular, speed, cadence, step length, step time difference, double support percent, stride length CV and stride time CV were significantly correlated with balance confidence and falls. The pattern of correlations was similar for all three groups indicating that patient reported measures (ABC-6 and falls) were correlated with performance-based measures (gait), independent of presence of ET and cognitive function.

Gait variables that were significantly correlated with falls were entered in a linear regression model as independent variables to test if they predicted falls (dependent variable) for people with ET. We also entered age into the model. Of all gait variables, speed was the only significant predictor of falls (Standardized $\beta=-0.25$, $t=-2.79$, $p<0.007$). Age was not a significant predictor of falls ($t=-0.16$, $p=0.87$) when it was entered into the model along with gait speed. We also examined if anticonvulsant medications had an influence on falls and balance confidence. Primidone was prescribed to 58 people with ET. Falls and ABC-6 scores were not different for people with ET who were prescribed Primidone compared with those who were not ($p>0.1$ for both analyses). In a separate analysis, ABC-6 and age were entered as independent variables to test if they predicted falls (dependent variable). ABC-6 was a significant predictor of falls (Standardized $\beta=-0.25$, $t=-2.3$, $p<0.02$), but age was not ($t=0.05$, $p=0.96$).

3.3 Cut-off Values for Predictors of falls

We constructed ROC curves to determine cut-off points for gait speed and ABC-6 to examine their performance in predicting fallers among people with ET (controls were excluded from this analysis). As seen in Table 3, a cut-off value of 0.9 m/s produced moderate sensitivity (0.7) and low-moderate (0.55) specificity. Results indicate that people with gait speed lower than 0.9 m/s had a greater likelihood of falls than those with speed greater than 0.9 m/s. For the ABC-6 scale, a cut-off score of 51% produced moderate sensitivity (0.73) and low-moderate specificity (0.59). The results indicate that people with balance confidence of less than 51% have a greater likelihood of falls.

4. Discussion

We have previously shown, using quantitative gait analysis, that people with ET with lower scores on a cognitive test (ET-LCS) had greater impairments during dual-task gait than people with ET with higher cognitive scores (ET-HCS), and healthy controls¹⁵. The purpose of the present study was to examine if ET subjects with lower cognitive scores have lower balance confidence and greater number of falls. Our study has three major findings. First, ET-LCS demonstrated the greatest *functional balance difficulty* compared with ET-HCS and controls. ET-LCS had lower balance confidence and greater number of falls. We have identified a subset of people with ET (with lower cognitive scores) who not only have greater gait impairments¹⁵, but also report experiencing functional difficulty with balance confidence and falls. Second, quantitative gait measures were significantly associated with balance confidence and falls. Finally, we have identified two measures (gait speed and ABC-6 score) that were significant predictors of fallers. Results of the present study and our previously published report on dual task gait¹⁵ highlight the relationship of cognitive and gait impairments with falls in people with ET. Similar results have been reported in the healthy elderly: older individuals with cognitive impairments were at a greater risk for falls, with an annual incidence as high as 80%²⁹. The risk for falls is also higher in older individuals with mild cognitive impairment and Alzheimer's disease^{30, 31}. While the mechanisms underlying increased fall risk in cognitively impaired elderly have not been clarified, several authors have suggested that impaired cognitive ability reduces attention capacity, which would normally be allocated to gait^{32–34}. Our results suggest that it may be beneficial to include assessment of cognitive function, balance confidence and gait as part of routine clinical examination in people with ET. Since ET-LCS had a greater number of falls, administering a cognitive test may help identify individuals at an increased risk for falls.

The short version of the ABC scale could be included to obtain patient reported outcomes on balance confidence. This may be particularly important for patients who do not report falls, but may be at an increased risk. Our results provide cut-off values (<51% confidence) to identify individuals with ET who may be at risk for falls. The ABC-6 scale has demonstrated clinical utility in identifying fallers among elderly living in the community³⁵, and for people with high-level gait disorders and Parkinson's disease²². Finally, clinicians should consider measurement of gait speed because speed less than 0.9 m/s increased the likelihood of falls. Gait speed is an important predictor of adverse outcomes such as falls, morbidity³⁶ and mortality³⁷ in older adults. Gait speed is considered a global measure of

function since speed correlates with muscle strength of the lower extremity, balance, cardiovascular fitness and neurological disease³⁶.

In summary, ABC-6 and gait speed demonstrated moderate sensitivity and low-to-moderate specificity in people with ET³⁸. Since ABC scale, gait speed and mMMSE can easily be administered in any clinical setting, our results provide a set of measures that can help identify people with ET at risk for falls.

Our study has implications for future research. We have identified a subset of individuals who are at a higher risk for falls, and have identified measures of gait and balance that are associated with falls. It will be important for future work to clarify the contributions of intrinsic factors (such as strength, balance, gait speed, dual-task ability etc.) and extrinsic factors (medication, environmental hazards) to fall risk in ET³⁹. This will be important in the design of rehabilitation therapy interventions to determine specific modifiable factors (such as gait speed, strength, balance, environmental modification) that may help to reduce fall risk in People with ET.

Balance confidence (ABC-6 scores) for patients in our study was lower than reported previously¹⁴, whereas the number of people with ET with falls was higher in our study compared with previous reports^{8, 14}. One explanation for this discrepancy is that patients in the present study were older than those in previous reports. Since tremor severity, gait and balance impairments worsen with age, patients in our study presented with clinical features of advanced ET.

The results of our study demonstrated that age was a significant factor in addition to group, in explaining differences in balance confidence and falls across groups. However, the presence of ET and cognitive limitations were more consistently associated with falls than age alone. While age is associated with declining balance confidence and falls, particularly in older people, recent evidence suggests that several other factors are more important predictors of falls⁴⁰. For instance, presence of neurological disease, decrease in muscle strength, imbalance, and cognitive impairment are more important predictors of falls, independent of age⁴¹. Recently we demonstrated that middle-aged people with severe ET had greater balance and gait impairments than older people with ET, highlighting the fact that presence of severe neurological disease (such as ET) can be a better predictor of balance impairment than age alone⁴².

Previous work has shown that people with ET with midline tremor (e.g. head) have greater balance impairments resulting from cerebellar pathology^{14, 43}. Emerging evidence on gait and balance impairments in ET support the suggestion that the cerebellum may be an important locus of pathology underlying motor impairments^{4, 5, 7-9}. In addition, there have been reports that cognitive impairments are also associated with ET^{10, 44-46}. The presence of cognitive impairments greater than that seen in typical aging implicates the possible involvement of neural pathways between the cerebellum and the frontal cortex¹¹.

Study Limitations

Our findings should be interpreted in light of study limitations. First, we collected retrospective data on balance confidence and fall history, which depend on the accuracy of participant recollection of events in the previous year. The negative effect of recall memory was applicable to participants in all three groups. Exclusion of demented subjects served to lessen the effects of poor recall. Despite this limitation, groups reported differences in balance confidence and falls. This conclusion was supported by the observation that the correlation between patient-reported measures (falls, balance confidence) and performance-based measures (gait) was similar across groups. Second, given the constraints of telephone contact, we were unable to administer a performance-based balance assessment, as we have previously reported¹⁴. Despite the lack of a performance-based balance test, our results demonstrated an association of gait measures with balance confidence and falls. In future work it will be important to evaluate balance confidence and falls in a prospective manner (such as daily recording of falls), and include performance-based measures of balance.

Conclusions

We have identified a sub-group of people with ET who demonstrate greater gait impairments and self-reported functional difficulty with balance, as well as falls. We have also identified easy-to-administer assessments (gait speed and ABC-6 scale) that are associated with falls in ET. Clinicians should consider inclusion of gait and balance into their routine clinical evaluation of ET.

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Table 1

Clinical Characteristics of participants

	ET-LCS	ET-HCS	Control	ET-LCS vs ET-HCS	ET-LCS vs Controls	ET-HCS vs Controls
N	63	69	48			
Mean Age, years (SD)	84.92 (5.71)	82.51 (5.64)	79.52 ^a (6.68)	<0.005	<0.0001	<0.008
Age Range	72 – 102	73 – 96	64–93	-	-	-
Mean Age of Tremor Onset, years (SD)	43.32 (23.42)	40.10 ^{NS} (21.84)	N/A	-	-	-
Mean mMMSE/57 (SD)	44.93 (5.4)	53.26 ^a (1.9)	NT	-	-	-
Orientation	9.32 (0.81)	9.72 ^b (0.71)	NT			
Registration	2.85 (0.36)	2.96 ^c (0.2)	NT			
Attention/Calculation	13.44 (2.05)	15.78 ^a (1.15)	NT			
Recall	1.59 (1.03)	2.46 ^a (0.71)	NT			
General Knowledge	3.1 (1.32)	4.17 ^a (0.89)	NT			
Language	15.02 (1.42)	16.29 ^a (0.88)	NT			
Construction	1.29 (0.69)	1.73 ^a (0.53)	NT			
Mean ABC-6 total score/100 (SD)	42.17 (26.4)	50.78 (29.6)	58.82 ^d (26.61)	<0.04	<0.01	0.07
Average number of falls /12 months (SD)	2.15 (3.21)	1.28 (2.27)	0.59 ^c (0.93)	<0.05	<0.0001	<0.01
Number of Fallers (Percent)	37/63 (58.7%)	35/69 (50.7%)	15/48 ^d (31.2%)			

ET-LCS= ET participants with lower cognitive scores; ET-HCS= ET participants with higher cognitive scores; mMMSE= modified Mini Mental State Examination; NT= Not tested; ABC-6 = Activities of Balance Confidence Scale- 6 item;

^a = p<0.0001;

^b = p<0.001;

^c =p<0.01;

^d =p<0.05; NS= Not significant; Fallers = > 2 in the past year.

Table 2

Correlation of balance confidence and falls with gait variables.

Gait Variable	ABC-6	Falls
Velocity (m/s)	0.62	-0.29
<i>p-value</i>	0.0001	0.0001
Cadence	0.37	-0.26
<i>p-value</i>	0.0001	0.0001
Step Length	0.59	-0.21
<i>p-value</i>	0.0001	0.005
Step time difference	-0.38	0.21
<i>p-value</i>	0.0001	0.002
Double Support %	-0.52	0.26
<i>p-value</i>	0.0001	0.001
Stride Length CV	-0.54	0.28
<i>p-value</i>	0.0001	0.0001
Stride Time CV	-0.49	0.27
<i>p-value</i>	0.0001	0.0001

Table 3

Results of linear regression and Receiver Operating Characteristic (ROC) curve analyses for Velocity and ABC-6 Total score

	Velocity (m/s)	ABC-6 Total Score
Linear Regression		
Standardized β	- 0.25	- 0.25
<i>t</i> -statistic	- 2.79	- 2.3
Significance	0.007	0.02
ROC Curve		
Area Under the Curve (S.E)	0.66 (0.05)	0.70 (0.05)
Significance	0.005	0.0001
95% CI	0.55 – 0.76	0.60 – 0.79
Cutoff Value	0.9	51.0
Optimal Sensitivity	0.7	0.73
Optimal Specificity	0.55	0.59

ABC-6 = Activities of Balance Confidence Scale- 6 item;