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TIMED UP AND GO PERFORMANCE IN OLDER PEOPLE WITH DIABETES MELLITUS: ASSOCIATIONS WITH SENSORIMOTOR FUNCTION, BALANCE, COGNITION, AND FALLS

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ABSTRACT

Background: The Timed up and Go Test (TUG) is often used as a mobility measure in older people. However, it is unclear whether the TUG is useful for identifying fall risk in people with diabetes mellitus (DM) and which physical and cognitive/psychological factors influence the performance of this test.

Objectives: To investigate whether slow TUG times (standard test and when performed with a secondary cognitive task (c-TUG)) are a risk factor for falls in older people with DM and to determine the relative contributions of a range of sensorimotor, balance and cognitive/psychological factors to TUG performance in this population.

Methods: Community-dwelling people (n=103, mean age 61.57, SD=6.3) underwent the TUG and c-TUG tests as well as quantitative tests of vision, peripheral sensation, strength, reaction time, balance, cognition, and fear of falling. Participants were then followed up for falls for six months.

Results: Negative binomial regression analyses revealed that each 1s increase in TUG and c-TUG times increased the risk of falling by 29% and 13%, respectively. Multiple regression analyses identified vibration sense ($p<0.001$), knee extension strength ($p=0.001$, $r^2=0.430$), edge contrast sensitivity ($p=0.002$), neuropathy examination score ($p=0.001$, $r^2=0.498$) and controlled leaning balance ($p=0.033$) as significant and independent explanatory predictors of TUG performance. The regression model for c-TUG was similar, vibration sense ($p=0.042$), knee extension strength ($p=0.009$, $r^2=0.256$), neuropathy examination score ($p=0.156$, $r^2=0.272$) and sway path-floor ($p=0.042$) except that the MOCA cognitive assessment ($p=0.015$) was included instead of edge contrast sensitivity. The combined explanatory variable models explained 43% and 26% of the variance in TUG and c-TUG times, respectively.

Conclusions: Slow TUG and c-TUG times significantly increased the risk of falls in community-dwelling older people with DM. Poor TUG and c-TUG performances were related independently to decreased vibration sense, lower limb weakness, and poor balance, with the c-TUG additionally influenced by cognitive function.

Keywords: Timed Up and Go test, lower limb strength, reaction time, balance, vision, accidental falls, Diabetes.

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INTRODUCTION

Diabetes mellitus (DM) affects approximately 8.5% of people aged over 18 years [1], and more than 16% of people aged over 65 years [2] DM affects people across the globe, with two-thirds of the world diabetic population living in the developing countries [3]. In Sri Lanka, the prevalence of DM has increased dramatically last 30 years with the prevalence of Diabetes mellitus of adults, reaching 8.6% in 2017 [4].

Falls represent one of the important health care problems for people with DM. Approximately 39% of people with DM fall once or several times within a year [5]. Falls can result in injuries ranging from bruises and abrasions through to dislocations, sprains, fractures, and traumatic brain injury [6]. Falls can also lead to decreased functioning in daily life, social isolation, fear of falling, loss of independent living, and impaired quality of life [7-11].

The TUG was developed for the general population of older people but has been increasingly used as a mobility assessment for people with DM. The TUG measures the time required for an individual to rise from a chair, walk three meters at a normal pace, turn, walk back to the chair, and sit down. The TUG has been validated against other mobility and balance measures such as the Berg balance test [12], the Functional Reach Test [12], and the Tinetti Mobility Index [13] and has demonstrated good inter-rater and test-retest reliability [14, 15]. Three studies have reported that older people with DM have slower TUG times than matched controls [16] and that in older people with DM, TUG times are associated with a fear of falling [17, 18].

No studies, however, have evaluated whether the TUG is a good prognostic ability for falls in DM older adults and whether performing this test with a secondary cognitive task adds value in terms of fall prediction. It is also generally considered that the TUG is dependent on physical factors such as strength and balance. Still, no studies have tested a wide variety of factors that impact performance in this test in older people with DM. Therefore, this prospective cohort study aimed to (i) determine whether the TUG is a good prognostic measure for falls; (ii) determine whether performing the TUG with a secondary cognitive task improves its prognostic ability; and (iii) document the impact of a broad range of sensorimotor, postural stability, cognitive and psychological factors to TUG performance in older community-dwelling people with DM.

METHODS

Study design

This study employed a cross-sectional and prospective cohort design with a six-month falls follow-up. All participants underwent baseline assessments, including assessments for neuropathy. Ethics approval was granted from the Ethics Review Committee of the Faculty of Medicine, University of Colombo, Sri Lanka, and from the National Hospital Colombo, Sri Lanka. Written informed consent was requested from each participant after reading out the information sheet describing the study in the native language.

Participants

Participants were recruited from March 2017 to May 2018 from endocrinology clinics at the National Hospital, Colombo, Sri Lanka. Inclusion criteria included having Diabetes for more than five years, aged 50-70 years, living in the community, able to understand instructions necessary for the assessments, and able to walk household distances without any assistance. Participants with significant central nervous system dysfunctions, musculoskeletal deformity, or lower limb pathologies that affect balance were excluded.

Baseline assessments

Timed Up and Go Test

In the standard test (TUG), participants were asked to stand up from a chair, walk forward for three meters fast as they can, turn towards the chair (180 degrees), walk 3m again to the chair and sit down [19]. The instructions were given as "stand up, walk as quickly and safely as possible to the marked line, turn through 180 degrees, walk back to the chair, and sit down again." Participants were also instructed to walk while counting backward in threes from a randomly chosen start number between 60 and 100 (c-TUG test) [19].

Demographics, health status, fear of falling

Participants have completed an interviewer-administered questionnaire related to demographic data, falls information in the previous year, diabetes-related factors, and medication use. Peripheral neuropathy was defined as the presence of three of the following a) a validated symptom score > 1 [20] , b) an examination DPN score > 4 [20], c) a nerve conduction time (tibial nerve velocity) < 40m/s [20] and d) a vibration perception threshold > 25V [20] (see details below). The level of concern about falls was assessed with the Icon-FES [21] scale, which uses pictures and matching short phrases to assess the level of concern related to falls for a collection of everyday activities.

Cognition and neuropsychological functioning

The Montreal Cognitive Assessment Test (MOCA) [22] was used to test general cognitive abilities. Trail Making Test (TMT) was used to test the cognitive-motor speed and task-switching ability, aspects of executive function [23]. TMT comprised of two parts, A and B, and Part A consisted of numbers that need to connect in order (e.g., 1-2-3). Part B consisted of both letters and numbers, which need to connect letters and numbers alternatively (e.g., 1-A-2-B). Then the time difference of part B-A was calculated to remove the effect of speed element from the test evaluation. Simple hand reaction time measured in milliseconds was tested with light as a stimulus and a finger click of a mouse button as the response.

Lower limb sensation

Tibial nerve conduction velocity was assessed with the Natus Xltek nerve conduction machine. Vibration perception thresholds of the big toe were measured using a

Biothesiometer (Bio-Medical Instrument co, Ohio, USA). Tactile sensitivity was assessed with a Semmes-Weinstein pressure aesthesiometer comprising 20 varying diameter nylon filaments with equal length. Testing was done by applying the filament to the center of the lateral malleolus of the right leg. Pressure measurements were expressed as logarithms of the bending force in milligrams. Lower limb proprioception was tested with a matching task of the lower limbs with participants sitting and eyes closed [24]. Errors in matching the great toes were tested with a protractor inscribed on a vertical clear acrylic sheet (60x60x1cm) kept between the participant's legs.

Vision

High contrast visual acuity was tested with a LogMAR letter chart [25] positioned 3 m in front of participants and measured under binocular conditions with participants wearing their distance correction glasses if applicable. Visual contrast sensitivity was tested using the Melbourne Edge Test (MET) [24], which comprised of 20 circular patches containing edges with reducing contrast. The participant was asked to identify the correct pattern of the orientation of the edge on the patches, which was measured in decibel units, where 1 dB = 10 log10 contrast.

Muscle strength, balance, gait, and mobility

Maximal isometric quadriceps strength was tested in both legs when the participant was seated on a high chair with feet not touching the ground. Hips and the knees should be flexed to 90 degrees [24]. A strain gauge was kept horizontally, which fixed to the back of the chair, and the other end containing straps fixed to the lower shin was 10cm above the ankle. Participants were asked to push against the strap with their maximum effort with three attempts. Also, the five-time sit to stand test was administered [26]. Participants were given a practice trial, and then the second trial was taken as the proper test.

Postural sway was assessed using a sway meter, which can be attached to the participant's waist using straps, and it can record the body displacement in quite standing [27]. Testing was done on the floor and a foam rubber mat (40×40×15cm thick) with their normal vision. Sway path (number of mm squares traversed by the sway meter pen) for each 30 s test was recorded. The controlled leaning balance was assessed with the coordinated stability test [28]. This test measures participants' ability to adjust body position in a steady and coordinated manner while placing them at or near the limits of their base of support.

Falls

Falls were defined as "unexpected events which resulted in the participant unintentionally coming to the ground, floor, or other lower-level" [29]. Participants were given six calendars at the baseline assessment and instructed to mark the falls occurred each month and post it to the research center using pre-paid envelopes. Participants whom calendars were not received on time were contacted by a research assistant to record the falls data.

Statistical analysis

Incidence rate ratios (IRRs) were calculated using negative binomial regression models assessing the associations between the TUG and c-TUG times and falls. These models estimate the number of occurrences of an event when the event (such as falls) has a Poisson variation with over-dispersion. The areas under the curve for Receiver-Operator Characteristic curves for the two TUG tests with 1+falls were assessed for statistical differences. The sensorimotor, postural stability, cognitive and psychological measures comprised continuous variables. Logs of the variables were analyzed for the right-skewed distributions. Pearson correlation coefficients were calculated to test the relationships between TUG and c-TUG times and the other test variables. Multiple regression was then used to identify the best set of independent and significant predictors of TUG. Explanatory strength, balance, sensory cognitive/ neuropsychological, and fear of falling scores were entered for the first step. DM diagnostic measures were then entered at step 2 to ascertain if disease-specific factors could explain further variance in TUG and c-TUG times. Standardized beta weights for the variables entered into the regression models are presented – these indicate the relative importance of each variable in explaining variance in TUG times. Analyses were conducted using SPSS and STATA statistical software.

RESULTS

The characterization of the 103 participants, including demographic, medication, diabetes mellitus, and fall-related measures, are described in Table 1.

Table 1: Demographic, medication, diabetes mellitus and fall-related measures for the sample (mean+SD unless stated)

Variable	Number (%) N= 103
Demographic	
Age (years)	61.6±6.0
Female, n (%)	68 (66%)
Height (cm)	156.6±7.8
Weight, (kg)	61.7±9.4
BMI	25.2±3.1
Medications	
Number of medications	6.8±2.6
Insulin dependent, n (%)	31 (30.1%)
Diabetes-related measures	
HbA1c (%)	8.2±1.8
Symptom score	1.4±1.4
Examination score	3.17±3.14
Diagnosed neuropathy, n (%)	51 (49.5%)
Fall-related measures	
1+ fall in previous year, n (%)	53 (51.5%)
Fear of falling	27.2±3.1

TUG performance with age and sex

The mean TUG and c-TUG completion times were 7.8±1.8 seconds and 12.4± 4.6 seconds respectively.

Test completion time for the men were less compared to women: 7.0± 1.4s vs 8.2 ± 1.9s (t=-3.15,df=101 ,p=0.220) for the TUG and 10.7± 2.9s vs 13.3 ± 5.1 for the c-TUG (t=-2.88,df=101,p=0.01). TUG and c-TUG times were not significantly associated with age (r=0.138, p=0.90 and r=0.059, p=0.55 respectively.

TUG performance and prospective falls

Table 2 presents the findings for the two TUG tests for the non-faller, single faller, and multiple faller groups. The negative binomial regression analyses revealed that for each 1s increase in TUG and c-TUG times increase the risk of falling by 29% and 13%, respectively. The complementary ROC comparisons contrasting non-fallers and 1+ fallers indicated the areas under the curve for the TUG (0.60; 95%CI=0.49-0.71) and c-TUG (0.62; 95%CI=0.50-0.73) tests were very similar - χ^2 for difference =0.05, df=1, p=0.82).

Table 2: TUG and c-TUG times for the non-faller, single faller and multiple faller groups (mean+SD)

Variable	No falls (n=66)	One fall (n=11)	Two plus falls (n=26)	IRR (95% CI)
TUG (s)	7.6±1.9	7.7±1.3	8.2±1.9	1.29 (1.03-1.62)
TUG cognitive (s)	11.7±3.6	11.5±2.8	14.1±5.0	1.13 (1.02-1.24)

Diabetes-specific, sensorimotor, balance, cognitive and psychological correlates of TUG

Table 3 shows the associations between TUG and c-TUG times and sensorimotor, balance, cognitive, psychological, and diabetes-specific measures. Several of these measures were significantly correlated with TUG and c-TUG times, with the strength of the associations ranging from weak to moderate.

Table 3: Diabetes specific, sensorimotor, balance and cognitive correlates of TUG and c-TUG times

Measure	Mean ± SD	TUG R (p)	c-TUG R (p)
Diabetes specific			
Symptom score	1.4±1.4	0.540(0.000)	0.318(0.001)
Examination score	3.2±3.1	0.467(0.000)	0.354(0.000)
Sensorimotor			
Tibial nerve velocity (ms^{-1})	40.4±5.6	0.008(0.940)	-0.094(0.373)
Vibration perception threshold (mV)	28.0±14.5	0.449(0.000)	0.170(0.086)
Tactile sensitivity (log_{10}mg pressure)	4.12±0.81	0.137(0.167)	0.170(0.086)
Proprioception (degree error)	2.5±1.3	0.105(0.292)	-0.046(0.647)
Visual acuity-high contrast (logMAR)	1.6±0.9	0.243(0.013)	0.140(0.159)
Edge contrast sensitivity (dB)	20.2±2.6	-0.312(0.001)	-0.234(0.017)
Knee extension strength (kg)	22.7±7.5	-0.487(0.000)	-0.432(0.000)
Balance			
Sway floor EO (mm)	71.9±32.5	0.143(0.151)	0.311(0.001)
Sway foam EO (mm)	201.1±92.8	0.186(0.061)	0.272 (0.005)
Coordinated stability score	11.3±9.2	0.428(0.000)	0.395(0.000)
Cognitive/Psychological			
MOCA score	22.9±3.2	-0.188(0.057)	-0.303(0.002)
Reaction time (ms)	258±51	0.170(0.087)	0.179(0.070)
Trials A (s)	66.6±28.3	0.169(0.088)	0.171(0.084)
Trials B (s)	172.5±87.3	0.204(0.039)	0.338(0.000)
Trials B-A (s)	103.6±71.3	0.159(0.109)	0.350(0.000)
Fear of falling score	27.4±7.5	0.346(0.000)	0.344(0.000)

* p<0.05, ** p<0.01, *** p<0.001

High scores in sway, coordinated stability, visual acuity, tactile sensitivity, reaction time, and psychological tests and low scores in the strength and contrast sensitivity tests indicate impairments

Multiple regression analysis identified vibration sense, knee extension strength, edge contrast sensitivity, and controlled leaning balance as the significant and independent explanatory predictors of TUG performance (Table 4). These variables explained 43% of the variance in TUG times. The inclusion of the DM examination score in the subsequent step explained a further 6.8% (p<0.001) of the variance in TUG times. The regression model for c-TUG was similar to that for the TUG, except that MOCA was included instead of edge contrast sensitivity. These variables explained 26% of the variance in c-TUG times. The inclusion of the DM examination score in the subsequent step explained only a further 1.6% of the variance in c-TUG times (p=0.156) (Table 4).

Table 4: Hierarchical multiple regression of TUG times and c-TUG times showing standardized Beta weights, and R^2 after the entry of each successive block of variables into the model

Predictor Variables for TUG times	Beta weights	p-value	r^2
Knee extension strength	-.279	0.001	0.430 ***
Coordinated stability	.189	0.033	
Edge contrast sensitivity	-.255	0.002	
Vibration sense	.297	<0.001	
Neuropathy examination score	.390	=0.001	0.498 **
Predictor Variables for c-TUG times			
Knee extension strength	-.249	0.009	0.256 ***
Sway path-floor	.189	0.042	
Vibration sense	.182	0.042	
MOCA	-.220	0.015	
Neuropathy examination score	.183	0.156	0.272 ^{NS}

*** p < 0.001 ** p < 0.01

DISCUSSION

In this cohort of community-living older people with DM, slow TUG, and c-TUG times were identified as significant risk factors for falls. The negative binomial regression analyses revealed that each 1s increase in TUG and c-TUG times increased the risk of falling by 29% and 13%, respectively, and the complementary ROC comparisons contrasting non-fallers and 1+ fallers indicating similar areas under the curve, i.e., 0.60 and 0.62, for the two tests.

These findings accord with systematic review evidence conducted by Barry et al. 2014 from studies of older people without DM that indicate while statistically significant, the TUG has only moderate diagnostic value with falls [30]. Besides, the finding of Menant et al. 2014 that undertaking the TUG while performing a secondary cognitive task provides no added value about discriminating fallers from non-fallers [31], also aligns with systematic review findings of Schoene et al. 2013 for the general population of older people [32].

Of the explanatory risk factors, knee extension strength explained the most variance in TUG performance – a finding that is consistent with previous studies done by Daubney et al. 1999, Kwan et al. 2011 [33, 34] of older people and confirms lower limb strength is a vital component of functional performance in older people with DM. However, vibration sense, visual contrast sensitivity, and controlled leaning balance were also identified as significant and independent predictors of TUG times, and it is likely these factors influence one or more of the TUG components: chair rising and sitting, walking and turning. Previous studies have found that vision is vital for judging distances which were by Lord et al. 2001 [35] and maintaining stability during standing done by Lord et al. 2000 [36] and stepping by Lord 2001 [37], and numerous studies conducted by Yiou et al. 2017, Conradsson et al., 2018, Day et al. 2018 have found balance control is essential for transfers, step initiation, gait stability and turning [38-40]. Further, the relatively large beta weight for vibration sense in the regression model suggests that loss of sensory integrity significantly impacts mobility task in older people with DM. Finally, DM examination scores provided additional significant explanation to TUG performance when added at the second step of the regression modelling. This measure comprises testing muscle strength, tendon reflex, and sensations of the lower limb, and complications related to disease severity are not captured by explanatory measures.

The associations between the sensorimotor, balance, psychological, and DM-specific factors and c-TUG times were generally weaker than that observed for TUG times. In contrast, MOCA scores were more strongly related to c-TUG times compared with TUG times, and the MOCA was included as an independent and significant predictor of c-TUG time in the multiple regression analysis. These findings reflect the c-TUG's cognitive component and how they limit the test performance of those with lower MOCA scores.

The study findings have a number of clinical implications. First, they indicate while useful, the TUG is likely to be insufficient to assess fall risk in older people with DM and needs to be complemented with disease-specific and impairment-level measures assessing vision, sensation, strength, processing speed, balance, and cognition. Second, it appears it is not necessary to conduct the c-TUG test as well as the TUG if the purpose of the assessment is to identify people with DM at risk of falls. Third, as lower limb strength, vision and balance were found to underpin TUG performance, interventions aimed at addressing impairments in these areas as well as strategies addressing the impact of co-morbidities may improve functional mobility in older people with DM.

The strengths of this study include the broad range of putative risk factors, the prospective falls surveillance, and the recruitment of a sample drawn from a community setting. It is acknowledged; however, the study has certain limitations. First, as the study was carried out in a single study cohort, the findings may only not be generalizable to some populations. Second, despite the range of factors available as possible predictors, over half the variance in TUG and c-TUG times were not accounted for. Fear of falling was included as a psychological measure in the assessment battery. While this measure was significantly correlated with TUG times, it did not meet the criteria for inclusion in the regression model as an independent predictor. Inclusion of complementary psychological measures such as depression and motivation as well as factors such as pain, lower limb power, and foot abnormalities may have improved the model.

CONCLUSION

This study provides evidence that slow TUG times are a significant risk factor for falls in older people with DM and presents information on important physical and cognitive factors that underpin performance in this test. The findings also suggest that the administration of the TUG under dual-task conditions does not further assist in identifying older people with DM at risk of falls.

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