



Full Length Article

Timed up-and-go test is a useful predictor of fracture incidence

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ABSTRACT

Purpose: The timed up-and-go (TUG) test is a validated screening tool to assess fall risk. This study evaluated the association between the TUG test and future fractures, which are a tangible clinical complication of falling.

Methods: We included 1,070,320 participants who participated in the National Screening Program for Transitional Ages for Koreans aged 66 years old from 2009 to 2014. Among them, 355,753 women underwent dual-energy X-ray absorptiometry. TUG times were classified as < 10 s or ≥ 10 s. The incidence of fractures, including vertebral, hip, and other sites, was determined using claims data from the National Health Information database.

Results: During the mean follow-up period of 4.4 ± 1.8 years, participants with slow TUG times had a significantly increased risk of fractures compared with those who had normal TUG times: any fractures (adjusted hazard ratio [aHR] = 1.08, 95% confidence interval [CI] = 1.06–1.10), vertebral fracture (aHR = 1.14, 95% CI = 1.11–1.16), hip fracture (aHR = 1.21, 95% CI = 1.13–1.29), and other fractures (upper arm, forearm, and lower leg; aHR = 1.02, 95% CI = 1.00–1.05). Among women with bone mineral density (BMD) results, slow TUG performance was associated with an increased risk of fracture independent of BMD.

Conclusions: The TUG test, as an indicator of physical performance, can provide information about future fracture risk above that provided by BMD. Conducting the TUG test to assess fracture risk should be considered to improve fracture risk assessment and propose interventions to improve physical performance, thereby reducing fracture risk.

1. Introduction

Fractures in older adults can adversely affect their quality of life and pose a serious socioeconomic burden [1,2]. The > 2 million fractures that occurred in the United States in 2005 were estimated to cost \$17 billion, and the incidence of fractures in the US is predicted to increase by almost 50% by 2025 [2]. The incidence of hip fractures in Koreans older than 50 years was reported to be 146.4 per 100,000 women and 61.7 per 100,000 men, and mortality associated with a hip fracture was 2.9 times higher in this older population than in the general population of Korea [3]. The socioeconomic burden posed by fractures is likely to increase as the population ages [4]. Fracture prevention is an important challenge in public health, and the early detection of individuals who

are at high risk of fracture is an effective preventive strategy. Although several clinical factors are associated with fracture risk, most fractures result from falls [5]. Bone mineral density (BMD) is a single strong predictor of fracture risk, but it reflects only the mineral content of bones without considering other clinical factors [6]. In addition, most fractures occur in individuals with low BMD, rather than in those with osteoporosis [7].

The timed up-and-go (TUG) test is a reliable screening tool to assess fall risk [8]. The clinical practice guidelines of the American and British Geriatrics Societies recommend using the TUG test as a primary functional assessment measure [9]. However, few studies have evaluated the association between the TUG test and future fractures, which are a tangible clinical complication of falling. A previous study of 1126

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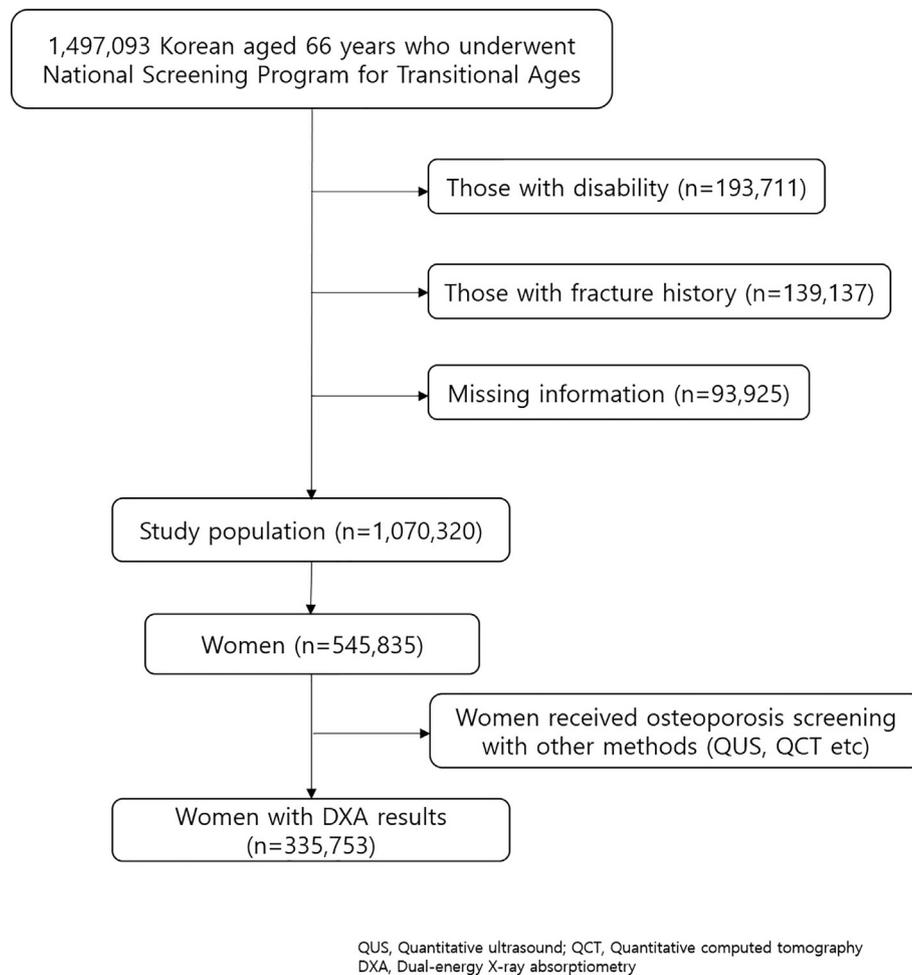


Fig. 1. Flow chart of the study population.

Australian women revealed that a slow TUG time (> 10.2 s) was associated with a higher risk of fracture than a fast TUG time (≤ 10.2 s) (hazard ratio [HR] = 2.48, 95% confidence interval [CI] = 1.02–6.02) [10]. The fracture risk was much higher in those with a slow TUG time and low BMD. However, that study used data from a small number of women who completed a 5-year randomized controlled trial, and the generalizability of its findings is uncertain. In addition, recall bias might have affected those results because the incidence of fractures was based on self-report. A prior cohort study in Korea reported a higher risk of fracture in those with poor TUG performance compared with those with good TUG performance (HR = 1.37, 95% CI = 1.21–1.56) [11]. However, that study did not consider BMD, which is a strong confounding factor.

We hypothesized that a slow TUG test result would be associated with an increased risk of fracture. To test that hypothesis, we investigated the association between TUG time and incident fractures while taking BMD into consideration.

2. Materials and methods

2.1. Study setting

This study used data from the National Health Information Database (NHID) of the Korean National Health Insurance Services (NHIS), which is the single government insurer that covers approximately 97% of the Korean population (the other 3% are Medicaid beneficiaries). For eligibility management, the Korean NHIS collects sociodemographic information, including age, sex, income (insurance premiums are based

on income level, not health status, in Korea), and place of residence. Vital statistics are regularly updated using death registry data from the Korean Statistical Office. To reimburse medical providers, NHIS collects all information about the use of medical facilities, as well as records of medical procedures and prescriptions, in the form of International Classification of Diseases, 10th revision (ICD-10) diagnostic codes.

Since 2007, NHIS has also provided the National Screening Program for Transitional Ages (NSPTA) to 66-year-old participants free of charge. The NSPTA program consists of anthropometric measurements, laboratory tests, and comprehensive geriatric assessments, including assessments of physical function (e.g., TUG test and unipedal balance test) and mental/cognitive function (e.g., screening for depression and cognitive impairment) [12]. It also provides free screening for osteoporosis to women; providers can choose among dual-energy X-ray absorptiometry (DXA), peripheral DXA, quantitative computed tomography (QCT), peripheral QCT, or quantitative ultrasound (QUS). NHID data have been widely used in epidemiologic studies and found to have sufficient validity [13–15].

2.2. Study population

This study initially included 1,497,093 Koreans aged 66 years who underwent the NSPTA from 2009 to 2014. We excluded people with registered disability status ($n = 193,711$), those with fracture history ($n = 139,137$), and those with missing information ($n = 93,925$), resulting in a final study population of 1,070,320. Fracture history was assessed using the ICD-10 code for any fracture, as detailed below. Among the 1,070,320 individuals, 335,753 women who had undergone

Table 1
Baseline characteristics of the study population.

	Total	TUG time		p
		< 10 s	≥ 10 s	
Number	1,070,320	799,240	271,080	
TUG time, seconds	8.3 ± 2.8	7.2 ± 1.5	11.5 ± 3.2	< 0.001
Sex, male	524,485 (49.0)	403,713 (50.5)	120,772 (44.5)	< 0.001
BMI, kg/m ²	24.3 ± 2.8	24.2 ± 2.9	24.4 ± 3.1	< 0.001
< 18.5	22,046 (2.1)	16,195 (2.0)	5851 (2.1)	< 0.001
18.5–23	344,529 (32.2)	261,067 (32.7)	83,462 (30.8)	
23–25	303,305 (28.3)	228,848 (28.6)	74,457 (27.5)	
25–30	364,567 (34.1)	268,521 (33.6)	96,046 (35.4)	
≥ 30	35,873 (3.3)	24,609 (3.1)	11,264 (4.2)	
Smoking				< 0.001
Never	724,104 (67.6)	532,876 (66.7)	191,228 (70.5)	
Former	202,921 (19.0)	158,734 (19.9)	44,187 (16.3)	
Current	143,295 (13.4)	107,630 (13.5)	35,665 (13.2)	
Drinking				< 0.001
None	748,480 (69.9)	552,534 (69.1)	195,946 (72.3)	
Moderate	268,497 (25.1)	206,308 (25.8)	62,189 (22.9)	
Heavy	53,343 (5.0)	40,398 (5.1)	12,945 (4.8)	
Income, lowest quintile	246,429 (23.0)	181,712 (22.7)	64,717 (23.9)	< 0.001
Regular PA, yes	278,816 (26.1)	213,785 (26.8)	65,031 (24.0)	< 0.001
Fall history ^a , yes	63,171 (5.9)	44,596 (5.6)	18,575 (6.9)	< 0.001
UBT, abnormal	150,646 (14.1)	97,566 (12.2)	53,080 (19.6)	< 0.001
Cognitive function, abnormal	141,052 (13.2)	101,897 (12.8)	39,155 (14.4)	< 0.001
Depressive mood	197,108 (18.4)	141,146 (17.7)	55,962 (20.6)	< 0.001
ADL, impaired	32,916 (3.1)	23,488 (2.9)	9428 (3.5)	< 0.001
Diabetes, yes	210,175 (19.6)	153,549 (19.2)	56,626 (20.9)	< 0.001
Hypertension, yes	565,013 (52.8)	415,684 (52.0)	149,329 (55.1)	< 0.001
CKD, ml/min/1.73 m ²				
GFR < 60	118,350 (11.1)	85,947 (10.8)	32,403 (12.0)	< 0.001
30 ≤ GFR < 60	111,335 (10.4)	80,647 (10.1)	30,688 (11.3)	< 0.001
GFR < 30	7015 (0.7)	5300 (0.7)	1715 (0.6)	
Cancer, yes	42,075 (3.9)	31,739(4.0)	10,336 (3.8)	< 0.001
BMD in women				< 0.001
Normal	71,138 (20.0)	55,896 (20.5)	15,242 (18.3)	
Osteopenia	154,044 (43.3)	119,266 (43.8)	34,778 (41.7)	
Osteoporosis	130,571 (36.7)	97,279 (35.7)	33,292 (40.0)	

TUG, timed up-and-go; BMI, body mass index; PA, physical activity; UBT, unipedal balance test; ADL, activities of daily living; CKD, chronic kidney disease; GFR, glomerular filtration rate; BMD, bone mineral density.

^a Fall history in the preceding 6 months.

DXA screening were included in a subgroup analysis; women who underwent other screening methods (most commonly QUS) were excluded to ensure the comparability of the bone density results (Fig. 1). Study participants were followed-up until an incident fracture, censoring (e.g., death), or the last follow-up date (31 December 2017), whichever came first. This study was approved by Samsung Medical Center's institutional review board (IRB number: SMC 2018-03-136), and consent from individual patients was waived because the data are public and anonymized under confidentiality guidelines.

2.3. Exposure: TUG test

The TUG test was administered by health providers at community clinics or hospitals on the day of the NSPTA. The TUG test records the time it takes a person to rise from a chair with armrests, walk 3 m, turn, walk back to the chair, and sit down again. The cut-off point at which the TUG test identifies persons as having a high risk of falling varies from 10 to 33 s depending on the study population [16]. For example, in a study of community-dwelling British elderly, a TUG time ≥ 12.6 s showed a significant association with future falls (adjusted odds ratio [aOR] = 3.94, 95% CI = 1.69–9.21), with 30% sensitivity and 89% specificity [8]. In this study, we divided the subjects into the following groups based on their TUG test results: (1) < 10 s and ≥ 10 s (two groups; primary analysis) or (2) < 10 s, 10–20 s, and ≥ 20 s (three groups; secondary analysis to verify the dose-response relationship) [17,18]. In the Korean NSPTA, TUG results for 66-year-olds are classified as normal if they are < 10 s, borderline between 10 and 20 s, and

abnormal if they are ≥ 20 s, based on expert consensus.

2.4. Outcome: fractures

Fractures were defined using ICD-10 codes as follows: vertebral (S22.0, S22.1, S32.0, M48.4 and M48.5), hip (S72.0 and S72.1), and other fractures, which were upper arm (S42.0, S42.2 and S42.3), forearm (S52.5 and S52.6), and lower leg (S82.3, S82.5 and S82.6) [19,20]. Individuals were deemed to have vertebral or other fractures when they had two or more outpatient visits with relevant diagnosis codes within 12 months. Hip fracture was defined as one hospitalization with the relevant diagnosis code. The category 'Any fractures' was defined as when individuals had at least one of these fracture types.

2.5. Covariates

BMD was measured by DXA (Hologic Inc., Bedford, MA, USA) at either the lumbar spine (from the first to the fourth lumbar vertebra) or in the femur. T-scores were calculated for women using the Asian (Japanese) reference curve supplied by the manufacturer. A normal density was defined as a T-score ≥ -1.0; osteopenia was defined as a T-score between -1.0 and -2.5; and osteoporosis was defined as a T-score ≤ -2.5, following World Health Organization definitions [21].

Individuals were assigned to one of five categories based on their body mass index (BMI, kg/m²): underweight (< 18.5), normal (18.5–23), overweight (23–25), obese (25–30), and severely obese (≥ 30), following the Asia-Pacific criteria of the World Health

Table 2
Hazard ratio for fractures according to baseline TUG times.

Fracture type	Sex	TUG time (s)	Number	Event	Duration (PYs)	Incidence rate	Unadjusted HR (95% CI)	Model 1 aHR (95% CI)	Model 2 aHR (95% CI)
Any	Total	< 10	799,240	61,021	3,508,755.6	17.4	1.00	1.00	1.00
		≥ 10	271,080	24,910	1,231,654.8	20.2	1.16 (1.14–1.18)	1.08 (1.07–1.10)	1.08 (1.06–1.10)
	Male	< 10	403,713	17,973	1,795,017.9	10.0	1.00	1.00	1.00
		≥ 10	120,772	6284	556,119.9	11.3	1.12 (1.09–1.16)	1.10 (1.07–1.13)	1.10 (1.06–1.13)
	Female	< 10	395,527	43,048	1,713,737.8	25.1	1.00	1.00	1.00
		≥ 10	150,308	18,626	675,534.9	27.6	1.09 (1.08–1.11)	1.08 (1.06–1.10)	1.07 (1.05–1.09)
Vertebral	Total	< 10	799,240	26,583	3,508,755.6	7.6	1.00	1.00	1.00
		≥ 10	271,080	11,538	1,231,654.8	9.4	1.23 (1.20–1.25)	1.14 (1.11–1.16)	1.14 (1.11–1.16)
	Male	< 10	403,713	8295	1,795,017.9	4.6	1.00	1.00	1.00
		≥ 10	120,772	2950	556,119.9	5.3	1.14 (1.09–1.19)	1.11 (1.06–1.16)	1.11 (1.06–1.16)
	Female	< 10	395,527	18,288	1,713,737.8	10.7	1.00	1.00	1.00
		≥ 10	150,308	8588	675,534.9	12.7	1.18 (1.15–1.21)	1.15 (1.12–1.18)	1.14 (1.11–1.17)
Hip	Total	< 10	799,240	2658	3,508,755.6	0.8	1.00	1.00	1.00
		≥ 10	271,080	1221	1,231,654.8	1.00	1.29 (1.21–1.38)	1.23 (1.14–1.31)	1.21 (1.13–1.29)
	Male	< 10	403,713	1244	1,795,017.9	0.7	1.00	1.00	1.00
		≥ 10	120,772	493	556,119.9	0.9	1.26 (1.14–1.40)	1.20 (1.08–1.33)	1.18 (1.07–1.31)
	Female	< 10	395,527	1414	1,713,737.8	0.8	1.00	1.00	1.00
		≥ 10	150,308	728	675,534.9	1.1	1.29 (1.18–1.41)	1.23 (1.13–1.35)	1.21 (1.11–1.32)
Other ^a	Total	< 10	799,240	31,780	3,508,755.6	9.1	1.00	1.00	1.00
		≥ 10	271,080	12,151	1,231,654.8	9.9	1.09 (1.07–1.11)	1.02 (1.00–1.05)	1.02 (1.00–1.05)
	Male	< 10	403,713	8434	1,795,017.9	4.7	1.00	1.00	1.00
		≥ 10	120,772	2841	556,119.9	5.1	1.09 (1.04–1.13)	1.07 (1.03–1.12)	1.07 (1.03–1.12)
	Female	< 10	395,527	23,346	1,713,737.8	13.6	1.00	1.00	1.00
		≥ 10	150,308	9310	675,534.9	13.8	1.01 (0.99–1.04)	1.01 (0.99–1.04)	1.01 (0.98–1.03)

TUG, timed up-and-go; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; PYs, person years.

Incidence rate indicates events per 1000 person-years.

Model 1 was adjusted for sex, body mass index, income, smoking, alcohol consumption, regular physical activity, fall history, and unipedal balance test. Model 2 was adjusted for the same variables as in model 1 + comorbidities (hypertension, diabetes, chronic kidney disease, cancer) and mental/cognitive function.

^a Other: fractures of upper arm, forearm, or lower leg.

Organization [22]. Participants were classified as non, past, or current smokers based on the smoking information they provided. Alcoholic drink consumption was classified as none (0 g/day), moderate (< 30 g/day), or heavy (≥ 30 g/day) based on daily alcohol consumption. Regular exercise was defined as ≥ 20 min of strenuous physical activity as least once a week. Income level was based on the monthly insurance premium because the insurance contribution is determined by income level, not health risk, in Korea.

An abnormal unipedal balance test (UBT) was defined as being unable to maintain posture for 5 s or less with closed eyes or 9 s or less with open eyes [23]. A history of falls was based on self-reported information. The Prescreening Korean Dementia Screening Questionnaire (KDSQ-P) was used to assess cognitive function [24]. Participants with a score ≥ 4 require further evaluation for cognitive function assessment. Depressive mood was assessed using three questions from the Geriatric Depression Scale to determine loss of interest, feelings of uselessness, and hopeless feelings. If participants answered “yes” to any of those questions, they were regarded as suffering from depression.

The following comorbidities were defined using claims data before the screening date: diabetes (at least one claim per year under ICD-10 codes E11–14 and at least one claim per year for the prescription of antidiabetic medication); hypertension (at least one claim per year under ICD-10 codes I10–13 or I15 and at least one claim per year for the prescription of antihypertensive agents or systolic/diastolic BP ≥ 140/90 mmHg); and cancer (ICD C-codes) [25]. Chronic kidney disease (CKD) was defined based on the glomerular filtration rate (GFR), as estimated by the Modification of Diet in Renal Disease (MDRD) equation, and the following GFR categories were recognized: ≥ 60, 30–60, and < 30 ml/min/1.73 m².

2.6. Statistical analysis

To examine differences in baseline characteristics according to TUG time, *t*-tests and chi-square tests were conducted. A Kaplan-Meier (KM) curve was used to depict the association between TUG time and fracture

risk. Hazard ratios for fractures according to TUG time were obtained using Cox proportional hazards regression analyses. We adjusted for sex, lifestyle variables (BMI, smoking, drinking, and physical activity), physical performance (history of falls and UBT), and household income in model 1. In model 2, mental health status (cognitive function and depressive mood) and comorbidities (CKD, cancer, diabetes, and hypertension) were added to model 1. Several sets of sensitivity analyses were performed. First, dose-response relationships were evaluated by estimating the fracture risk with TUG time in three categories (< 10, 10–20, ≥ 20). Second, we applied 9 s, 13.5 s and 15 s cut-offs to confirm the association with different cut-off points [16,26]. The 9 s cut-off was the optimal point that minimized the Euclidean distance between the receiver operating characteristic curve and the (0,1) point with 45% sensitivity and 59% specificity (Supplementary Fig. 1). Third, we included participants with disabilities and those with missing TUG times in the analysis. Stratified analyses by level of physical activity and BMI were also performed. Another stratified analysis by BMD level was conducted with subgroups of female participants who underwent DXA during the NSPTA. All statistical analyses were carried out using SAS (version 9.4; SAS Institute, Cary, NC, US).

3. Results

3.1. Baseline characteristics

The mean TUG time was 8.3 (standard deviation [SD] 2.8) seconds; 74.7% of the sample had a TUG time < 10 s (mean 7.2, SD 1.5), and 25.3% had a TUG time ≥ 10 s (mean 11.5 s, SD 3.2). More individuals with lower TUG times (< 10 s) were underweight (BMI < 18.5 kg/m², 2.1%) or obese (BMI ≥ 25 kg/m², 39.6%) compared with individuals with faster TUG times. Fewer individuals with slow TUG times engaged in regular physical activity compared with those who had low TUG times (24.0% vs. 26.8%). In addition, poor geriatric physical performance (a history of falls and UBT abnormality) and an abnormal mental health state (poor cognitive function or depressive mood) were more

Table 3
Hazard ratio for fractures according to baseline TUG times with dose-response relationships.

Fracture type	Sex	TUG time (s)	Number	Event	Duration (PYs)	Incidence rate	Unadjusted HR (95% CI)	Model 1 aHR (95% CI)	Model 2 aHR (95% CI)
Any	Total	< 10	799,240	61,021	3,508,755.6	17.4	1.00	1.00	1.00
		10–20	266,001	24,335	1,208,600.0	20.1	1.15 (1.14–1.17)	1.08 (1.06–1.10)	1.08 (1.06–1.09)
		≥ 20	5079	575	23,054.7	24.9	1.43 (1.32–1.55)	1.21 (1.12–1.32)	1.20 (1.11–1.30)
	Male	< 10	403,713	17,973	1,795,017.9	10.0	1.00	1.00	1.00
		10–20	118,795	6153	546,949.7	11.3	1.12 (1.09–1.15)	1.10 (1.06–1.13)	1.09 (1.06–1.12)
		≥ 20	1977	131	9170.2	14.3	1.42 (1.19–1.68)	1.29 (1.09–1.53)	1.27 (1.07–1.51)
	Female	< 10	395,527	43,048	1,713,737.8	25.1	1.00	1.00	1.00
		10–20	147,206	18,182	661,650.4	27.5	1.09 (1.07–1.11)	1.07 (1.06–1.09)	1.07 (1.05–1.09)
		≥ 20	3102	444	13,884.5	32.0	1.27 (1.16–1.39)	1.19 (1.08–1.30)	1.17 (1.07–1.29)
Vertebral	Total	< 10	799,240	26,583	3,508,755.6	7.6	1.00	1.00	1.00
		10–20	266,001	11,253	1,208,600.0	9.3	1.22 (1.19–1.25)	1.13 (1.11–1.16)	1.13 (1.11–1.16)
		≥ 20	5079	285	23,054.7	12.4	1.61 (1.44–1.81)	1.34 (1.19–1.50)	1.32 (1.17–1.48)
	Male	< 10	403,713	8295	1,795,017.9	4.6	1.00	1.00	1.00
		10–20	118,795	2891	546,949.7	5.3	1.13 (1.09–1.18)	1.11 (1.06–1.16)	1.11 (1.06–1.15)
		≥ 20	1977	59	9170.2	6.4	1.38 (1.07–1.78)	1.24 (0.96–1.60)	1.22 (0.94–1.58)
	Female	< 10	395,527	18,288	1,713,737.8	10.7	1.00	1.00	1.00
		10–20	147,206	8362	661,650.4	12.6	1.17 (1.14–1.20)	1.14 (1.11–1.17)	1.14 (1.11–1.17)
		≥ 20	3102	226	13,884.5	16.3	1.51 (1.33–1.73)	1.35 (1.19–1.54)	1.34 (1.17–1.53)
Hip	Total	< 10	799,240	2658	3,508,755.6	0.8	1.00	1.00	1.00
		10–20	266,001	1176	1,208,600.0	1.0	1.27 (1.18–1.36)	1.21 (1.13–1.29)	1.19 (1.11–1.27)
		≥ 20	5079	45	23,054.7	1.9	2.53 (1.88–3.40)	2.06 (1.53–2.77)	1.96 (1.45–2.63)
	Male	< 10	403,713	1244	1,795,017.9	0.7	1.00	1.00	1.00
		10–20	118,795	477	546,949.7	0.9	1.24 (1.12–1.38)	1.19 (1.07–1.32)	1.17 (1.05–1.30)
		≥ 20	1977	16	9170.2	1.7	2.47 (1.51–4.04)	1.94 (1.18–3.18)	1.83 (1.11–3.01)
	Female	< 10	395,527	1414	1,713,737.8	0.8	1.00	1.00	1.00
		10–20	147,206	699	661,650.4	1.1	1.26 (1.15–1.38)	1.21 (1.11–1.33)	1.19 (1.09–1.31)
		≥ 20	3102	29	13,884.5	2.1	2.49 (1.72–3.59)	2.09 (1.44–3.02)	1.97 (1.36–2.85)
Others ^a	Total	< 10	799,240	31,780	3,508,755.6	9.1	1.00	1.00	1.00
		10–20	266,001	11,906	1,208,600.0	9.9	1.09 (1.07–1.11)	1.02 (1.00–1.05)	1.02 (1.00–1.05)
		≥ 20	5079	245	23,054.7	10.6	1.18 (1.04–1.33)	1.03 (0.91–1.17)	1.02 (0.90–1.16)
	Male	< 10	403,713	8434	1,795,017.9	4.7	1.00	1.00	1.00
		10–20	118,795	2785	546,949.7	5.1	1.08 (1.04–1.13)	1.07 (1.02–1.12)	1.07 (1.02–1.11)
		≥ 20	1977	56	9170.2	6.1	1.30 (0.99–1.69)	1.22 (0.94–1.59)	1.22 (0.93–1.58)
	Female	< 10	395,527	23,346	1,713,737.8	13.6	1.00	1.00	1.00
		10–20	147,206	9121	661,650.4	13.8	1.01 (0.99–1.04)	1.01 (0.99–1.04)	1.01 (0.99–1.03)
		≥ 20	3102	189	13,884.5	13.6	1.00 (0.87–1.16)	0.98 (0.85–1.13)	0.97 (0.84–1.12)

TUG, timed up-and-go; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; PYs, person years.

Incidence rate indicates events per 1000 person-years.

Model 1 was adjusted for sex, body mass index, income, smoking, alcohol consumption, regular physical activity, fall history, and unipedal balance test. Model 2 was adjusted for the same variables as in model 1 + comorbidities (hypertension, diabetes, chronic kidney disease, cancer) and mental/cognitive function.

^a Others: fractures of upper arm, forearm, or lower leg.

prevalent in those with slower TUG times. Among women with BMD results, the prevalence of osteoporosis was higher in those with slower TUG times (35.7% vs. 40.0%) (Table 1).

3.2. Association between TUG time and incidence of fracture

The median follow-up duration was 4.4 (SD 1.8) years in the normal TUG group and 4.5 (SD 1.9) years in the slow TUG group. The incidence rate (per 1000 person-years) of fractures was higher among those with a slow TUG test result than among those with a normal TUG test result: any fractures (20.2 vs. 17.4), vertebral fracture (9.4 vs. 7.6), hip fracture (1.0 vs. 0.8), and other fractures (9.9 vs. 9.1) (Table 2).

Compared with those who had normal TUG times, participants with slow TUG times had a significantly increased risk of fractures: any fractures (adjusted hazard ratio [aHR] = 1.08, 95% CI = 1.06–1.10), vertebral fracture (aHR = 1.14, 95% CI = 1.11–1.16), hip fracture (aHR = 1.21, 95% CI = 1.13–1.29), and other fracture (aHR = 1.02, 95% CI = 1.00–1.05). There was no significant difference in this association by subject sex (Table 2). Supplementary Fig. 2 depicts the KM curves for the association of fracture risk with baseline TUG times.

Secondary analysis with three TUG groups showed a significant dose-response relationship: any fractures (aHR = 1.08, 95% CI = 1.06–1.09 in 10–20 s and aHR = 1.20, 95% CI = 1.11–1.30 in ≥ 20 s); vertebral fracture (aHR = 1.13, 95% CI = 1.11–1.16 in 10–20 s and aHR = 1.32, 95% CI = 1.17–1.48 in ≥ 20 s); hip fracture (aHR = 1.19, 95% CI = 1.11–1.27 in 10–20 s and aHR = 1.96, 95%

CI = 1.45–2.63 in ≥ 20 s) (Table 3).

In the analysis with different cut-off points, a high risk of fractures with a slow TUG time was consistently observed (Supplementary Table 1). In the analysis including those with any disability and those with missing TUG times, the highest risk of fracture was observed in those with any disability (Supplementary Table 2).

When we stratified participants by physical activity level, a higher risk of hip fracture was evident in individuals without regular physical activity (aHR 1.29 vs. 0.88). Results stratified by BMI level showed that the effect of a slow TUG time was most prominent among underweight individuals (aHR = 1.40, 95% CI = 1.19–1.64) (Supplementary Table 3).

3.3. Risk of fracture according to TUG time among women who underwent DXA

Among women with BMD results, slow TUG performance was associated with an increased risks of all fractures (aHR = 1.08, 95% CI = 1.05–1.10), vertebral fracture (aHR = 1.16, 95% CI = 1.12–1.20), and hip fracture (aHR = 1.22, 95% CI = 1.08–1.37), but not the risk of other fractures (aHR = 1.01, 95% CI 0.97–1.04). When stratified by BMD status, the overall association did not seem to depend BMD status. However, the risk of vertebral fractures tended to be more prominent in women with normal BMD (aHR = 1.27, 95% CI = 1.14–1.41) than in women with osteoporosis (aHR = 1.07, 95% CI = 1.02–1.12). Conversely, among those with a slow TUG time, the risk of a hip

Table 4
Hazard ratio for fractures according to baseline TUG time among 355,753 women stratified by bone mineral density.

Fracture type	BMD	TUG time (s)	Number	Event	Duration (PYs)	Incidence rate	Unadjusted HR (95% CI)	Model 1 aHR (95% CI)	Model 2 aHR (95% CI)
Any	Total	< 10	272,441	27,873	1,145,491.5	24.3	1.00	1.00	1.00
		≥ 10	83,312	9549	355,868.1	26.8	1.10 (1.08–1.13)	1.08 (1.05–1.11)	1.08 (1.05–1.10)
	Normal	< 10	55,896	3860	237,314.9	16.3	1.00	1.00	1.00
		≥ 10	15,242	1204	65,723.5	18.3	1.13 (1.05–1.20)	1.09 (1.02–1.17)	1.09 (1.02–1.16)
	Osteopenia	< 10	119,266	11,558	502,223.0	23.0	1.00	1.00	1.00
		≥ 10	34,778	3648	149,837.2	24.4	1.06 (1.02–1.10)	1.03 (0.99–1.07)	1.03 (0.99–1.07)
Osteoporosis	< 10	97,279	12,455	405,953.6	30.7	1.00	1.00	1.00	
	≥ 10	33,292	4697	140,307.4	33.5	1.09 (1.05–1.13)	1.07 (1.03–1.10)	1.06 (1.03–1.10)	
Vertebral	Total	< 10	272,441	11,317	1,145,491.5	9.9	1.00	1.00	1.00
		≥ 10	83,312	4256	355,868.1	12.0	1.21 (1.16–1.25)	1.16 (1.12–1.20)	1.16 (1.12–1.20)
	Normal	< 10	55,896	1225	237,314.9	5.2	1.00	1.00	1.00
		≥ 10	15,242	459	65,723.5	7.0	1.35 (1.21–1.50)	1.28 (1.15–1.42)	1.27 (1.14–1.41)
	Osteopenia	< 10	119,266	4218	502,223.0	8.4	1.00	1.00	1.00
		≥ 10	34,778	1529	149,837.2	10.2	1.21 (1.14–1.28)	1.15 (1.09–1.22)	1.14 (1.08–1.21)
Osteoporosis	< 10	97,279	5874	405,953.6	14.5	1.00	1.00	1.00	
	≥ 10	33,292	2268	140,307.4	16.2	1.11 (1.06–1.17)	1.07 (1.02–1.13)	1.07 (1.02–1.12)	
Hip	Total	< 10	272,441	934	1,145,491.5	0.8	1.00	1.00	1.00
		≥ 10	83,312	381	355,868.1	1.1	1.30 (1.16–1.47)	1.24 (1.10–1.39)	1.22 (1.08–1.37)
	Normal	< 10	55,896	144	237,314.9	0.6	1.00	1.00	1.00
		≥ 10	15,242	50	65,723.5	0.8	1.25 (0.90–1.72)	1.15 (0.83–1.59)	1.12 (0.81–1.56)
	Osteopenia	< 10	119,266	385	502,223.0	0.8	1.00	1.00	1.00
		≥ 10	34,778	137	149,837.2	0.9	1.18 (0.97–1.43)	1.13 (0.93–1.38)	1.11 (0.92–1.36)
Osteoporosis	< 10	97,279	405	405,953.6	1.0	1.00	1.00	1.00	
	≥ 10	33,292	194	140,307.4	1.4	1.38 (1.16–1.63)	1.31 (1.11–1.56)	1.29 (1.08–1.53)	
Other ^a	Total	< 10	272,441	15,622	1,145,491.5	13.6	1.00	1.00	1.00
		≥ 10	83,312	4912	355,868.1	13.8	1.01 (0.98–1.05)	1.01 (0.98–1.04)	1.01 (0.97–1.04)
	Normal	< 10	55,896	2491	237,314.9	10.5	1.00	1.00	1.00
		≥ 10	15,242	695	65,723.5	10.6	1.01 (0.93–1.10)	0.99 (0.91–1.08)	0.99 (0.91–1.08)
	Osteopenia	< 10	119,266	6955	502,223.0	13.9	1.00	1.00	1.00
		≥ 10	34,778	1982	149,837.2	13.2	0.96 (0.91–1.01)	0.95 (0.91–1.00)	0.95 (0.90–0.99)
Osteoporosis	< 10	97,279	6176	405,953.6	15.2	1.00	1.00	1.00	
	≥ 10	33,292	2235	140,307.4	15.9	1.05 (0.99–1.10)	1.04 (0.99–1.09)	1.04 (0.99–1.09)	

TUG, timed up-and-go; BMD, bone mineral density; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; PYs, person years.

Incidence rate indicates events per 1000 person-years.

Model 1 was adjusted for sex, body mass index, income, smoking, alcohol consumption, regular physical activity, fall history, and unipedal balance test. Model 2 was adjusted for the same variables as in model 1 + comorbidities (hypertension, diabetes, chronic kidney disease, cancer) and mental/cognitive function.

^a Other: fractures of upper arm, forearm, or lower leg.

fracture was more prominent in women with osteoporosis (aHR = 1.29, 95% CI = 1.08–1.53) than in women with normal BMD (aHR = 1.12, 95% CI = 1.08–1.37) (Table 4). When we included BMD status as a confounding factor instead of a stratification, the results were consistent: slow TUG performance was associated with a higher risk of a future fracture (Supplementary Table 4).

4. Discussion

To our knowledge, this study is the first to demonstrate that slow TUG performance is significantly associated with an increased risk of fractures in a very large study population. In particular, women with a slow TUG time had an increased risk of fractures independent of BMD status. A slow TUG time was significantly associated with a higher fracture risk, even in women with a normal BMD.

TUG time reflects walking speed, muscle strength and balance, sit-to-walk transition time, turning, walking, and walk-to-sit transition time. All these components are known to be associated with fracture risk. The Osteoporosis Prospective Risk Assessment study reported that decreased walking speed was associated with a high risk of fractures independent of BMD (HR = 1.37, 95% CI = 1.14–1.64) [27]. Impaired postural balance, assessed by a one-leg standing test, was previously associated with an increased risk of hip fracture [28]. Quadriceps muscle strength, which plays an important role in knee extension during walking, was also shown to be an independent determinant of fracture risk [29]. The TUG test is a single test that can assess general physical performance; it is simple to perform, reliable, and can easily be conducted as part of a routine examination, with high interrater and test-retest reliability [30].

In this study, the HR for the association between hip fracture and a slower versus faster TUG time (aHR 1.21) was higher than that for a vertebral fracture (aHR 1.14) or other fracture (aHR 1.02). Most hip fractures result from falls, whereas a smaller proportion of vertebral fractures results from falls [31]. Among women with osteoporosis, the risk of a hip fracture was greater (aHR 1.19) than among women with normal BMD (aHR 1.12) or osteopenia (aHR 1.11), but the confidence intervals overlapped, suggesting that a slow TUG time and osteoporosis might contribute synergistically to hip fracture. People with a slow TUG time might be more prone to high-energy trauma, such as falls, in which low BMD is a strong risk factor for hip fracture. In addition, a slow TUG time might reflect poor mobility and muscle weakness, and the subsequent low physical load on the hip bone could lead to further deterioration of hip BMD, further increasing the risk of a fracture [32]. Consistent with this explanation, we found that a higher risk of fracture was prominently observed among those in the slow TUG time group who did not engage in regular physical activity, perhaps because of poor mobility.

Women with a normal BMD and slow TUG time had a higher HR for vertebral fracture than women with a normal BMD and fast TUG time, which indicates that the TUG test could add information above that provided by BMD in predicting vertebral fractures. When stratified by BMD level, a slow TUG time had a stronger effect on vertebral fracture when BMD was normal (aHR 1.27) than when BMD was consistent with osteopenia (aHR 1.14) or osteoporosis (aHR 1.07). This is contrary to the effect of BMD on the association between TUG time and hip fracture. The exact mechanism for this finding needs further investigation, but possible reasons are a high incidence of low-trauma fracture without osteoporosis of the spine, [33] and a relatively lower

contribution of low BMD to vertebral fracture than other fracture types [34].

In this study, a slow TUG time was marginally associated with fracture risk at other sites (forearms, upper arms, and lower legs). Even though most of those fractures result from falls, a slow TUG time was not strongly associated with a risk of fracture at those sites. This result could be related to the U-shaped relationship between walking speed and falls [35]. In contrast to the notion that a slow walking speed is associated with falls or fractures, more physically active persons with a faster walking speed could be exposed more to outdoor environmental hazards than those with a slower walking speed [36]. In particular, distal forearm fractures tend to occur in women with a low BMD who are relatively healthy and have good neuromuscular function [37].

Our study has several clinical implications. The fracture risk assessment tool (FRAX) is widely used to estimate fracture probability and has an area-under-the-curve value of 0.69 for predicting major osteoporotic fractures based on clinical risk factors and femoral BMD [38]. TUG time could potentially provide additional information if incorporated into the FRAX model. Physical performance predicted the incidence of fractures independently of FRAX probability in the Osteoporotic Fractures in Men Study cohort [39]. Second, appropriate management techniques, such as adequate weight-bearing and muscle-strengthening exercises, should be considered for those with slow TUG times to improve their physical performance, as well as their bone mass [40]. In conjunction with nonpharmacologic strategies, physicians could also consider pharmacotherapy for those with a slow TUG performance and a low BMD, in accordance with accepted guidelines [41]. In our study, the effect of a slow TUG time was greater in people with the lowest BMI, which is also a well-known risk factor for fractures, suggesting a synergic interaction in fracture risk between a slow TUG time and being underweight. Special attention needs to be paid to the individuals at highest risk.

Our study had several limitations that could limit the generalizability of our results. First, because we used claims data, our definition of fracture is subject to ascertainment bias, and we could not determine whether any fracture was the result of falls. The TUG test is widely used to assess mobility and the risk of falls, and we assume that the mechanisms underlying our findings of a higher risk of fracture according to TUG time correlate with the risk of falling or poor mobility. However, there is no reason to believe that individuals with a slow TUG time are more susceptible than others to traumatic fracture. Second, our follow-up period was relatively short (mean follow-up: 4.4 years, up to 8.0 years). The incidence of fracture increases with age, and the results of our study might have been more pronounced if the follow-up period was longer. Third, we could not consider racial differences in fracture incidence or BMD based on our sample population. Asian females have the lowest BMD and a lower risk of fracture than other ethnicities [42]. Therefore, replicative studies in various races are needed. Fourth, there might have been selection bias; the individuals who participated in the DXA screening program might have been healthier and better educated than those who did not participate [43].

4.1. Conclusions

The TUG test as an indicator of physical performance can provide additional information about the risk of a future fracture above that provided by BMD. This study supports the use of the TUG test to assess fracture risk and suggests the need for interventions to improve physical performance and reduce fracture risk.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bone.2019.07.018>.

Declaration of Competing Interest

All authors state that they have no conflicts of interest.

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