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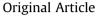
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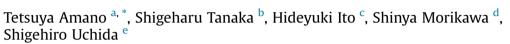


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Quantifying walking ability in Japanese patients with knee osteoarthritis: Standard values derived from a multicenter study



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ABSTRACT

Background: We aimed to determine useful parameters for quantifying walking ability in patients with knee osteoarthritis.

Methods: This study included 621 Japanese patients with knee osteoarthritis scheduled to undergo total knee arthroplasty at any of 14 participating hospitals. Sex, age, body mass index, osteoarthritis severity (Kellgren-Lawrence grade), laterality, prior contralateral surgery, and pain were analyzed for their influence on walking ability, which was evaluated in terms of the 5-m walk test and the Timed Up and Go test outcomes during preoperative hospitalization. Patients were stratified based on dichotomized values of the independent influencing factors of walking ability, and the standard values for parameters describing walking ability were obtained.

Results: Multiple regression analysis revealed that sex, age, and Kellgren-Lawrence grade were factors influencing walking ability (5-m walk test and Timed Up and Go test outcomes). Therefore, the patients were stratified by sex, age, and Kellgren-Lawrence grade. The standard values (median values) for walking time on the 5-m walk test among patients aged 60-74/75-89 years were: 3.90/4.64 vs. 4.27/5.12 s for men vs. women with Kellgren–Lawrence grade III; 4.26/5.60 vs. 4.80/6.05 s for men vs. women with Kellgren-Lawrence grade IV. Regarding walking speed on the 5-m test, the standard values were: 1.28/1.08 vs. 1.17/0.98 m/s for men vs. women with Kellgren-Lawrence grade III; 1.17/0.89 vs. 1.04/0.83 m/s for men vs. women with Kellgren-Lawrence grade IV. Finally, the standard values for time on the Timed Up and Go test were: 8.52/10.30 vs. 9.30/11.74 s for men vs. women with Kellgren -Lawrence grade III; 9.40/12.90 vs. 10.05/13.20 s for men vs. women with Kellgren-Lawrence grade IV. Conclusions: The standard values reported in this study can be used to quantify walking ability decline in patients with knee osteoarthritis and to aid in the decision to consider total knee arthroplasty.

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1. Introduction

Osteoarthritis (OA) is a common complaint for which patients seek treatment, with knee OA being the most frequent type of arthropathy worldwide [1,2]. Conservative therapies such as pharmacotherapy, orthosis therapy, and physical therapy are generally

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effective and represent the first choice for the treatment of knee OA [3–6]. However, the decline in walking ability represents a clinical symptom that remains problematic in patients with knee OA undergoing conservative therapies [7]. Astephen et al. [8] reported that walking speed in severe knee OA subjects just prior to total joint replacement surgery was significantly slower than that in asymptomatic subjects and in subjects clinically diagnosed with moderate knee OA. Upon following up knee OA patients for 1 year, van Dijk et al. [9] found recognizable progression of activity restriction, mediated by a decrease in walking ability. Treatment should be planned and adapted according to the condition and

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disease progress in each individual patient because knee OA is a degenerative condition, with age representing an important risk factor associated with advanced stage and more severe symptoms of OA. Although a quantitative evaluation of the patient's condition is paramount, no specific parameter has gained widespread adoption for quantitative evaluation of the decline in walking ability, which represents a key development in patients with knee OA.

Owing to its safety and effectiveness, total knee arthroplasty (TKA) is the most commonly used surgical therapy for knee OA [10]. TKA is mainly indicated when adequate pain relief and functional improvement are not achieved with physical therapy combined with orthosis therapy and pharmacotherapy, but it is also widely indicated for end-stage knee OA with strong functional decline. TKA indication is based on age, OA stage, pain due to functional deterioration, activity level, and the patient's expectations [11,12]. Due to advances in surgical techniques, TKA indications have expanded to include younger and more active patients [13,14]. However, there is no objective measure of the appropriateness of TKA because it is difficult to objectively evaluate the limits of conservative therapy.

This study aimed to identify adequate parameters for the quantitative evaluation of walking ability in patients with knee OA.

2. Materials and methods

2.1. Patients and study design

This cross-sectional, multicenter study was conducted in 14 participating hospitals between July 2013 and December 2017. This study included data pertaining to 621 Japanese patients with knee OA (492 women and 129 men; mean age ±standard deviation, 75.1 \pm 6.5 years). The selection criteria were: 1) hospitalization for scheduled TKA; 2) age between 60 and 89 years; 3) diagnosis of OA of Kellgren–Lawrence (K-L) grade III or IV; and 4) ability to walk independently or using a T-cane. The exclusion criteria were: 1) major neurological findings, such as motor paralysis; 2) cognitive or mental dysfunction; and 3) significant functional disorders affecting joints other than the knee. This study was conducted based on the guidelines laid down in the Helsinki Declaration and the ethical guidelines of our institution. This study was approved by the Research Ethics Committee of Tokoha University (approval no. R-2017-510H). All patients provided written informed consent for participation.

2.2. Data collection

The following factors were assessed preoperatively: individual factors including sex, age, and body mass index (BMI); OA severity as K-L grade; laterality (bilateral or unilateral knee OA); prior history of contralateral surgery; and pain. The degree of perceived spontaneous pain in the knee joint was evaluated using a numerical rating scale (NRS) that ranged from 0 (no pain) to 10 (worst pain imaginable) [15].

2.3. Functional tests of walking ability

Walking ability was evaluated using two tests commonly employed to assess walking mobility: the 5-m walk test (5 mWT) and the Timed Up and Go test (TUGT) [16]. The 5mWT was conducted as an in-room test consisting of an 11-m linear walking exercise along an initial, 3-m acceleration zone, a central, 5-m timed zone, and a final, 3-m deceleration zone. The 5 mWT started from the moment the patient's lower limb crossed the starting line (i.e., the line between the initial, 3-m acceleration zone and the 5-m timed zone), and ended when the patient crossed the end line (i.e., the line between the 5-m timed zone and the final, 3-m deceleration zone). The outcome measures included the time it took for the patient to walk the entire 5-m zone at maximum speed (walking time, measured in sec), as well as the walking speed (m/sec), calculated as the distance (5 m) divided by the walking time. In the TUGT, the patient was instructed to rise from a chair, walk 3 m, turn, walk back, and sit back down in the chair as quickly as they could. The TUGT outcome measure was the total time it took for the patient to complete the test and return to the starting position (i.e., seated in the chair). The two functional tests (i.e., 5mWT and TUGT) were performed during preoperative hospitalization.

2.4. Statistical analysis

We first examined the factors affecting walking ability, and then stratified patients based on dichotomized values of such factors in order to determine the standard values for the 5mWT and TUGT outcomes in knee OA patients scheduled for TKA. Factors previously reported to affect walking ability in patients with knee OA include sex, advanced age, obesity, disease severity, and pain [17-20]. Laterality and previous history of contralateral surgery may also have an influence on walking ability. In this study, multiple regression analysis was used to determine the independent factors affecting walking ability in patients with knee OA. The independent variables tested for their effect on walking ability were sex, age, BMI, K-L grade, laterality, contralateral surgery, and pain on the NRS. The dependent variables describing walking ability were walking time on the 5 mWT, walking speed on the 5 mWT, and time on the TUGT. The independent variables were entered into the multiple regression model using the stepwise method. In the regression models used to determine the importance of each factor, qualitative variables were coded as follows: sex, men = 1, women = 0; K-L grade, grade III = 1, grade IV = 0; laterality, unilateral knee OA = 1, bilateral knee OA = 0; contralateral surgery, yes = 1, no = 0. In these models, other variables (age, BMI, and pain score) were treated as quantitative data. Finally, the patients were then stratified based on dichotomized values of the independent influencing factors, and the standard values for walking time on the 5mWT, walking speed on the 5mWT, and time on the TUGT were obtained. The software used to analyze the collected data was SPSS (version 22.0; IBM Corp., Tokyo, Japan), and the significance level was set at p < 0.05.

3. Results

The average Functional Independence Measure score was 121.6 ± 5.1 points, and a decline in activities of daily living was recognized mainly for items assessing locomotion and transfers. Descriptive statistics for individual factors and preoperative walking ability are shown in Table 1.

Multiple regression analysis revealed that the independent factors affecting walking time on the 5 mWT (p < 0.001, R = 0.354, $R^2 = 0.125$) were age (p < 0.001, $\beta = 0.269$), K-L grade (p < 0.001, $\beta = -0.192$), and sex (p = 0.003, $\beta = -0.114$). The factors influencing walking speed on the 5 mWT (p < 0.001, R = 0.417, $R^2 = 0.174$) were also age (p < 0.001, $\beta = -0.337$), K-L grade (p < 0.001, $\beta = 0.200$), and sex (p < 0.001, $\beta = 0.337$), K-L grade (p < 0.001, $\beta = 0.200$), and sex (p < 0.001, $\beta = 0.131$). Specifically, older age, higher OA severity (K-L grade IV vs. III), and female sex were associated with worse 5 mWT results, both in terms of walking time, and in terms of walking speed (Table 2). Additionally, multiple regression analysis revealed that the independent factors influencing the TUGT results (p < 0.001, R = 0.435, $R^2 = 0.189$) were age (p < 0.001, $\beta = -0.326$), K-L grade (p < 0.001, $\beta = -0.146$), and sex (p = 0.001, $\beta = -0.127$). Specifically, younger age, male sex, and lower OA severity (K-L grade III vs. IV) were associated with better TUGT results (Table 3).

Table 1

Individual factors and walking ability prior to total knee arthroplasty for knee osteoarthritis (n = 621).

Type of characteristic	Characteristic	Value
Individual factors	Sex: women / men	492 (79.2%) / 129 (20.8%)
	Age, years	75.1 ± 6.5
	BMI, kg/m ²	25.5 ± 3.8
	OA severity: K-L grade IV / III	366 (58.9%) /
		255 (41.1%)
	Laterality: bilateral / unilateral	427 (68.8%) /
		194 (31.2)
	Contralateral surgery: no / yes	432 (69.6%) /
		189 (30.4%)
	Pain on the NRS, points	2.7 ± 2.9
Walking ability	Walking time on the 5mWT, sec Walking speed on the 5mWT, m/sec	5.11 ± 2.15 1.02 ± 0.33
	Time on the TUGT, sec	11.84 ± 4.14

Data are presented as mean ± standard deviation or n (%). BMI, body mass index; OA, osteoarthritis; K-L grade, Kellgren–Lawrence grade; NRS, numerical rating scale; 5 mWT, 5-m walk test; TUGT, Timed Up and Go test.

Table 2

Factors affecting walking ability reflected in the 5-m walk test.

Walking time	В	95% CI (lower limit, upper limit)	β	p-value
Intercept Age K-L grade Sex	-0.742 0.089 -0.838 -0.603	-2.620, 1.136 0.065, 0.114 -1.164, -0.512 -0.999, -0.207	0.269 -0.192 -0.114	0.438 <0.001 <0.001 0.003
Walking time	В	95% CI (lower limit, upper limit)	β	p-value
Intercept Age K-L grade Sex	2.220 -0.017 0.133 0.105	1.943, 2.497 -0.021, -0.013 0.085, 0.181 0.047, 0.164	-0.337 0.200 0.131	<0.001 <0.001 <0.001 <0.001

Model for walking time: R = 0.354, $R^2 = 0.125$, ANOVA: p < 0.001.

Model for walking speed: R = 0.417, $R^2 = 0.174$, ANOVA; p < 0.001.

B, partial regression coefficient; CI, confidence interval; β , standardized partial regression coefficient; K-L grade, Kellgren–Lawrence grade.

Table 3

Factors affecting walking ability reflected in the Timed Up and Go test.

Time	В	95% CI (lower limit, upper limit)	β	p-value
Intercept Age K-L grade Sex	-5.893 0.246 -1.226 -1.292	-9.368, -2.418 0.200, 0.292 -1.831, -0.621 -2.024, -0.560	0.386 -0.146 -0.127	0.001 <0.001 <0.001 0.001

R= 0.435, $R^2=$ 0.189, ANOVA: p < 0.001.

B, partial regression coefficient; CI, confidence interval; β , standardized partial regression coefficient; K-L grade, Kellgren–Lawrence grade.

The standard values for 5mWT and TUGT results were obtained after stratifying the patients by sex, age, and K-L grade, which were the independent influencing factors of walking ability on multiple regression analysis. The standard values for walking time and walking speed on the 5mWT are shown in Table 4, while those for time on the TUGT are shown in Table 5.

4. Discussion

Our results are consistent with those of Brunner et al. [21], who assessed 6345 healthy subjects (4489 men, 1856 women; age, 50-73 years) and reported that walking speed was significantly higher among men and that it decreased with age. Our study also revealed OA severity as a factor influencing walking speed in patients with knee OA. Christiansen et al. [22] examined walking ability on the 6-min walk test in 50 patients with unilateral knee OA and 17 age-matched, healthy controls, and reported that knee OA patients could walk significantly shorter distances and at significantly lower walking speed. Additionally, Shimada et al. [23] reported that, among 959 community-dwelling elderly people (396 men, 563 women; average age, 74.8 years), the walking speed on the 5mWT was 1.99 ± 0.43 m/s and 1.71 ± 0.41 m/s for men and women, respectively. It may not be entirely appropriate to refer to the average values of parameters describing walking ability in community-dwelling elderly people when attempting to obtain a quantitative evaluation of walking ability decline in patients with knee OA. In this study, we aimed to determine adequate standard values for the quantitative evaluation of walking ability indicative of the need for TKA. Therefore, we measured walking ability directly in the target population, namely in knee OA patients hospitalized for scheduled TKA. We thus believe that the values reported in this study will be useful for judging the appropriateness of TKA in Japanese patients with knee OA.

For the 5 mWT results, we provide standard values for both walking time (sec) and walking speed (m/sec), which is obtained by dividing the length of the central, timed zone (i.e., 5 m) by the walking time. We believe that, in the clinical setting, walking time (sec) may be more useful than walking speed (m/sec) because no additional calculation is required. In their meta-analysis covering almost 3000 community-dwelling elderly Japanese people (948 men, 1992 women; age, 60–90 years), Ando et al. [24] reported a reference value of 2.86 s (95% confidence interval, 2.69–3.02 s) for walking time on the 5 mWT. In our study, which included elderly Japanese patients with knee OA scheduled for TKA, the standard range for walking time on the 5 mWT was 3.90-5.60 s for men and 4.27–6.05 s for women. These results confirm the fact that walking time on the 5 mWT differs greatly between patients with end-stage knee OA and the general population of communitydwelling elderly people. The standard values for walking time on

Table 4

Standard values for walking time and walking speed in the 5-m walk test among patients with knee OA (n = 621).

Walking time, sec		n	60-74 years	n	75–89 years
K-L grade III	Male	26	3.90 (3.30–4.89)	34	4.64 (4.02-5.41)
-	Female	89	4.27 (3.62-5.03)	106	5.12 (4.10-6.58)
K-L grade IV	Male	31	4.26 (3.62-5.15)	38	5.60 (4.32-6.80)
	Female	121	4.80 (4.00-5.90)	176	6.05 (5.00-7.32)
Walking speed, m/sec		n	60-74 years	n	75–89 years
K-L grade III	Male	26	1.28 (1.02–1.52)	34	1.08 (0.92-1.24)
	Female	89	1.17 (0.99-1.38)	106	0.98 (0.76-1.22)
K-L grade IV	Male	31	1.17 (0.97-1.38)	38	0.89 (0.74-1.16)
	Female	121	1.04 (0.85-1.25)	176	0.83 (0.68-1.00)

For each category defined in terms of OA severity, sex, and age, data are provided as median (interquartile range). The number of patients included in each category is also given. OA, osteoarthritis; K-L grade, Kellgren–Lawrence grade.

Table 5

Standard values for the time taken by patients with knee OA to complete the Timed Up and Go test ($n = 621$).

Time, sec		n	60-74 years	n	75—89 years
K-L grade III	Male	26	8.52 (7.19–9.87)	34	10.30 (8.95–12.13)
	Female	89	9.30 (7.96–11.00)	106	11.74 (10.00–14.37)
K-L grade IV	Male	31	9.40 (8.20–10.85)	38	12.90 (9.20–14.50)
	Female	121	10.05 (8.40–12.76)	176	13.20 (10.63–15.64)

For each category defined in terms of OA severity, sex, and age, data are provided as median (interquartile range). The number of patients included in each category is also given. OA, osteoarthritis; K-L grade, Kellgren–Lawrence grade.

the 5 mWT can be easily utilized in the clinical setting to quantify walking ability decline and thus help evaluate the need for TKA in Japanese patients with knee OA.

Shimada et al. [23] evaluated 959 community-dwelling elderly people (396 men, 563 women; age, 65–84 years) and reported TUGT results of 5.4 \pm 1.1 s and 7.9 \pm 2.3 s for men aged 65–69 years and 80-84 years, respectively, compared to 5.9 \pm 1.0 s and 9.6 ± 3.0 s for women aged 65–69 years and 80–84 years, respectively. These previous findings by Shimada et al. are consistent with the results obtained in our study regarding TUGT results and walking speed, as well as with observations from other studies: men walk significantly faster than women, walking speed decreases significantly with age [25], and OA severity is also an important correlate of walking speed. Furthermore, Tsonga et al. [26] reported that, among patients with severe knee OA (K-L grade III or IV), the preoperative TUGT result was 13.05 ± 4.13 s. However, these previously reported TUGT results were not stratified by age or knee OA severity, which are influencing factors for walking ability, and thus such values may not be suitable for use as standard values when quantifying the decline in walking ability. In our study, the standard value for time on the TUGT was provided for each category of patients, defined in terms of age, sex, and OA severity; moreover, all data pertain to measurements performed during preoperative admission among patients with knee OA indicated for TKA. Thus, the standard values reported in our study can be used in the clinical setting for quantifying walking ability decline in patients with knee OA, and thus potentially informing the need for TKA.

Kuptniratsaikul et al. [19] reported significant correlations of walking ability with sex, age, and radiographic severity of knee OA. Additionally, Elbaz et al. [27] reported that, in both male and female patients with knee OA, K-L grade worsening was accompanied by a significant decrease in walking speed. While they established that sex, age, and OA severity influenced walking ability in patients with knee OA, there was no clustering based on these variables identified as influencing factors. The strength of our study is that multivariate analysis allowed us to stratify knee OA patients based on the influencing factors of walking ability, and to extract the standard values for parameters of walking ability in each category of patients, defined in terms of age, sex, and OA severity. In addition, we expect that the standard values reported in our study can be easily adopted in clinical practice because the 5 mWT and TUGT can be conducted easily and inexpensively in the clinical setting. Therefore, we believe that the standard values for pre-TKA 5 mWT and TUGT results reported in our study will be of use to clinicians and patients alike, providing valuable tools to quantify walking ability decline and aiding in the decision to consider TKA.

Several limitations to the present study should be considered. Firstly, we did not investigate walking ability during the entire period between the onset of knee OA and the time of TKA, or before and after conservative therapy. Further study is warranted to clarify the influence of conservative therapy on walking ability in this population. Secondly, we did not investigate the effect of other factors affecting walking ability in the elderly, such as angina pectoris, arteriosclerosis obliterans, hypertension, chronic obstructive pulmonary disease, or sarcopenia. Thus, the results of our study may not be generalizable to patients with such diseases.

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Conflicts of interest

None.

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1030

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