



## 2. Methods

### 2.1. Participants

Eligibility criteria included presence of dementia, hospital inpatients, no severe cardiopulmonary or respiratory insufficiency, ability to push against the dynamometer with their leg, and desire to participate in the study. A sample size of 46 was derived by insertion of power (0.95),  $\alpha$  (0.05), and effect size (0.50) values in the Hulley matrix<sup>[27]</sup>; this study planned to recruit about 50 patients with dementia. The study was approved by the ethics committee at Niigata University of Health and Welfare. All subjects and their families were briefed about the aims of the study and the testing procedure prior to participation. Written informed consent was obtained from all the subjects and/or their family. This study was performed in accordance with the Declaration of Helsinki.

### 2.2. Knee extension strength

Isometric strength assessment by the hand-held dynamometer (HHD) for people with dementia has been used to quantify maximal strength and may offer several advantages over free weights, including ease of transport, time efficiency, and low cost. Intraclass correlation coefficients, used to characterize the reliability of the knee extension strength tests using HHD, have ranged from 0.95 to 0.98, which is considered good in elderly people with dementia.<sup>[11]</sup> Therefore, knee extension strength was assessed with an HHD ( $\mu$ Tas MT-1; Anima, Tokyo, Japan) in this study. The dynamometer pad is 55 × 55 mm, and its front side is curved to fit the shape of areas to be measured on the extremities. The measurement range of this dynamometer is 0.1 to 999.9 N, with a recording interval of 0.1 N. For knee extensor assessment, subjects were seated in an elevated hard chair with knees flexed 90°, feet over the floor, and arms on their thighs. The dynamometer was placed perpendicular to the leg just above the malleoli. Subjects were instructed to push against the dynamometer by attempting to straighten their knees. They were asked to increase force gradually to a maximum voluntary effort. They then maintained maximum effort for additional 5 seconds. Throughout the session, each subject was given consistent verbal encouragement and praise as reinforcement. During all tests, the dynamometer was stabilized by the belt and the examiner's hands. A study has shown a strong relationship between force measured by the equipment and the subject's body weight in strength measurements.<sup>[28]</sup> The variability (relative dispersion) of the force scores was reduced by normalization against body weight. Thus, to predict the gait functional abilities with walking aid using strength measurement, torque (Nm), as determined by force (N) and lower leg length (m), was normalized against body weight (Nm/kg), and this value is termed the "normalized knee extension strength."

### 2.3. Cognitive impairment

In addition to the effect of lower limb weakness, the cognitive impairments of sample subjects were also assessed. The Mini-Mental State Examination (MMSE) is widely used for assessing cognitive mental status, both in clinical practice and research.<sup>[29]</sup> It assesses the subject's orientation, attention, immediate and short-term recall, language, and ability to follow simple verbal and written commands. MMSE scores range from 0 to 30, with lower scores indicating greater cognitive impairment.<sup>[29]</sup>

### 2.4. Walking aids

Gait performance was assessed by determining the walking aid that enables the subject to walk 10 m independently. The subjects were instructed to walk on a 10-m walkway. The use of a walking aid such as a cane or a walker was accepted for the performance tests. Walking aids for independent walking were graded on a 4-point scale: 0 = unable to walk with aids; 1 = able to walk with a walker; 2 = able to walk with a cane; 3 = able to walk without walking aids. These evaluations were completed by the physical therapists who had regular contact with the patient during rehabilitation interventions.

### 2.5. Data analysis

Spearman rank correlation coefficient was obtained to compare the independence level for gait with each walking aid with knee extension strength, MMSE score, age, and body mass index (BMI) to assess whether gait ability is related with knee extension strength, cognitive impairment, and age. In addition, difference in sex between the independence levels for gait with each walking aid was analyzed by Chi-Squared test.

To determine the association between knee extension strength (explanatory variable) and independence level for gait with each walking aid (dependent variable), ordinal logistic modeling analysis was used.<sup>[30]</sup> The principle of ordinal logistic modeling is to fit the probability ( $P$ ) of multiple dichotomous responses (Eq. 1) to a linear model (Eq. 2):

$$g(x) = \frac{1}{1 + e^{-f(x)}} \quad (1)$$

$$f(x) = \beta_0 + \beta_1 x + e \quad (2)$$

where  $x$  is the explanatory variable,  $\beta_i$  is the partial regression coefficient, and  $e$  is the residual between actual and predicted data. Therefore, for multilevel ordinal responses, cumulative probability is calculated at each level to model the odds to a simple regression. In this study, the probability of 4 levels of gait performance with walking aids was evaluated in relationship with knee extension muscle strength.

Previous studies noted<sup>[10,11]</sup> that the predictive values were 0.70 to 0.83 for normalized knee extension strength predicting lower extremity functions including walking in patients with dementia. Considering previous prediction accuracy, 80% of the probability [ $g(x)$  value] for knee extension strengths discriminating between 0 and 1 point, between 1 and 2 points, and between 2 and 3 points of gait abilities was estimated by Eqs. (1) and (2). All statistical analyses were performed using the R 3.4.0 software (R Foundation for Statistical Computing, Vienna, Austria).

## 3. Results

Fiftysix people with dementia (45 women and 11 men) were recruited from a nursing home. The characteristics of the subjects are presented in Table 1. Subjects' age ranged from 72 to 100 years. The MMSE score for the 56 subjects ranged from 6 to 23 points. Normalized knee extensor strength for the 54 subjects in this study ranged from 0.06 to 0.43 Nm/kg (average, 0.21 Nm/kg; SD, 0.09 Nm/kg), ranging from 0.14 to 0.43 Nm/kg (average, 0.34 Nm/kg; SD, 0.44 Nm/kg) for the 16 subjects who were able to walk without walking aid (walking grade, 3 points), ranging from 0.14 to 0.39 Nm/kg (average, 0.38 Nm/kg; SD, 0.52 Nm/kg) for the 11 subjects who were able to walk with a cane (walking grade, 2 points),

**Table 1**  
**Characteristics of patients who satisfied the eligibility criteria (n=56).**

		P*
Age (years)	84.5±5.9	.332
Sex		.563
Female	45 (80.4)	
Male	11 (19.6)	
Body Mass Index	21.1±4.1	.290
Mini-Mental State Examination	16 [12–18]	.120
Gait performance		
Freehand	16 (28.6)	
Cane	11 (19.6)	
Walker	19 (33.9)	
Unable	10 (17.9)	

Values are mean±SD, n (%), or median [interquartile range].  
 \*Spearman rank correlation coefficients or Chi-Squared test.

ranging from 0.06 to 0.43 N m/kg (average, 0.28 N m/kg; SD, 0.42 N m/kg) for the 19 subjects who were able to walk with a walker (walking grade, 1 point), ranging from 0.10 to 0.27 N m/kg (average, 0.33 N m/kg; SD, 0.56 N m/kg) for the 10 subjects who were unable to walk with walking aid (walking grade, 0 point).

The independence level for gait with each walking aid was significantly correlated with knee extension strength (Spearman rank correlation coefficients,  $r=0.35$ ,  $P<.0001$ ). However, the correlations between the independence level for gait with each walking aid and MMSE score, age, and BMI were not significant (Spearman’s rank correlation coefficients: MMSE score,  $P=.120$ , age,  $P=.332$ , BMI,  $P=.290$ ; Table 1). In addition, the number of women and men was not significantly different between the independence level for gait with each walking aid (chi-squared test,  $P=.563$ ; Table 1).

Figure 1 shows the results of the ordinal logistic modeling of the data set for knee extension strength and gait performance. For each walking aid needed for independent gait, the fit of ordinal logistic modeling was statistically significant, indicating that the results in the data set could be validly interpreted as logistic

**Table 2**  
**Coefficients of normalized knee extension strength for gait performance score.**

β	SEM	Z	P
6.56	3.00	2.19	.028

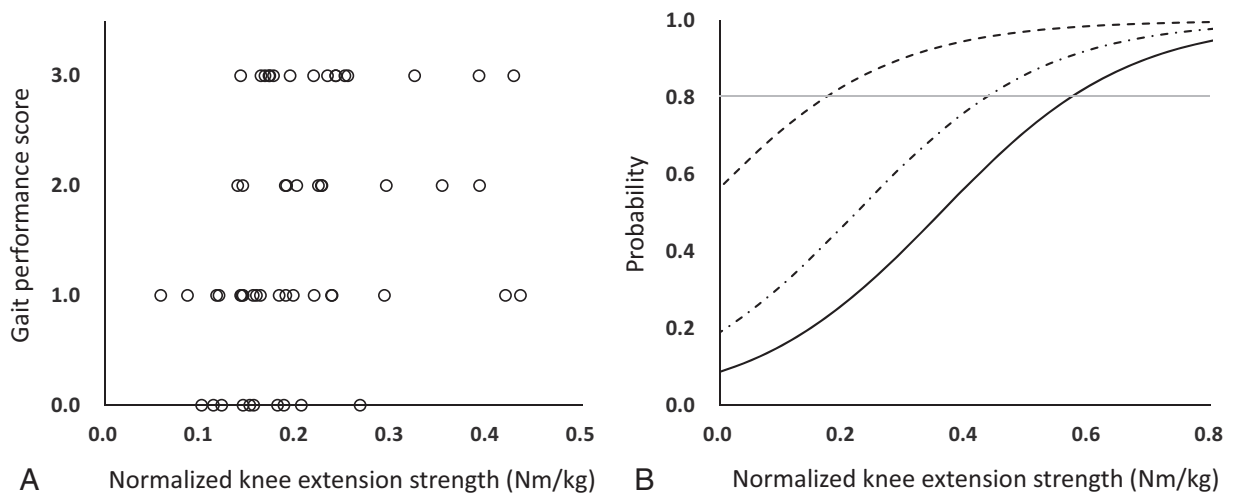
SEM=standard error of the mean.

probability. The logistic curves discriminating 0 point (unable to walk with aids) from 1 point (able to walk with a walker), 1 point from 2 points (able to walk with a cane), and 2 points from 3 points (able to walk without walking aid) were in a stepwise fashion fit ( $P=.028$ ; Table 2). To reach at least 80% probability [g(x) value] for gait to be discriminated between 0 and 1 point, between 1 point and 2 points, and between 2 and 3 points, the normalized knee extension strengths were 0.17, 0.43, and 0.57 N m/kg, respectively (Fig. 2).

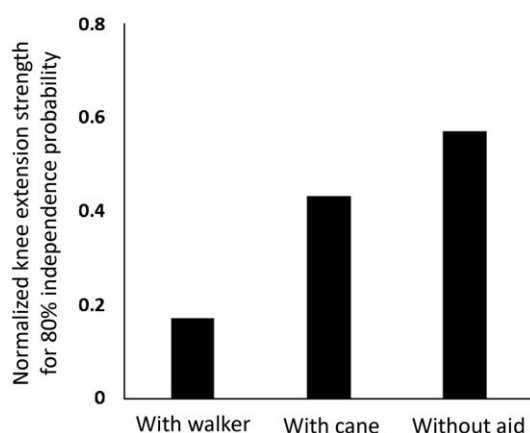
**4. Discussion**

Lower limb strength is one of the essential activities in everyday life. In the present study, the relationship between gait performance with walking aid and knee extension strength was investigated by applying ordinal logistic modeling to data collected from patients with dementia. The results of this study indicated that the independence level of gait performance with walking aid and knee extension strength were correlated and that there are threshold levels of strength that could predict gait performance with particular walking aid in people with dementia. Although several lines of research have characterized the relationship between gait performance and knee extension strength,<sup>[10–14]</sup> independence probabilities for gait performance with particular walking aid in relationship to knee extension strength were detected.

Previous studies suggested that 0.6 N m/kg of knee extension strength was needed to walk independently without walking aid.<sup>[10,11]</sup> The present data agree with the previous data in which muscle force was necessary for gait performance.<sup>[10–14]</sup>



**Figure 1.** Scatterplots (A) and logistic probability plots (B) showing the relation between gait performance with walking aid and normalized knee extension strength. The logistic curve that discriminated 0 point (unable to walk with aids) from 1 point (dotted line: able to walk with a walker), 1 point from 2 points (chain line: able to walk with a cane) and 2 points from 3 points (solid line: able to walk without walking aids) were in a stepwise fashion fit ( $P=.028$ ). Gray line denotes the 80% probability level [g(x) value] for gait with walker, with cane, and without aid.



**Figure 2.** Bar graphs of normalized knee extension strengths needed to reach at least 80% probability for gait with walker, with cane, and without aid. The normalized knee extension strength for gait with walker, with cane, and without aid was 0.17, 0.43, and 0.57 Nm/kg, respectively.

An additional new observation in the present study was that the knee extension strength stochastically predicted independence level of gait performance with walking aid including cane and walker. In this study, the threshold levels of knee extension strength for patients with dementia who could walk independently with particular walking aid were clearly demonstrated. In fact, the results of this study indicated that knee extension strength of 0.17, 0.43, and 0.57 Nm/kg is needed to reach 80% independence probability for gait with walker, with cane, and without walking aid, respectively. Comparison of personal strengths with the threshold level for independence gait with walking aid makes it possible to tailor individual training with targets that more closely matched achievable levels for specific knee extension strength and gait performance with walking aid. Hence, rehabilitative regimen can be designed with allowance for variability in the independence levels of knee extension strength and gait performance with walking aid. Therefore, threshold levels contribute toward prediction of the extent or duration of the gait disturbance and lower limb weakness and to an increasingly evidence-based approach for advocating rehabilitative training for patients with dementia.

Dementia and institutionalization may drastically reduce the physical activity levels and accelerate sarcopenia and muscle weakness in the elderly, resulting in an accelerated decline in aspects of overall function including gait ability in frail patients.<sup>[31]</sup> Resistance training, as a countermeasure for this risk, has been increasingly studied as a method for reducing impairments and recovering function in frail elderly persons.<sup>[21–25]</sup> Thomas and Hageman<sup>[23]</sup> evaluated the potential of a resistance-exercise training intervention (3 sessions per week over 6 weeks) to improve neuromuscular strength and function in the lower extremities among community-dwelling people with dementia and reported some gains in muscle strength and functional performance. Teri et al<sup>[24]</sup> demonstrated that home-based exercise training (performed over a 3-month period), combined with training of caregivers in behavioral management techniques, improved physical health and depression in patients with dementia. Rolland et al<sup>[22]</sup> reported the effectiveness of a simple exercise training program (1 hour twice weekly) over a 1-year period in attenuating the decline in the ability of patients with dementia to perform the activities of daily living. Recently, Santana-Sosa et al<sup>[25]</sup> showed that a short-term (12-week)

training program for patients with dementia combining resistance, joint mobility, and coordination exercises, performed in a nursing home dwelling, improved their overall functional capacity. Hauer et al<sup>[21]</sup> found that 3 months of progressive resistance and functional training resulted in significant increases in strength and functional performance in elderly patients with dementia. However, in those studies, the patients with dementia were capable of walking independently,<sup>[21,22]</sup> which suggests that the patients in these studies had a better functional status than the patients in the present study. The results suggest that the period required to reach the threshold levels can be estimated during resistance training programs. In addition, preventive training based on normalized knee extensor strength is needed for people with normalized knee extensor strength near 0.17 to 0.57 Nm/kg. These findings will contribute to an increasingly evidence-based approach to strengthen training for patients with dementia. Further research can be carried out based on the results of this study to develop a training protocol for people with dementia and to determine whether strength and gait performance among people with dementia can be improved by training.

#### 4.1. Limitations

A potential limitation of the present study was the sample size, which was estimated using the Hulley matrix method.<sup>[27]</sup> Lower limb weakness in patients with dementia is based on a complex combination of factors, such as the effects of increasing age,<sup>[15]</sup> inactivity,<sup>[32]</sup> failure of reciprocal control,<sup>[33]</sup> and lack of gain in maximal effort.<sup>[34]</sup> In future studies, a larger number of participants will be needed to investigate the relation between gait ability and multiple important covariates. With further detailed examination classifying participants by their covariates and the inclusion of a large number of patients, the results of our study might be more generally applicable. Furthermore, this study had a higher number of female subjects than male subjects because of their greater numbers in the aged population. This higher number of female subjects might have biased the results of this study. Therefore, further detailed studies are needed to classify participants by sex to define more clearly the relationships between knee extension strengths and lower extremity functions in subjects with dementia.

#### 5. Conclusions

Using ordinal logistic modeling, the normalized knee extensor strength was indicated to be a significant predictor of gait performance with walking aids. Resistance training based on normalized knee extensor strength is needed for people with normalized knee extensor strength in the range of 0.17 to 0.57 Nm/kg for improvement of strength and independent gait. The findings of this study will contribute to an increasingly evidence-based approach to resistance training and prescription of walking aids for patients with dementia. These findings, including normalized strength assessment, may serve as a clinically meaningful index for rehabilitation assessment and training of patients with dementia and may be especially relevant to rapidly aging societies.

#### Author contributions

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