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Association between locomotive syndrome and the Japanese version of the EQ-5D-5L in middle-aged and elderly people in Japan

Satoshi Tanaka[1], Kei Ando[1], Kazuyoshi Kobayashi[1], Taisuke Seki[1],
Takashi Hamada[1], Masaaki Machino[1], Kyotaro Ota[1], Masayoshi Morozumi[1],
Shunsuke Kanbara[1], Sadayuki Ito[1], Naoki Ishiguro[1],
Yukiharu Hasegawa[2] and Shiro Imagama[1]

[1]*Department of Orthopaedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Aichi, Japan*
[2]*Department of Rehabilitation, Kansai University of Welfare Science, Osaka, Japan*

ABSTRACT

The Japanese version of the EuroQol 5 dimension, 5 level version (EQ-5D-5L) can now be used to quantitatively evaluate the health-related quality of life (QoL) in Japan. Locomotive syndrome (LS) is a concept advocated in Japan to describe a condition requiring care for musculoskeletal disorders. However, no detailed study on the relationship between this index and LS in Japanese health checkup has been reported. We aimed to evaluate the relationship between the Japanese version of the EQ-5D-5L and LS. We enrolled 477 participants who were undergoing health checkups in Japan. All participants were administered the 25-question Geriatric Locomotive Functional Scale for the diagnosis of LS and the Japanese version of the EQ-5D-5L. We performed statistical analysis to compare the non-LS and LS patients; moreover, the risk factors and cut-off values were calculated and verified. The Japanese version of the EQ-5D-5L index was significantly lower in patients with LS than in non-LS patients and was significantly related to LS in logistic regression analysis. In subgroup analysis targeting the five dimensions of the EQ-5D-5L, it was seen that mobility, pain/discomfort, and self-care were significantly involved in LS. The cut-off value of the EQ-5D-5L index for LS was 0.875. The Japanese version of the EQ-5D-5L index was significantly related to LS in Japan. This index will be a useful tool that can easily measure health-related quality of life in middle-aged and elderly Japanese people. Future studies should investigate the relationship of not only LS but also various diseases with the Japanese version of the EuroQol 5 dimension, 5 level version.

Keywords: community-dwelling people, Japanese version EQ-5D-5L, locomotive syndrome, QoL, Yakumo Study

INTRODUCTION

Health-related quality of life (QoL) has been gaining importance in research, clinical practice, and health planning due to the production of complementary information regarding health

indicators relevant to morbidity and mortality.[1,2] Evaluating the general health of the population is a specific application proposed for health-related QoL instruments.[3] The EuroQol 5 dimension (EQ-5D) is a questionnaire for quantitatively evaluating QoL in various health conditions. The Japanese version of the three-level EQ-5D (EQ-5D-3L) was completed in 1997 and certified as an official version by the EuroQol Group.[4] It is based on an interview survey conducted in the general population using the time trade-off method.[5] The EQ-5D-3L is a simple, five-dimensional scale. However, because only three levels can be distinguished for each health condition, the sensitivity is insufficient and the ceiling effect, which results in high scores for responses, was found to be a problem. To solve these problems, the EuroQol Group made it possible to calculate a more detailed QoL index by increasing the number of levels for each dimension from three to five. However, since the scoring algorithm of the EQ-5D-5L is created independently by each country, the QoL index calculated for the same health condition varies among countries.

In 2015, the Japanese scoring algorithm of the EQ-5D-5L was reported[6] and the Japanese version of the EQ-5D-5L became available. With the aging of the general population in Japan, the promotion of musculoskeletal health and improvements in life expectancy have become important public health issues. In 2007, the Japanese Orthopedic Association proposed the concept of locomotive syndrome (LS) to identify individuals with musculoskeletal disorders who are at high risk of requiring long-term care at some point. The 25-question Geriatric Locomotive Function Scale (GLFS-25) was developed as an evidence-based screening tool to quantify LS. The validity and reliability of this scale have been confirmed.[7] In recent years, several studies investigating the relationship between LS and health-related QoL have been reported, and it is known that patients diagnosed with LS have significantly lower QoL scores.[7-9] However, to our knowledge, there is no report investigating the relationship between LS and the Japanese version of the EQ-5D-5L in Japanese people. With this in mind, the aim of our study was to evaluate the relationship between LS and the Japanese version of the EQ-5D-5L administered during general health checkups in Japan. This represents the first report of its kind. The study also aimed to determine the cut-off value of the EQ-5D-5L index for LS.

MATERIALS AND METHODS

Participants

The participants were healthy Japanese middle-aged and elderly adults who attended an annual public health check-up provided by the local government in Japan in 2018. This checkup has been held annually since 1982 in the town of Yakumo in a rural area of southern Hokkaido, Japan, with the data forming the basis of the Yakumo Study, which includes voluntary orthopedic assessment and physical function examinations in addition to internal medical examinations, psychological tests, and a health-related QoL survey.[10-17]

The inclusion criteria for this study were as follows: completion of all questions on the GLFS-25 and the Japanese version of the EQ-5D-5L. The exclusion criteria were as follows: a history of spinal, hip, or knee surgery; severe knee injury; severe osteoarthritis; history of fracture of the hip and spine; and treatment for diabetes, kidney disease, or heart disease.

Among the 546 individuals who participated in the annual check-up in 2018, 483 participants fully completed the Japanese version of the EQ-5D-5L and GLFS-25 survey. Of these 483 participants, six were subsequently excluded due to the above-mentioned criteria. Therefore, 477 participants were finally included in the study. The study protocol was approved by the ethics committee for human research and the institutional review board at our university. All participants provided written informed consent. The study procedures were carried out in accordance with

the principles of the Declaration of Helsinki.

GLFS-25

The GLFS-25 is a self-administered questionnaire consisting of 25 items graded on a 5-point scale, from no impairment (0 points) to severe impairment (4 points). The sum of the 25 item scores yields a total possible score in the range 0–100, with increasing values indicating increasing severity of LS. The validity and reliability of this new index have been reported to be satisfactory, with a score cut-off of ≥16 points indicative of LS and with individuals with a GLFS-25 score ≤15 points classified into the non-LS group.[7] For this study, we used the Japanese version of the GLFS-25, the Locomo 25.

EQ-5D-5L

The EQ-5D-5L[18] is a self-administered questionnaire and descriptive system comprising five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with five levels of severity (no problems, slight problems, moderate problems, severe problems, and extreme problems). The responses for the five dimensions can be combined into a 5-digit number describing the respondent's health state (from "11111" meaning no problems at all to "55555" meaning extreme problems in all five dimensions). A total of 3,125 possible health states are defined in this way. Health states may be converted into a single health index by applying a formula that attaches values (also called weights) to each response. To obtain the EQ-5D-5L index, we used the Japanese version of the EQ-5D-5L[19] value, which is estimated using the crosswalk methodology developed by the EuroQol Group.[20]

Average percent body fat measurement

The Inbody 770 BIA unit (Inbody Co., LTD, Seoul, Korea) was used, which differentiates tissues (such as fat, muscle, and bone) based on their electrical impedance. Individuals grasped the handles of the analyzer, in which electrodes are embedded, and stood on the platform, with the soles of the feet in contact with electrodes (two electrodes for each foot and hand).

Statistical Analysis

Statistical analyses were performed with SPSS version 25.0 for Mac (SPSS Inc., Chicago, IL, USA). Continuous variables are expressed as means (standard deviation: SD) and categorical variables as percentages. The Mann-Whitney *U*-test and Fisher's exact test were used to examine the differences in variables between male and female participants. Participants were classified into the LS and non-LS groups based on a GLFS-25 cut-off score of ≥16 points. To compare variables between the non-LS and LS groups, the Mann-Whitney *U*-test, Fisher's exact test, and generalized linear model (GLM) were used. GLM analysis was used to adjust for age and sex, which are known factors related to LS.[21,22] To determine the risk factors associated with LS, logistic regression analysis with the step-wise method was performed. All variables (p <0.25) that showed a certain degree of difference in univariate analysis were used as covariates. To identify the cut-off value of EQ-5D-5L index for LS, Youden's Index[23] was used with a receiver operating characteristics (ROC) curve. In all analyses, p-values <0.05 were considered statistically significant.

RESULTS

The baseline characteristics of the study participants are summarized in Table 1. The average

Table 1 Demographic, EQ-5D-5L index, and GLFS-25 data of the participants

Variables	Total	Male	Female	p-value
Number of participants	477	196	281	
Age (years)	64.1 (10.1)	65.8 (9.6)	62.9 (10.2)	**0.003****
BMI (kg/m^2)	23.6 (3.6)	24.5 (3.2)	23.0 (3.7)	**<0.001*****
PBF (%)	29.2 (7.1)	24.1 (4.6)	32.7 (6.4)	**<0.001*****
EQ-5D-5L index	0.886 (0.117)	0.884 (0.128)	0.888 (0.109)	0.84
EQ-5D-5L dimensions				
Mobility	1.22 (0.57)	1.26 (0.60)	1.20 (0.56)	0.16
Self-care	1.05 (0.29)	1.07 (0.37)	1.03 (0.21)	0.21
Usual activities	1.16 (0.50)	1.16 (0.50)	1.16 (0.50)	0.79
Pain/discomfort	1.78 (0.75)	1.77 (0.77)	1.79 (0.73)	0.59
Anxiety/depression	1.25 (0.59)	1.26 (0.66)	1.25 (0.55)	0.60
GLFS-25	7.2 (8.5)	6.4 (9.3)	7.8 (7.8)	**0.001****
Prevalence of LS (%)	12.6	9.2	14.9	0.069

<0.01, *<0.001, Mann-Whitney *U*-test, Fisher's exact test.

Parameter values are shown as the mean (standard deviation) or numbers.
Bold indicates a statistically significant difference.
BMI, body mass index; PBF, percent body fat; EQ-5D-5L, EuroQol 5 dimension, 5 level version;
GLFS-25, 25-question geriatric locomotive function scale; LS, locomotive syndrome.

age of the 477 participants was 64.1 years (range: 40–88; SD: 10.1); 196 were male and 281 were female. The average body mass index (BMI) was 23.6 kg/m^2 and average percent body fat (PBF) was 29.2%. Significant differences were observed between male and female participants for all variables except for EQ-5D-5L and the prevalence of LS.

Comparative study data for the non-LS and LS groups are summarized in Table 2. Although age (p = 0.004), PBF (p = 0.012), EQ-5D-5L index (p < 0.001), and EQ-5D-5L severity for all five dimensions (p < 0.001) were different between the non-LS and LS groups, sex and BMI were not significantly different. Furthermore, controlling for age and sex revealed a significant difference between the two groups for the same variable.

A summary of the logistic regression analysis for risk factors of LS is shown in Table 3. Covariates included age, sex, BMI, PBF, and EQ-5D-5L index. This analysis showed that EQ-5D-5L index (odds ratio [OR] < 0.001; p < 0.001), age (OR = 1.052; p = 0.008), and male sex (OR = 0.366; p = 0.011) were significant risk factors for LS.

In addition, in subgroup analysis of the five dimensions of EQ-5D-5L, we investigated which dimensions were related to LS using logistic regression analysis (Table 4). Mobility (OR = 4.293; p < 0.001), pain/discomfort (OR = 3.283; p < 0.001), and self-care (OR = 5.338; p = 0.030) were significantly related to LS.

The ROC curve for the predictive value of the EQ-5D-5L index for the presence or absence of LS had an area under the curve (AUC) of 0.867 (Fig. 1, Table 5). Based on Youden's index,[23] the cut-off value of EQ-5D-5L index was determined to be 0.875 for LS. An EQ-5D-5L index of <0.875 indicated the presence of LS with 85.0% sensitivity, 73.4% specificity, 31.6% positive predictive value, 96.9% negative predictive value, and 73.8% correct diagnosis rate (Fig. 1, Table 5, 7). The participants were divided into two groups (low and high) and compared using this cut-off value. As a result, there was no significant difference in age, sex, BMI, and PBF

Table 2 Comparison between the non-LS and LS groups

Variables	Non-adjusted			Age and sex-adjusted		
	non-LS (N = 417)	LS (N = 60)	p-value	Non-LS (N = 417)	LS (N = 60)	p-value
Age (years)	63.6 (10.0)	67.6 (10.3)	**0.004****			
Sex (male/female)	110/155	11/19	0.069			
BMI (kg/m²)	23.5 (3.5)	24.2 (3.9)	0.12	23.7 (0.2)	24.4 (0.5)	0.18
PBF (%)	28.9 (7.0)	31.1 (7.8)	**0.012***	28.0 (0.4)	30.3 (0.8)	**0.012***
EQ-5D-5L index	0.910 (0.08)	0.718 (0.18)	**<0.001****	0.911 (0.006)	0.712 (0.013)	**<0.001****
EQ-5D-5L dimensions						
Mobility	1.11 (0.36)	2.02 (1.00)	**<0.001****	1.11 (0.03)	2.03 (0.06)	**<0.001****
Self-care	1.01 (0.10)	1.32 (0.73)	**<0.001****	1.01 (0.01)	1.39 (0.02)	**<0.001****
Usual activities	1.07 (0.31)	1.77 (0.95)	**<0.001****	1.08 (0.03)	1.79 (0.05)	**<0.001****
Pain/discomfort	1.67 (0.64)	2.60 (0.92)	**<0.001****	1.66 (0.04)	2.59 (0.09)	**<0.001****
Anxiety/depression	1.18 (0.48)	1.75 (0.95)	**<0.001****	1.17 (0.03)	1.79 (0.07)	**<0.001****

*<0.05, **<0.01, ***<0.001, Mann-Whitney *U*-test, Fisher's exact test.

Parameter values are shown as the mean (standard deviation) or numbers for non-adjusted data and corrected mean (standard error) or numbers of the mean for age and sex-adjusted data.
Bold indicates a statistically significant difference.
BMI, body mass index; PBF, percent body fat; EQ-5D-5L, EuroQol 5 dimension, 5 levels version; LS, locomotive syndrome.

Table 3 Logistic regression model for the prediction of LS

Variables	Coefficient (ß)	Odds ratio	95% CI	p-value
EQ-5D-5L index	-15.188	<0.001	<0.001–<0.001	**<0.001****
Age	0.051	1.052	1.013–1.093	**0.008***
Sex (male)	-1.006	0.366	0.168–0.797	**0.011***

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

All variables (p <0.25) that showed a certain degree of difference in univariate analysis were used as covariates. The dependent variable was the LS. Covariates were age, sex, BMI, PBF, and EQ-5D-5L index.
LS, locomotive syndrome; EQ-5D-5L, EuroQol 5 dimensions, 5 level version; BMI, body mass index; PBF, percent body fat; CI, confidence interval.

Table 4 Logistic regression model for the prediction of LS in subgroup analysis

Variables	Coefficient (ß)	Odds ratio	95% CI	p-value
Mobility	1.457	4.293	2.556–7.211	**<0.001****
Pain/discomfort	1.189	3.283	2.020–5.336	**<0.001****
Self-care	1.675	5.338	1.179–24.163	**0.030***

*<0.05, ***<0.001

All variables (p <0.25) that showed a certain degree of difference in univariate analysis were used as covariates. The dependent variable was LS. Covariates were EQ-5D-5L dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression).
LS, locomotive syndrome; CI, confidence interval; EQ-5D-5L, EuroQol 5 dimensions, 5 level version.
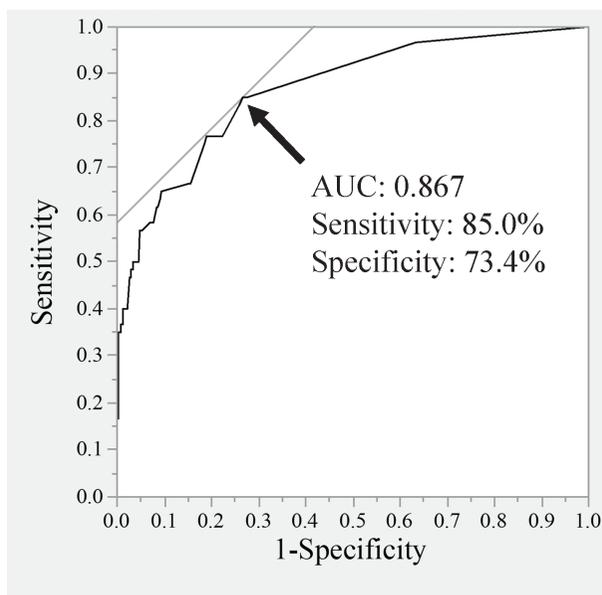
Fig. 1 Receiver operating characteristic (ROC) curve of the EuroQol 5 dimension, 5 level version (EQ-5D-5L) index and locomotive syndrome (LS) with an area under the curve (AUC) of 0.618, sensitivity of 85%, and specificity of 73.4%

Table 5 The AUC, cut-off value, sensitivity, and specificity of the EQ-5D-5L index for the presence or absence of LS

AUC	SE	p-value	95% CI	Cut-off value	Sensitivity, specificity (%)
0.867	0.027	< 0.001	0.814–0.919	0.875	85.0, 73.4

AUC, area under curve; EQ-5D-5L, EuroQol 5 dimensions, 5 level version; LS, locomotive syndrome; SE, standard error; CI, confidence interval.

Table 6 Comparison of demographic and GLFS-25 data between individuals with a low (<0.875) and high (≥0.875) EQ-5D-5L index

Variables	EQ-5D-5L index		p-value
	low (N = 158)	high (N = 319)	
Age (years)	64.6 (10.3)	63.8 (10.0)	0.45
Sex (male/female)	68/90	128/191	0.55
BMI (kg/m^2)	23.9 (3.8)	23.5 (3.5)	0.25
PBF (%)	29.4 (7.2)	29.1 (7.1)	0.48
GLFS-25	13.4 (11.0)	4.2 (4.4)	**<0.001*****

***<0.001, Mann-Whitney *U*-test, Fisher's exact test.

Parameter values are shown as mean (SD).
Bold indicates the significant difference.
EQ-5D-5L, EuroQol 5 dimensions, 5 level version; BMI, body mass index; GLFS-25, 25-question geriatric locomotive function scale.

Table 7 Cross-tabulation of LS and non-LS cases and the low (<0.875) and high (≥0.875) EQ-5D-5L groups

EQ-5D-5L index	LS	non-LS	Total	p-value	Risk ratio	Odds ratio	PPV (%)	NPV (%)	Correct diagnosis rate (%)
Low	50	108	158						
High	10	309	319						
Total	60	417	477	**<0.001**	10.1	14.3	31.6	96.9	75.3

Fisher's exact test.

Bold indicates a statistically significant difference.

EQ-5D-5L, EuroQol 5 dimensions, 5 level version; LS, locomotive syndrome; PPV, positive predictive value;

NPV, negative predictive value.

between the two groups (Table 6). However, there was a significant relationship between low EQ-5D-5L index and LS (p < 0.001; Table 6,7). The risk ratio of LS among individuals with a low EQ-5D-5L index was 10.1, with an OR of 14.3 (Table 7).

DISCUSSION

This is the first report to examine the relationship between LS, which is a concept proposed in Japan, and the Japanese version of the EQ-5D-5L in Japanese people involved in a large-scale general health check-up. In this study, we demonstrated that the Japanese version of the EQ-5D-5L index was significantly related to LS. Among the five dimensions of the EQ-5D-5L, those that were particularly related to LS were mobility, pain/discomfort, and self-care. The cut-off value was 0.875, the sensitivity was 85%, and the specificity was 73.4%, indicating the usefulness of this measure.

Since the concept of LS was announced, research on LS has been conducted using various approaches.[21,22,24] Regarding health-related QoL, the association with the EQ-5D-3L[7,9] and SF-36[8] has been reported and a relationship between reduced QoL and LS has been described. Furthermore, the EQ-5D-3L has been reported to be associated not only with LS but also with various diseases, such as osteoarthritis and osteoporosis.[25,26] However, the EQ-5D-5L has not been developed extensively and there are still few reports regarding its use. Therefore, this paper can serve as a reference to researchers hoping to investigate the relationship between other diseases and the Japanese version of the EQ-5D-5L.

It has been reported that the concept of LS strongly reflects musculoskeletal disorders and is often found in elderly people and women.[21,22] Therefore, when comparing and examining LS, it is necessary to consider the influence of age and sex. In this study, the EQ-5D-5L index was significantly lower in the LS group than in the non-LS group, and similar results were obtained after correcting for age and sex using statistical methods. Furthermore, in order to account for bias in the demographic data, not only age and gender but also BMI and PBF were added as independent variables in logistic regression analysis. This analysis showed that lower EQ-5D-5L index, which is indicative of low health-related QoL, is significantly associated with LS. In addition, among the five dimensions of the EQ-5D-5L, mobility, pain/discomfort, and self-care were significantly related to LS. In other words, higher scores in these dimensions were associated with the presence of LS. This result has not been reported previously. In the future, it is important to focus on not only the EQ-5D-5L index but also each of the five dimensions separately.

In previous studies, cut-off values of the EQ-5D-3L index for various diseases have been reported. Morgan et al[27] reported a mean EQ-5D-3L index for diabetes without vascular complica-

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tions of 0.735, and Dhillon et al[25] reported that the mean EQ-5D-3L index for patients with osteoporosis is 0.65. Iizuka et al[9] reported that the mean EQ-5D-3L index for patients suspected of having LS based on the use of "loco-check" was 0.76. In this study, the cut-off value of the Japanese version of the EQ-5D-5L for LS was 0.875. There are differences in the target disease between the 3L and 5L versions and the Japanese version. However, our impression was that the cut-off value was relatively high. The reason for this is that in this study, not all residents took part in the study. The participants were health check-up examiners, suggesting that they might be more interested in health than the general population. However, the AUC of the ROC curve was very high (0.867), suggesting that the data were reliable.

There are several limitations to this study that should be identified. First, our study sample was drawn exclusively from a rural area, where the living and working environment is likely to contribute to the risk of LS. Second, we did not include data regarding physical function, muscular strength, or muscle mass. Third, there is a possibility that several complicated conditions such as chronic physical and mental diseases have not been investigated in detail. Finally, this was a cross-sectional study. Thus, a longitudinal study is necessary in order to clarify whether there is a causal relationship between LS and the factors assessed using the EQ-5D-5L. Based on the results of this research, we plan to perform a longitudinal study in the future.

In conclusion, this study assessed the relationship between LS and the Japanese version of the EQ-5D-5L in middle-age and elderly Japanese people. Low EQ-5D-5L index was significantly associated with LS and was also a significant risk factor for LS. This is the first study to report these findings. Among the five dimensions of the EQ-5D-5L, mobility, pain/discomfort, and self-care were particularly related to LS. The cut-off value of EQ-5D-5L index for LS formulated from the ROC curve was 0.875: the AUC was 0.867, sensitivity 85%, and specificity 73.4%. The risk ratio for individuals with an EQ-5D-5L index <0.875 having LS was 10.1, with an OR of 14.3. The Japanese version the EQ-5D-5L is a useful tool that can easily measure health-related QoL in middle-aged and elderly people. Based on the present results, it will be helpful in the future to investigate the relationship between not only LS but also various diseases and the Japanese version of the EQ-5D-5L.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

REFERENCES

1) Black N. Patient reported outcome measures could help transform healthcare. *BMJ*. 2013;346:f167.
2) Garratt A, Schmidt L, Mackintosh A, Fitzpatrick R. Quality of life measurement: bibliographic study of patient assessed health outcome measures. *BMJ*. 2002;324(7351):1417.

3) Aaronson N, Alonso J, Burnam A, et al. Assessing health status and quality-of-life instruments: attributes and review criteria. *Qual Life Res*. 2002;11(3):193–205.

4) Brauer CA, Rosen AB, Greenberg D, Neumann PJ. Trends in the measurement of health utilities in published cost-utility analyses. *Value Health*. 2006;9(4):213–218.

5) Tsuchiya A, Ikeda S, Ikegami N, et al. Estimating an EQ-5D population value set: the case of Japan. *Health Econ*. 2002;11(4):341–353.

6) Ikeda S, Shiroiwa T, Igarashi I, et al. Developing a Japanese version of the EQ-5D-5L value set [in Japanese]. *J Natl Inst Public Health*. 2015;64(1):47–55.

7) Seichi A, Hoshino Y, Doi T, Akai M, Tobimatsu Y, Iwaya T. Development of a screening tool for risk of locomotive syndrome in the elderly: the 25-question Geriatric Locomotive Function Scale. *J Orthop Sci*. 2012;17(2):163–712.

8) Hirano K, Imagama S, Hasegawa Y, Ito Z, Muramoto A, Ishiguro N. The influence of locomotive syndrome on health-related quality of life in a community-living population. *Mod Rheumatol*. 2013;23(5):939–944.

9) Iizuka Y, Iizuka H, Mieda T, Tajika T, Yamamoto A, Takagishi K. Association between "loco-check" and EuroQol, a comprehensive instrument for assessing health-related quality of life: a study of the Japanese general population. *J Orthop Sci*. 2014;19(5):786–791.

10) Tanaka S, Ando K, Kobayashi K, et al. A low phase angle measured with bioelectrical impedance analysis is associated with osteoporosis and is a risk factor for osteoporosis in community-dwelling people: the Yakumo study. *Arch Osteoporos*. 2018;13(1):39.

11) Tanaka S, Ando K, Kobayashi K, et al. The decrease in phase angle measured by bioelectrical impedance analysis reflects the increased locomotive syndrome risk in community-dwelling people: the Yakumo study. *Mod Rheumatol*. 2019;29(3):496–502. doi: 10.1080/14397595.2018.1469582.

12) Tanaka S, Ando K, Kobayashi K, et al. The decreasing phase angles of the entire body and trunk during bioelectrical impedance analysis are related to locomotive syndrome. *J Orthop Sci*. 2019;24(4):720–724. doi: 10.1016/j.jos.2018.12.016.

13) Tanaka S, Ando K, Kobayashi K, et al. Utility of the serum cystatin c level for diagnosis of osteoporosis among middle-aged and elderly people. *Biomed Res Int*. 2019;2019:5046852.

14) Imagama S, Hasegawa Y, Matsuyama Y, et al. Influence of sagittal balance and physical ability associated with exercise on quality of life in middle-aged and elderly people. *Arch Osteoporos*. 2011;6(1–2):13–20.

15) Tanaka S, Ando K, Kobayashi K, et al. Increasing postural sway in balance test is related to locomotive syndrome risk: a cross-sectional study. *J Orthop Sci*. 2019;24(5):912–917. doi: 10.1016/j.jos.2019.01.011.

16) Imagama S, Hasegawa Y, Ando K, et al. Staged decrease of physical ability on the locomotive syndrome risk test is related to neuropathic pain, nociceptive pain, shoulder complaints, and quality of life in middle-aged and elderly people - the utility of the locomotive syndrome risk test. *Mod Rheumatol*. 2017;27(6):1051–1056.

17) Tanaka S, Ando K, Kobayashi K, et al. Serum cystatin C is associated with locomotive syndrome risk and can be an early predictor in community-living people: the Yakumo study. *Mod Rheumatol*. 2018;28(6):1035–1040.

18) Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level verion of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20(10):1727–1736.

19) Shiroiwa T, Ikeda S, Noto S, et al. Comparison of value set based on DCE and/or TTO data: scoring for EQ-5D-5L health states in Japan. *Value Health*. 2016;19(5):648–654.

20) Oppe M, Devlin NJ, van Hout B, Krabbe PF, de Charro F. A program of methodological research to arrive at the new international EQ-5D-5L valuation protocol. *Value Health*. 2014;17(4):445–453.

21) Muramoto A, Imagama S, Ito Z, Hirano K, Ishiguro N, Hasegawa Y. Physical performance tests are useful for evaluating and monitoring the severity of locomotive syndrome. *J Orthop Sci*. 2012;17(6):782–788.

22) Hirano K, Imagama S, Hasegawa Y, Wakao N, Muramoto A, Ishiguro N. Impact of back muscle strength and aging on locomotive syndrome in community living Japanese women. *Nagoya J Med Sci*. 2013;75(1–2):47–55.

23) Youden WJ. Index for rating diagnostic tests. *Cancer*. 1950;3(1):32–35.

24) Tanaka S, Ando K, Kobayashi K, et al. Relationship between locomotive syndrome and body composition among community-dwelling middle-age and elderly individuals in Japan: the Yakumo study. *Mod Rheumatol*. 2019;29(3):491–495. doi: 10.1080/14397595.2018.1465645.

25) Dhillon V, Hurst N, Hannan J, Nuki G. Association of low general health status, measured prospectively by Euroqol EQ5D, with osteoporosis, independent of a history of prior fracture. *Osteoporos Int*. 2005;16(5):483–489.

26) Fransen M, Edmonds J. Reliability and validity of the EuroQol in patients with osteoarthritis of the knee. *Rheumatol*. 1999;38(9):807–813.

27)   Morgan CL, McEwan P, Morrissey M, Peters JR, Poole C, Currie CJ. Characterization and comparison of health-related utility in people with diabetes with various single and multiple vascular complications. *Diabet Med*. 2006;23(10):1100–1105.