

The risk factors for development or progression of locomotive syndrome: a systematic review

Yoshitaka Iwamoto^{1,2}, Takeshi Imura³, Kazuhiko Hirata¹, Yasunari Ikuta⁴,
Kai Ushio⁵, Yukio Mikami⁵, Nobuo Adachi⁴, Makoto Takahashi^{2,6}
and Ryo Tanaka⁷

¹*Division of Rehabilitation, Department of Clinical Practice and Support,
Hiroshima University Hospital, Hiroshima, Japan*

²*Department of Neuromechanics, Graduate School of Biomedical and Health Sciences,
Hiroshima University, Hiroshima, Japan*

³*Department of Rehabilitation, Faculty of Health Sciences, Hiroshima Cosmopolitan University,
Hiroshima, Japan*

⁴*Department of Orthopedic Surgery, Graduate School of Biomedical and Health Sciences,
Hiroshima University, Hiroshima, Japan*

⁵*Department of Rehabilitation Medicine, Hiroshima University Hospital, Hiroshima, Japan*

⁶*Center for Advanced Practice and Research of Rehabilitation, Graduate School of
Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan*

⁷*Graduate School of Humanities and Social Sciences, Hiroshima University,
Higashi-Hiroshima, Japan*

ABSTRACT

Locomotive syndrome is a decline in mobility and is believed to occur before the occurrence of frailty and sarcopenia; therefore, early detection of risk factors is important. However, systematic reviews have not been conducted. A systematic review of observational studies was performed to identify risk factors for the development or progression of locomotive syndrome. We searched the electronic databases of MEDLINE, Scopus, Web of Science, Ichushi Web (in Japanese), and Cumulative Index to Nursing and Allied Health Literature. Studies that used the development or progression of locomotive syndrome as an outcome and were written in English or Japanese were included. However, studies with nonadult participants and review articles were excluded. The quality of the eligible studies was evaluated using the Cochrane risk-of-bias instrument. This study included 79 observational studies (8 cohort and 71 cross-sectional studies). A meta-analysis was not performed. All studies were conducted in Japan. The eight cohort studies included 2,343 participants aged 57.0–79.3 years upon study initiation. The risk factors for developing locomotive syndrome were objectively assessed by parameters of motor function and muscle strength, such as short one-leg standing time and weak grip strength. The progression of locomotive syndrome was associated with the preoperative risk stage of locomotive syndrome and postoperative surgical failure syndrome. Locomotive syndrome can be detected through the regular assessment of motor function and muscle strength. To prevent locomotive syndrome in middle-aged and older people, an examination by an expert is necessary.

Keywords: locomotive syndrome, risk factor, systematic review

Abbreviations:

JOA: Japanese Orthopaedic Association

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Corresponding Author: Yoshitaka Iwamoto, RPT, PhD

Division of Rehabilitation, Department of Clinical Practice and Support, Hiroshima University Hospital,
1-2-3 Kasumi, Hiroshima 734-8551, Japan

Tel: +81-82-257-5566, Fax: +81-82-257-5594, E-mail: iwamo10@hiroshima-u.ac.jp

TUG: Timed Up & Go Test

DAS28-CRP: Disease Activity Score 28-C-reactive protein

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INTRODUCTION

Locomotive syndrome is a concept proposed by the Japanese Orthopaedic Association (JOA) in 2007.¹ In this condition, motor function is impaired because of disorders of the locomotor system.¹ This concept can raise health awareness among older adults regarding their locomotor system (consisting of bones, muscles, joints, and peripheral nerves) and prevent them from needing nursing care or becoming bedridden.

The global population is aging continuously, and Japan is one of the most aged countries worldwide. Although healthy life expectancy has increased along with average life expectancy, significant differences exist between them.² Healthy life expectancy is the period during which a person can live independently, both physically and mentally, without requiring daily nursing care.² In other words, the large gap between average life expectancy and healthy life expectancy means that older adults have difficulty living an independent life and that social security benefit costs increase. Thus, being in a state requiring nursing care must be avoided among older adults.

Fractures, falls, and osteoarthritis are common conditions requiring care, with approximately 30% of those requiring care suffer from these musculoskeletal dysfunctions.³ Therefore, the prevention and treatment of locomotive syndrome are important to prevent care needs and reduce social security benefit costs. In our systematic review of treatments for locomotive syndrome, oral glucosamine intake, electrical stimulation, and exercise were found to be effective in improving locomotive syndrome.⁴ However, to manage locomotive syndrome at an earlier stage, its onset and progression must be prevented.

Numerous cross-sectional and cohort studies have attempted to identify risk factors for the development or progression of locomotive syndrome; however, no systematic review of these reports has been conducted. Therefore, this systematic review was conducted to address the following clinical questions: (1) What declines in physical function are risk factors in the development and progression of locomotive syndrome? (2) What diseases are risk factors for the development and progression of locomotive syndrome? (3) What are the effects of these risk factors?

METHODS

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines.⁵ It was registered in the University Hospital Medical Information Network ([UMIN] trial ID: UMIN000046584).

Search strategy

We searched the electronic databases of MEDLINE, Scopus, Web of Science, Ichushi Web (in Japanese), and Cumulative Index to Nursing and Allied Health Literature (CINAHL). The following terms were used: “locomotive syndrome,” “risk factor,” “health correlates,” “population at risk,” “risk score,” “risk factor score,” and variants. No restrictions were set for the date, and the literature search was conducted on December 16, 2021.

Selection criteria

Studies that used the development or progression of locomotive syndrome as an outcome and articles written in English or Japanese were included.

Studies with nonadult participants and review articles were excluded.

Selection process

The search results from the databases were compiled into a spreadsheet using Microsoft Excel 2019. After removing duplicates, the titles and abstracts were reviewed separately by two reviewers (Y Iwamoto and TI), and this primary screening was conducted based on predefined criteria. The selected papers were organized. Again, two reviewers (Y Iwamoto and TI) separately reviewed the content, and secondary screening based on predefined criteria was performed to select eligible papers. If the opinions of the two reviewers (Y Iwamoto and TI) differed, the decision was left to the third reviewer (RT).

Data extraction

One reviewer (Y Iwamoto) extracted information about the participants, risk factors, and locomotive syndrome on a pre-prepared Microsoft Excel 2019 spreadsheet, and another (TI) validated the content.

Quality assessment

To assess the risk-of-bias (RoB) in each article, two reviewers (Y Iwamoto and TI) conducted separate evaluations using a set of predesigned criteria based on the Cochrane RoB instrument.⁶ If the opinions of the two reviewers (Y Iwamoto and TI) differed, the decision was left to the third reviewer (RT). Based on the Cochrane Handbook,⁷ the RoB was assessed only in cohort studies.

RESULTS

Study selection and characteristics

Figure 1 shows the process of selecting eligible papers. In total, 360 papers were systematically extracted from MEDLINE, Scopus, Web of Science, Ichushi Web, and CINAHL. Two papers were added after the manual search, and duplicates were then removed, leaving 218 papers. Furthermore, 92 papers were selected based on their titles and abstracts. After examining the full text, 79 papers were selected for inclusion. Nine of the excluded articles did not assess the development or progression of locomotive syndrome as an outcome, two included children, and two were review articles. Of the 79 eligible articles, only 8 were cohort studies, and the remaining 71 were cross-sectional studies. Based on the guidelines of the National Health and Medical Research Council,⁸ this study considered only the results obtained from the cohort study risk factors for locomotive syndrome. Moreover, the cross-sectional study results are listed in a separate table as potential risk factors (Appendix).

Table 1 presents the contents of the studies covered. In total, the eight cohort studies included 2,343 participants aged 57.0–79.3 years upon study initiation. All studies were conducted in Japan, and the follow-up period ranged from 1 to 10 years. Shen et al used a historical cohort approach, and their study had a long follow-up period.⁹ Only two studies used the three indices recommended by the JOA for the evaluating of locomotive syndrome,^{10,11} and others were determined only using questionnaires.

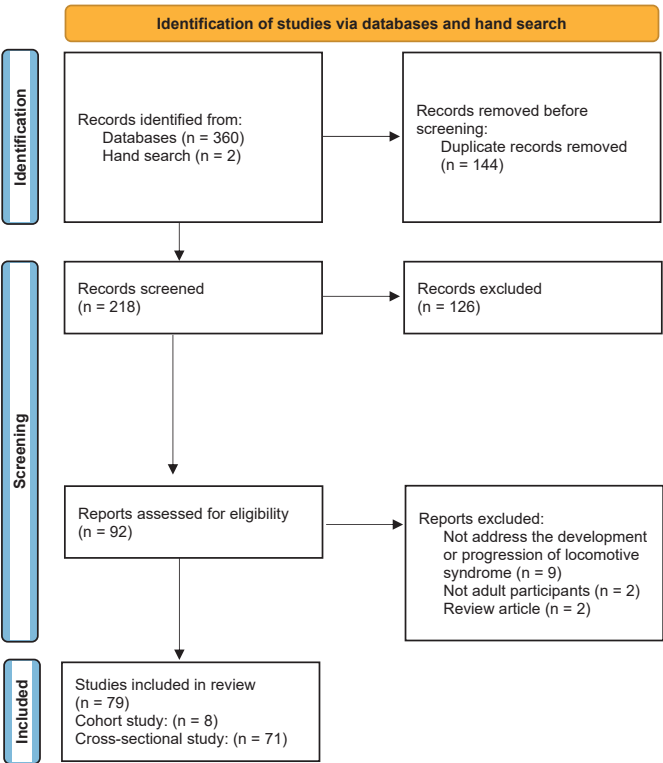


Fig. 1 Flow diagram of included and excluded studies

Table 1 Summary of included studies

First author, year	Population and setting	Age [years]	Sex (male/female)	Factor(s) included in the study	LS assessment (criteria)	Prevalence of LS at endpoint (LS/all participants)	Significant predictors	Follow-up rate (baseline/endpoint)	Follow-up
Kobayashi et al, ¹² 2019	519 healthy volunteers who attended a local government basic health checkup	63.1 ± 7.9*	87/118*	Age, 10-m gait time, GLFS-25, one-leg standing time, back muscle strength, RDQ	GLFS-25 (LS ≥ 16)	10.2% (21/205)	GLFS-25 OR = 1.437 (95% CI 1.143, 1.808) One-leg standing time OR = 0.958 (95% CI 0.924, 0.994) Back muscle strength OR = 0.961 (95% CI 0.869, 0.984)	42.2% (219/519)*	5 years
Kobayashi et al, ¹³ 2020	88 healthy elderly adults who attended the annual public health check-up*	61.6 ± 7.9*	31/57*	Grip strength	GLFS-25 (LS ≥ 16)	13.6% (12/88)	Grip strength ^b	N/A ^c	10 years
Ono et al, ¹⁷ 2021	1177 participants were from small, agricultural communities located in mountainous area	79.3 ± 3.5	660/517	SF	GLFS-25 (LS ≥ 16)	19.5% (104/533)	N/A ^d	63.6% (748/1177)	2 years
Shen et al, ⁹ 2021 ^e	568 alumni of physical education university	Middle-aged: 57.0 Elderly: 69.0–73.0 ^f	568/0	Sports club membership	Loco-check	Middle-aged: 14.6% (40/274) Elderly: 38.8% (114/294)	Engagement in exercise of increased cardiovascular intensity; for moderate-intensity exercise HR = 0.48 (95% CI 0.22, 1.06); for high-intensity exercise HR = 0.44 (95% CI 0.20, 0.97)	83.2% (568/683)	Middle-aged: 35.0 years Elderly: 47.0–51.0 years
Kita et al, ¹⁴ 2018	119 patients attending orthopaedic clinic and receiving physiotherapy or exercise therapy	76.6 ± 6.5	14/115	Age, sex, height, weight, maximum step height, TUG test, right-leg standing, left-leg standing	GLFS-5 (LS ≥ 6)	52.4% (43/82)	Maximum step height OR = 0.39 (95% CI 0.18, 0.84) TUG test OR = 6.09 (95% CI 1.44, 25.81)	68.9% (82/119)	1.89 years
Sobue et al, ¹⁵ 2021	246 RA patients consecutively visited hospital	60.9 ± 10.9*	82.8% (female)*	DAS28-CRP	GLFS-25 (LS ≥ 16)	25.9% (15/58)	2nd year DAS28-CRP ≥ 1.88 OR = 9.9 (95% CI 1.6, 60.2) 4th year DAS28-CRP ≥ 3.11 OR = 12.8 (95% CI 2.2, 74.0) 5-year mean DAS28-CRP ≥ 1.99 OR = 4.8 (95% CI 1.0, 22.9)	37.0% (91/246)	5 years

Fujita et al, ¹¹ 2020	357 patients who underwent lumbar spinal surgery for LSS	72.8 ± 5.5 ^a	95/71 ^a	Age, sex, BMI, preoperative factors, medical history, FBSS, preoperative stage of 2 in the stand-up test	GLFS-25 Stand-up test Two-step test	100% (166/166)	FBSS OR = 0.2 (95% CI 0.04, 1.05) ^b Preoperative stage of 2 in the stand-up test OR = 0.2 (95% CI 0.05, 0.102) ^c	46.5% (166/357)	1 year
Shimizu et al, ¹⁰ 2021	101 patients who underwent surgery for LSS	69.3 ± 8.1	46/55	Age, sex, BMI, BMD, preoperative grip strength, presence of spondylolisthesis, presence of DISH, type of leg symptom, presence of multi-level treatment, use of instrumentation, SVA before surgery and 1 year after surgery	GLFS-25 Stand-up test Two-step test	94.1% (95/101)	N/A ^d	100% (101/101)	1 year

BMD: bone mineral density
BMI: body mass index
DAS28-CRP: Disease Activity Score 28-C-reactive protein
DISH: diffuse idiopathic skeletal hyperostosis
FBSS: failed back surgery syndrome
GLFS-25: 25-Question Geriatric Locomotive Function Scale
GLFS-5: 5-Question Geriatric Locomotive Function Scale
LS: locomotive syndrome
N/A: not applicable
OR: odds ratio
RDQ: Roland-Morris Disability Questionnaire
SF social frailty
SVA: sagittal vertical axis
TUG: Timed-Up & Go Test
*: at the endpoint

a: 219 means 205 eligible participants at the endpoint plus 14 identified as LS at baseline.
b: Odds rate was not calculated in that study.
c: There was no description of the number of participants at baseline.
d: There was no statistically significant predictor.
e: Study design was a historical cohort.
f: They grouped with age and did not show group average.
g: They investigated risk factors associated with non-improvement in risk level of locomotive syndrome.

Quality assessment

Table 2 shows the RoB of the eligible articles. In one article, six items were rated as probably no (PN) or definitely no (DN). Two articles had three items rated PN or DN. Three articles had two items rated PN or DN. Two articles had only one item rated PN or DN.

Table 2 Results of risk of bias assessment

	Kobayashi et al, ¹² 2019	Kobayashi et al, ¹³ 2020	Ono et al, ¹⁷ 2021	Shen et al, ⁹ 2021	Kita et al, ¹⁴ 2018	Sobue et al, ¹⁵ 2021	Fujita et al, ¹¹ 2020	Shimizu et al, ¹⁰ 2021
1. Was selection of exposed and non-exposed cohorts drawn from the same population?	PY	DY	PY	PY	PY	PY	PY	PY
2. Can we be confident in the assessment of exposure?	PY	PN	DY	DN	DN	DY	DY	PN
3. Can we be confident that the outcome of interest was not present at start of study?	PY	DN	PY	DN	DN	PY	DY	DY
4. Did the study match exposed and unexposed for all variables that are associated with the outcome of interest or did the statistical analysis adjust for these prognostic variables?	PY	PN	PY	PY	PY	PY	PY	PN
5. Can we be confident in the assessment of the presence or absence of prognostic factors?	PY	PN	PY	PY	PN	PY	PY	PN
6. Can we be confident in the assessment of outcome?	PY	PY	PY	PN	PN	PY	DY	DY
7. Was the follow up of cohorts adequate?	DN	N/A	DN	PY	PN	DN	DN	DY
8. Were co-intervention similar between groups?	PY	PN	PN	PN	PN	PN	DN	PN

PY: probably yes
 DY: definitely yes
 PN: probably no
 DN: definitely no

Risk factors for locomotive syndrome

One-leg standing time, back strength, grip strength, step-up ability, and Timed Up & Go Test (TUG) time were identified as risk factors for the development or progression of locomotive syndrome. Kobayashi et al conducted a 5-year follow-up study on community-dwelling older adults and reported that high 25-Geriatric Locomotive Function Scale scores, short one-leg standing time, and weak back strength upon study initiation were risk factors for the development of locomotive syndrome.¹² In a follow-up study, the same research group revealed that the prevalence of locomotive syndrome was significantly higher after 10 years in the group with a weaker grip strength compared to those with a stronger grip strength upon study initiation.¹³ Kita et al conducted a follow-up study on patients with orthopedic problems for approximately 2 years. The results showed that participants who could climb high steps and had a shorter TUG time had a lower risk of developing locomotive syndrome.¹⁴

High Disease Activity Score 28-C-reactive protein (DAS28-CRP) scores were identified as risk factors for the development or progression of locomotive syndrome. Sobue et al focused on disease severity and found that higher DAS28-CRP scores were a risk factor for the development of locomotive syndrome in patients with rheumatoid arthritis during a 5-year follow-up study.¹⁵

Failed back surgery syndrome was identified as a risk factor for the development or progression of locomotive syndrome. The JOA has established three risk stages for locomotive syndrome: stages 1, 2, and 3.¹⁶ Based on studies that examined the progression of locomotive syndrome risk stages before and after surgical intervention for lumbar spinal stenosis, stage 2 preoperative classification according to the stand-up test and failed back surgery syndrome were identified as risk factors.¹¹

In addition, Shen et al focused on middle-aged and older adults who graduated from a school of physical education.⁹ They showed that increased cardiovascular intensity was associated with a lower risk of locomotion.⁹ Ono et al examined whether social frailty is a risk factor for the development of locomotive syndrome; however, the results showed no association between them.¹⁷

In this systematic review, we could not perform a meta-analysis and could not address the magnitude of the effect of the integrated risk factors.

DISCUSSION

Risk factors for the development or progression of locomotive syndrome were one-leg standing time, back strength, grip strength, step-up ability, and TUG time. Balance ability is associated with mobility capacity in the older population.¹⁸ In addition, a one-legged standing time of less than 10 s suggests serious mobility dysfunction,¹⁹ and the JOA also recommends practicing one-legged standing to prevent locomotive syndrome.²⁰ Back strength is associated with the quality of life in middle-aged and older men²¹ and postmenopausal women with osteoporosis.²² Grip strength is often used as an indicator of overall muscle strength²³ and can predict functional decline.²⁴ Sometimes back pain occurs during back muscle strength measurement,²⁵ and grip strength, which is more easily and safely measured, may be useful. Both TUG and step-up ability assess complex movements. TUG is often used to safely and simply assess mobility function and predict activities of daily living.²⁶ Compared with the 10-meter walk, TUG is considered more predictive of locomotive syndrome development because it includes standing, sitting, and changing direction.

DAS28-CRP scores can be used to assess disease activity in patients with rheumatoid arthritis.²⁷ These patients are more likely to develop locomotive syndrome, and DAS28-CRP scores are correlated with 25-Geriatric Locomotive Function Scale scores.²⁸ Because DAS28-CRP scores are also associated with disease-dependent functional decline, disease activity must be evaluated

to prevent locomotive syndrome.

Failed back surgery syndrome refers to persistent or recurrent pain that occurs after lumbar spine surgery.²⁹ Surgical treatment for patients with lumbar spinal stenosis can improve locomotive syndrome; however, failed back surgery syndrome prevents improvement and is often complicated by depression, economic and personal stress, loss of employment and productivity, and low self-esteem.²⁹ The subsequent decrease in activity may induce the progression of locomotive syndrome.

Comparing the results of this study with those of previous systematic reviews that have examined the risk factors for sarcopenia and frailty, which represent physical and mental function decline among older individuals, is extremely interesting. The risk factors for sarcopenia and frailty were sociodemographic,³⁰⁻³² physical,^{31,33} biological,³¹ and lifestyle factors,^{30,31,34-37} but not expert-rated motor function and muscle strength. In contrast, this review showed that motor function and muscle strength, which were examined by experts, were risk factors for locomotive syndrome, namely, one-leg standing time,¹² back muscle strength,¹² grip strength,¹³ step-up ability,¹⁴ and TUG time.¹⁴ Motor function (walking speed) and muscle strength (grip strength) measures are used in the diagnostic criteria for sarcopenia and frailty.^{38,39} However, unlike sarcopenia and frailty, walking speed and grip strength are not used as diagnostic criteria for locomotive syndrome. Therefore, there was no agreement on whether improvement of these motor functions reduces the risk of locomotive syndrome. In the present review, we confirm the fact that there is evidence from cohort studies that these motor function impairments are a risk factor for locomotive syndrome. In addition, we confirm the fact that evidence from cohort studies has shown that impaired balance functions such as one-leg standing time and TUG may be a risk factor for locomotive syndrome. This supports the usefulness of motor function measures for the prevention of locomotive syndrome for professionals. Moreover, the prevention of locomotive syndrome may inhibit the development of sarcopenia and frailty in the future.⁴⁰ Therefore, experts should accurately measure motor function and detect risk factors.

How should we treat the risk factors for the development or progression of locomotive syndrome identified in this review? In our systematic review of intervention effects on locomotive syndrome, oral glucosamine intake, electrical stimulation, and exercise were found to be effective in improving locomotive syndrome.⁴ First, active evaluation of motor function and muscle strength by an expert is necessary. Such assessments may be routinely performed in medical institutions. However, this review revealed that motor function and muscle strength decline can predict the development of locomotive syndrome not only in individuals with the disease but also in community-dwelling older adults. Therefore, motor function and muscle strength should be assessed not only in older individuals but also in the general population from middle age onward by experts. Furthermore, early detection of risk factors is important. In the study by Kobayashi et al, the mean values after the follow-up period in the group with weak grip strength were below the diagnostic criteria for sarcopenia according to the Asian Working Group³⁹ in both men and women (26.5 and 17.5, respectively¹³). This finding may indicate that grip strength evaluation is important for not only the diagnosis of sarcopenia but also the prognosis of locomotive syndrome.

This review had several limitations. First, the studies could not be categorized according to risk factors because a meta-analysis was not performed given the small number of cohort studies. However, this is the first systematic review of the development or progression of locomotive syndrome. We hope that experts will further conduct cohort studies, including motor function assessment, in the future. Second, all eight studies analyzed in this study were conducted in Japan, and whether the results can be generalized to diverse racial groups is unclear. Locomotive syndrome is a concept proposed by the JOA and is not well-known overseas. However, population aging will occur in other developed countries as well as in Japan, and the decline in mobility among older individuals will become a major social issue. Therefore, the concept of

locomotive syndrome will expand, and similar assessments will be performed in other countries worldwide. Third, no cohort study has investigated the association between nutritional status or lifestyle habits and the development or progression of locomotive syndrome. Nutritional status and lifestyle habits were found to be risk factors for sarcopenia and frailty.^{32-34,36,37,41} Therefore, they may affect the development or progression of locomotive syndrome. Accordingly, further studies are required to investigate these relationships in the future.

To the best of our knowledge, this is the first systematic review of the risk factors for the development and exacerbation of locomotive syndrome. In total, 71 cross-sectional and 8 cohort studies were selected. The cohort studies showed that the risk factors were expert-rated motor functions such as one-leg standing time, back muscle strength, and grip strength.

CONFLICT OF INTEREST

The authors declare no conflicts of interest associated with this manuscript.

AUTHOR CONTRIBUTIONS

Conceptualization: All authors; Methodology: Iwamoto, Imura, Takahashi, Tanaka; Formal analysis and investigation: Iwamoto, Imura, Takahashi, Tanaka; Writing - original draft preparation: Iwamoto; Writing - review and editing: All authors; Funding acquisition: Tanaka; Resources: All authors; Supervision: Imura, Hirata, Ikuta, Ushio, Mikami, Adachi, Takahashi, Tanaka.

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APPENDIX

Akabori et al 2015	The percentage of people with pre-LS was lower in the group that frequently ate natto and raw vegetables.
Akahane et al 2017	Logistic regression analysis revealed that older age, sex, current smoking status, number of existing teeth, and presence of periodontal disease were associated with LS.
Akahane et al 2019	LS was associated with functional inconvenience in performing common daily activities involving the lower extremities and spine.
Anees et al 2020	The risk of LS is high with grade III knee osteoarthritis as compared to grade II.
Arai et al 2019	JST-IC and social participation were factors related to LS among the elderly.
Asakura et al 2016	After adjusting for age and sex, body weight, BMI, and K6 scores in patients with LS were significantly higher, and EQ-5D scores were significantly lower than in those without LS.
Endo et al 2018	The number of sites of musculoskeletal pain was associated with the degree of LS risk stage.
Fujimoto 2017	In women, the relationship between depressive tendencies and LS was found to be related.
Fujita et al 2019	LSS severity is potentially associated with the progression of LS.
Fujita et al 2017	In LS group, age and BMI were higher and knee extension strength was lower.
Hirano et al 2012a	A decrease in BMS and an increase in SIA were significantly associated with LS.
Hirano et al 2012b	A decrease in BMS and an increase in SIA were significantly associated with LS.
Hirano et al 2013	An increase in age and a decrease in BMS were significantly associated with LS.
Iizuka et al 2015	The young adult mean of the speed of sound, LBP, shoulder pain and knee pain were found to be factors significantly affecting the presence of locomotive dysfunction as identified based on the GLFS-25 scores.
Ikemoto et al 2016	Functional decline in grip strength, TUG and one-leg standing and degree of depression were significantly associated with LS.
Ishigaki et al 2016	The results of GLFS-25 were correlated with the results of rising assessment and the two-step test, and with the thoracolumbar extension range of motion, but not with the kyphotic index or thoracolumbar rotation range of motion.
Ito et al 2017	BMI, perceived ill-health, social activities, and awareness of social resources were risk factors for LS.
Kashiwabara et al 2017	Ground golf players have a lower risk of being judged as having LS risk levels 1 and 2 than elderly people of the same age.
Kitagawa et al 2020	Handgrip measurement was useful in detecting LS.
Kobashi 2016	Age and BMI were associated with LS in males and females.
Mahali et al 2018	There was a positive correlation between the scores of the GLFS-25 and EQ-5D questionnaires and a negative correlation with the visual level of health. Level of quality of life in the two groups with LS and without LS was significantly different.

Maruya et al 2018	The finding is that the risk stage of the 2-step test is related to cognitive functions, even at an initial risk stage.
Matsugi et al 2015	Age and TUG were significantly associated with LS.
Matsugi et al 2017	In the overall and gender analyses, an increase in BMI was associated with an increase in LS prevalence independently of age and grip strength, but in the late elderly, there was no clear relationship between an increase in BMI and LS prevalence, and age and grip strength were related.
Matsumoto et al 2016a	Using multivariate logistic regression analysis with adjustment factors, of the autocorrelation coefficients only gait variability in the vertical axis remained a significant independent associated with the LS.
Matsumoto et al 2016b	Based on the multiple regression analysis adjusted for age and gender, there was a significant relationship between the risk of falling and LS compared with the non-locomotive and pre-LS groups.
Mitani et al 2018	The prevalence rates of LS and metabolic syndrome correlate positively in women.
Mochizuki et al 2019	This study demonstrated that to prevent LS, we should aim to control pain and maintain a low HAQ-DI in elderly and younger patients with RA, and improve disease activity and maintain a higher basal metabolic rate, and legs muscle mass in younger patients with RA.
Muramoto et al 2012a	Knee pain, LBP, one-leg standing time, TUG, and BMS was significantly associated with the GLFS-25 score.
Muramoto et al 2012b	BMS was independently associated with LS in men, and knee pain and BMS were independently associated with LS in women.
Muramoto et al 2013	The results of all the physical performance tests (TUG, one-leg standing time, BMS, 10-m gait time, maximum stride) correlated significantly with the GLFS-25 scores of both genders even after adjusting for age except for grip strength.
Muramoto et al 2014	Central obesity is significantly associated with LS, and WC can be a useful parameter to assess the risk of LS in elderly women.
Muramoto et al 2016	LBP and knee pain were greater, physical performance tests were poorer, SIA was greater, and LLA was smaller in LS group compared to non-LS group even after adjustment by age.
Nagilla et al 2021	Older age and number of lost tooth affect the prevalence of LS.
Nakamura et al 2015	Unipedal stance time less than 15 s was significantly related to LS.
Nakamura et al 2016	Participants with BMI ≥ 23.5 kg/m ² had significantly higher risk for LS than those with BMI < 23.5 kg/m ² .
Nishimura et al 2020	Knee pain, LBP and physical activity levels are key factors related to LS even in young and middle-aged adults.
Ohtsuki et al 2019	Age, BMI, AD, UCLA activity score, and FBC were also related to LS.
Okada et al 2016	LS was negatively associated with social engagement, loss of social engagement, life satisfaction, and self-rated health.
Sadeghimahalli et al 2019	Age, female gender, positive history of chronic disease, and positive history of chronic pain were the predictors of LS among elders.
Saito et al 2017	Depressive states and age are independent factors for LS.
Sasaki et al 2012	In the elderly group, abdominal circumference was significantly associated with LS.

Seichi et al 2014	A significant difference was seen between each group mean for individual average one-leg standing times.
Seko et al 2021	Leg press strength measurement with a knee flexion angle of 60° by pull-type HHD is useful as a method to reflect LS.
Shibata et al 2020	For those with a one-leg standing time of either leg reaching 60 seconds, the proportion of LS subjects is higher in the group with a left-right difference of 10 seconds or more.
Shinkai et al 2020	Multiple logistic regression analysis revealed significant association with increased BMI, Timed-Up-and-Go delay, decreased grip strength, and aging.
Shiratani et al 2017	Logistic regression analysis revealed that for aged men, severe of living arrangement, Philadelphia Geriatric Center moral and Frontal Assessment Battery, were significantly associated with presence of LS.
Sobue et al 2019	GLFS-25 and HAQ-DI were positively and strongly correlated.
Sudo et al 2014	Patients with LS had a slower gait speed, a shorter stride length, a shorter time to stand on one leg, and a longer time to stand up five times.
Tajika et al 2017	Logistic regression analysis applied after adjustment for age, sex, height, and weight revealed a significant association between LS and each of non-dominant hand grip and the Hand 10 questionnaire score.
Takenaka et al 2019	The significant factor of the GLFS-25 score was trunk-extensor strength.
Tanaka et al 2018	The serum cystatin C level is significantly related to LS risk and can be an early predictor.
Tanaka et al 2019a	Among the four posturographic variables by balance test, increase in back-and-forth sway was the most remarkable variable associated with LS risk together with BMS, BMI, and TUG by logistic regression analysis.
Tanaka et al 2019b	The ECW/TBW ratio is predictive of LS.
Tanaka et al 2019c	Compared to muscle mass, phase angle more strongly reflects LS risk and becomes significantly reduced at later LS risk stages.
Tanaka et al 2019d	The phase angle was significantly related to LS, and the decreased phase angle was a significant risk factor of LS together with the TUG result.
Tanaka et al 2019e	The increase in WC measured by BIA was significantly associated with LS risk.
Tanaka et al 2019f	Low phase angle was significantly related with LS.
Tanaka et al 2020a	The Japanese version of the EQ-5D-5L index was significantly related to LS in Japan.
Tanaka et al 2020b	An increase in the ECW/TBW ratio may reflect LS risk.
Tavares et al 2017	A significantly higher risk of LS in the presence of chronic pain and with a worse self-perceived health.
Terai et al 2021	Age, locomotor symptoms, especially spine or hip/knee joint complaints, and exercise habits were associated with the development of LS.
Tsuruta et al 2018	High ratios of participants in the LS group were also found to have anxiety about their physical strength compared to participants in the non-LS group. A strong association between LS and pain in both the back and hip joint was shown, and the mean PCS score of the participants in the LS group was significantly lower than that of participants in the non-LS group.

Uesugi et al 2019	This higher risk group was higher in weight, body fat mass, and body fat percentage than low risk group. This group was lower in energy intake and physical activity amount of 3 Mets or more than the low risk group.
Wakimoto et al 2018	WHO-5 score was significantly associated with LS.
Yamada et al 2019	Albumin level and PNI were negatively correlated with GLFS-25.
Yamada et al 2021	Increased age in participants aged ≥ 40 years, female sex, overweight status, hypertension, frequency of physical activity/sports, and a history of orthopaedic surgery were related factors in all stages.
Yamaguchi et al 2018	Faster gait speed was a significant predictor of the negative two-step test, negative 25-question geriatric locomotive function scale, and absence of LS.
Yoshihara et al 2019	Higher HbA1c and lower albumin are associated with the prevalence of LS in Japanese middle-aged and elderly individuals.
Yoshimura et al 2019	LS in participants with obesity was more frequent than those without obesity, while LS in participants with an exercise habit was less frequent than those without an exercise habit.
Yoshinaga et al 2019	Interventions to prevent LS are important during its early stages, especially for females, and lifestyle-related signs of LS, such as pain in the locomotive organs, lifestyle-related disease, drug treatment, and a lower subjective evaluation of health must not be overlooked.

AD: alcohol drinking
 BIA: bioelectrical impedance analysis
 BMI: body mass index
 BMS: back muscle strength
 ECW/TBW: extracellular water/total body water
 EQ-5D: EuroQol 5-dimensions
 EQ-5D-5L: EuroQol 5-dimensions 5-levels
 FBC: frequency of breakfast consumption
 GLFS-25: 25-Geriatric Locomotive. Function Scale
 HAQ-DI: Health Assessment Questionnaire Disability Index
 HHD: Hand Held Dynamometer
 JST-IC: Japan Science and Technology Agency Index of Competence
 LBP: low back pain
 LLA: lumber lordosis angle
 LS: locomotive syndrome
 LSS: lumber spinal stenosis
 PCS: physical component summary
 PNI: Prognostic Nutritional Index
 RA: rheumatoid arthritis
 SIA: spinal inclination angle
 TUG: Timed-Up & Go Test
 UCLA: University of California, Los Angeles
 WC: waist circumference
 WHO: World Health Organization