Associations Between Symptoms and Quality of Life in Lumbar Degenerative Disease and Cognitive Dysfunction in a Japanese Community: A Cross-sectional Study

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Research article

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Abstract

**Background:** Lumbar degenerative disease (LDD) and dementia are increasing in super-aging societies and are both related to physical dysfunction and pain. However, the relationship between these diseases remains unclear. This cross-sectional study aimed to investigate the rate of comorbidity of lumbar spinal stenosis (LSS) and mild cognitive impairment (MCI) by age and sex and clarify the association between LSS presence, LDD symptoms, quality of life (QOL) related to low back pain, and cognitive impairment in a Japanese population.

**Methods:** We enrolled 1097 participants (men 437; women 660; mean age 54.6 years) from a medical checkup program. LSS was diagnosed using a self-administered questionnaire, and LDD symptoms were evaluated using visual analog scale (VAS: low back pain, pain, numbness of the lower limb). QOL related to low back pain was evaluated using the Japanese Orthopedic Association Back-Pain Evaluation Questionnaire (JOABPEQ: pain, lumbar function, and gait function), and Kellgren-Lawrence grading was performed to evaluate lumbar degeneration using lateral radiographs of the lumbar spine. Cognitive function was measured using the Mini Mental State Examination (MMSE), and we defined MCI as a summary score of MMSE £27. Logistic and multiple linear regression analyses were performed to analyze the association between MCI, summary score of MMSE and LSS factors.

**Results:** The comorbidity rate of MCI and LSS was 0.9% in men and 0.7% in women. It was 2.1% in those aged ≥65 years in both sexes, and this rate increased with age. Lumbar function in JOABPEQ (OR 0.979, 95% CI 0.961 to 0.998) and lower limb pain in VAS (OR 1.020, 95% CI 1.002 to 1.039) were associated with MCI in men. The presence of LSS, lumbar function, and gait function in JOABPEQ were associated with MMSE in both sexes, while lower limb numbness and pain in VAS were associated with MMSE in men.

**Conclusion:** The comorbidity rate of LSS and MCI increased with age. The presence of LSS, certain symptoms of LDD, and deterioration of QOL due to low back pain were related to cognitive dysfunction. Treatment of LDD could help to improve both LDS symptoms and cognitive dysfunction.

**Background**

Lumbar degenerative disease (LDD), such as lumbar spinal stenosis (LSS), degenerative spondylolisthesis and spondylosis deformity, is more prevalent among middle-aged and elderly individuals. LDD causes low back pain, intermittent claudication, bladder and rectal disturbance, numbness and lower limb pain, and deterioration in muscle power of the lower limbs as well as standing and walking abilities [1-3]. The number of people whose quality of life (QOL) is impaired by LDD is expected to increase in a super-aging society.

Mild cognitive impairment (MCI) is a pre-stage of dementia, and people with MCI are in a high-risk group for developing dementia [4]. However, MCI can be improved if risk factors of cognitive dysfunction are reduced [5, 6]. Thus, reducing the risk of cognitive impairment is important to prevent the development of...
Several reports have shown that cognitive impairment is related with pain and physical dysfunctions [7-9], which are typical symptoms of musculoskeletal disease. Cognitive function certainly decays with age, thereby increasing the prevalence of MCI in the future.

Previous studies investigating the association between cognitive function and musculoskeletal diseases reported that MCI was related with the occurrence of knee osteoarthritis [10] and that delayed union of osteoporotic vertebral fracture decreased cognitive function [11]. However, the association between LDD and cognitive function remains unclear, although both LDD and cognitive impairment are related to pain and physical dysfunction. Hence, clarifying the relationship between LDD and cognitive impairment may be important for improving ADL in elderly people. This study aimed to investigate the rate of comorbidity of MCI and LSS by age and sex, and to clarify the relationship between MCI/MMSE score and the risk factors of LDD—LSS presence, LDD symptom, QOL score depending on low back pain and radiographical lumbar degeneration in a community-dwelling Japanese population.

Materials And Methods

Participants

Our analysis was based on data collected from a medical checkup program in 2016. In brief, this program was initiated in 2005, and it was conducted over a 10-year period. In addition to orthopedic surgeons, gynecologists, urologists, endocrine physicians, cardiologist physicians, gastroenterologists, neurologists, and otolaryngologists were involved in this project. As one aspect of the multiple-focused check, we collected questionnaires and radiographic images related to musculoskeletal disorder.

For this cross-sectional study, 1149 participants were enrolled. Participants were asked to complete some self-administered questionnaires assessing their daily habits, medical histories, and LDD. They also underwent a cognitive screening test and a lateral lumbar radiograph in the neutral position. We excluded those who did not answer the questionnaire entirely, did not undergo cognitive screening test and radiographic examination, or had medical histories of lumbar spine surgeries. Of all participants, 52 were excluded (19 men, 33 women). Of those excluded, 36 (13 men, 23 women) did not answer questionnaires entirely, 13 (4 men, 9 women) did not undergo radiography, and 3 (2 men, 1 woman) had previous lumbar surgery. Finally, 1097 people (20-93 years old, 437 men, 660 women) were included in this study. The mean ages were 53.6 years old in men and 55.3 years old in women. All participants were provided a thorough explanation that the data collected would be analyzed, and gave written informed consent.

Diagnosis of LSS

LSS was detected using self-administered questionnaires consisting 15 questions associated with neurological disorders. We diagnosed LSS when the scores were 13 points or greater (sensitivity: 84%, specificity: 78%) [12].
**Evaluation of cognitive function**

Cognitive function was measured using the Mini Mental State Examination (MMSE) [13]. This is a 30-item cognitive screening test that measures orientation, registration, short-term memory, attention and concentration, and language and construction capacity. The full score of MMSE is 30 points, with 0 being the worst cognitive function. We defined the participant as having MCI when MMSE was 27 points or less, because this cut-off value had the greatest sensitivity (66.3%) and specificity (72.9%) of diagnosing MCI in a previous report [14]. We defined the participants whose MMSE was score 27 points or less as MCI+ group, and the participants whose MMSE score was over 27 points as MCI- group.

**Assessment of symptoms of LDD, and quality of life associated with low back pain**

The severities of the symptoms of LDD were evaluated with the visual analogue scale (VAS), for the most severe low back pain, lower limb pain and numbness during the past three months. The most severe score is 100 mm, and 0 mm means no symptoms.

Deterioration of quality of life (QOL) due to low back pain was evaluated using the Japanese Orthopedics Association Back Pain Evaluation Questionnaire (JOABPEQ) [15]. There have been several reports that JOABPEQ was useful for evaluating QOL in patients with lumbar disc herniation, LSS, and other lumbar diseases [16-18]. It consists of five domains: pain, gait function, lumbar function, social life, and mentality, and each domain is scored out of 100 points. Three of the five domains: pain, gait function and lumbar function were used for analysis in this study. Research assistants supported the participants who could not answer these questionnaires by themselves.

**Measurement of lumbar degeneration on radiography**

Lateral radiographs of the lumbar spine were taken, with the participants standing naturally, with their forearms crossed and hands on the chest. Radiographs were evaluated by a single orthopedic surgeon (KK) using Kellgren-Lawrence grading (KL) [19] in each intervertebral level (L1/2, L2/3, L3/4, L4/5, and L5/S1). To determine the severities of lumbar degeneration, the values of KL were summed from L1/2 to L5/S. According to this summed value, 0 corresponded to a normal lumbar spine and 20 expressed the most severe degenerative lumbar spine [20].

**Medical histories and daily habits**

All participants provided data related to their medical histories and daily habits which were previously reported as related to cognitive impairment [21-25]. Medical histories related to diabetes mellitus (DM), hypertension (HT), and depression were collected. We collected data pertaining to their duration of
education (6 to 20 years), daily smoking habits (0, ex-smoker or never smoked; 1, current smoker), alcohol consumption (0, ex-drinker or never drank or social drinker; 1, habitual drinker) and exercise (0, no exercise habit; 1, having exercise habits over 2 times during one week).

**Statistical analyses**

Descriptive statistics were used to investigate the prevalence of MCI and LSS by age and sex. To compare characteristics between MCI+ and MCI- groups, we used the Mann-Whitney U test with the presence of MCI as the dependent variable and age, BMI, VAS, JOABPEQ, summed KL, and education periods as independent variables. To analyze the correlation between MCI and LDD parameters, logistic regression analysis was performed with MCI as the dependent variable and the presence of LSS, VAS, JOABPEQ and summed KL grades as the independent variables. For adjusting for age, duration of education, DM, HT, depression, smoking, alcohol consumption, and exercise, they were also included as independent variables. To analyze the correlation between MMSE and LDD parameters, multiple linear regression analysis was performed with MMSE as the dependent variable and the presence of LSS, VAS, JOABPEQ, and summed KL grades as the independent variables. All statistical tests were performed using SPSS ver. 22.0 (SPSS Inc., Chicago, IL, USA), and statistical significant was set at 0.05.

**Results**

**Prevalence of MCI and LSS by age and sex**

In men, 48 individuals (11%) had MCI. The prevalence of MCI increased with age and was 29% (35/123) in those aged ≥65 years. Eleven individuals (2.5%) were diagnosed with LSS and the prevalence of LSS also increased with age. In women, 45 individuals (6.8%) had MCI. The prevalence increased with age and was 18% (37/211) in those aged ≥65 years. Twenty individuals (3.0%) were diagnosed with LSS. The comorbidity rate of MCI and LSS was 0.8% in all participants, 0.9% in men and 0.7% in women (Table 1). The comorbidity rate was 2.1% (7/334) in those aged ≥65 years, and increased with age. The rate of MCI was 29% (9/31) in participants with LSS in both sexes, 36% (4/11) in men, and 25% (5/20) in women. The rate of LSS was 9.8% (9/92) in participants with MCI in both sexes, 8.5% (4/47) in men, and 11% (5/45) in women.
Table 1
MCI and LSS prevalence, JOABPEQ, VAS, medical histories and daily habits by age and sex.

|                        | Men (437) | Total       | 20s (25) | 30s (83) | 40s (72) | 50s (83) | 60s (106) | 70s (50) | over 80 (18) |
|------------------------|-----------|-------------|----------|----------|----------|----------|-----------|----------|--------------|
| BMI                    | 23.7 ± 3.0| 22.9 ± 3.9  | 23.3 ± 3.2| 24.6 ± 3.2|          |          |           |          |              |
| LSS                    | 11 (2.5)  | 0 (0)       | 1 (1.2)  | 1 (1.4)  |          |          |           |          |              |
| MCI                    | 47 (11)   | 1 (4.0)     | 0 (0)    | 3 (4.2)  |          |          |           |          |              |
| Comorbidity of LSS and MCI | 4 (0.9)  | 0 (0)       | 0 (0)    | 0 (0)    | 0 (0)    |          |           |          |              |
| MMSE                   | 29.2 ± 1.6| 29.5 ± 1.2  | 29.7 ± 0.5| 29.6 ± 0.9|          |          |           |          |              |
| VAS (mm)               |           |             |          |          |          |          |           |          |              |
| Low back pain          | 17.1 ± 21.9| 5.4 ± 13.0  | 15.4 ± 19.4| 17.2 ± 23.3|          |          |           |          |              |
| Pain of lower limb     | 5.1 ± 14.1| 3.4 ± 11.8  | 3.3 ± 10.4| 4.4 ± 9.7 |          |          |           |          |              |
| Numbness of lower limb | 4.6 ± 13.6| 1.1 ± 3.2   | 3.0 ± 10.4| 4.1 ± 10.0|          |          |           |          |              |
| JOABPEQ                |           |             |          |          |          |          |           |          |              |
| Pain                   | 85.6 ± 26.5| 93.1 ± 20.7 | 86.2 ± 24.9| 87.5 ± 25.5|          |          |           |          |              |
| Lumbar function        | 93.0 ± 14.2| 97.7 ± 5.7  | 98.0 ± 8.7| 97.0 ± 7.0|          |          |           |          |              |
| Gait function          | 94.8 ± 14.2| 100.0 ± 0  | 98.7 ± 6.1| 99.4 ± 3.5|          |          |           |          |              |
| KL                     | 4.8 ± 4.3  | 1.0 ± 1.4   | 1.6 ± 2.2| 2.5 ± 2.7 |          |          |           |          |              |
| Education periods (year)| 12.2 ± 12.2| 13.2 ± 2.2  | 12.7 ± 1.6| 12.5 ± 1.4|          |          |           |          |              |
| DM                     | 33 (7.5)  | 0 (0)       | 0 (0)    | 2 (2.8)  |          |          |           |          |              |
| HT                     | 125 (29)  | 0 (0)       | 2 (2.4)  | 8 (11)   |          |          |           |          |              |
| Depression             | 3 (0.7)   | 0 (0)       | 0 (0)    | 0 (0)    |          |          |           |          |              |
| Smoking                | 127 (29)  | 8 (32)      | 40 (48)  | 22 (31)  |          |          |           |          |              |
| Alcohol                | 305 (70)  | 7 (28)      | 63 (76)  | 46 (64)  |          |          |           |          |              |
| Exercise               | 80 (18)   | 5 (20)      | 14 (17)  | 11 (15)  |          |          |           |          |              |
| Men (437)              | 50s (83)  | 60s (106)   | 70s (50) | over 80 (18) |          |          |           |          |              |
|                        | BMI  | ±2.6 | 23.7 | ±2.9 | 23.4 | ±2.6 | 23.7 | ±3.9 |
|------------------------|------|------|------|------|------|------|------|------|
| **BMI**                | 23.6 | ±2.6 | 23.7 | ±2.9 | 23.4 | ±2.6 | 23.7 | ±3.9 |
| **LSS**                | 2    | (2.4) | 4    | (3.8) | 1    | (2.0) | 2    | (11) |
| **MCI**                | 0    | (0)  | 18   | (17) | 15   | (30) | 10   | (56) |
| Comorbidity of LSS and MCI | 0    | (0)  | 2    | (8.0) | 1    | (4.0) | 1    | (4.0) |
| **MMSE**               | 29.7 | ±0.5 | 28.9 | ±1.7 | 28.2 | ±2.1 | 26.1 | ±3.1 |
| **VAS (mm)**           |      |      |      |      |      |      |      |      |
| Low back pain          | 18.3 | ±23.6 | 18.1 | ±20.8 | 18.9 | ±22.7 | 23.1 | ±30.2 |
| Pain of lower limb     | 4.7  | ±13.4 | 7.2  | ±18.0 | 7.0  | ±17.7 | 3.7  | ±11.6 |
| Numbness of lower limb | 3.3  | ±12.3 | 6.0  | ±15.3 | 7.1  | ±19.7 | 9.0  | ±21.0 |
| **JOABPEQ**            |      |      |      |      |      |      |      |      |
| Pain                   | 86.1 | ±26.3 | 83.7 | ±27.0 | 83.1 | ±29.1 | 79.4 | ±35.1 |
| Lumbar function        | 94.9 | ±10.7 | 88.7 | ±18.8 | 86.3 | ±17.0 | 82.9 | ±20.1 |
| Gait function          | 97.5 | ±8.4  | 91.7 | ±17.8 | 90.0 | ±16.0 | 69.4 | ±29.2 |
| **KL**                 | 4.7  | ±3.1  | 7.7  | ±4.3  | 7.5  | ±3.7  | 10.2 | ±4.7  |
| Education periods (year)| 12.2 | ±1.7  | 12.3 | 2.2   | 10.8 | ±2.2  | 10.3 | ±2.7  |
| **DM**                 | 3    | (3.6) | 18   | (17)  | 6    | (12)  | 4    | (22.2) |
| **HT**                 | 18   | (22)  | 51   | (48)  | 34   | (68)  | 12   | (68)  |
| Depression             | 1    | (1.2) | 2    | (1.9) | 0    | (0)   | 0    | (0)   |
| Smoking                | 33   | (40)  | 20   | (19)  | 4    | (8.0) | 0    | (0)   |
| Alcohol                | 65   | (78)  | 78   | (74)  | 35   | (70)  | 11   | (61)  |
| Exercise               | 11   | (13)  | 17   | (16)  | 19   | (38)  | 3    | (17)  |
| Women (660) Total      |      |      |      |      |      |      |      |      |
| BMI                    | 22.5 | ±3.5 | 21.0 | ±4.0 | 20.9 | ±3.6 | 22.6 | ±3.9 |
| LSS                    | 20   | (3.0) | 0    | (0)   | 0    | (0)   | 0    | (0)   |
| MCI                    | 45   | (6.8) | 0    | (0)   | 1    | (1.1) | 1    | (0.9) |
| Comorbidity of LSS and MCI | 5    | (0.8) | 0    | (0)   | 0    | (0)   | 0    | (0)   |
| **MMSE**               | 29.4 | ±1.3 | 29.8 | ±0.5 | 29.8 | ±0.5 | 29.8 | ±0.6 |
### Table 1: VAS (mm) and JOABPEQ Scores

| Category                  | Value 1   | Value 2   | Value 3   | Value 4   | Value 5   | Value 6   | Value 7   |
|---------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| **VAS (mm)**              |           |           |           |           |           |           |           |
| Low back pain             | 18.3 ±22.1| 13.6 ±20.8| 12.1 ±17.3| 17.0 ±21.7|
| Pain of lower limb        | 6.3 ±15.6 | 1.2 ±5.7  | 1.4 ±5.8  | 6.2 ±16.5 |
| Numbness of lower limb    | 5.1 ±14.6 | 0.2 ±1.0  | 0.7 ±3.3  | 4.2 ±12.1 |
| **JOABPEQ**               |           |           |           |           |           |           |           |
| Pain                      | 86.7 ±23.9| 91.6 ±18.0| 93.2 ±16.1| 88.5 ±22.4|
| Lumbar function           | 90.5 ±17.0| 97.1 ±10.4| 96.9 ±9.0 | 94.8 ±12.2|
| Gait function             | 90.6 ±19.2| 98.1 ±6.4 | 98.7 ±5.0 | 97.2 ±8.7 |
| KL                        | 3.4 ±3.6  | 1.3 ±1.8  | 1.0 ±1.8  | 1.4 ±1.9  |
| Education periods (year)  | 12.1 ±12.1| 13.8 ±1.5 | 13.0 ±1.6 | 12.9 ±1.6 |
| DM                        | 25 (3.8)  | 1 (2.9)   | 1 (1.1)   | 0 (0)     |
| HT                        | 167 (25)  | 1 (2.9)   | 1 (1.1)   | 7 (6.5)   |
| Depression                | 4 (0.6)   | 0 (0)     | 0 (0)     | 0 (0)     |
| Smoking                   | 70 (11)   | 3 (8.8)   | 19 (20)   | 21 (19)   |
| Alcohol                   | 183 (28)  | 6 (18)    | 35 (37)   | 43 (40)   |
| Exercise                  | 109 (17)  | 2 (5.9)   | 15 (16)   | 16 (15)   |
| Women (660)               |           |           |           |           |
| 50s (125)                 |           |           |           |           |
| 60s (178)                 |           |           |           |           |
| 70s (94)                  |           |           |           |           |
| over 80 (26)              |           |           |           |           |
| BMI                       | 22.3 ±2.8 | 22.9 ±3.3 | 23.5 ±3.6 | 23.3 ±2.7 |
| LSS                       | 5 (4.0)   | 4 (2.2)   | 7 (7.4)   | 4 (15)    |
| MCI                       | 3 (2.4)   | 13 (7.3)  | 16 (17)   | 11 (42)   |
| Comorbidity of LSS and MCI| 1 (0.8)   | 0 (0)     | 2 (2.1)   | 2 (7.7)   |
| MMSE                      | 29.6 ±0.8 | 29.3 ±1.2 | 28.4 ±1.8 | 27.7 ±2.3 |
| **VAS (mm)**              |           |           |           |           |           |           |           |
| Low back pain             | 17.9 ±21.7| 17.2 ±20.8| 25.2 ±23.9| 35.9 ±31.1|
| Pain of lower limb        | 7.6 ±17.4 | 6.3 ±14.9 | 8.7 ±16.2 | 15.5 ±28.3|
| Numbness of lower limb    | 7.0 ±16.7 | 4.9 ±13.9 | 8.3 ±18.1 | 13.2 ±27.8|
| **JOABPEQ**               |           |           |           |           |           |           |           |
|                      | Pain   | ±24.1 | 88.3 | ±22.1 | 77.1 | ±30.1 | 74.7 | ±32.7 |
|----------------------|--------|-------|------|-------|------|-------|------|-------|
| Lumbar function      | 92.0   | ±14.0 | 89.1 | ±16.4 | 80.6 | ±24.0 | 78.5 | ±25.5 |
| Gait function        | 94.5   | ±11.8 | 89.1 | ±18.7 | 77.4 | ±26.3 | 61.5 | ±37.1 |
| KL                   | 2.7    | ±2.8  | 4.4  | ±3.1  | 6.7  | ±3.7  | 8.8  | ±4.9  |
| Education periods    | 12.7   | ±1.4  | 11.6 | ±1.7  | 10.4 | ±1.8  | 9.8  | ±2.5  |
| (year)               |        |       |      |       |      |       |      |       |
| DM                   | 7      | (5.6) | 5    | (2.8) | 9    | (9.6) | 2    | (7.7) |
| HT                   | 20     | (16)  | 66   | (37)  | 52   | (55)  | 20   | (77)  |
| Depression           | 1      | (0.8) | 3    | (1.7) | 0    | (0)   | 0    | (0)   |
| Smoking              | 15     | (12)  | 11   | (6.2) | 1    | (1.1) | 0    | (0)   |
| Alcohol              | 42     | (34)  | 40   | (23)  | 11   | (12)  | 6    | (23)  |
| Exercise             | 23     | (18)  | 30   | (17)  | 21   | (22)  | 6    | (23)  |

Data are presented as mean ± SD or as n (%). MCI, mild cognitive impairment; LSS, lumbar spinal canal stenosis; JOABPEQ, Japan Orthopedics Association Back Pain Evaluation Questionnaires; VAS, visual analog scale; KL, Kellgren-Lawrence grade; MMSE, Mini Mental State Examination; MCI, mild cognitive impairment; DM, diabetes mellitus; HT, hyper tension

**Comparison of characteristics between MCI+ and MCI- groups**

We investigated the differences of parameters between the group with MCI and that without MCI using the Mann-Whitney U test. Age and the prevalence of LSS and KL were significantly higher in the MCI+ group than in the MCI- group in both sexes. In men, lumbar function and gait function of JOABPEQ were lower in the MCI+ than in the MCI- group. In women, all three domains of JOABPEQ were lower in the MCI+ group than in the MCI- group, and pain and numbness of lower limb of VAS were higher in the MCI+ group than in the MCI- group (Table 2).
Table 2
Differences in demographic characteristics between groups with and without MCI.

|        | Men (437) | MCI- (389) | MCI+ (48) | p     |
|--------|-----------|------------|-----------|-------|
|        | Mean or (n) | SD or (%) | Mean or (n) | SD or (%) |   |
| Age    | 51.4 14.8 | 70.7 13.0 | <0.001    |       |   |
| BMI    | 23.7 3.0 | 23.3 3.2 | 0.32      |       |   |
| LSS    | (7) (1.8) | (4) (8.3) | 0.026     |       |   |
| JOABPEQ|           |           |           |       |   |
| Pain   | 86.3 25.6 | 79.8 32.1 | 0.082     |       |   |
| Lumbar function | 94.3 12.2 | 82.1 22.7 | <0.001    |       |   |
| Gait function | 96.1 12.3 | 84.1 22.2 | <0.001    |       |   |
| VAS (mm) |           |           |           |       |   |
| Low back pain | 16.5 21.4 | 21.8 25.4 | 0.11      |       |   |
| Pain of lower limb | 4.5 12.3 | 10.6 23.5 | 0.19      |       |   |
| Numbness of lower limb | 3.9 11.6 | 9.8 24.3 | 0.44      |       |   |
| KL     | 4.4 4.3 | 8.4 4.4 | <0.001    |       |   |
| Education periods (year) | 12.4 2.0 | 10.6 2.6 | <0.001    |       |   |
| DM     | (26) (6.7) | (7) (15) | 0.056     |       |   |
| HT     | (97) (25) | (28) (58) | <0.001    |       |   |
| Depression | (3) (0.8) | (0) (0) | 0.72      |       |   |
| Smoking | (119) (31) | (8) (17) | 0.036     |       |   |
| Alcohol | (274) (70) | (31) (65) | 0.33      |       |   |
| Exercise | (72) (19) | (8) (17) | 0.51      |       |   |
| Women (660) | MCI- (615) | MCI+ (45) | p       |       |   |
|        | Mean or (n) | SD or (%) | Mean or (n) | SD or (%) |   |
| Age    | 54.1 15.1 | 71.2 10.6 | <0.001    |       |   |
| BMI    | 22.4 3.5 | 22.9 3.4 | 0.13      |       |   |
| LSS    | (15) (2.4) | (5) (11) | 0.01      |       |   |
| JOABPEQ|           |           |           |       |   |
| Pain   | 87.4 23.2 | 77.5 30.7 | 0.009     |       |   |
|                                | Mean ± SD | Median | 25th | 75th | P-value |
|--------------------------------|-----------|--------|------|------|---------|
| Lumbar function                | 91.4      | 15.6   | 77.6 | 27.4 | <0.001  |
| Gait function                  | 91.8      | 17.7   | 74.0 | 29.2 | <0.001  |
| VAS (mm)                       |           |        |      |      |         |
| Low back pain                  | 17.9      | 21.8   | 22.8 | 26.5 | 0.18    |
| Pain of lower limb             | 5.8       | 15.8   | 12.2 | 21.0 | 0.003   |
| Numbness of lower limb         | 4.7       | 13.7   | 11.0 | 23.3 | 0.003   |
| KL                             | 3.2       | 3.5    | 6.2  | 3.7  | <0.001  |
| Education periods (year)       | 12.2      | 1.9    | 10.4 | 1.7  | <0.001  |
| DM                             | (23)      | (3.7)  | (2)  | (4.4) | 0.53    |
| HT                             | (141)     | (23)   | (26) | (58) | <0.001  |
| Depression                     | (4)       | (0.7)  | (0)  | (0)  | 0.76    |
| Smoking                        | (68)      | (11)   | (2)  | (4.4) | 0.13    |
| Alcohol                        | (175)     | (29)   | (8)  | (18) | 0.091   |
| Exercise                       | (101)     | (16)   | (8)  | (18) | 0.48    |

Date are presented as mean ± SD or as n (%). Comparison between groups with and without MCI using Mann-Whitney U test. MCI, mild cognitive impairment; LSS, lumbar spinal canal stenosis; JOABPEQ, Japan Orthopedics Association Back Pain Evaluation Questionnaires; VAS, visual analog scale; KL, Kellgren-Lawrence grade; MMSE, Mini Mental State Examination; MCI, mild cognitive impairment; DM, diabetes mellitus; HT, hyper tension

The association between presence of LSS, symptoms of LDD, QOL related to LDD and MCI

We showed the association between LDD factors (presence of LSS, symptoms related to LDD, and QOL score related to LDD) and MCI using logistic regression analysis with MCI as the dependent variable. In men, lumbar function of JOABPEQ (OR 0.979, 95% CI 0.961 to 0.998) and pain of lower limb of VAS (OR 1.020, 95% CI 1.002 to 1.039) were significantly associated with MCI. In women, there was no significant relationship between MCI and any factors related to LDD (Table 3).
|                | Men       | OR   | 95% CI    | p     |
|----------------|-----------|------|-----------|-------|
| LSS            | 0.14      |      |           |       |
| JOABPEQ        |           |      |           |       |
| Pain           | 0.49      |      |           |       |
| Lumbar function| 0.979     | 0.961| 0.998     | 0.027 |
| Gait function  | 0.54      |      |           |       |
| VAS            |           |      |           |       |
| Low back pain  | 0.61      |      |           |       |
| Pain of lower limb | 1.020   | 1.002| 1.039     | 0.032 |
| Numbness of lower limb | 0.17    |      |           |       |
| KL             | 0.22      |      |           |       |

|                | Women     | OR   | 95% CI    | p     |
|----------------|-----------|------|-----------|-------|
| LSS            | 0.29      |      |           |       |
| JOABPEQ        |           |      |           |       |
| Pain           | 0.48      |      |           |       |
| Lumbar function| 0.087     |      |           |       |
| Gait function  | 0.20      |      |           |       |
| VAS            |           |      |           |       |
| Low back pain  | 0.37      |      |           |       |
| Pain of lower limb | 0.30    |      |           |       |
| Numbness of lower limb | 0.41    |      |           |       |
| KL             | 0.87      |      |           |       |

Logistic regression analysis was performed with MCI as the dependent variable. Factors related to LDD were independent variables. For adjusting for age, education periods, DM, HT, depression, smoking, alcohol consumption and exercise were also included as independent variables. MCI, mild cognitive impairment; LDD, degenerative disease of the lumbar; LSS, lumbar spinal canal stenosis; JOABPEQ, Japan Orthopedics Association Back Pain Evaluation Questionnaires; VAS, visual analog scale; KL, Kellgren-Lawrence grade.
The association between presence of LSS, symptoms of LDD, QOL related to LDD and MMSE

We showed the association between the factors of LDD and MMSE using multiple linear regression analysis with MMSE as the dependent variable. The presence of LSS ($\beta = -0.214, 95\% \text{ CI} -3.018 \text{ to } -1.344$), lumbar function and gait function of JOABPEQ (lumbar function: $\beta = 0.161, 95\% \text{ CI} 0.008 \text{ to } 0.028$; gait function: $\beta = 0.106, 95\% \text{ CI} 0.002 \text{ to } 0.022$) and VAS of lower limb symptoms (pain of lower limb: $\beta = -0.141, 95\% \text{ CI} -0.026 \text{ to } -0.007$; numbness of lower limb: $\beta = -0.105, 95\% \text{ CI} -0.022 \text{ to } -0.002$) were related to MMSE significantly in men. The presence of LSS ($\beta = -0.093, 95\% \text{ CI} -1.211 \text{ to } -0.168$) and two domains of JOABPEQ (lumbar function: $\beta = 0.164, 95\% \text{ CI} 0.007 \text{ to } 0.018$; gait function: $\beta = 0.149, 95\% \text{ CI} 0.005 \text{ to } 0.015$) were associated with MMSE significantly in women (Table 4).
Table 4
The impact of parameters related to LDD on MMSE

|         | β     | 95% CI       | p    |
|---------|-------|--------------|------|
| **Men** |       |              |      |
| LSS     | -0.214| -3.018 -1.344| <0.001|
| JOABPEQ |       |              |      |
| Pain    | 0.063 |              |      |
| Lumbar function | 0.161| 0.008 - 0.028| <0.001|
| Gait function | 0.106| 0.002 - 0.022| 0.009|
| VAS     |       |              |      |
| Low back pain | 0.25 | | |
| Pain of lower limb | -0.141| -0.026 - 0.007| 0.001|
| Numbness of lower limb | -0.105| -0.022 - 0.002| 0.015|
| KL      | 0.66  |              |      |
| **Women** |       |              |      |
| LSS     | -0.093| -1.211 - 0.168| 0.010|
| JOABPEQ |       |              |      |
| Pain    | 0.27  |              |      |
| Lumbar function | 0.164| 0.007 - 0.018| <0.001|
| Gait function | 0.149| 0.005 - 0.015| <0.001|
| VAS     |       |              |      |
| Low back pain | 0.72 | | |
| Pain of lower limb | 0.27 | | |
| Numbness of lower limb | 0.31 | | |
| KL      | 0.28  |              |      |

Multiple linear regression analysis was performed with MMSE as the dependent variable, and factors related to LDD as independent variables. For adjusting for age, education periods, DM, HT, depression, smoking, alcohol consumption and exercise, they were also included as independent variables. LDD, degenerative disease of the lumbar; MMSE, Mini Mental State Examination; LSS, lumbar spinal canal stenosis; JOABPEQ, Japan Orthopedics Association Back Pain Evaluation Questionnaires; VAS, visual analog scale; KL, Kellgren-Lawrence grade.
Discussion

Summary of the current study

This population-based study was conducted to clarify the relationship between LDD and cognitive impairment. Initially, we found that the rate of comorbidity of MCI and LSS was 2.1% in those aged ≥65 years. Second, we analyzed the relationship between LSS presence, LDD symptoms, deterioration of QOL due to low back pain, radiographical lumbar degenerations, and cognitive impairment. Lower limb pain and deterioration of QOL due to low back pain were significantly associated with MCI in men. LSS presence, and deterioration of QOL due to low back pain were significantly related to MMSE in both sexes, and pain and numbness of the lower limb were significantly associated with MMSE in men.

Prevalence of MCI and LSS, comorbidity of MCI and LSS

The prevalence of MCI and LSS in general populations have been reported previously. The prevalence of MCI was 3.0% to 42% [26, 27], and had a strong association with aging [28]. Here, the prevalence of MCI was 8.5%, and had relation with aging. The range of prevalence of MCI was great in this and previous population studies, one reason being that the diagnostic tools used for MCI were different: such as Clinical Dementia Rating, MMSE, Montreal Cognitive Assessment, Psychogeriatric Assessment Scale, or Wechsler Memory Scale-Revised. We defined MCI as a summary score of MMSE ≤ 27 in this study. MMSE is a useful screening tool for evaluating cognitive function. Thus, this study’s results may be useful as base data for screening for cognitive impairment in a medical checkup program. Moreover, the age-ranges of the subjects were different, and major cut-off age was 65 years old in previous studies. We collected data from the participants whose age-range was from 20 years old to 93 years old in this study. Hence, the prevalence of MCI we showed would be reasonable compared with past reports.

The prevalence of LSS was 10.1% in men and 8.9% in women and was associated with age in the ROAD study, a nationwide study of the Japanese population [29]. In that study, LSS was diagnosed using lumbar MRI, medical histories, and physical test performed by an orthopedic surgeon, and based on North American Spine Society guideline. The current study showed that the prevalence of LSS was 2.5% in men and 3.0% in women and increased with age. The prevalence of LSS was lower in our study than that in the ROAD study because the diagnostic tool used for LSS was different, wherein we used a self-administered diagnostic support tool for LSS. However, the diagnostic support tool we used had good sensitivity (84%) and specificity (78%) for diagnosing LSS [12]. Thus, LSS prevalence in the current study was meaningful as a base data for screening. LSS prevalence increases with age according to past and current studies [29].

To the best of our knowledge, there has been no report on the comorbidity of MCI and LSS to date. The comorbidity rates of MCI and LSS were 0.8% and 2.1%, respectively in those aged ≥65 years in our study. The rate of MCI was 29% in participants with LSS, and the rate of LSS was 9.8% in participants with MCI in both sexes. The prevalence of MCI and LSS has been proven to increase with age, and the comorbidity...
rate of MCI and LSS also increased with age in this study. We showed a high rate of comorbidity of MCI and LSS, and one third of the people with LSS had MCI in a Japanese dwelling population. This study was held as part of a medical checkup program, and almost all subjects would be interested in health. Thus, the comorbidity rate of MCI and LSS may increase if people who are not interested in health and who cannot go outside because of decaying mobility capability were enrolled as subjects in a similar study. The percentage of elderly persons in Japan will highly increase in the future, suggesting that the comorbidity rate of MCI and LSS will correspondingly further increase. Hence, when we examine and treat people with LSS, we should always consider the cognitive impairment as a potential comorbidity.

The relationship between LDD and cognitive function

Several reports were showed the links between musculoskeletal disease and cognitive function previously. Baseline MMSE summary score and the prevalence of MCI were significantly associated with the incidence of knee osteoarthritis [10]. Delayed union of vertebral fracture decreased MMSE summary score in a longitudinal study [11]. However, to the best of our knowledge, there has been no report on LDD and cognitive impairment. This study is the first report showing that the presence of LSS, symptoms of LDD, and deterioration of QOL due to low back pain are associated with MCI and MMSE summary score.

Here, pain and numbness of lower limbs was associated with MCI and MMSE in men. The relationship between pain and cognitive impairment were also reported previously. Pain was a serious symptom secondary to neuropsychiatric symptoms in patients with dementia [30] and approximately 50% of people with dementia experienced pain regularly [31]. Chronic and neuropathic pain are particularly associated with cognitive impairment [7, 8]. A past report showed that severe pain led to cognitive impairment in a longitudinal study [3]. We showed that neuropathic pain and numbness due to LDD were associated with cognitive dysfunction. A few reports showed the difference of pain threshold between men and women. Calvo-Perxas [32] showed gender differences in depression and pain, and suggested that mild to severe pain showed an association with depression in men, although only severe pain was associated with depression in women. They suggested that the frequency of pain, rather than severity of pain, was related with the deterioration of the central nervous system in men. In our report, the symptoms of the lower limbs might be associated with cognitive function in only men because of gender differences in the central sensitization of pain.

Several reports have showed the relations between physical dysfunction and cognitive impairment. Gait speed, standing balance, stand-up time and leg strength declined more in cognitive impairment subjects compared with healthy subjects [1, 33, 34], and these physical functions decayed prior to cognitive decline [9]. In the current study, deteriorations of QOL, which were related with lumbar function and gait function, were associated with the prevalence of MCI in men and decline of MMSE scores in both sexes. Physical dysfunction may cause cognitive dysfunction through deterioration of QOL in people with LDD. The effect of intervention of pain and physical dysfunction on cognitive function is controversial. We should do an interventional study on whether LDD treatment also improves cognitive function.
Limitations

There were several limitations to our study. First, we used only the MMSE for evaluating cognitive function. Although MMSE is a standard measure of cognitive function, MMSE could evaluate only global cognitive function. We should study the relationships between LDD and specific cognitive functions such as memory and language, among others. Second, although more than 1000 participants were included in this study, the study population may not be representative of the general population because participants were recruited from only one area of Japan. Further, we could not clarify the causal relationship between LDD and cognitive impairment because this was a cross-sectional study. Hence, a longitudinal study investigation, the causal relationship between LDD and cognitive function is necessary in the future.

Nevertheless, this is the first study to have investigated the relationship between LDD and cognitive impairment in a Japanese population to the best of our knowledge, and our results provide valuable information to improve QOL of elderly people in a super-aging society. This health promotion project started from 2005 and provides continuous data, enabling longitudinal study to clarify further relationships between LDD and cognitive impairment.

Conclusions

Our results indicated that the comorbidity rate of MCI and LSS was 0.8% in all participants, and 2.1% in those aged ≥65 years, and this comorbidity rate increased along with age. Deterioration of QOL related to lumbar function and pain of lower limb were associated with MCI in men. Deterioration of QOL related to lumbar and gait function, and LSS presence were associated with summary score of MMSE in both sexes, while pain and numbness of lower limb were associated with summary score of MMSE in men. Treatment of LDD may be useful in bringing improvement of cognitive function.

List Of Abbreviations

LDD - Lumbar degenerative disease
LSS - Lumbar spinal stenosis
MCI - Mild cognitive impairment
QOL - Quality of life
VAS - Visual analog scale
JOABPEQ - Japanese Orthopedic Association Back-Pain Evaluation Questionnaire
MMSE - Mini Mental State Examination

Declarations
**Ethics approval and consent to participate**

For this cross-sectional survey, the ethics committee of Hirosaki University, Graduate School of Medicine approved the study, and all participants provided written informed consent before participation.

**Consent for publication**

Not applicable

**Availability of data and material**

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

**Competing Interests**

The authors declare that they have no competing interests.

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**Authors’ contributions**

Conceived and designed the experiments: KK, WK, SN, YI

Performed the experiments: KK, WK, GK, SO

Analyzed the data: KK, SO

Wrote the paper: KK, WK

Revised the paper critically for important intellectual content: GK, HK, ST, TA, KI, SN, YI

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