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# Prevalence and distribution of intervertebral disc degeneration over the entire spine in a population-based cohort: the Wakayama Spine Study

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SUMMARY

*Objectives:* The purposes of this study were to investigate the prevalence and distribution of intervertebral disc degeneration (DD) over the entire spine using magnetic resonance imaging (MRI), and to examine the factors and symptoms potentially associated with DD.
*Design:* This study included 975 participants (324 men, mean age of 67.2 years; 651 women, mean age of 66.0 years) with an age range of 21–97 years in the Wakayama Spine Study. DD on MRI was classified into Pfirrmann's system (grades 4 and 5 indicating DD). We assessed the prevalence of DD at each level in the cervical, thoracic, and lumbar regions and the entire spine, and examined DD-associated factors and symptoms.
*Results:* The prevalence of DD over the entire spine was 71% in men and 77% in women aged <50 years, and >90% in both men and women aged >50 years. The prevalence of an intervertebral space with DD was highest at C5/6 (men: 51.5%, women: 46%), T6/7 (men: 32.4%, women: 37.7%), and L4/5 (men: 69.1%, women: 75.8%). Age and obesity were associated with the presence of DD in all regions. Low back pain was associated with the presence of DD in the lumbar region.
*Conclusion:* The current study established the baseline data of DD over the entire spine in a large population of elderly individuals. These data provide the foundation for elucidating the causes and mechanisms of DD.


## Introduction

Intervertebral disc degeneration (DD) is thought to be the first step in degenerative spinal changes[1], and is typically followed by the gradual formation of osteophytes, disc narrowing, and spinal stenosis[2,3]. Furthermore, DD is considered to be one of the causes of several symptoms (neck pain or low back pain)[4–7]. Therefore, in terms of developing preventive strategies for spinal disorders, it will be important to obtain fundamental data on DD (prevalence, distribution, associated factors, etc.) in a population-based cohort.

We believe that the analysis of DD over the entire spine would provide more useful data than that of DD in the cervical, thoracic, or lumbar regions, separately. In particular, investigations on the extent of DD in these three regions using whole spine magnetic resonance imaging (MRI) could provide useful data concerning intra-individual factors in the development of DD. Several studies have examined degenerative changes in only cervical and lumbar discs because of the high susceptibility to DD in these regions[8–12]. As well, several previous studies have investigated the aging process of the intervertebral discs in the cervical and lumbar regions using MRI in population-based cohorts[13,14]. However, degenerative changes in the thoracic region and correspondingly over the entire spine are poorly understood, because DD in the thoracic region is considered to be an uncommon problem[15,16]. In particular, the stabilization of the thoracic region by the thoracic cage, which

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reduces the mechanical stress imposed on the intervertebral discs, is believed to reduce the incidence of degenerative diseases in this region[17].

Consistent with the above-mentioned previous studies, a population-based cohort analysis of DD in the different spinal regions using MRI could be used to examine the distribution of DD over the entire spine. However, to our knowledge, no previous studies have performed this type of investigation with a population-based cohort.

From the perspective of discogenic pain, the association between DD and symptoms remains controversial, although several reports have found that DD was a source of low back pain[4,5]. Moreover, reports on the association between the presence of DD in the cervical and thoracic regions and neck pain are rare[6,7]. Further, these studies were not performed with population-based cohorts and did not use whole spine MRI. Thus, no study has assessed neck pain and low back pain within individuals using whole spine MRI. To clarify the points described above, we established a population-based cohort study in which participants underwent whole spine MRI and were examined for symptoms associated with spinal disorders. This is our first report of DD over the entire spine based on a cross-sectional examination of a baseline population.

The aims of this study were to examine (1) the prevalence and distribution of DD over the entire spine using MRI in a population-based cohort, (2) the factors associated with DD (age, gender, and body mass index [BMI]) in the cervical, thoracic, and lumbar regions, and (3) the association between DD and symptoms (neck pain and low back pain).

## Methods

### *Participants*

The present study, entitled the Wakayama Spine Study, was performed with a sub-cohort of the second visit of the ROAD (Research on Osteoarthritis/osteoporosis Against Disability) study, which was initiated as a nationwide, prospective study of bone and joint diseases in population-based cohorts; the cohorts were established in three communities with different characteristics (i.e., urban, mountainous, and coastal regions) in Japan. A detailed profile of the ROAD study has already been described elsewhere[18,19]. Here, we briefly summarize the profile of the present study. The second visit of the ROAD study began in 2008 and was completed in 2010. All the participants in the baseline study were invited to participate in the second visit. In addition to the former participants, inhabitants aged 60 years and older in the urban area and those aged 40 years and younger in the mountainous and coastal areas who were willing to participate in the ROAD survey were also included in the second visit (both the mountainous and coastal areas were in Wakayama prefecture). Finally, 2674 individuals (900 men, 1774 women) participated in the second visit of the ROAD study, and comprised 1067 individuals (353 men, 714 women) in the urban area, 742 individuals (265 men, 477 women) in the mountainous area, and 865 individuals (282 men, 583 women) in the coastal area. Among these three communities in the ROAD study, the mountainous and coastal areas from which we invited all 1607 participants (547 men, 1060 women) to the Wakayama Spine Study are located in Wakayama prefecture. Of the 1607 participants, a total of 1011 individuals provided written informed consent and attended the Wakayama Spine Study with MRI examinations[20,21]. Among the 1011 participants, those who had MRI-sensitive implanted devices (e.g., pacemakers) and other disqualifiers were excluded. Consequently, 980 individuals underwent MRI of the whole spine. Furthermore, one participant who had undergone a previous cervical operation and four participants who had undergone a previous posterior lumbar fusion were excluded from the analysis. Finally, whole spine MRI results were available for 975 participants (324 men, 651 women) with an age range of 21–97 years (mean, 67.2 years for men and 66.0 years for women). Table I shows the demographic and baseline characteristics of the 975 participants in the present study.

For the purpose of analysis, the participants were divided into five age groups: (1) under 50 years, (2) 50–59 years, (3) 60–69 years, (4) 70–79 years, and (5) 80 years and over. The anthropometric measurements included height, weight, and BMI (weight [kg]/height$^2$ [m$^2$]). BMI was categorized according to the guidelines for Asians proposed by the World Health Organization and was thus defined as follows: underweight, less than 18.5; normal, 18.5–23; overweight, 23–27.5; and obesity, greater than 27.5[22]. Experienced orthopedists also asked all participants the following question regarding neck pain and low back pain: "Have you experienced neck pain on most days during the past month, in addition to now?" and "Have you experienced low back pain on most days during the past month, in addition to now?" Those who answered "yes" were defined as having neck pain or low back pain based on previous studies[23–26].

### *MRI*

A mobile MRI unit (Excelart 1.5 T, Toshiba, Tokyo, Japan) was used in the present study, and whole spine MRI was performed for all participants on the same day as the examination. The participants were supine during the MRI, and those with rounded backs used triangular pillows under their head and knees. The imaging protocol included sagittal T2-weighted fast spin echo (FSE) (repetition time [TR]: 4000 ms/echo, echo time [TE]: 120 ms, field of view [FOV]: 300 × 320 mm), and axial T2-weighted FSE (TR: 4000 ms/echo, TE: 120 ms, FOV: 180 × 180 mm).

Sagittal T2-weighted images were used to assess the intervertebral space from C2/3 to L5/S1. C2/3 to C7/T1, T1/2 to T12/L1, and L1/2 to L5/S1 were defined as the cervical region, thoracic region, and lumbar region, respectively. DD grading was performed by an

**Table I**
Characteristics of participants

| | Overall | Men | Women |
|---|---|---|---|
| **No. of participants** | **975** | **324** | **651** |
| **Age strata (years)** | | | |
| <50 | 125 | 38 | 87 |
| 50–59 | 175 | 59 | 116 |
| 60–69 | 223 | 65 | 158 |
| 70–79 | 261 | 89 | 172 |
| ≧80 | 191 | 73 | 118 |
| **Demographic characteristics** | | | |
| Age, years | 66.4 ± 13.5 | 67.2 ± 13.9 | 66.0 ± 13.4 |
| Height, cm | 156.4 ± 9.4 | 164.6 ± 7.2 | 151.5 ± 7.2 |
| Weight, kg | 56.8 ± 11.5 | 64.5 ± 11.6 | 53.0 ± 9.4 |
| BMI (kg/m$^2$) | 23.3 ± 3.6 | 23.6 ± 3.4 | 23.1 ± 3.7 |
| **BMI (WHO-Asian category) (*N*)** | | | |
| Underweight | 61 | 16 | 45 |
| Normal | 425 | 124 | 300 |
| Overweight | 361 | 139 | 221 |
| Obesity | 128 | 44 | 84 |
| **Baseline characteristics** | | | |
| **Symptoms (%)** | | | |
| Neck pain | 24.9 | 19.4 | 27.7 |
| Low back pain | 43 | 36.7 | 42.1 |
| **Life style (%)** | | | |
| Smoking | 10.7 | 25.2 | 4.1 |
| Alcohol consumption | 31.4 | 56.8 | 18.8 |

BMI category for Asian was based on World Health Organization (WHO) guidelines defining underweight (<18.5), normal (18.5–23), overweight (23–27.5), and obese (>27.5). Values are the means ± standard deviation.

orthopedist (MT) who was blind to the background of the subjects. The degree of DD on MRI was classified into five grades based on Pfirrmann's classification system[27], with grades 4 and 5 indicating DD. As shown in Fig. 1, the signal intensity for grade 4 was intermediate to hypointense to the cerebrospinal fluid (dark gray), while the structure is inhomogeneous. Meanwhile, for grade 5, the signal intensity is hypointense to the cerebrospinal fluid (black), and the structure is likewise inhomogeneous. In addition, the disc space is collapsed. It has been reported that loss of signal intensity is significantly associated with the morphological level of the DD and is also associated with both the water and proteoglycan content in a disc[28]. Therefore, we used a grading based on signal intensity and disc height. For evaluating intraobserver variability, 100 randomly selected magnetic resonance images of the entire spine were rescored by the same observer (MT) more than 1 month after the first reading. Furthermore, to evaluate interobserver variability, 100 other magnetic resonance images were scored by two orthopedists (MT and RK) using the same classification. The intraobserver and interobserver variability for DD, as evaluated by kappa analysis, was 0.94 and 0.94, respectively.

"Prevalence of DD", which was defined as "the proportion of the number of participants who had DD at each intervertebral space or region or over the entire spine divided by the total number of participants", was used to describe the frequency of the presence of DD. In the analysis, to clarify the associated factors using multiple logistic regression analysis, we entered a variable of prevalence state (1, presence; 0, absence) of DD as a dependent variable.

*Statistical analysis*

Multiple logistic regression analysis was used to estimate the association between the presence of DD in each region (cervical, thoracic, and lumbar) as dependent variables and the age group, gender, and BMI category as nominal independent variables after adjustment for the age group, gender and BMI category, mutually.

Additionally, multiple logistic regression analysis was used to estimate the association between the presence of neck pain or low back pain and the presence of DD in each region after adjustment for age, gender, and BMI. Furthermore, in cases in which the presence of DD was significantly associated with a symptom, we examined as a sub-analysis the association between the presence of neck pain or low back pain and the number of DD (categorized into "0", "1 or 2", "3 or more" for ready assessment) in each region using multiple logistic regression analysis after adjustment for age, gender, and BMI. All statistical analyses were performed using JMP version 8 (SAS Institute Japan, Tokyo, Japan).

## Results

As shown in Table II, the prevalence of DD in the cervical and thoracic regions and over the entire spine increased with the elevation of the age strata in both men and women. For both genders, the prevalence of DD in the lumbar region was also increased with the elevation of the age strata up to the 70-year-old age group but decreased in the 80-year-old age group. Table III

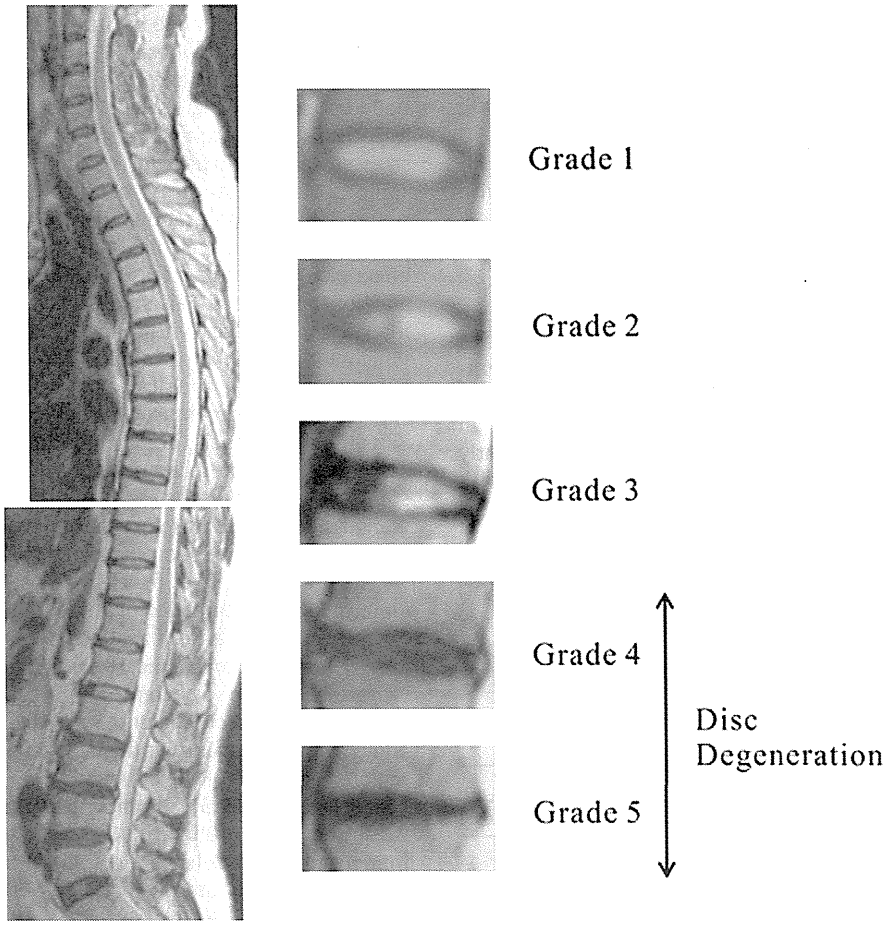


**Fig. 1.** Mid-sagittal view on T2-weighted images of the whole spine MRI with Pfirrmann classification. The grade is described according to Pfirrmann classification. Grades 4 and 5 were considered degenerated. The signal intensity for grade 4 was intermediate to hypointense to the cerebrospinal fluid (dark gray), while the structure is inhomogeneous. Meanwhile, for grade 5, the signal intensity is hypointense to the cerebrospinal fluid (black), and the structure is also inhomogeneous. Additionally, the disc space is collapsed.

shows the prevalence of intervertebral spaces with DD over the entire spine for the participants in this study. The three highest prevalence levels of DD in the intervertebral spaces in the cervical, thoracic, and lumbar regions were as follows. The prevalence at C5/6 was 51.5% (95% CI: 46.1–56.3) in men and 46% (95% CI: 42.2–49.9) in women, followed by the prevalence at C6/7 of 43.5% in men and 33.3% in women, and at C4/5 of 38.6% in men and 35.8% in women. The prevalence at T6/7 was 32.4% (95% CI: 27.5–37.6) in men and 37.7% (95% CI: 34.1–41.5) in women, followed by the prevalence at T7/8 of 31.8% in men and 36.2% in women, and at T5/6 of 28.4% in men and 35.9% in women. The prevalence at L4/5 was 69.1% (95% CI: 63.9–73.9) in men and 75.8% (95% CI: 72.3–78.9) in women, followed by that at L5/S1 of 66.7% in men and 70.9% in women, and at L3/4 of 59.3% in men and 61.9% in women.

An older age was significantly associated with the presence of DD in each region. Gender was not significantly associated with the presence of DD in each region, although men demonstrated a tendency for a greater number of DD than women in the cervical region. In addition, overweight status (BMI: 23–27.5) was a significantly associated factor in the cervical and thoracic regions, and obesity (BMI: >27.5) was a significantly associated factor in all regions compared with participants of a normal weight (BMI: 18.5–23) (Table IV).

The participants with DD in the cervical region did not significantly differ in terms of the presence of neck pain (OR 0.88, 95% CI: 0.63–1.22, $P = 0.53$). The presence of DD in the thoracic region was not significantly associated with neck pain (OR 0.84, 95% CI: 0.60–1.19, $P = 0.33$) and low back pain (OR 1.08, 95% CI: 0.80–1.47, $P = 0.60$). However, the presence of DD in the lumbar region was significantly associated with low back pain (OR 1.57, 95% CI: 1.02–2.49, $P < 0.05$). Moreover, in a sub-analysis, we investigated the association between low back pain and the number of DD in the lumbar region ("0", "1 or 2", "3 or more"). The presence of low back pain was significantly higher in participants with three or more DD (OR 1.75, 95% CI: 1.11–2.81, $P < 0.05$), but not in those with one or two DD (OR 1.34, 95% CI: 0.84–2.20, $P = 0.22$), as compared with participants without DD.

## Discussion

This study is the first to report the prevalence and distribution of DD over the entire spine using whole spine MRI in a population-based cohort. The prevalence of DD over the entire spine and in each of the three spinal regions was higher in older participants. In addition, we noted that the presence of DD was significantly associated with low back pain in the lumbar region but not with neck pain in the cervical region.

Battié *et al.* reviewed the prevalence of DD in the lumbar region and noted that it ranged from 20% to 83%[29]. Consistent with the observations of this review, other reported prevalence levels of DD in the lumbar region have shown wide variation between samples and have often been quite high because the studies had certain drawbacks, including relatively small sample sizes[1,30], narrow age ranges[5,31], and asymptomatic subjects[32]. However, no previous study has assessed the prevalence of DD over the entire spine using whole spine MRI. We noted that the prevalence of DD over the entire spine exceeded 70% in participants less than 50 years of age and was greater than 90% in participants older than 50 years of age.

Little epidemiological data are available concerning DD in the intervertebral space using MRI assessments in a population-based cohort. Matsumoto *et al.*[4] reported that the prevalence of DD in the cervical region was the highest at C5/6 (86% in men and 89% in women over the age of 60 years). In addition, Hanagai *et al.*[33] and Kanayama *et al.*[34] reported that the prevalence of DD in the lumbar region was the highest at L4/5 (67%; mean age 68.4 years) and L5/S1 (49.5%; mean age 39.7 years), respectively. In the present study, the prevalence of DD was the highest at C5/6 (51.5% in men and 46.0% in women) and L4/5 (69.1% in men and 75.8% in women). The prevalence of cervical DD in the previous study by Matsumoto *et al.*[4] was higher than that in the present study. However, the subjects were recruited from volunteers in the hospital rather than a population; thus, the capacity for strict comparisons are limited. Furthermore, few studies have reported age-related DD in the thoracic region. Matsumoto *et al.* reported that the highest prevalence of DD occurred at T7/8 (30.9%; mean age 48.0 y) followed by T6/7 in the thoracic region; however, all 94 participants in this report were asymptomatic[35]. In the present study, we confirmed a high prevalence of DD at T6/7 in the thoracic region. This finding is supported by results from thoracic MRI investigations demonstrating a high prevalence of DD in asymptomatic individuals.

The distribution of prevalence of DD was similar to the alignment of the spine in the sagittal plane, such as cervical lordosis (C3–C7), thoracic kyphosis (T1–T12), and lumbar lordosis (L1–L5)[36]. The high prevalence of DD in the lumbar region can potentially be explained by mechanical stress. Our results support the hypothesis that compressive stress affected DD, since compressive stresses are the highest in the mid-thoracic region of the entire spine[37]. Mechanical stress on the thoracic intervertebral disc is reduced due to stabilization by the thoracic cage, and therefore, the thoracic intervertebral disc may be affected by the detrimental effect of compressive stress caused by posture on the sagittal balance of the spine[38]. This study also provides the first mapping of intervertebral spaces with DD over the entire spine by MRI analysis, which adds to our knowledge of the distribution of prevalence of DD in the cervical, thoracic, and lumbar regions, which has been reported only fragmentarily in previous reports.

Our current results confirmed that age was a significant factor associated with the presence of DD in all three regions. Previous studies reported that the association of DD to factors such as height, weight, and gender was uncertain; however, age, obesity, smoking, and occupation have been suggested to be DD-associated factors[39–42]. The previous studies focused almost entirely on the lumbar region, and the identification of associated factors may be challenging for this region because it is affected to a greater extent by various factors, including mechanical stress. Moreover, it remains unknown what other factors (beyond age) are associated with DD in the cervical and thoracic regions[6,13]. In the present study, overweight and obesity significantly influenced DD in the cervical and thoracic regions (cervical; OR: overweight 1.38 [95% CI 1.00–1.90], obesity 1.60 [95% CI 1.04–2.51], thoracic; OR: overweight 1.64 [95% CI 1.17–2.29], obesity 3.12 [95% CI 1.91–5.19]), and obesity also significantly influenced DD in the lumbar region (OR: 2.56 [95% CI 1.20–6.14]). In a previous study, Samartzis *et al.* reported that DD in the lumbar region was significantly associated with overweight and obesity[39]. However, DD in the cervical and thoracic region did not demonstrate a significant association with BMI, as reported by Okada *et al.*[6] and Matsumoto *et al.*[35]. Of note, the previous studies were

**Table II**
Prevalence of DD by age strata in men and women

| | Entire spine | | Cervical | | Thoracic | | Lumbar | |
|---|---|---|---|---|---|---|---|---|
| | Men | Women | Men | Women | Men | Women | Men | Women |
| Age strata (years) | | | | | | | | |
| <50 | 71.0 | 77.0 | 26.3 | 27.9 | 15.7 | 11.4 | 55.2 | 71.2 |
| 50–59 | 91.5 | 93.1 | 47.4 | 49.1 | 49.1 | 35.3 | 86.4 | 91.3 |
| 60–69 | 98.4 | 95.5 | 66.1 | 54.4 | 61.5 | 63.2 | 96.9 | 94.3 |
| 70–79 | 95.8 | 99.4 | 80.9 | 72.0 | 73.0 | 79.6 | 96.6 | 96.5 |
| ≧80 | 93.2 | 97.4 | 86.3 | 85.5 | 79.4 | 88.9 | 82.1 | 84.5 |

Values are percentage.

**Table III**
Prevalence of intervertebral spaces with DD over the entire spine by age strata in men and women

| Age strata (years) | C2/3 | C3/4 | C4/5 | C5/6 | C6/7 | C7/T1 | T1/2 | T2/3 | T3/4 | T4/5 | T5/6 | T6/7 | T7/8 | T8/9 | T9/10 | T10/11 | T11/12 | T12/L1 | L1/2 | L2/3 | L3/4 | L4/5 | L5/S1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Men** | | | | | | | | | | | | | | | | | | | | | | | |
| Total | 28.3 | 30.2 | 38.6 | 51.5 | 43.5 | 26.8 | 20.3 | 23.4 | 22.2 | 24.0 | 28.4 | 32.4 | 31.8 | 28.7 | 31.4 | 25.0 | 24.0 | 17.5 | 30.0 | 51.5 | 59.3 | 69.1 | 66.7 |
| <50 | 10.5 | 10.5 | 13.1 | 15.7 | 13.1 | 5.2 | 5.2 | 7.8 | 7.8 | 5.2 | 10.5 | 7.8 | 5.2 | 2.6 | 2.6 | 2.6 | 0.0 | 0.0 | 2.6 | 10.5 | 7.8 | 34.2 | 47.3 |
| 50–59 | 6.7 | 11.8 | 15.2 | 37.2 | 27.1 | 10.1 | 8.4 | 6.7 | 11.8 | 11.8 | 16.9 | 23.7 | 27.1 | 16.9 | 20.3 | 16.9 | 13.5 | 5.1 | 15.2 | 35.5 | 61.0 | 74.5 | 50.8 |
| 60–69 | 35.3 | 36.9 | 49.2 | 50.7 | 40.0 | 21.0 | 20.0 | 24.6 | 23.0 | 27.6 | 27.6 | 35.3 | 32.3 | 36.9 | 41.5 | 23.0 | 24.6 | 18.4 | 40.0 | 60.0 | 69.0 | 76.9 | 75.3 |
| 70–79 | 35.9 | 35.9 | 49.4 | 64.0 | 51.6 | 34.8 | 24.7 | 26.9 | 25.8 | 30.3 | 33.7 | 38.2 | 41.5 | 35.9 | 40.4 | 37.0 | 31.4 | 26.9 | 39.3 | 69.6 | 73.0 | 79.7 | 79.7 |
| ≧80 | 39.7 | 42.4 | 47.9 | 67.1 | 65.7 | 46.5 | 32.8 | 39.7 | 32.8 | 32.8 | 41.0 | 42.4 | 36.9 | 35.6 | 35.6 | 30.1 | 35.6 | 24.6 | 39.7 | 56.1 | 58.9 | 63.0 | 65.7 |
| **Women** | | | | | | | | | | | | | | | | | | | | | | | |
| Total | 21.9 | 24.8 | 35.8 | 46.0 | 33.3 | 13.6 | 15.2 | 23.1 | 29.8 | 31.7 | 35.9 | 37.7 | 36.2 | 34.2 | 32.7 | 28.7 | 23.8 | 20.0 | 31.7 | 49.7 | 61.9 | 75.8 | 70.9 |
| <50 | 2.2 | 3.4 | 10.3 | 20.6 | 10.3 | 1.1 | 0.0 | 1.1 | 4.5 | 0.0 | 1.1 | 4.5 | 3.4 | 5.7 | 4.5 | 4.5 | 1.1 | 0.0 | 4.5 | 12.6 | 18.3 | 49.4 | 56.3 |
| 50–59 | 11.2 | 9.4 | 23.2 | 36.2 | 23.2 | 3.4 | 6.8 | 12.0 | 15.5 | 15.5 | 16.3 | 18.1 | 19.8 | 12.9 | 13.7 | 10.3 | 6.9 | 6.9 | 15.6 | 35.6 | 55.6 | 73.9 | 70.4 |
| 60–69 | 13.9 | 20.8 | 31.0 | 43.6 | 29.1 | 11.3 | 13.2 | 18.3 | 29.7 | 32.2 | 37.9 | 39.8 | 31.6 | 32.2 | 30.3 | 19.6 | 15.8 | 14.5 | 25.3 | 55.0 | 66.4 | 85.4 | 75.9 |
| 70–79 | 33.7 | 34.8 | 46.5 | 53.4 | 42.4 | 16.2 | 22.0 | 34.3 | 41.2 | 44.7 | 50.0 | 50.0 | 47.0 | 45.9 | 44.7 | 42.4 | 34.3 | 26.1 | 44.7 | 64.5 | 80.2 | 86.0 | 81.9 |
| ≧80 | 40.6 | 46.6 | 57.6 | 66.9 | 52.5 | 32.2 | 27.1 | 40.6 | 45.7 | 51.6 | 57.6 | 61.0 | 66.9 | 61.8 | 57.6 | 56.7 | 52.9 | 46.1 | 57.2 | 62.3 | 67.5 | 69.2 | 58.9 |

*Values are percentage.*

conducted with asymptomatic healthy subjects. Therefore, based on our findings, obesity appears to have some influence on the process of DD over the entire spine.

An association between DD in the lumbar region and low back pain was previously demonstrated in a twin study[43]. Moreover, Okada *et al.*[6] reported an association between neck pain and DD in the cervical region, whereas Arana *et al.*[7] found an association between neck pain and DD in the upper thoracic region. Of interest, no agreement has been reached regarding the most appropriate definition of neck pain and low back pain in population cohorts[7]. Nonetheless, we observed a significant association between the presence of DD in the lumbar region and low back pain.

The present study has several limitations. First, it was a cross-sectional study, and therefore, the transition to DD cannot be clarified. Second, the participants included in the present study may not represent the general population, since they were recruited from only two local areas. To confirm whether the participants of the Wakayama Spine Study are representative of the Japanese population, we compared the anthropometric measurements and frequencies of smoking and alcohol consumption between the general Japanese population and the study participants. No significant differences in BMI were observed (men: 24.0 and 23.7, $P = 0.33$; women: 23.5 and 23.1, $P = 0.07$). Further, the proportion of current smokers and those who consumed alcohol (those who regularly smoked or consumed alcohol more than once per month) in men and the proportion of those who consumed alcohol in women were significantly higher in the general Japanese population than in the study population, whereas there was no significant difference in the proportion of current smokers in women (male smokers, 32.6% and 25.2%, $P = 0.015$; female smokers, 4.9% and 4.1%, $P = 0.50$; men who consumed alcohol, 73.9% and 56.8%, $P < 0.0001$; women who consumed alcohol, 28.1% and 18.8%, $P < 0.0001$). These results suggest the likelihood that in this study, participants had healthier lifestyles than those of the general Japanese population[44]. This "healthy" selection bias should be taken into consideration when generalizing the results obtained from the Wakayama Spine Study. Third, the Pfirrmann classification introduced a comprehensive MRI grading system based on the assessment of structure, the distinction of the nucleus and annulus fibrosis, the signal intensity[28], and the height of the intervertebral discs[27]. However, bony endplate alterations, osteophyte changes, spinal stenosis, and disc protrusion are not covered by the Pfirrmann classification. Therefore, it is necessary to perform investigations that include these morphological changes. Finally, the accurate measurement of obesity, such as abdominal obesity and/or body composition, might reveal that obesity has a stronger association with DD; however, the present study examined only BMI as a measurement of obesity. Thus, we plan to examine the girth of the abdomen and body composition using electrical impedance in the assessment of human body composition (the BIA method) in a future study.

In conclusion, this study is the first one to investigate the prevalence of DD over the entire spine in a large population of individuals to establish baseline data for a prospective longitudinal

**Table IV**
Multiple logistic regression of the association with presence of DD with age, BMI, and gender

| | Cervical | Thoracic | Lumbar |
|---|---|---|---|
| | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| **Age group (years)** | | | |
| <50 | 1 | 1 | 1 |
| 50–59 (vs <50) | 2.45 (1.5–4.06)** | 4.60 (2.53–8.76)*** | 4.47 (2.44–8.48)*** |
| 60–69 (vs <50) | 3.62 (2.26–5.91)*** | 12.0 (6.77–22.7)*** | 9.95 (5.02–21.3)*** |
| 70–79 (vs <50) | 7.87 (4.86–12.9)*** | 24.9 (13.8–47.6)*** | 15.0 (7.26–34.5)*** |
| ≧80 (vs <50) | 16.9 (9.68–30.5)*** | 47.0 (24.5–95.6)*** | 2.94 (1.71–5.13)** |
| **Men (vs women)** | 1.20 (0.89–1.64) | 0.88 (0.64–1.21) | 0.70 (0.45–1.09) |
| **BMI (WHO-Asian category)** | | | |
| Underweight (vs normal) | 0.91 (0.49–1.70) | 1.36 (0.71–2.67) | 0.81 (0.38–1.84) |
| Normal | 1 | 1 | 1 |
| Overweight (vs normal) | 1.38 (1.00–1.90)* | 1.64 (1.17–2.29)* | 1.14 (0.71–1.85) |
| Obesity (vs normal) | 1.60 (1.04–2.51)* | 3.12 (1.91–5.19)*** | 2.56 (1.20–6.14)* |

BMI category for Asian was based on World Health Organization (WHO) guidelines defining underweight (<18.5), normal (18.5–23), overweight (23–27.5), and obese (>27.5). OR = odds ratio, CI = confidential interval.
*$P < 0.05$, **$P < 0.001$, ***$P < 0.0001$.

study. The prevalence of intervertebral spaces with DD was the highest at C5/6, T6/7, and L4/5 in the cervical, thoracic, and lumbar regions, respectively. DD in the cervical, thoracic, and lumbar regions was significantly associated with age and obesity. A significant positive association was observed between the presence of DD in the lumbar region and low back pain.

### Author contributions

All authors worked collectively to develop the protocols and method described in this paper. MT, NY, SM, HO, YI, KN, NT, and TA were principal investigators responsible for the fieldwork in the Wakayama Spine study. MT and SM performed the statistical analysis. All authors contributed to the analysis and interpretation of results. MT wrote the report. All authors read and approved the final manuscript.

### Role of the funding source

The sponsors had no role in study design, data collection, data analysis, data interpretation, or in writing of the report.

### Conflict of interest

The authors declare no conflicts of interest.

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ORIGINAL ARTICLE

# Prevalence of diffuse idiopathic skeletal hyperostosis (DISH) of the whole spine and its association with lumbar spondylosis and knee osteoarthritis: the ROAD study

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**Abstract** We aimed to assess the prevalence of diffuse idiopathic skeletal hyperostosis (DISH) and its association with lumbar spondylosis (LS) and knee osteoarthritis (KOA) using a population-based cohort study entitled Research on Osteoarthritis/osteoporosis Against Disability (ROAD). In the baseline ROAD study, which was performed between 2005 and 2007, 1,690 participants in mountainous and coastal areas underwent anthropometric measurements and radiographic examinations of the whole spine (cervical, thoracic, and lumbar) and both knees. They also completed an interviewer-administered questionnaire. Presence of DISH was diagnosed according to Resnick criteria, and LS and KOA were defined as Kellgren-Lawrence (KL) grade ≥3. Among the 1,690 participants, whole-spine radiographs of 1,647 individuals (97.5 %; 573 men, 1,074 women; mean age, 65.3 years) were evaluated. Prevalence of DISH was 10.8 % (men 22.0 %, women 4.8 %), and was significantly higher in older participants (presence of DISH 72.3 years, absence of DISH 64.4 years) and mainly distributed at the thoracic spine (88.7 %). Logistic regression analysis revealed that presence of DISH was significantly associated with older age [+1 year, odds ratio (OR): 1.06, 95 % confidence interval (CI): 1.03–1.14], male sex (OR: 5.55, 95 % CI: 3.57–8.63), higher body mass index (+1 kg/m$^2$, OR: 1.08, 95 % CI: 1.02–1.14), presence of LS (KL2 vs KL0: 1, OR: 5.50, 95 % CI: 2.81–10.8) (KL ≥3 vs KL0: 1, OR: 4.09, 95 % CI: 2.08–8.03), and presence of KOA (KL ≥3 vs KL0: 1, OR: 1.89, 95 % CI: 1.14–3.10) after adjusting for smoking, alcohol consumption, and residential area (mountainous vs coastal). This cross-sectional population-based study clarified the prevalence of DISH in general inhabitants and its significant association with LS and severe KOA.

**Keywords** Prevalence · Diffuse idiopathic skeletal hyperostosis · Knee osteoarthritis · Lumbar spondylosis · ROAD study

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## Introduction

Diffuse idiopathic skeletal hyperostosis (DISH) is characterised by calcification and ossification of soft tissue such as entheses and joint capsules [1]. Resnick and Niwayama specifically defined DISH as the radiographic finding of calcification or ossification along the anterolateral aspects of at least 4 contiguous vertebral levels (across 3 disc spaces), with relative preservation of disc height in the involved vertebral segments and without degenerative disc disease [2]. In 1998, Mata and co-workers [3] developed a

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scoring system such that the presence of DISH could be assessed reproducibly. This system scores individuals who fulfill the Resnick criteria by numerically classifying each vertebral level based on the amount of ossification and whether partial or complete bridging of the disc space is present [3].

Although some reports have indicated a significant association between DISH and ossification of the posterior longitudinal ligament (OPLL) [4–7], DISH is thought to be an asymptomatic condition in many affected individuals; however, several clinical symptoms have been described including pain, limited range of spinal motion, and increased susceptibility to unstable spinal fractures after trivial trauma [8]. In addition, dysphagia and airway obstruction at the cervical levels [8, 9], as well as radiculopathy and spinal injury after spinal fracture [10–12], have been reported as clinical manifestations of DISH.

Although the condition is recognised in many parts of the world [13–20], there are relatively few population-based studies concerning its prevalence. Such data are important in order to characterise the burden of the disease. In addition, regarding its characteristics, several epidemiologic studies have reported that DISH is observed mainly in the elderly, and that prevalence increases with age [18, 19]. Men are affected by DISH much more frequently than women [20]. Although metabolic disturbance is hypothesised to be a factor [21, 22], the aetiology of the condition remains unknown.

Based on the definition of DISH as the radiographic finding of calcification or ossification, it appears that the condition might be associated with osteoarthritis (OA) of the spine. The severity of OA, as observed on radiography, was determined according to Kellgren-Lawrence (KL) grading as follows [23]: KL0, normal; KL1, slight osteophytes; KL2, definite osteophytes; KL3, joint or intervertebral space narrowing with large osteophytes; and KL4, bone sclerosis, joint or intervertebral space narrowing, and large osteophytes. KL2 is commonly used as the diagnostic criterion for lumbar spondylosis (LS) or OA at other sites. Thus, LS—defined as KL2 (defined as the definite presence of osteophytes)—could easily be associated with DISH. However, there are few reports to confirm the association between DISH and severe LS with the criterion of KL3 (defined as the presence of intervertebral space narrowing) or KL4 (defined as the presence of bone sclerosis). In addition, there are few reports to clarify the association between DISH and OA at other sites, such as the knees.

We conducted a survey, known as the Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study, using a population-based cohortto determine the prevalence of DISH using lateral whole-spine radiography in recently examined subjects, which included men and women in Japan. Another aim of our study was to clarify the association of DISH with LS and knee osteoarthritis (KOA) based on KL grade.

## Materials and methods

### Outline of the ROAD study

We conducted the present study using the cohorts established in 2005 for the ROAD study—a nationwide, prospective study of OA comprising population-based cohorts in several communities in Japan. Details of the cohort profile have been reported elsewhere [24, 25]. Briefly, from 2005 to 2007, we developed a baseline database that included clinical and genetic information of 3,040 residents of Japan (1,061 men, 1,979 women) with a mean age of 70.3 (SD, 11) years [men: 71 (SD, 10.7) years, women: 69.9 (SD, 11.2) years]. Subjects were recruited from resident registration listings in three communities with different characteristics: 1,350 subjects (465 men, 885 women) from an urban region in Itabashi, Tokyo; 864 (319 men, 545 women) from a mountainous region in Hidakagawa, Wakayama; and 826 (277 men, 549 women) from a coastal region in Taiji, Wakayama.

Participants completed an interviewer-administered questionnaire of 400 items that included lifestyle information, such as occupation, smoking habits, alcohol consumption, family history, medical history, physical activity, reproductive variables, and health-related quality of life. The questionnaire was prepared by modifying the questionnaire used in the Osteoporotic Fractures in Men Study (MrOS) [26]; some new items also were added to the modified questionnaire. Participants were asked whether they took prescription medication daily or nearly every day (no = 0, yes = 1). If the participants did not know the reason for the prescribed medication, they were asked to bring their medication to the medical doctor (NY).

Anthropometric measurements, including height (cm), body weight (kg), arm span (cm), bilateral grip strength (kg), and body mass index (BMI, kg/m$^2$) were recorded for each patient. Medical information was recorded by experienced orthopaedic surgeons on systematic, local, and mental status, including information on back, knee, and hip pain; swelling and range of motion of the joints; and patellar and Achilles tendon reflexes.

### Eligible subjects of the present study

In the ROAD study, radiographic examination of the thoracic spine was performed only in subjects in mountainous and coastal regions. These subjects also underwent blood and urinary examinations. In the present study, among 1,690 subjects (596 men, 1,094 women) in mountainous and

coastal regions in the ROAD study, we excluded 43 whose radiograph quality was so poor that it was difficult to observe the sites of thoracic–lumbar junction and lumbosacral junction; thus, we analysed 1,647 participants (573 men, 1,074 women) ranging in age from 23 to 94 years (mean: 65.3 years, men: 66.3 years, women: 64.7 years).

Study participants provided written informed consent, and the study was approved by the ethics committees of the University of Wakayama Medical University (No. 373) and the University of Tokyo (No. 1264 and No. 1326).

### Radiographic assessment

Plain radiographs of the cervical, thoracic, and lumbar spine in the anteroposterior and lateral views, and bilateral knees in the anteroposterior view with weight-bearing and foot-map positioning were obtained. DISH was diagnosed according to the following criteria, defined by Resnick and Niwayama [2]: (1) flowing ossification along the lateral aspect of at least 4 contiguous vertebral bodies, (2) relative preservation of intervertebral disc height in the involved segments, and (3) absence of epiphyseal joint bony enclosing and sacroiliac joint erosion. In the assessment of lateral radiographs, since it was difficult to read the C7/Th1 to T3/4 vertebral levels, 'whole spine' in the present study implies radiographs assessed from the C0/1 to C6/7, Th4/5 to Th12/L1, and L1/L2 to L5/S1 levels.

The radiographic severity of OA was determined according to the above-mentioned KL grade [20]. Radiographs of each site (i.e., vertebrae and knees) were examined by a single experienced orthopaedic surgeon (SM) who was blinded to the participants' clinical status. In the present study, the maximum grade, diagnosed in at least 1 intervertebral level of the lumbar spine or at least 1 knee joint, was regarded as the subject's KL grade.

### Statistical analysis

All statistical analyses were performed using STATA statistical software (STATA Corp., College Station, TX, USA). Differences in proportions were compared using the Chi-square test. Differences in continuous variables were tested for significance using analysis of variance for comparisons among multiple groups or Scheffe's least significant difference test for pairs of groups.

To test the association between the presence of DISH and LS and/or KOA, we used logistic regression analysis. In the analysis, we used presence of DISH as the objective variable (absence = 0, presence = 1), and severity of prevalent LS (KL0, 1 = 0 vs. KL2 = 1; KL0, 1 = 0 vs. KL3 or 4 = 2) and KOA (KL0, 1 = 0 vs. KL2 = 1; KL0, 1 = 0 vs. KL3 or 4 = 2) as explanatory variables, in addition to basic characteristics such as age (+1 year), sex (men = 1, women = 0), BMI (+1 kg/m$^2$), and regional differences (mountainous area = 0, coastal area = 1). Other potential associated factors were selected with significant or marginal ($p < 0.1$) association with DISH status in a simple linear analysis. The selected explanatory variables for logistic regression analysis are described in the Results section.

## Results

Prevalence of DISH was 10.8 % (men: 22.0 %, women: 4.8 %), and was significantly higher in men than in women. Figure 1 shows the prevalence of DISH according to age and sex. Prevalence increased with age in both men and women. Prevalence in subjects classified by age-strata—<50, 50–59, 60–69, 70–79, and ≥80 years—was 1.8, 11.7, 15.4, 32.6, and 39.6 % in men, and 0.7, 1.5, 3.5, 7.6, and 11.8 % in women, respectively.

Table 1 shows the baseline characteristics of the 1,647 participants with and without DISH. In total, subjects with DISH tended to be older, taller, heavier, and have higher BMI than those without DISH ($p < 0.0001$). In the comparison classified by sex, age was significantly higher in those with DISH in both men and women ($p < 0.0001$). In women, mean weight and BMI were significantly higher in those with DISH than in those without DISH (weight: $p < 0.05$, BMI: $p < 0.0001$).

Prevalence of DISH was lower in individuals residing in a coastal area. Individuals with DISH had a higher frequency of smoking and alcohol consumption ($p < 0.05$). The difference in the residing area was significantly observed in men. However, in the comparison classified by sex, differences in smoking and drinking were diluted (Table 1).

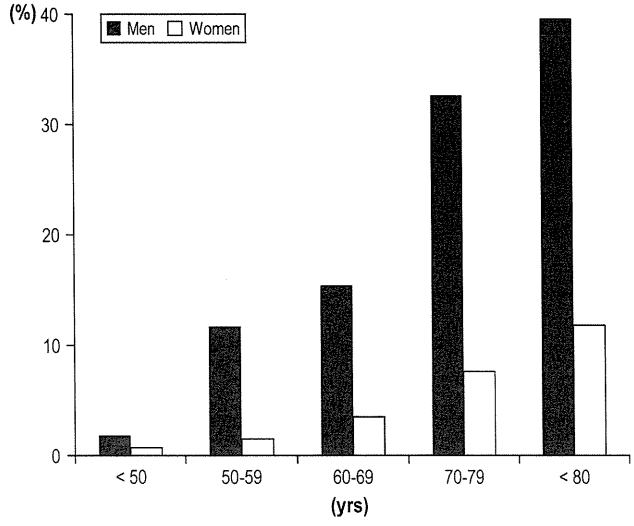


**Fig. 1** Prevalence of diffuse idiopathic skeletal hyperostosis (DISH) according to sex and age

**Table 1** Mean values (standard deviations) of the anthropometric measurements and the prevalence of lifestyle factors for the participants classified by presence or absence of DISH

| | Total ($n$ = 1647) | | | Men ($n$ = 573) | | | Women ($n$ = 1074) | | |
|---|---|---|---|---|---|---|---|---|---|
| | DISH (−) $n$ = 1470 | DISH (+) $n$ = 177 | $p$ | DISH (−) $n$ = 447 | DISH (+) $n$ = 126 | $p$ | DISH (−) $n$ = 1023 | DISH (+) $n$ = 51 | $p$ |
| Age (years) | 64.4 (12.1) | 72.3 (8.4) | <0.0001*** | 64.6 (12.1) | 72.4 (8.2) | <0.0001*** | 64.3 (12.2) | 71.9 (8.8) | <0.0001*** |
| Height (cm) | 154.7 (9.2) | 158.6 (8.8) | <0.0001*** | 163.7 (7.3) | 162.5 (6.7) | 0.0918 | 150.8 (7.0) | 148.9 (5.5) | 0.0589 |
| Weight (kg) | 55.9 (10.6) | 60.1 (10.5) | <0.0001*** | 62.3 (11.0) | 62.1 (10.0) | 0.8806 | 51.9 (8.8) | 55.0 (10.3) | 0.0126* |
| BMI (kg/m$^2$) | 22.9 (3.4) | 23.8 (3.3) | 0.0005*** | 23.2 (3.2) | 23.5 (2.9) | 0.3378 | 22.8 (3.4) | 24.7 (3.9) | 0.0001*** |
| Residing in the coastal area (%) | 50.48 | 40.11 | 0.009** | 50.3 | 35.7 | 0.004** | 50.5 | 51.0 | 0.951 |
| Current smoking habit (regularly, ≥1 month) (%) | 11.9 | 21.3 | <0.001*** | 29.9 | 29.0 | 0.858 | 3.8 | 2.0 | 0.506 |
| Current alcohol consumption (regularly, ≥1 month) (%) | 38.7 | 48.0 | 0.017* | 68.5 | 61.1 | 0.122 | 25.7 | 15.7 | 0.108 |
| Presence of LS (KL grade ≥2) (%) | 59.1 | 93.8 | <0.001*** | 72.0 | 94.4 | <0.001*** | 53.4 | 92.2 | <0.001*** |
| Presence of LS (KL grade ≥3) (%) | 35.6 | 48.0 | 0.001** | 35.4 | 45.2 | 0.043* | 35.7 | 54.9 | 0.005** |
| Presence of KOA (KL grade ≥2) (%) | 48.2 | 65.5 | <0.001*** | 35.5 | 58.7 | <0.001*** | 53.8 | 83.3 | <0.001*** |
| Presence of KOA (KL grade ≥3) (%) | 18.4 | 34.5 | <0.001*** | 11.0 | 27.0 | <0.001*** | 21.7 | 54.2 | <0.001*** |

*DISH* diffuse idiopathic skeletal hyperostosis, *BMI* body mass index, *LS* lumbar spondylosis, *KOA* knee osteoarthritis, *KL grade* Kellgren-Lawrence grade

*DISH (−)* absence of DISH, *DISH (+)* presence of DISH

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 1 also shows the prevalence of LS and KOA defined by KL grade ≥2 and grade ≥3, according to DISH status. In total, the prevalence of LS was higher in those with DISH than in those without DISH ($p = 0.001$). A similar tendency was observed in the prevalence of KOA ($p < 0.001$). This tendency also was noted in the comparison classified by sex.

We classified subjects with DISH into 4 types: (1) cervical, ossification along the lateral aspect of at least 4 contiguous vertebral bodies only in the cervical region (C0/1–C6/7); (2) thoracic, ossification along the lateral aspect of at least 4 contiguous vertebral bodies only in the thoracic region (Th4/5–Th12/L1); (3) lumbar, ossification along the lateral aspect of at least 4 contiguous vertebral bodies only in the lumbar region (L1/2–L5/S1); and (4) diffuse, ossification along the lateral aspect of at least 4 contiguous vertebral bodies in more than 2 regions or through more than 2 regions. Table 2 shows the prevalence of DISH classified by location in the spine. A total of 89 % was shown to be thoracic, whereas the remaining was diffuse; there were no subjects with cervical-type or lumbar-type DISH.

Figure 2 shows the distribution of DISH classified by vertebral level (Th4/5–LS/S1). Among diffuse-type DISH, although 2 subjects had ossification in the cervical region, the cervical site is excluded from the figure. Figure 2 shows that ossification was observed mainly in the middle-lower thoracic sites (Th7/8–Th9/10).

Logistic regression analysis was performed with DISH as the objective variable, LS and KOA as explanatory variables, and patient characteristics including age, sex, BMI, regional differences, smoking, and alcohol consumption as potential risk factors. Presence of DISH was significantly associated with presence of LS (KL2 vs KL0: 1, KL ≥3 vs KL0: 1) and KOA (KL ≥3 vs KL0: 1). Among other potential associated factors, older age, male sex, and higher BMI remained as significantly associated with the presence of DISH (Table 3).

**Table 2** Number (proportion, %) of DISH (+) patients classified by spinal ossification site

| Type of DISH | Total | Men | Women |
|---|---|---|---|
| Cervical type | 0 (0.0 %) | 0 (0.0 %) | 0 (0.0 %) |
| Thoracic type | 157 (88.7 %) | 111 (88.1 %) | 46 (90.2 %) |
| Lumbar type | 0 (0.0 %) | 0 (0.0 %) | 0 (0.0 %) |
| Diffuse type | 20 (11.3 %) | 15 (11.9 %) | 5 (9.8 %) |
| Total | 177 (100.0 %) | 126 (100.0 %) | 51 (100.0 %) |

Cervical type: Ossification along the lateral aspect of at least four contiguous vertebral bodies existing only in the cervical region (C0/1–C6/7)

Thoracic type: Ossification along the lateral aspect of at least four contiguous vertebral bodies existing only in the thoracic region (Th4/5–Th12/L1)

Lumbar type: Ossification along the lateral aspect of at least four contiguous vertebral bodies existing only in the lumbar region (L1/2–L5/S1)

Diffuse type: Ossification along the lateral aspect of at least four contiguous vertebral bodies existing in more than 2 regions or through more than 2 regions

Finally, to clarify the association of DISH with LS and KOA, we performed logistic regression analysis using DISH as an objective variable, LS and KOA as explanatory variables, and patient characteristics including age, sex, BMI, regional differences, smoking, and alcohol consumption as potential risk factors. Presence of DISH was significantly associated with presence of LS (KL2 vs KL0: 1, KL ≥3 vs KL0: 1) and KOA (KL ≥3 vs KL0: 1) independently (Table 4).

## Discussion

In the present study, using lateral whole-spine radiographs of recently examined population-based samples, we estimated that the prevalence of DISH was one-tenth of the population, which consisted of participants from the ROAD study. The subjects with DISH tended to be older and had bigger body build than those without DISH. In addition, DISH was observed more frequently in men than

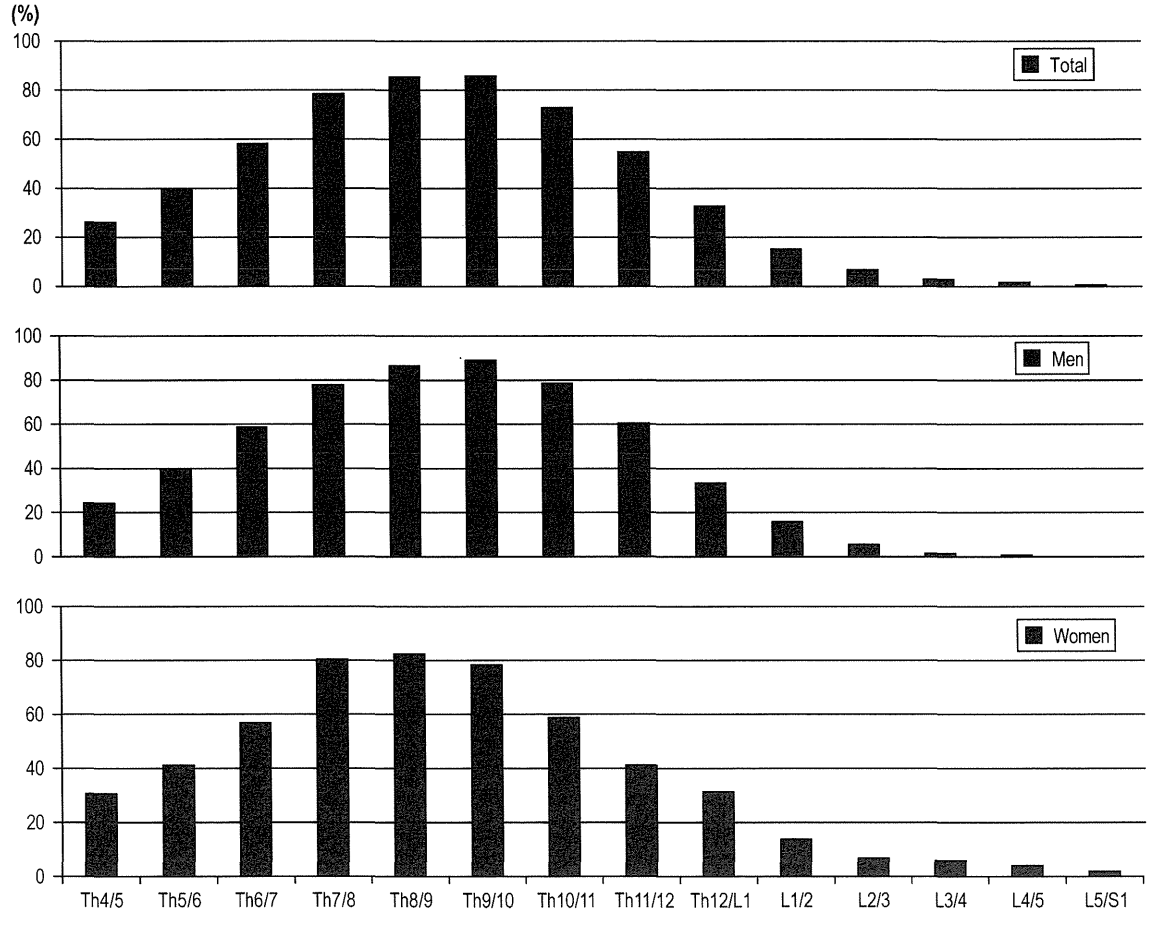


**Fig. 2** Prevalence of diffuse idiopathic skeletal hyperostosis (DISH) in each vertebral level, classified by sex

**Table 3** Odds ratios of lumbar spondylosis or knee osteoarthritis, and potentially associated factors for the presence of DISH vs. absence of DISH

| Explanatory variables | Category | OR | 95 % CI | *p* |
|---|---|---|---|---|
| Lumbar spondylosis | | | | |
| Presence of LS | 0: KL grade = 0, 1, 1: KL grade = 2 | 5.80 | 2.97–11.3 | <0.001*** |
| | 0: KL grade = 0, 1, 2: KL grade ≥3 | 4.54 | 2.34–8.84 | <0.001*** |
| Age (years) | +1 year | 1.07 | 1.05–1.09 | <0.001*** |
| Gender | 1: men, 0: women | 4.61 | 3.05–6.99 | <0.001*** |
| Region | 0: mountainous area, 1: coastal area | 0.88 | 0.61–1.26 | 0.475 |
| BMI (kg/m$^2$) | +1 kg/m$^2$ | 1.11 | 1.05–1.17 | <0.001*** |
| Smoking | 0: ex or never smoker, 1: current smoker | 1.65 | 1.04–2.63 | 0.034* |
| Alcohol consumption | 0: ex or never drinker, 1: current drinker | 0.82 | 0.56–1.22 | 0.329 |
| Knee osteoarthritis | | | | |
| Presence of KOA | 0: KL grade = 0, 1, 1: KL grade = 2 | 1.34 | 0.85–2.10 | 0.211 |
| | 0: KL grade = 0, 1, 2: KL grade ≥3 | 2.15 | 1.32–3.52 | 0.002** |
| Age (years) | +1 year | 1.07 | 1.04–1.09 | <0.001*** |
| Gender | 1: men, 0: women | 6.90 | 4.48–10.6 | <0.001*** |
| Region | 0: mountainous area, 1: coastal area | 0.95 | 0.65–1.37 | 0.771 |
| BMI (kg/m$^2$) | +1 kg/m$^2$ | 1.09 | 1.03–1.15 | 0.002** |
| Smoking | 0: ex or never smoker, 1: current smoker | 1.52 | 0.95–2.42 | 0.079 |
| Alcohol consumption | 0: ex or never drinker, 1: current drinker | 0.85 | 0.58–1.26 | 0.431 |

*DISH* diffuse idiopathic skeletal hyperostosis, *BMI* body mass index, *LS* lumbar spondylosis, *KOA* knee osteoarthritis, *KL grade* Kellgren-Lawrence grade

*OR* odds ratios, *95 % CI* 95 % confidence interval

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

**Table 4** Odds ratios of lumbar spondylosis and knee osteoarthritis, and potentially associated factors for the presence of DISH vs. absence of DISH

| Explanatory variables | Category | OR | 95 % CI | *p* |
|---|---|---|---|---|
| Presence of LS (KL grade = 2) | vs. KL grade = 0, 1 | 5.50 | 2.81–10.8 | <0.001*** |
| Presence of LS (KL grade ≥3) | vs. KL grade = 0, 1 | 4.09 | 2.08–8.03 | <0.001*** |
| Presence of KOA (KL grade = 2) | vs. KL grade = 0, 1 | 1.22 | 0.77–1.92 | 0.404 |
| Presence of KOA (KL grade≥ 3) | vs. KL grade = 0, 1 | 1.89 | 1.14–3.10 | 0.013** |
| Age (years) | +1 year | 1.06 | 1.03–1.14 | <0.001*** |
| Gender | 1: men, 0: women | 5.55 | 3.57–8.63 | <0.001*** |
| Region | 0: mountainous area, 1: coastal area | 0.88 | 0.60–1.29 | 0.522 |
| BMI (kg/m$^2$) | +1 kg/m$^2$ | 1.08 | 1.02–1.14 | 0.008** |
| Smoking | 0: ex or never smoker, 1: current smoker | 1.59 | 1.00–2.55 | 0.052 |
| Alcohol consumption | 0: ex or never drinker, 1: current drinker | 0.81 | 0.54–1.21 | 0.298 |

*DISH* diffuse idiopathic skeletal hyperostosis, *BMI* body mass index, *LS* lumbar spondylosis, *KOA* knee osteoarthritis, *KL grade* Kellgren-Lawrence grade

*OR* odds ratios, *95 % CI* 95 % confidence interval

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

in women, and the most common site was the thoracic vertebrae. Presence of DISH was significantly associated with the presence of KOA and LS, after adjusting for potential associated factors.

There have been several epidemiologic studies on DISH in many parts of the world [12–19]. The results indicate that DISH is observed mainly in men and the elderly; prevalence increases with age, and it is distributed mostly in the thoracic spine. These results are supported by the results of the present study. However, there are considerable differences in the prevalence. Weinfeld et al. [20] reported that genetic or hereditary differences are

important predisposing factors for DISH. Their previous study involved patients from ethnic populations, including 667 white, 144 black, 72 Native American, 11 Hispanic, and 30 Asian patients. They showed that the Asian, black, and Native American populations had a remarkably lower prevalence of DISH; however, their study population was small. In a recent study, Kim et al. [18] reported that race influences the prevalence of DISH. Their prevalence of DISH was 5.4 % in men and 0.8 % in women aged over 80 years in a Korean population, which is remarkably lower than the prevalence in our study, despite the similar race. Our prevalence was similarly high as the white population in Weinfield's report. Therefore, it is believed that genetic factors influence the prevalence of DISH more than race.

The present study clarified that most cases of DISH were observed in the thoracic vertebrae. There were no cases of DISH located in only the cervical or lumbar region. All cases of DISH in the cervical region were categorised as diffuse-type. Even if subjects were categorised into diffuse-type DISH, thoracic vertebrae were found to be the most affected. In addition, among the thoracic vertebrae, we found the predilection site to be the middle thoracic vertebrae (Th7–Th9). Holton et al. [27] reported that the distribution of the lowest level of DISH in 298 male subjects aged ≥65 years was 38 % in the thoracic region, 49 % in the thoracolumbar region, and 13 % in the lumbar region. It is interesting that DISH has predilection sites, which might be due to anatomic alignment of the vertebrae. For example, the middle thoracic vertebrae are likely to be affected by compressive mechanical stress because the Th8 is located nearly at the top in physiologic kyphosis. DISH originates mainly from the thoracic spine and extends to the cervical and/or lumbar spine by mechanical stress. In the present cross-sectional study, we could not evaluate whether DISH tends to occur in the thoracic vertebrae and then forms in the lumbar spine secondarily; however, we were able to follow-up on the ROAD study and clarify the disease course of thoracic DISH.

Regarding the definition of DISH, it might be easy to imagine that LS, defined by KL2 (defined as radiographically definite osteophytes), is associated with DISH. However, there are few reports to confirm the association between DISH and severe LS with the criterion of KL3 or 4. In the present study, we confirmed the significant association between DISH and LS, not only with the criterion of KL2, but also with KL ≥3. In addition, there are few reports to clarify the association between DISH and OA of other sites. In the present study, we also confirmed the significant association between DISH and KOA. In fact, the OR of the presence of DISH for KOA significantly increased according to the severity of KOA. The effects of LS and KOA coexisted independently. This result suggests that DISH and OA might be in a similar vein of disease, for example, the so-called 'bone proliferative group'. There have been several reports regarding the association between DISH and OPLL [4–7]. Resnick et al. [4] described 4 patients with coexisting DISH and cervical OPLL, and found OPLL in 50 % of 74 additional patients with DISH after reviewing their cervical spine radiographs. However, there has been no report on the association of DISH and OA; thus the etiology of ossification might not be similar to that of OA. Therefore, with only the results of the present study, we cannot definitely claim that DISH and OA are in a similar disease group, even though DISH tends to have similar associated factors, such as age, overweight (bigger BMI), and mechanical stress, as OA.

Another hypothesis is that there might be hidden associated factors that might affect both DISH and OA. We considered risk factors for metabolic syndrome as potential confounders. Several constitutional and metabolic abnormalities have been reported to be associated with DISH including obesity, large waist circumference, hypertension, diabetes mellitus, hyperinsulinemia, dyslipidemia, and hyperuricemia [21, 28–30]. In addition, both LS and KOA are well known to be associated with obesity [31]. We have already reported on the presence of hypertension and impaired glucose tolerance, and shown that the accumulation of metabolic risk factors is associated with the presence and occurrence of KOA [32, 33]. In addition, we found that current smoking, a known risk factor for cardiovascular disease as well as metabolic risk factors, was significantly associated with DISH. These findings may indicate that DISH is a candidate surrogate index for metabolic risk factors as a predictor of OA, or vice versa. We could not evaluate this hypothesis at present, but we would clarify the association including the causal relationships between DISH, OA, and metabolic risk factors in a further study.

Alternatively, we considered associated factors for inflammation or cartilage metabolic turnover as potential confounders between DISH and OA. These factors might coexist as risk factors for DISH and OA. Thus, there might be a direct or indirect pathway between DISH and OA via hidden associated factors, which should be investigated in a further study.

This study has several limitations. First, although the ROAD study includes a large number of participants, these subjects may not truly represent the general population. To address this, we compared the anthropometric measurements and frequencies of smoking and alcohol consumption between study participants and the general Japanese population; no significant differences were found, with the exception that male ROAD study participants aged 70–74 years were significantly smaller in terms of body structure than the overall Japanese population ($p < 0.05$)

[25]. This difference should be considered when evaluating potential risk factors in men aged 70–74 years; factors such as body build, particularly greater weight, are known to be associated with LS and KOA. Therefore, our results may be an underestimation of the prevalence of these conditions. Second, in the present study, we used only the data of the baseline study. Thus, we were not able to confirm a causal relationship between DISH status and other associated factors, as mentioned above. Nevertheless, we have performed a follow-up study, so we will be able to clarify the causal relationship between DISH status and OA in the near future. Third, this study could not evaluate the cervicothoracic junction (C7–Th4) because we assessed only radiographs. Although most cases of DISH existed in the inferior thoracic spine, as Fig. 2 shows, the lack of findings in the C7/C1–Th3/Th4 levels might have underestimated the prevalence of DISH. To evaluate the cervicothoracic junction, it would be necessary to use computed tomography or magnetic resonance imaging of the whole spine, which appeared impossible to perform on more than 1,600 subjects. Fourth, LS defined by KL2 may have been included in cases of DISH, but there is no method to confirm the overlap of the presence of DISH and LS of KL2 using the radiographic diagnostic criteria. DISH is observed mainly in the thoracic region, and only the diffuse type expands partly into the lumbar region. Therefore, there is a small possibility that LS of KL2 might be contaminated into DISH. Finally, in the present study, we could not evaluate other sites of OA besides the knee and lumbar spine, such as the hands or hip. To evaluate DISH and other sites of OA, we should evaluate the presence or occurrence of OA at other sites in a further study.

In conclusion, in the present population-based study, we found that the prevalence of DISH was 10.8 % in the overall population. Prevalence was significantly higher in older subjects, and mainly distributed at the thoracic spine. Logistic regression analysis revealed that the presence of DISH was significantly associated with older age, male sex, higher BMI, and presence of severe KOA.

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ORIGINAL ARTICLE

# Association of physical activities of daily living with the incidence of certified need of care in the long-term care insurance system of Japan: the ROAD study

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**Abstract**
*Background* The present study aimed to investigate association of physical activities of daily living with the incidence of certified need of care in the national long-term care insurance (LTCI) system in elderly Japanese population-based cohorts.
*Methods* Of the 3,040 participants in the baseline examination, we enrolled 1,773 (699 men, 1,074 women) aged 65 years or older who were not certified as in need of care-level elderly at baseline. Participants were followed during an average of 4.0 years for incident certification of need of care in the LTCI system. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used assess function. Associated factors in the baseline examination with the occurrence were determined by multivariate Cox proportional hazards regression analysis. Receiver operating characteristic curve analysis was performed to evaluate cut-off values for discriminating between the occurrence and the non-occurrence group.
*Results* All 17 items in the WOMAC function domain were significantly associated with the occurrence of certified need of care in the overall population. Cut-off values of the WOMAC function score that maximized the sum of sensitivity and specificity were around 4–6 in the overall population, in men, and in women. Multivariate Cox hazards regression analysis revealed that a WOMAC function score ≥4 was significantly associated with occurrence with the highest hazard ratio (HR) for occurrence after adjusting for confounders in the overall population (HR [95 % confidence interval (CI)] 2.54 [1.76–3.67]) and in women [HR (95 % CI) 3.13 (1.95–5.02)]. A WOMAC function score ≥5 was significantly associated with the highest HR for occurrence in men [HR (95 % CI) 1.88 (1.03–3.43)].
*Conclusions* Physical dysfunction in daily living is a predictor of the occurrence of certified need of care. Elderly men with a WOMAC function score ≥5 and women with a score ≥4 should undergo early intervention programs to prevent subsequent deterioration.

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## Introduction

Japan is a super-aged society experiencing an unprecedented aging of the population. The proportion of the population aged 65 years or older was 23 % in 2010, and is expected to reach 30.1 % in 2024 and 39 % in 2051 [1]. This leads to an increasing proportion of disabled elderly requiring support or long-term care, imposing enormous economic and social burdens on the country. The Japanese Government started the national long-term care insurance (LTCI) system in 2000 based on the Long-Term Care Insurance Act [2]. The aim was to certify need of care-level elderly and to provide suitable care services according to the level of care required [7 levels, including requiring support (levels 1 and 2) and requiring long-term care (levels 1–5)]. The total number of certified need of care-level elderly was reported to be 5 million in 2011 [2]. Certification of need of care in the national LTCI system is an important outcome in Japan not only because of its massive social and economic burdens, but also because it is urgently necessary to reduce risk and decrease the number of disabled elderly requiring care in their activities of daily living (ADLs). It is critically important to accumulate epidemiologic evidence, including identification of predictors, to establish evidence-based prevention strategies. However, no studies have determined the association of physical ADLs with the incidence of certified need of care in the national LTCI system using large-scale, population-based cohorts. The objective of the present study was to investigate the association of physical ADLs with the incidence of certified need of care in the national LTCI system and determine its predictors in elderly participants of large-scale, population-based cohorts of the research on osteoarthritis/osteoporosis against disability (ROAD) study.

## Subjects and methods

### Participants

The analysis was based on data collected from cohorts established in 2005 for the ROAD study. Details of the cohorts have been reported elsewhere [3, 4]. Briefly, a baseline database was created from 2005 to 2007, which included clinical and genetic information on 3,040 residents of Japan (1,061 men, 1,979 women). Participants were recruited from resident registration listings in three communities, namely, an urban region in Itabashi, Tokyo, and rural regions in Hidakagawa and Taiji, Wakayama. Participants in the urban region in Itabashi were recruited from those of a cohort study [5] in which the participants were randomly drawn from the register database of Itabashi ward residents, with a response rate in the age group >60 years of 75.6 %. Participants in the rural regions in Hidakagawa and Taiji were recruited from resident registration lists, with response rates in the groups aged >60 years of 68.4 and 29.3 %, respectively. Inclusion criteria were the ability to (1) walk to the survey site, (2) report data, and (3) understand and sign an informed consent form. For the present study, we enrolled 1,773 participants (699 men, 1,074 women; mean age 75.4 years) aged 65 years or older who were not certified as in need of care-level elderly in the national LTCI system at baseline. All participants provided written informed consent, and the study was conducted with approval from the ethics committees of the participating institutions.

### Baseline procedures

Participants completed an interviewer-administered questionnaire containing 400 items that included lifestyle information, such as smoking habits, alcohol consumption, and physical activity. At baseline, anthropometric measurements, including height and weight, were taken, and body mass index (BMI) [weight (kg)/height$^2$ (m$^2$)] was estimated based on the measured height and weight.

### Assessment of physical ADLs

We used the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for assessment of physical ADLs. The WOMAC is a health status instrument, consisting of three domains: pain, stiffness, and physical function. We used the WOMAC function domain to evaluate physical ADLs. It consisted of 17 items: assessing difficulties in descending stairs, ascending stairs, rising from sitting, standing, bending to floor, walking on a flat surface, getting in/out of car/bus, going shopping, putting on socks/stockings, rising from bed, taking off socks/stockings, lying in bed, getting into/out of bath, sitting, getting on/off toilet, heavy domestic duties, and light domestic duties. Each item in the domain is graded on either a 5-point Likert scale (scores of 0–4) or a 100-mm visual analog scale [6, 7]. In the present study, we used the Likert scale (version LK 3.0). Items were rated from 0 to 4; 0, no difficulty; 1, mild difficulty; 2, moderate difficulty; 3, severe difficulty; 4, extreme difficulty. The domain score ranges from 0 to 68. Japanese versions of the WOMAC have been validated [8].

### Certification of need of care in the LTCI system

The nationally uniform criteria for long-term care need certification was established objectively by the Japanese Government, and certification of need of care-level elderly

is determined based on evaluation results by the Certification Committee for Long-term Care Need in municipalities in accordance with basic guidelines formulated by the Government. The process of eligibility for certification of need of care in the LTCI system was described in detail by Chen et al. [9]. An elderly person who requires help with ADLs or the caregiver contacts the municipal government to request official certification of care needs. After the application, a trained official visits the home to assess the current physical status of the elderly person, including presence or absence of muscle weakness or joint contracture of limbs, and difficulties in sitting-up, standing-up, maintaining sitting or standing position, transferring from one place to another, standing on one leg, walking, bathing, dressing, and other ADLs. Mental status, including dementia, also is assessed. These data are analyzed to calculate a standardized score for determination of the level of care needs (certified support, levels 1–2; or long-term care, levels 1–5). In addition, the primary physician of the applicant assesses physical and mental status, including information on diseases causing ADL disability and the extent of disabilities caused by them. Finally, the Certification Committee for Long-term Care Need reviews the data and determines the certification and its level.

### Follow-up and definition of incident certified need of care

After the baseline ROAD survey, participants who were not certified as in need of care-level elderly at baseline were followed for incident certification of need of care in the LTCI system. Incident certified need of care was defined as the incident certified 7 levels, including requiring support (levels 1–2) and requiring long-term care (levels 1–5). Information on the presence or absence of certification of need of care and its date of occurrence were collected by the resident registration listings in three communities every year up to 2010, and were used for analyses in the present study.

### Statistical analysis

All statistical analyses were performed using STATA statistical software (STATA, College Station, TX, USA). Differences in values of the parameters between the two groups were tested for significance using the unpaired Student's *t* test, the Mann–Whitney's *U* test, and Chi-square test. We used receiver operating characteristic (ROC) curve analysis to determine a cut-off value of the WOMAC function score for discriminating two distinct groups: an occurrence and a non-occurrence group of certified need of care. Cut-off values were determined that maximized the sum of sensitivity and specificity. Factors associated with the occurrence of certified need of care were determined using Cox proportional hazards regression analysis; hazard ratios (HRs) and 95 % confidence intervals (CIs) were determined after adjusting for region, age, sex, and BMI. Smoking habit and alcohol consumption were not included as confounders because they were not significantly associated with the incidence of certified need of care.

## Results

Of the 1,773 participants who were not certified as in need of care-level elderly at baseline, information on

**Table 1** Baseline characteristics of population at risk for the certified need of care in the LTCI system

| | Men | Women |
|---|---|---|
| No. of subjects | 699 | 1,074 |
| Age (years) | 75.6 (5.1) | 75.2 (5.3) |
| Height (cm) | 160.9 (6.0) | 147.9 (6.0)[b] |
| Weight (kg) | 59.4 (9.1) | 50.0 (8.3)[b] |
| BMI (kg/m$^2$) | 22.9 (2.9) | 22.8 (3.4) |
| Smoking (%) | 21.0 | 3.2[c] |
| Alcohol consumption, % | 61.2 | 23.0[c] |
| WOMAC function domain | | |
| Descending stairs, pts[a] | 0 (0, 0, 1, 1) | 0 (0, 0, 1, 2)[d] |
| Ascending stairs, pts[a] | 0 (0, 0, 1, 1) | 0 (0, 0, 1, 2) |
| Rising from sitting, pts[a] | 0 (0, 0, 0, 1) | 0 (0, 0, 1, 1)[d] |
| Standing, pts[a] | 0 (0, 0, 0, 1) | 0 (0, 0, 1, 1)[d] |
| Bending to floor, pts[a] | 0 (0, 0, 0, 1) | 0 (0, 0, 1, 1) |
| Walking on a flat surface, pts[a] | 0 (0, 0, 0, 1) | 0 (0, 0, 0, 1) |
| Getting in/out of car/bus, pts[a] | 0 (0, 0, 0, 1) | 0 (0, 0, 1, 1)[d] |
| Going shopping, pts[a] | 0 (0, 0, 0, 1) | 0 (0, 0, 0, 1)[d] |
| Putting on socks/stockings, pts[a] | 0 (0, 0, 0, 1) | 0 (0, 0, 0, 1)[d] |
| Rising from bed, pts[a] | 0 (0, 0, 0, 1) | 0 (0, 0, 0, 1)[d] |
| Taking off socks/stockings, pts[a] | 0 (0, 0, 0, 1) | 0 (0, 0, 0, 1)[d] |
| Lying in bed, pts[a] | 0 (0, 0, 0, 0) | 0 (0, 0, 0, 1)[d] |
| Getting into/out of bath, pts[a] | 0 (0, 0, 0, 0) | 0 (0, 0, 0, 1)[d] |
| Sitting, pts[a] | 0 (0, 0, 0, 0) | 0 (0, 0, 0, 0)[d] |
| Getting on/off toilet, pts[a] | 0 (0, 0, 0, 1) | 0 (0, 0, 1, 2)[d] |
| Heavy domestic duties, pts[a] | 0 (0, 0, 0, 1) | 0 (0, 0, 0, 1)[d] |
| Light domestic duties, pts[a] | 0 (0, 0, 0, 1) | 0 (0, 0, 0, 1)[d] |
| Total, pts[a] | 1 (0, 0, 5, 12) | 2 (0, 0, 8, 17)[d] |

Except where indicated otherwise, values are mean (SD)

*LTCI* long-term care insurance system, *BMI* body mass index, *WOMAC* the Western Ontario and McMaster Universities Arthritis Index

[a] Median (10, 25, 75, and 90 percentile)

[b] $P < 0.05$ vs men by unpaired Student's *t* test

[c] $P < 0.05$ vs men by Chi-square test

[d] $P < 0.05$ vs men by Mann–Whitney *U* test

**Table 2** Association of physical activities of daily living with the occurrence of certified need of care in the LTCI system

| Physical activity | Overall population | | Men | | Women | |
|---|---|---|---|---|---|---|
| | HR (95 % CI) | *P* value | HR (95 % CI) | *P* value | HR (95 % CI) | *P* value |
| Descending stairs, pts | 1.47 (1.26, 1.72) | <0.001 | 1.29 (0.96, 1.74) | 0.089 | 1.56 (1.30, 1.87) | <0.001 |
| Ascending stairs, pts | 1.47 (1.25, 1.73) | <0.001 | 1.29 (0.93, 1.77) | 0.123 | 1.55 (1.29, 1.86) | <0.001 |
| Rising from sitting, pts | 1.58 (1.34, 1.88) | <0.001 | 1.38 (0.95, 1.99) | 0.092 | 1.67 (1.37, 2.03) | <0.001 |
| Standing, pts | 1.64 (1.41, 1.91) | <0.001 | 1.39 (1.02, 1.90) | 0.037 | 1.73 (1.45, 2.06) | <0.001 |
| Bending to floor, pts | 1.57 (1.32, 1.85) | <0.001 | 1.61 (1.15, 2.27) | 0.006 | 1.57 (1.29, 1.90) | <0.001 |
| Walking on a flat surface, pts | 1.57 (1.30, 1.90) | <0.001 | 1.25 (0.88, 1.77) | 0.22 | 1.78 (1.41, 2.23) | <0.001 |
| Getting in/out of car/bus, pts | 1.76 (1.47, 2.10) | <0.001 | 1.60 (1.14, 2.26) | 0.007 | 1.85 (1.50, 2.29) | <0.001 |
| Going shopping, pts | 1.72 (1.46, 2.03) | <0.001 | 1.55 (1.14, 2.11) | 0.005 | 1.81 (1.48, 2.21) | <0.001 |
| Putting on socks/stockings, pts | 1.60 (1.33, 1.92) | <0.001 | 1.41 (0.98, 2.03) | 0.065 | 1.71 (1.37, 2.12) | <0.001 |
| Rising from bed, pts | 1.68 (1.40, 2.03) | <0.001 | 1.41 (0.98, 2.02) | 0.066 | 1.83 (1.47, 2.29) | <0.001 |
| Taking off socks/stockings, pts | 1.64 (1.37, 1.98) | <0.001 | 1.48 (1.01, 2.16) | 0.046 | 1.72 (1.39, 2.13) | <0.001 |
| Lying in bed, pts | 1.82 (1.44, 2.30) | <0.001 | 1.96 (1.13, 3.40) | 0.017 | 1.79 (1.38, 2.32) | <0.001 |
| Getting into/out of bath, pts | 1.71 (1.43, 2.04) | <0.001 | 1.64 (1.15, 2.33) | 0.006 | 1.75 (1.43, 2.15) | <0.001 |
| Sitting, pts | 2.21 (1.73, 2.82) | <0.001 | 1.92 (1.14, 3.22) | 0.014 | 2.32 (1.75, 3.06) | <0.001 |
| Getting on/off toilet, pts | 1.87 (1.52, 2.29) | <0.001 | 1.51 (1.00, 2.27) | 0.05 | 2.09 (1.63, 2.68) | <0.001 |
| Heavy domestic duties, pts | 1.27 (1.09, 1.49) | 0.003 | 1.20 (0.89, 1.62) | 0.238 | 1.33 (1.10, 1.60) | 0.003 |
| Light domestic duties, pts | 1.68 (1.41, 2.01) | <0.001 | 1.49 (1.07, 2.07) | 0.019 | 1.80 (1.45, 2.24) | <0.001 |

Hazard ratios (HRs) and 95 % confidence intervals (CIs) were determined by Cox proportional hazards regression analysis after adjusting for age, sex, body mass index, and region in the overall population, and after adjusting for age, body mass index, and region in men and in women, respectively

*LTCI* long-term care insurance system

certification of need of care could be obtained in 1,760 (99.3 %) during the average 4.0-year follow-up. Fifty-four men and 115 women were certified as in need of care-level elderly in the national LTCI system, whereas, 1,591 remained uncertified during the follow-up period. The average period for the certification was 2.3 years. Among the above 54 men and 115 women, those who were certified as requiring long-term care level 1, 2, 3, 4, and 5 were 7, 9, 2, 4, 3 men, and 12, 17, 9, 4, 4 women, respectively. One hundred and twenty-six participants died and eight moved away. Incidence of certified need of care in the LTCI system was 2.3/100 person-years in the overall population, and 2.0/100 person-years in men and 2.5/100 person-years in women. Table 1 shows the baseline characteristics of the population at risk for occurrence of certified need of care in the LTCI system. The score of each item in the WOMAC function domain was significantly higher in women than in men in almost all items.

We then investigated association of each item in the WOMAC function domain with the occurrence of certified need of care in the LTCI system (Table 2). All 17 items in the WOMAC function domain were significantly associated with the occurrence of the certified need of care in the overall population and in women. In men, standing, bending to floor, getting in/out of car/bus, going shopping, taking off socks/stockings, lying in bed, getting into/out of bath, sitting, and light domestic duties were significantly associated with the occurrence of certified need of care, whereas other ADLs were not. In addition, the value of HR for each item in the association was higher in women than in men in 15 of 17 items.

Next we determined cut-off values of total score of the WOMAC function domain for discriminating two groups: an occurrence and a non-occurrence group of certified need of care using ROC curve analysis. The area under ROC curve was 0.70 in the overall population, 0.61 in men, and 0.74 in women (Fig. 1). The cut-off value of the WOMAC function score that maximized the sum of sensitivity and specificity was 6, 5, and 6 in the overall population, in men, and in women, respectively. In addition, the sensitivity/specificity was 57.3/75.0 % in the overall population, 45.7/75.0 % in men, and 64.4/72.6 % in women, respectively (Table 3). Furthermore, the cut-off value by which the sum was the second largest was 4 in the overall population, 4 in men, and 4 in women, and the sensitivity/specificity was 65.3/66.7 % in the overall population, 50.0/70.0 % in men, and 72.1/64.5 % in women, respectively (Table 3).

Because ROC curve analysis is a univariate analysis, we performed multivariate Cox hazards regression analysis to determine the cut-off value of the WOMAC function score for best discriminating between an occurrence and a non-