Impact of Pain on Incident Risk of Disability in Elderly Japanese

Cause-specific Analysis

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ABSTRACT

Background: Although several cross-sectional studies have reported that pain is associated with functional disability in the elderly, data regarding a longitudinal association between pain and disability are inconsistent. This study aimed to investigate the association of pain severity with subsequent functional disability due to all causes as well as stroke, dementia, and joint disease/fracture.

Methods: The authors conducted a prospective cohort study of 13,702 Japanese individuals aged 65 yr or older. Information regarding pain severity during the previous 4 weeks and other lifestyle factors was collected *via* questionnaire in 2006. Data on the incidence of functional disability were retrieved from the Long-term Care Insurance database. Cox proportional hazards regression analysis was used to estimate the multivariate-adjusted hazard ratios for incident functional disability.

Results: The authors documented 2,686 (19.6%) cases of incident functional disability. The multivariate hazard ratio of functional disability was 1.15 (95% CI, 1.02 to 1.31) among respondents with moderate pain and 1.31 (95% CI, 1.12 to 1.54) among respondents with severe pain in comparison with those without pain (P trend < 0.001). These positive associations were particularly remarkable for disability due to joint disease/fracture: the multivariate hazard ratio was 1.88 (95% CI, 1.37 to 2.58) for moderate pain and 2.76 (95% CI, 1.93 to 3.95) for severe pain (P trend < 0.001). There was a negative association between pain severity and disability due to dementia (P trend = 0.041) and no significant association between pain severity and disability due to stroke.

Conclusions: Among elderly Japanese individuals, the authors found a significant positive association between pain severity and future incident functional disability. **(ANESTHESIOLOGY 2017; 126:688-96)**

PAIN is a common and major complaint of the elderly.[1–3] According to the Comprehensive Survey of Living Conditions conducted in 2013 by the Ministry of Health, Labour, and Welfare of Japan (Tokyo), more than 37% of the Japanese population aged 65 yr old or older complained of pain, a prevalence comparable to that reported in other developed countries.[2,4,5] As the aging population continues to rise in an unprecedented manner globally, the number of patients afflicted with significant pain will also increase rapidly.[6,7]

Pain has been reported to have a strong relationship with functional limitation and disability in several cross-sectional studies.[1,8–12] For example, Scudds and Robertson[10] showed that pain of severe or greater intensity was significantly associated with disability (odds ratio, 4.32; 95% CI, 2.01 to 9.01) in community-dwelling senior citizens in Canada. However, studies of the longitudinal relationship between pain and disability have yielded inconsistent results. To our knowledge, there have been six longitudinal studies that have examined the association between pain and the incident risk of functional disability; five of these studies suggested that pain may predict future functional disability.[13–17] In contrast, Andrews *et al.*[18] demonstrated that the association between pain and future activities of daily living (ADL) disability disappeared

What We Already Know about This Topic

- The longitudinal effects of pain on disability in the elderly remain unclear
- The authors thus evaluated the association of pain severity with subsequent functional disability among 13,702 elderly Japanese

What This Article Tells Us That Is New

- Moderate pain increased the risk of functional disability by 15%, and severe pain increased the risk by 31%
- Risk was especially great for joint disease and fractures

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after adjustment for possible confounding factors including baseline ADL difficulties and mobility limitations. The differing findings in these studies may be partially attributable to methodologic limitations such as small sample size, not population based, younger study populations, lower follow-up rates, and discrepancies in the definitions and assessments of pain and disability.

Furthermore, none of these studies assessed the cause of disability. Major common causes of functional disability include stroke, dementia, and joint disease/fracture. Most of the previous studies adopted self-reported ADLs or instrumental ADLs as study outcomes, and it is difficult to detect the direct cause of disability in these studies. With the aging of populations worldwide, the extension of a disability-free life span has become major public health goal. In order to devise an efficient strategy to prevent disability due to pain, an investigation of the cause-specific impact of pain on disability and a greater understanding of the pathway from pain to disability is urgently needed.

The aim of this study was to investigate the association between pain severity and incident functional disability and to reveal the cause-specific impact of pain severity on functional disability in the elderly Japanese population.

Materials and Methods

Study Population and Design

The details of the Ohsaki Cohort 2006 Study have been described elsewhere.[19–24] In brief, a baseline questionnaire was distributed to all 31,694 residents aged 65 yr old or older in Ohsaki City, Miyagi Prefecture, northeastern Japan, between December 1, 2006, and December 15, 2006. The survey included questions regarding body pain, as well as past medical history, blood pressure, educational level, smoking, alcohol consumption, body weight and height, motor function, psychologic distress score (Kessler Psychological Distress Scale [K6]),[25,26] and social support. In this analysis, the 23,091 individuals who returned the questionnaires formed the study cohort. We excluded 6,333 persons who did not provide us with written consent for access to their Long-term Care Insurance (LTCI) information, 2,102 persons who had already been certified as disabled by the LTCI before the starting date of follow-up (March 30, 2007), 62 persons who had died or moved before the starting date of follow-up, 188 persons for whom the Doctor's Opinion Paper (DOP) was unavailable, and 704 persons who failed to answer questions regarding pain severity in the baseline questionnaire. Ultimately, 13,702 subjects were analyzed in the study.

Assessment of Pain

Pain was evaluated according to the subject's response to the question "How much pain have you experienced during the past 4 weeks?" and used a six-point verbal rating scale with the words "none," "very mild," "mild," "moderate," "severe," and "very severe."[27–29] Because of the small number of subjects, we reclassified these six categories into four categories by combining "severe" and "very severe" into a single "severe" pain category and "very mild" and "mild" into a single "mild" pain category to facilitate interpretation. To confirm the validity of this classification, we performed the same analysis using the original six categories as a sensitivity analysis.

Case Ascertainment

The primary outcome was incident functional disability, defined as a disability certification by the LTCI in Japan. The LTCI is a mandatory social insurance system in Japan for care of the elderly disabled population.[30–33] People aged 40 yr old or older pay a premium, and those aged 65 yr old or older are eligible for formal care giving services. In this study, we confirmed incident functional disability when eligible persons were certified as disabled by the Municipal Care Need Certification Committee (Ohsaki, Miyagi, Japan). Certification was determined using a questionnaire developed by the Ministry of Health, Labour, and Welfare and the DOP reported by the primary doctor.[34] The LTCI certification was found to be associated with a patient's ability to perform ADLs in a community-based study[35] and has previously been used as a measure of incident functional disability among elderly individuals in epidemiologic studies.[21,36,37]

We obtained a data set including information on LTCI certification, death, or emigration from Ohsaki City based on an agreement with the Ohsaki City Government related to Epidemiologic Research and Privacy Protection.

Cause of Disability

Cause of disability was investigated based on the DOP in the LTCI according to a standardized physicians' manual issued by the Ministry of Health, Labour, and Welfare.[34] The primary cause of disability was coded by trained physicians according to the International Classification of Diseases and Related Health Problems, Tenth Revision.

We focused on three major causes (stroke, dementia, and joint disease/fracture) of functional disability. We identified disability due to stroke as codes I60 to I69, those due to dementia as codes F00 to F03 and G30, and those due to joint disease and fracture as codes M00 to M25 and M40 to M54.

Ethical Issues

We considered the return of the questionnaires as implied consent to participate in the study involving the baseline survey data and subsequent follow-up data regarding death and emigration. We also obtained written consent for LTCI certification status along with the questionnaires at the baseline survey. The Ethics Committee of Tohoku University Graduate School of Medicine, Sendai, Japan, reviewed and approved the study protocol.

Statistical Analysis

We counted the person-years of follow-up for each subject from April 1, 2007, until the date of incident functional

disability, date of emigration from the study area, date of death, or the end of the study period (November 30, 2012), whichever occurred first. In our analysis, deaths without LTCI certification were treated as censored.

Statistical differences in baseline characteristics among the four categories of pain severity were tested using ANOVA for continuous variables and the chi-square test for categorical variables.

Kaplan–Meier estimates with log-rank tests were used to compare the cumulative proportion of participants remaining free from disability during the follow-up period between the pain severity categories.

We used the multiple adjusted Cox proportional hazards model to calculate the hazard ratios (HRs) and 95% CIs for incident disability for each pain severity category, considering the no-pain category as the reference. Multivariate models were adjusted for the following variables. Model 1 was sex and age adjusted. To examine whether the association between pain and functional disability was attributable to physical health, lifestyle, and psychosocial factors, model 2 was further adjusted for a history of stroke, myocardial infarction, hypertension (individuals with self-measured systolic blood pressure greater than or equal to 140 mmHg or diastolic blood pressure greater than or equal to 90 mmHg were also defined as hypertensive), diabetes mellitus, cancer, arthritis, osteoporosis and fracture, educational level, smoking status, alcohol consumption, body mass index, motor function score, psychologic distress score, and social support. Body mass index was calculated as the self-reported body weight (kg) divided by the square of the self-reported body height (m). We used the K6 to measure psychologic distress. We classified individuals with scores of greater than or equal to 13 as having psychologic distress, based on previous studies.[25,26] The Kihon Checklist was developed by the Ministry of Health, Labour, and Welfare of Japan to screen for functional decline in the community-dwelling elderly population. With regard to the motor function score in the Kihon Checklist, respondents were asked about their current motor function status by using five binary questions yielding a total point score ranging from 0 to 5. We classified individuals with scores of greater than or equal to 3 as having limited motor function as done in previous studies.[20] Previous validation studies reported that the motor function score of the Kihon Checklist correlates with objective measurements of motor function.[20,38] The presence of social support available to each individual was assessed by asking the question "Is there someone to whom you can talk when in trouble?"

To test for linear trend, the *P* values for the test of the linear trend (*P* trend) were also calculated by considering pain severity categories as an ordinal variable (score 1, 2, 3, and 4 for no, mild, moderate, and severe pain, respectively) in the corresponding Cox models.

We further estimated the association between pain severity and incident functional disability according to cause of disability. The Cox models were applied to estimate HRs and 95% CIs for incident functional disability due to stroke, dementia, and joint disease/fracture.

We also analyzed the association between pain severity and incident functional disability with the exclusion of 1,111 cases of incident disability occurring during the first 2 yr of follow-up to examine the possibility of reverse causality.

All of the above analyses were planned *a priori*. After examination of the data, we conducted two additional analyses that we describe in the Results.

All data were analyzed using SAS version 9.3 (SAS, Inc., USA) except for Kaplan–Meier curves, which were drawn using SPSS version 22.0 (SPSS, Inc., USA). All statistical tests described here were two sided, and differences at $P < 0.05$ were accepted as significant.

Results

During the 5.7 yr of follow-up between April 1, 2007, and November 30, 2012, 132 individuals were lost to follow-up because they moved away from the study area without incident disability; therefore, the follow-up rate was 99.0%. Incident functional disability was documented in 2,686 cases, accounting for 19.6% of the participants overall. The total number of deaths was 1,682 (12.3%), and among them, 762 (5.6%) participants died without incident disability. Kaplan–Meier curves, shown in figure 1, indicated the cumulative proportion of participants remaining free from disability with respect to pain severity. The cumulative disability-free proportion of participants who reported greater pain severity was lower throughout the follow-up period ($P < 0.001$).

Table 1 shows the baseline characteristics of the participants according to pain severity. Participants who reported greater pain severity were more likely to be women, obese, less educated, lack social support, have limited motor function, suffer from psychologic distress, and have a history of hypertension, myocardial infarction, arthritis, osteoporosis, and falls or fractures.

Table 2 shows the relationship between pain severity and incident functional disability with HRs and associated 95% CIs. We found that pain severity was associated with incident functional disability in model 1. In model 2, the multivariate HRs were 1.00 (reference) for no pain, 0.99 (95% CI, 0.89 to 1.10) for mild pain, 1.15 (95% CI, 1.02 to 1.31) for moderate pain, and 1.31 (95% CI, 1.12 to 1.54) for severe pain (P trend < 0.001). Conversely, there was no significant association between pain severity and all-cause mortality (P trend = 0.735). Because 762 cases of death among 1,682 total cases (45.3%) were censored in the analysis, we conducted an additional analysis (survival analysis) using the competing-risks regression model in order to avoid the possibility of an overestimation of the detrimental effects of pain severity against incident functional disability.[39] The competitive event was defined as a disability-free death. Even in a competing-risks model, the positive relation between pain severity and incident functional disability remained statistically significant (see appendix).

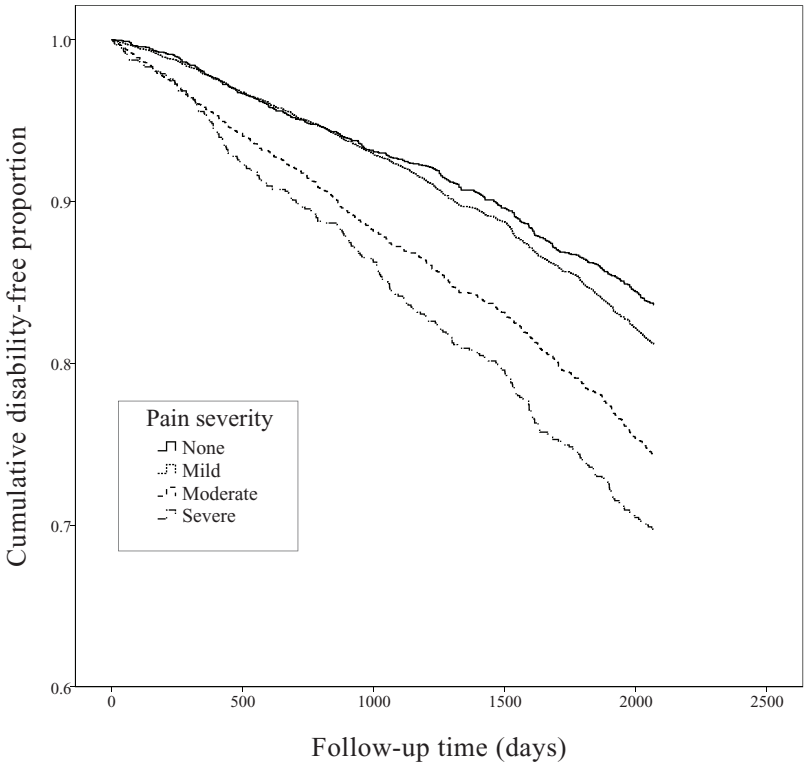

Fig. 1. Kaplan–Meier survival curves for the cumulative proportion of participants remaining free from disability with respect to pain severity (n = 13,702).

Table 3 shows the association between pain severity and incident functional disability due to three major causes. Functional disability developed in 405 individuals due to stroke, 453 individuals due to dementia, and 536 individuals due to joint disease/fracture. There was a significant relationship between pain and incident functional disability only for individuals in the joint disease/fracture group. In model 2, the multivariate HRs were 1.00 (reference) for no pain, 1.25 (95% CI, 0.93 to 1.69) for mild pain, 1.88 (95% CI, 1.37 to 2.58) for moderate pain, and 2.76 (95% CI, 1.93 to 3.95) for severe pain (*P* trend < 0.001). On the other hand, we found a negative association between pain severity and disability in the dementia group. The corresponding data for dementia were 1.00 (reference), 0.76 (95% CI, 0.60 to 0.96), 0.70 (95% CI, 0.52 to 0.94), and 0.74 (95% CI, 0.49 to 1.12) (*P* trend = 0.041). For the stroke group, there was no significant association between pain severity and disability.

To examine possible reverse causality for the association between pain and incident disability, we reanalyzed the association after excluding 1,111 participants who developed incident disability during the first 2 yr of follow-up; however, the results did not change substantially (table 4). The multivariate HRs (model 2) were 1.00 (reference) for no pain, 1.08 (95% CI, 0.94 to 1.24) for mild pain, 1.16 (95% CI, 0.98 to 1.37) for moderate pain, and 1.38 (95% CI, 1.12 to 1.71) for severe pain (*P* trend = 0.003). In addition, we analyzed the 2-yr excluded association between pain severity and incident disability due to the three major causes after excluding the above 1,111 participants. The results did not change substantially from the results shown in table 3 (data not shown). Because participants who reported greater pain severity tended to have a more significant history of joint disease/fracture, we conducted an additional analysis (sensitivity analysis) in which we excluded 4,670 individuals with a history of joint disease/fracture (arthritis, osteoporosis, and falls or fractures) at baseline. Even after excluding those participants, the positive relationship between pain severity and incident functional disability did not change substantially (table 5).

Table 6 shows the results of a sensitivity analysis that we performed to confirm the validity of our classification of pain severity. The associations between pain and incident disability did not change substantially for disability due to all causes and disability due to joint disease/fracture (table 7).

Discussion

In this population-based cohort study, we found that pain severity was significantly associated with an increased risk of incident functional disability. In addition, the association was particularly remarkable for disability due to joint disease/fracture. There was a negative association between pain severity and disability due to dementia, and there was no significant association between pain severity and disability due to stroke. To our knowledge, this is the first study to show an association between pain severity and the risk of incident

Table 1. Baseline Characteristics According to Pain Severity (n = 13,702)

Characteristics	Pain Severity				*P* Value
	None	Mild*	Moderate	Severe†	
No. of participants	3,000	6,847	2,899	956	
Demographic					
Age, yr (mean ± SD)	73.2 ± 6.0	73.7 ± 5.8	74.5 ± 6.0	74.3 ± 5.8	
Female, %	44.2	54.5	63.2	65.9	< 0.0001
Body mass index (≥ 25), %	23.1	26.0	29.1	33.4	< 0.0001
Socioeconomic status measures, %					
Educational level (≤ 15 yr)	27.3	27.0	30.7	31.6	< 0.0001
Lack of social support‡	8.1	8.9	10.7	12.5	< 0.0001
Limited motor function, %§	8.0	16.1	33.3	44.4	< 0.0001
Psychologic distress, %‖	1.5	2.8	6.5	12.0	< 0.0001
History of disease, %					
Stroke	3.2	2.3	3.2	3.4	0.006
Hypertension	36.8	43.2	48.9	49.8	< 0.0001
Myocardial infarction	4.1	4.2	7.0	6.6	< 0.0001
Cancer	9.3	8.1	9.0	9.4	0.1353
Arthritis	4.1	13.9	26.9	34.3	< 0.0001
Osteoporosis	3.8	9.3	17.4	23.3	< 0.0001
Fall or fracture	10.2	14.9	20.2	27.2	< 0.0001
Health-related behaviors, %					
Current smoker	15.4	11.9	9.6	9.1	< 0.0001
Current alcohol drinker	39.6	34.9	29.3	29.3	< 0.0001

*Combined category of original two categories "very mild" and "mild." †Combined category of original two categories "severe" and "very severe." ‡To consult when you are in trouble. §Motor function score in Kihon Checklist greater than or equal to 3. ‖Kessler six-item psychologic distress scale greater than or equal to 13.

Table 2. Relation between Pain and Incident Functional Disability

Incident Functional Disability	Pain Severity				*P* Trend
	None	Mild*	Moderate	Severe†	
No. of participants	3,000	6,847	2,899	956	
Person-years of follow-up	15,047	34,489	13,793	4,397	
Total no. of cases	466	1,234	709	277	
Unadjusted	1.00 (reference)‡	1.16 (1.04–1.29)	1.67 (1.49–1.88)	2.06 (1.78–2.39)	< 0.001
Model 1§	1.00 (reference)	1.08 (0.97–1.20)	1.43 (1.27–1.60)	1.82 (1.57–2.11)	< 0.001
Model 2‖	1.00 (reference)	0.99 (0.89–1.10)	1.15 (1.02–1.31)	1.31 (1.12–1.54)	< 0.001

*Combined category of original two categories "very mild" and "mild." †Combined category of original two categories "severe" and "very severe." ‡Hazard ratio (95% CI). §Model 1 was adjusted for age and sex (among all participants). ‖Model 2 was adjusted as for model 1 plus history of disease (stroke, myocardial infarction, hypertension, diabetes mellitus, cancer, arthritis, osteoporosis, or fracture [yes, no]), educational level (age at last school graduation: less than or equal to 15 yr, 16 to 18 yr, greater than or equal to 19 yr, or missing), smoking (never, former, current, or missing), alcohol drinking (never, former, current, or missing), body mass index (in kg/m^2: less than 18.5, 18.5 to 24.9, greater than or equal to 25.0, or missing), motor function score (less than 3, greater than or equal to 3, or missing), psychologic distress score (less than 13, greater than or equal to 13, or missing), social support (whether participant had a consultant when in trouble [yes, no, or missing]).

functional disability stratified according to the major causes of disability.

Although many cross-sectional studies have reported a strong association between pain and functional disability,[1,8–12] the existing data regarding a longitudinal association between pain and disability were inconsistent. Several studies demonstrated a positive association between pain and functional disability,[13–17] but one large population-based cohort study in 2013 by Andrews *et al.*[18] showed a null association between pain and ADL disability or death. The inconsistency between these studies may be partially attributable to methodologic limitations such as small sample size, not population based, younger study populations, lower follow-up rates, and discrepancies in the definitions and assessments of pain and disability.

Our study has several strengths including (1) older participants (aged 65 yr old or older); (2) a large population-based cohort of 13,702 persons; (3) a follow-up rate of almost 100%; and (4) an objective and chronologically intermittent case ascertainment. The current study is the first large population-based prospective study demonstrating a positive association between pain severity and future functional disability.

Table 3. Relation between Pain and Cause-specific Incident Functional Disability

Incident Functional Disability	Pain Severity				*P* Trend
	None	Mild*	Moderate	Severe†	
Person-years of follow-up	15,047	34,489	13,793	4,397	
Stroke (405)					
No. of cases	82	194	95	34	
Unadjusted	1.00 (reference)‡	1.03 (0.80–1.34)	1.27 (0.95–1.71)	1.43 (0.96–2.14)	0.026
Model 1§	1.00 (reference)	1.05 (0.81–1.36)	1.27 (0.94–1.71)	1.47 (0.98–2.20)	0.024
Model 2‖	1.00 (reference)	0.98 (0.75–1.27)	1.05 (0.76–1.43)	1.07 (0.70–1.64)	0.669
Dementia (453)					
No. of cases	109	216	95	33	
Unadjusted	1.00 (reference)	0.87 (0.69–1.09)	0.96 (0.73–1.26)	1.05 (0.71–1.55)	0.872
Model 1	1.00 (reference)	0.78 (0.62–0.98)	0.76 (0.58–1.00)	0.87 (0.59–1.28)	0.184
Model 2	1.00 (reference)	0.76 (0.60–0.96)	0.70 (0.52–0.94)	0.74 (0.49–1.12)	0.041
Joint disease/fracture (536)					
No. of cases	55	217	176	88	
Unadjusted	1.00 (reference)	1.72 (1.28–2.32)	3.52 (2.60–4.76)	5.55 (3.96–7.77)	< 0.001
Model 1	1.00 (reference)	1.48 (1.10–1.99)	2.65 (1.95–3.59)	4.30 (3.06–6.03)	< 0.001
Model 2	1.00 (reference)	1.25 (0.93–1.69)	1.88 (1.37–2.58)	2.76 (1.93–3.95)	< 0.001

*Combined category of original two categories "very mild" and "mild." †Combined category of original two categories "severe" and "very severe." ‡Hazard ratio (95% CI). §Adjusted as for model 1 in table 2. ‖Adjusted as for model 2 in table 2.

Table 4. Relation between Pain and Incident Functional Disability (2-yr Disability Incident Excluded; n = 12,591)

Incident Functional Disability	Pain Severity				*P* Trend
	None	Mild*	Moderate	Severe†	
No. of participants	2,801	6,386	2,574	830	
Person-years of follow-up	14,762	33,830	13,356	4,231	
Total no. of cases	267	773	384	151	
Unadjusted	1.00 (reference)‡	1.27 (1.10, 1.46)	1.62 (1.38, 1.89)	2.04 (1.67, 2.49)	< 0.001
Model 1§	1.00 (reference)	1.16 (1.00, 1.33)	1.37 (1.17, 1.60)	1.77 (1.45, 2.16)	< 0.001
Model 2‖	1.00 (reference)	1.08 (0.94, 1.24)	1.16 (0.98, 1.37)	1.38 (1.12, 1.71)	0.003

*Combined category of original two categories "very mild" and "mild." †Combined category of original two categories "severe" and "very severe." ‡Hazard ratio (95% CI). §Adjusted as for model 1 in table 2. ‖Adjusted as for model 2 in table 2.

Table 5. Additional Analysis: Relation between Pain and Incident Functional Disability (Past History Excluded; n = 9,032)

Incident Functional Disability	Pain Severity				*P* Trend
	None	Mild*	Moderate	Severe†	
No. of participants	2,516	4,638	1,487	391	
Person-years of follow-up	12,686	23,498	7,120	1,856	
Total no. of cases	362	760	325	86	
Unadjusted	1.00 (reference)‡	1.13 (1.00–1.29)	1.61 (1.38–1.87)	1.64 (1.30–2.07)	< 0.001
Model 1§	1.00 (reference)	1.11 (0.98–1.26)	1.48 (1.27–1.72)	1.59 (1.26–2.01)	< 0.001
Model 2‖	1.00 (reference)	1.03 (0.91–1.17)	1.25 (1.07–1.45)	1.23 (0.96–1.56)	0.004

*Combined category of original two categories "very mild" and "mild." †Combined category of original two categories "severe" and "very severe." ‡Hazard ratio (95% CI). §Adjusted as for model 1 in table 2. ‖Adjusted as for model 2 in table 2 except for history of arthritis, osteoporosis, and fracture.

In the current study, we also found a negative association between pain severity and disability due to dementia. Whether pain predicts future cognitive function is an important question that needs to be answered. Some cross-sectional studies have reported that pain has been associated with poorer cognitive function, suggesting that pain may require attention and may compete for limited attentional resources.[40–42] On the other hand, several recent cohort studies reported that a longer duration of nonsteroidal antiinflammatory drug (NSAID) treatment can reduce the risk of Alzheimer disease or dementia in patients with rheumatoid arthritis.[43,44] It has been proposed that NSAIDs

Table 6. Relation between Pain and Incident Functional Disability

Incident Functional Disability	Pain Severity*						
	None	Very Mild	Mild	Moderate	Severe	Very Severe	*P* Trend
No. of participants	3,000	1,925	4,922	2,899	822	134	
Person-years of follow-up	15,047	9,762	24,727	13,793	3,789	608	
Total no. of cases	466	314	920	709	237	40	
Unadjusted	1.00 (reference)†	1.04 (0.90–1.20)	1.20 (1.08–1.35)	1.67 (1.49–1.88)	2.05 (1.75–2.40)	2.15 (1.56–2.97)	< 0.001
Model 1‡	1.00 (reference)	1.05 (0.91–1.21)	1.09 (0.97–1.22)	1.43 (1.27–1.60)	1.86 (1.59–2.18)	1.61 (1.17–2.23)	< 0.001
Model 2§	1.00 (reference)	1.01 (0.87–1.16)	0.98 (0.88–1.10)	1.15 (1.02–1.31)	1.34 (1.13–1.58)	1.19 (0.86–1.65)	0.001

*Original six categories. †Hazard ratio (95% CI). ‡Adjusted as for model 1 in table 2. §Adjusted as for model 2 in table 2.

Table 7. Relation between Pain and Cause-specific Incident Functional Disability (Joint Disease/Fracture)

Incident Functional Disability	Pain Severity*						
	None	Very Mild	Mild	Moderate	Severe	Very Severe	*P* Trend
No. of participants	3,000	1,925	4,922	2,899	822	134	
Person-years of follow-up	15,047	9,762	24,727	13,793	3,789	608	
Total number of cases	55	41	176	176	78	10	
Unadjusted	1.00 (reference) †	1.15 (0.77–1.72)	1.95 (1.44–2.64)	3.52 (2.60–4.76)	5.71 (4.04–8.06)	4.55 (2.32–8.92)	< 0.001
Model 1‡	1.00 (reference)	1.10 (0.74–1.65)	1.61 (1.19–2.18)	2.66 (1.96–3.60)	4.51 (3.19–6.39)	3.17 (1.62–6.23)	< 0.001
Model 2§	1.00 (reference)	1.01 (0.67–1.51)	1.34 (0.98–1.82)	1.90 (1.38–2.61)	2.88 (1.99–4.16)	2.27 (1.15–4.50)	< 0.001

*Original six categories. †Hazard ratio (95% CI). ‡Adjusted as for model 1 in table 2. §Adjusted as for model 2 in table 2.

decrease brain inflammation and act as protective agents for neural injury in the brain. Although the impact of NSAID treatment upon dementia risk is an interesting question, our study did not assess medication use.

To minimize the effects of reverse causality, we repeated all analyses after excluding participants who developed incident functional disability in the first 2 yr of follow-up. However, the association between pain severity and incident functional disability did not change (table 4). In addition, even in the sensitivity analysis excluding participants with a history of joint disease/fracture (arthritis, osteoporosis, and falls or fractures) at baseline, the positive association did not change substantially (table 5). These findings suggest that the current results are unlikely to be attributable to reverse causality.

This study had several limitations. First, changes in pain severity during the follow-up period were not measured. In particular, we did not have information regarding pain treatment and medication. Second, not all candidates applied for LTCI certification; therefore, we cannot rule out the possibility of detection bias. Third, we measured psychologic distress with the K6 instead of using a clinical diagnosis made by a psychiatrist; therefore, data regarding psychologic distress might be limited.

With the aging population, the number of elderly individuals with disability is rapidly increasing.[6] Functional disability threatens the quality of life of the elderly.[45] In addition, late-life functional disability significantly increases the LTC burden and increases demands on the social security system. Organisation for Economic Co-operation and Development reported that government and private market spending on LTC in 2010 was as much as 1.5% of the gross domestic product of Organisation for Economic Co-operation and Development countries and will double or triple by 2050.[6] Disabled or frail patients have been found to be at a much higher risk of adverse postoperative outcomes such as mortality, morbidity, and institutionalization after surgery.[46,47] Therefore, it is crucial to develop effective measures to detect and treat risk factors for incident functional disability. Our results emphasize the clinical importance of the prompt identification and management of pain in older adults to extend their healthy life expectancy. The assessment of pain is easy and inexpensive, and the presence of pain should be routinely assessed during general medical examinations in elderly patients. The presence of pain should warrant appropriate pain relief treatment and additional interventions, including rehabilitation services, to improve the patient's functional status.

In conclusion, this study has shown a strong longitudinal relationship between pain severity and functional disability. The relationship was particularly remarkable among individuals who developed disability due to joint disease/fracture.

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Competing Interests

The authors declare no competing interests.

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Address correspondence to Dr. Kaiho: Division of Epidemiology, Department of Health Informatics and Public Health, Tohoku University School of Public Health, Graduate School of Medicine 2-1, Seiryo-machi, Aoba-ku, Sendai, Miyagi 980–8575, Japan. yu.kaiho@med.tohoku.ac.jp. Information on purchasing reprints may be found at www.anesthesiology.org or on the masthead page at the beginning of this issue. ANESTHESIOLOGY's articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

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Appendix. Additional Analysis: Relation between Pain and Incident Functional Disability (Competing-risks Model#)

	Pain Severity				
Incident Functional Disability	None	Mild*	Moderate	Severe†	*P* Trend
No. of participants	3,000	6,847	2,899	956	
Person-years of follow-up	15,047	34,489	13,793	4,397	
Total no. of cases	466	1,234	709	277	
Unadjusted	1.00 (reference)‡	1.17 (1.05–1.30)	1.67 (1.49–1.88)	2.05 (1.76–2.38)	< 0.001
Model 1§	1.00 (reference)	1.11 (0.99–1.23)	1.42 (1.26–1.61)	1.82 (1.56–2.13)	< 0.001
Model 2‖	1.00 (reference)	1.03 (0.92–1.15)	1.17 (1.02–1.33)	1.36 (1.15–1.60)	< 0.001

*Combined category of original two categories "very mild" and "mild." †Combined category of original two categories "severe" and "very severe." ‡Hazard ratio (95% CI). §Model 1 was adjusted for age and sex (among all participants). ‖Model 2 was adjusted as for model 1 plus history of disease (stroke, myocardial infarction, hypertension, diabetes mellitus, cancer, arthritis, osteoporosis, or fracture [yes, no]), educational level (age at last school graduation: less than or equal to 15 yr, 16 to 18 yr, greater than or equal to 19 yr, or missing), smoking (never, former, current, or missing), alcohol drinking (never, former, current, or missing), body mass index (in kg/m^2: less than 18.5, 18.5 to 24.9, greater than or equal to 25.0, or missing), motor function score (less than 3, greater than or equal to 3, or missing), psychologic distress score (less than 13, greater than or equal to 13, or missing), social support (whether participant had a consultant when in trouble [yes, no, or missing]). #Competitive event was defined as disability-free death.