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ORIGINAL ARTICLE

Alexithymia, Depression, Inflammation, and Pain in Patients With Rheumatoid Arthritis

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Objective. **We previously reported that depression and inflammation have independent effects on pain severity in patients with rheumatoid arthritis (RA). Alexithymia is a personality trait characterized by deficits in cognitive processing and regulation of emotions. A broad association between alexithymia and various health problems has been suggested, including depression, inflammation, and pain. The objective of this study was to examine the independent influence of alexithymia on pain perception and its relationship to depression and inflammation.**
Methods. **We evaluated 213 RA outpatients who completed self-administered questionnaires, including the Beck Depression Inventory-II (BDI-II) to measure depression severity, the 20-item Toronto Alexithymia Scale (TAS-20) to measure degree of alexithymia, and a visual analog scale to quantify perceived pain. Serum C-reactive protein (CRP) levels were measured to quantify inflammation severity.**
Results. **An initial significant positive association between the TAS-20 score and pain severity ($P = 0.01$) lost significance after controlling for BDI-II score and CRP level using regression analysis. An interaction was observed among alexithymia, depression, and inflammation with regard to perceived pain. Among those without alexithymia, pain severity increased linearly with the CRP tertile levels regardless of the presence of depression ($P < 0.001$ for trend). No linear association between pain severity and CRP level was observed among those with alexithymia. Moreover, depressed patients with alexithymia (BDI-II score ≥14 and TAS-20 score ≥61) reported severe pain even at low CRP levels.**
Conclusion. **Alexithymia might have a substantial role in pain perception as well as depression in patients with RA. A biopsychosocial approach is essential to achieve better pain control.**

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic disease in which an autoimmune disorder causes inflammation of the joints and surrounding tissues. Patients with RA experience persistent pain, arising from inflammation. This pain is also known to possess a strong emotional component and is affected by mood and psychosocial factors (1). We previously reported the independent influences of depression severity and inflammation on perceived pain in patients with RA (2). Both the depression score and the serum levels of C-reactive protein (CRP), a biomarker of inflammation, were significantly associated with pain, even after controlling for each other and for clinical covariates by regression analysis.

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Significance & Innovations

- Alexithymia, which is a personality trait characterized by the inability to identify and describe one's own feelings and a preference for externally oriented thinking rather than introspection, is considered as a risk factor that is broadly associated with various mental and physical health problems.
- This is the first study to evaluate the interrelationships between alexithymia, depression, inflammation, and perceived pain intensity in patients with rheumatoid arthritis (RA).
- Alexithymia might have played a substantial role in pain perception, and when it was coupled with depression, it could separate the perception of pain from the physical effects of inflammation.
- Therefore, to achieve appropriate pain control in all patients with RA, the assessment of alexithymia and use of biopsychosocial approaches would be required, in addition to traditional pharmaceutical interventions.

Alexithymia is defined as a personality construct with difficulties in affective self-regulation (3). It has been proposed to be a cluster of cognitive and affective characteristics that are commonly observed among classic psychosomatic patients for whom therapy has been unsuccessful (4). Individuals with alexithymia tend to experience difficulties in identifying and describing their inner feelings and have a limited imaginary capacity and a preference for externally oriented thinking rather than introspection (3). To date, alexithymia has been reported to have a broad association with various mental and physical problems, including depression (5), inflammation (6–8), and pain (9). Furthermore, alexithymia is suspected to be an important psychosocial factor affecting disease control and health promotion (10–12).

Pain is a personal, subjective experience produced by multiple influences and is composed of sensory, affective, and cognitive dimensions (13). Considering the construct of alexithymia reflecting deficits in cognitive processing and the regulation of emotions, alexithymia may play some role in pain perception. A high prevalence of alexithymia has been observed in patients with chronic pain (9), including those with RA (14,15). Numerous observational and some experimental studies revealed positive associations between alexithymia and pain intensity and sensitivity (16). However, there are some conflicting reports; alexithymia has been suggested to be associated with poor awareness of physical symptoms, such as cardiac pain, resulting in a delay of seeking treatment (17). One possible reason for this inconsistency may be the influence of negative affect. Alexithymia has been reported to be associated with negative affect (5), which is substantially associated with pain (1). Pain and depression often coexist and each increases the gravity of the other, since they share several pathophysiologic pathways, including neuroendocrine and immune activities (18). The independent effect of alexithymia on pain perception has rarely been examined so far. Hosoi et al examined 129 patients with neuromuscular disorders and found that the association between alexithymia and pain intensity is greatly diminished when controlling for baseline negative affect (19). Another shortcoming of previous studies is that most of them evaluated the output of pain without considering the inputs of pain (13). According to recent experimental studies, those with alexithymia may be insensitive to their own physical sensation when the external stimuli are not strong enough (16,20).

The purpose of this study was to examine the independent impact of alexithymia on pain perception among patients with RA. From accumulating evidence, we hypothesized that the association of perceived pain severity is altered by the level of inflammation and by the presence of depression and alexithymia. It is speculated that RA patients with alexithymia may report more severe pain than the level estimated from CRP results when they are depressed because they are unable to modulate their own feelings and tend to amplify bodily sensations due to psychological distress (21). On the other hand, patients with alexithymia may be less responsive to inflammation when they are not depressive because of their external focus of attention (17).

To our knowledge, this is the first study assessing the interrelationships between alexithymia, depression, inflammation, and pain perception. We explored how alexithymia may intervene in the association we had observed in the previous study.

PATIENTS AND METHODS

We conducted a secondary analysis of data from the observational study focusing on the association between the psychosocial factors and clinical evaluations in patients with RA. The study protocol followed has been described in detail in a previous publication (2). The Research Ethics Committee of Nagoya City University Graduate School of Medical Sciences, Japan approved the research protocol.

Subjects. The study subjects were selected from among patients who met the criteria of the American College of Rheumatology (22) and attended the Outpatient Rheumatology Clinic of Nagoya University Hospital (Nagoya, Japan) between March 7 and April 18, 2003. During this period, trained research assistants invited 321 eligible patients to participate in the study after briefly explaining the protocol. Of these 321 patients, 303 provided written informed consent for participation and completed the self-administered questionnaires. Finally, a total of 218 patients, who completed all of the clinical examinations and questionnaire surveys, were included in the current study.

Measures. All of the patients who agreed to participate in the study were asked to complete self-administered questionnaires that reported their sociodemographic characteristics, smoking and drinking habits, year of RA onset, and current perceived pain severity using a visual analog scale. The details of the questionnaire have been described in a previous study (2). In addition, the questionnaire included a battery of well-validated self-reporting inventories for evaluation of psychosocial factors. Alexithymia was evaluated using the Japanese version (23) of the 20-item Toronto Alexithymia Scale (TAS-20) (24,25), which is the most internationally popular instrument to assess alexithymia (12). Total TAS-20 scores range from 20–100, and a score of ≥61 was suggested for use in alexithymia screening by the original authors (25). Depression severity was assessed using the Japanese version (26) of the Beck Depression Inventory-II (BDI-II) (27). BDI-II scores range from 0–63, and a score of ≥14 indicates the presence of at least mild to moderate symptoms of depression (27,28).

As part of routine clinical examinations, experienced rheumatologists who were unaware of patients' participation in this study assessed the number of swollen and/or tender joints along with the Steinbrocker functional classification (29) and made a global assessment of disease severity for each of their patients. Serum CRP levels were measured using standard methodology (30) on a JCA-BM 2250 autoanalyzer (JEOL) with CRP-Latex (II) X2 SEIKEN reagents from Denka Seiken. Inter- and intraassay variations of the measurements for CRP were <10%.

Blood sampling, clinical assessment, and the self-administered questionnaire were completed on the same day. The time intervals between them were <12 hours (2–4 hours for most patients).

Statistical analysis. Data were analyzed using SPSS for Windows (IBM SPSS statistics 19). All statistical tests were 2-sided. A P value of less than 0.05 was considered significant, and a value between 0.05 and 0.1 was considered marginally significant. Each variable was visually inspected to validate the assumption of a normal distribution. The CRP data were natural log–transformed after adding 1 to each value, since these data were skewed and 2 of the subjects had values of 0.

The background characteristics of the patients were initially compared on the basis of the presence of alexithymia using the chi-square test for categorical variables and the *t*-test for continuous variables. A TAS-20 score of 61 was used as the cutoff to define the presence of alexithymia (25). To explore the relationships between variables, Pearson's correlation coefficients were calculated.

Thereafter, linear regression analyses were performed to evaluate the independent association of the TAS-20, the BDI-II, and the log-transformed CRP with perceived pain severity. The dependent variable was pain severity, and each variable was individually entered as an independent variable initially. Subsequently, CRP, TAS-20, and BDI-II scores were entered into the same model in succession. Variables to be entered as potential confounders into the final model were selected from those that exhibited a significant correlation with perceived pain and any of the TAS-20, BDI-II, or CRP scores (31).

To confirm the hypotheses that RA patients with alexithymia perceive more severe pain than expected, based on their level of inflammation and depression, interaction terms between the TAS-20, the BDI-II, and CRP were entered into the regression model. Upper and lower tertiles were used as cutoff points to categorize CRP level into 3 groups. Further, the subjects were divided into 4 groups according to the presence or absence of depression (BDI-II score ≥14) and alexithymia (TAS-20 score ≥61). Regression analysis was conducted separately to estimate the impact of CRP level on pain severity perceived by the groups. Finally, average pain severity by the low, middle, and high levels of CRP by the presence of depression and alexithymia adjusted for covariates was estimated by using analysis of covariance. Upper and lower tertiles were used as cutoff points to categorize CRP into 3 levels.

RESULTS

Background characteristics and the presence of alexithymia. The mean ± SD age of the subjects was 60 ± 12 years and 81.7% were women. In total, 46 patients (21.6%) had alexithymia according to the TAS-20 cutoff score of ≥61. The demographic, laboratory, and psychosocial variables, organized on the basis of the presence of alexithymia, are shown in Table 1. Subjects with alexithymia were more likely to be unmarried, be living alone, have incomplete higher education, and have severe physical disabilities compared with those without alexithymia. Both the pain and BDI-II scores of those with alexithymia were higher compared with those without alexithymia. There were no differences in age, sex, disease duration, or CRP level between those with and without alexithymia.

Interrelationships between variables. Pearson's correlation coefficients between the variables TAS-20 score, BDI-II score, and CRP level, along with the potential covariates physical function, age, living status, and educational level, are listed in Table 2. TAS-20 score revealed statistically significant correlations with BDI-II score, physical function, and years of education. TAS-20 score was not significantly associated with CRP level, whereas BDI-II score was positively associated with CRP level and physical function. In addition, age was significantly correlated only with physical function.

Perceived pain severity was significantly correlated with TAS-20 and BDI-II scores, CRP level, age, the total number of swollen joint counts, physical function, and years of education (data are not shown in the table because equivalent data are shown in Table 3). However, sex was only marginally associated with CRP level ($r = 0.13$, $P = 0.06$) and living status ($r = -0.12$, $P = 0.07$) and was not associated with pain, TAS-20 score, or BDI-II score. Therefore, the combined data of men and women were used for further analysis.

Independent influence of alexithymia on perceived pain. To investigate the independent influence of alexithymia on perceived pain, a hierarchical regression analysis was conducted. The standardized beta coefficient of each variable is shown in Table 3. When TAS-20 and BDI-II scores were entered into the same model, the association between TAS-20 score and perceived pain severity

Table 1. Demographic, clinical, and psychosocial characteristics of the patients with RA by the presence of alexithymia*

Variables	Total (n = 213) Value	Total (n = 213) Range	Alexithymic, TAS-20 ≥61 (n = 46)	Nonalexithymic, TAS-20 <61 (n = 167)	*P*
Sociodemographic characteristics					
Age, years	60.0 ± 12.0	18–85	61.2 ± 10.6	59.4 ± 12.4	0.35
Women, %	81.7		80.4	82.6	0.73
Married, %	75.8		62.8	79.0	0.03
Living alone, %	10.6		21.7	7.8	0.01
Current smoker, %	14.6		15.2	13.8	0.80
Education >12 years, %	22.0		11.9	24.6	0.02
Total income >$60,000/year, %	23.3		8.7	26.4	0.05
Clinical characteristics					
RA disease duration, years	11.7 ± 10.6	0.2–60.8	13.0 ± 11.0	11.3 ± 10.6	0.40
Functional disability	2.1 ± 0.7	1–4	2.3 ± 0.6	2.0 ± 0.7	0.01
Rheumatologist global severity	35.6 ± 17.5	0–91	37.0 ± 15.3	35.1 ± 18.0	0.50
Total number of tender joints	2.8 ± 3.9	0–27	2.8 ± 3.3	2.7 ± 4.0	0.86
Total number of swollen joints	4.2 ± 5.4	0–40	3.0 ± 3.0	4.4 ± 5.9	0.03
CRP, mg/liter	2.1 ± 2.4	0–13.9	2.2 ± 2.6	2.1 ± 2.3	0.78
Perceived pain	34.6 ± 24.3	0–100	44.2 ± 22.8	32.1 ± 24.4	0.003
Depressive symptoms (BDI-II)	12.9 ± 9.6	0–48	23.0 ± 11.1	10.3 ± 7.0	< 0.001

* Values are the mean ± SD unless indicated otherwise. RA = rheumatoid arthritis; TAS-20 = 20-item Toronto Alexithymia Scale; CRP = C-reactive protein; BDI-II = Beck Depression Inventory-II.

was attenuated and inverted, whereas the impact of BDI-II score on the pain level was unaltered. By further adding CRP level into the model, the association between TAS-20 score and the pain level became insignificant. However, BDI-II score and CRP level were both independently associated with perceived pain severity even after controlling for age, total number of swollen joints, functional disability, and educational level.

Interaction between alexithymia, depression, inflammation, and perceived pain. A marginally significant interaction was confirmed between perceived pain and the variables TAS-20 score, BDI-II score, and CRP level by adding the interaction terms in the trivariable model ($P = 0.07$). Further, a significant interaction was observed between perceived pain and the variables BDI-II score and CRP level only among those with alexithymia ($P = 0.03$).

Table 2. Pearson's correlation coefficients between alexithymia, depression, C-reactive protein (CRP) level, and covariates

Variables	Alexithymia*	Depression†	CRP‡	Total no. of swollen joint counts	Functional disability§	Age
Depression†						
r	0.58	1.00				
P	< 0.001					
CRP‡						
r	0.01	0.17	1.00			
P	1.00	0.01				
Total no. of swollen joint counts						
r	−0.08	0.05	0.47	1.00		
P	0.27	0.44	< 0.001			
Functional disability§						
r	0.14	0.29	0.36	0.27	1.00	
P	0.04	< 0.001	< 0.001	< 0.001		
Age						
r	−0.01	0.07	0.08	0.11	0.21	1.00
P	0.85	0.28	0.26	0.12	0.002	
Years of education						
r	−0.23	−0.19	−0.09	−0.02	−0.12	−0.35
P	0.001	0.01	0.19	0.73	0.07	< 0.001

* Measured with the 20-item Toronto Alexithymia Scale.
† Measured with the Beck Depression Inventory-II.
‡ Each CRP value was natural log–transformed after adding 1.
§ Determined according to Steinbrocker functional classification.

Table 3. Linear regression analyses showing the contribution of alexithymia, depression, natural log–transformed C-reactive protein (CRP) level, and covariates to perceived pain severity in rheumatoid arthritis patients

	Univariable model		Bivariable model*		Trivariable model†		Multiadjusted model‡	
Dependent variables	Standardized β	P	Standardized β	P	Standardized β	P	Standardized β	P
Alexithymia§	0.17	0.01	−0.13	0.08	−0.07	0.28	−0.08	0.25
Depression¶	0.45	< 0.001	0.53	< 0.001	0.43	< 0.001	0.40	< 0.001
CRP#	0.45	< 0.001			0.38	< 0.001	0.35	< 0.001
Age	0.16	0.02					0.07	0.26
Total no. of swollen joint counts	0.20	0.004					−0.03	0.66
Functional disability**	0.34	< 0.001					0.10	0.12
Education >12 years	−0.18	0.009					−0.06	0.32

* $R^2 = 0.22$, $F[2,210] = 28.7$, $P < 0.001$.
† $R^2 = 0.36$, $F[3,209] = 38.3$, $P < 0.001$.
‡ $R^2 = 0.22$, $F[7,205] = 17.6$, $P < 0.001$.
§ Measured with the 20-item Toronto Alexithymia Scale.
¶ Measured with the Beck Depression Inventory-II.
# Each CRP value was natural log–transformed after adding 1.
** Determined according to Steinbrocker functional classification.

Average pain severity reported by subjects with low, middle, and high CRP levels, arranged according to the presence or absence of depression and alexithymia and adjusted for age and functional disability, is displayed in Figure 1. Among those without alexithymia, perceived pain severity increased linearly with the level of CRP, regardless of the presence of depression. Among nondepressed patients with alexithymia, the high CRP level subgroup revealed higher average pain severity compared with that in the middle and low CRP level subgroups, but no difference was observed between the middle and low CRP level subgroups. Moreover, among depressed patients with alexithymia, pain severity was comparable across all CRP levels.

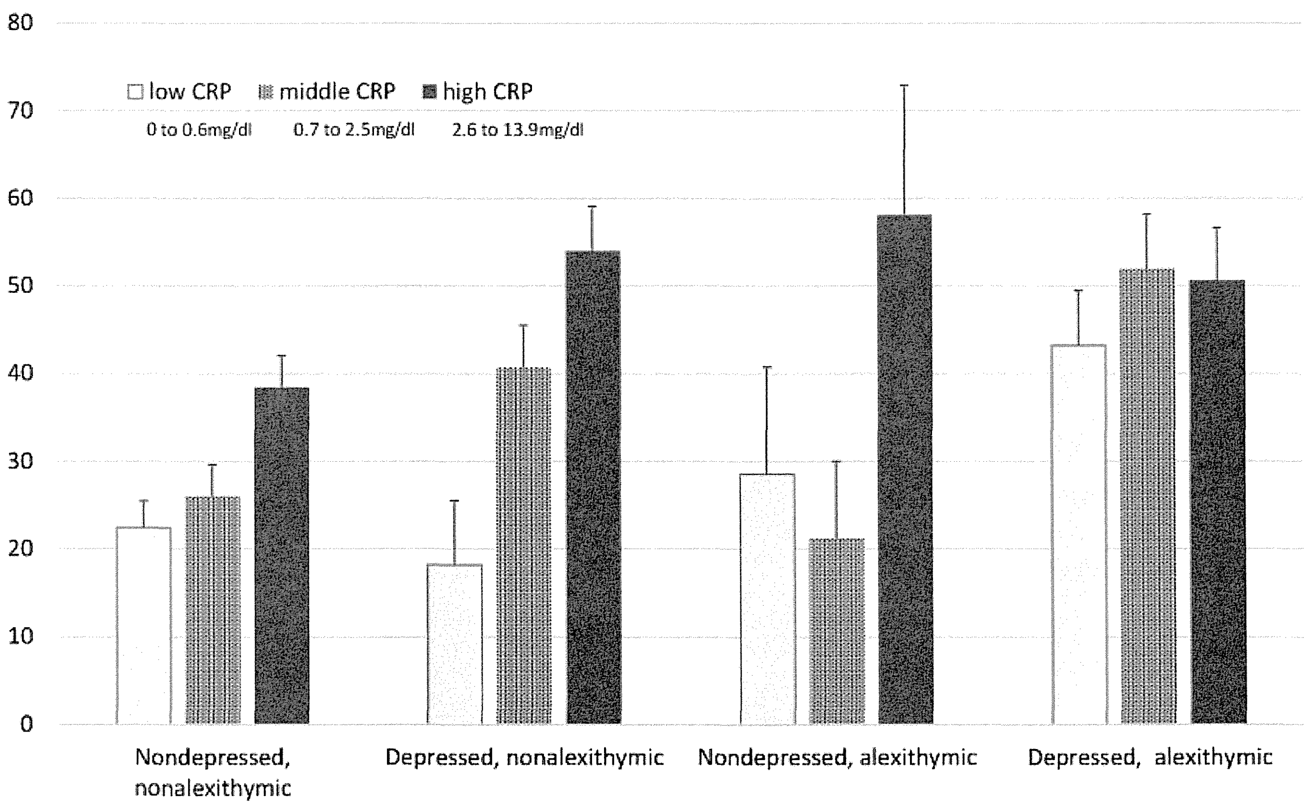

Figure 1. Average pain severity reported by subjects with low, middle, and high C-reactive protein (CRP) levels, arranged according to the presence or absence of depression (Beck Depression Inventory-II score ≥14 or <14) and alexithymia (20-item Toronto Alexithymia Scale score ≥61 or <61), adjusted for age and functional disability. Upper and lower tertiles were used as cutoff points to categorize CRP into 3 levels (0–0.6, 0.7–2.5, and 2.6–13.9 mg/dl).

Table 4. Effect of CRP level on perceived pain severity (increase of 1 mg/dl) by the presence of depression and alexithymia*

		Unadjusted		Adjusted	
	N	$\beta \pm$ SE	*P*	$\beta \pm$ SE	*P*
Nonalexithymic, nondepressed (TAS-20 <61, BDI-II <14)	120	14.5 ± 2.9	< 0.001	12.6 ± 3.5	0.001
Nonalexithymic, depressed (TAS-20 <61, BDI-II ≥14)	47	24.0 ± 4.8	< 0.001	23.3 ± 5.8	< 0.001
Alexithymic, nondepressed (TAS-20 ≥61, BDI-II <14)	12	18.9 ± 7.7	0.04	18.3 ± 10.0	0.13
Alexithymic, depressed (TAS-20 ≥61, BDI-II ≥14)	34	7.0 ± 5.5	0.21	2.7 ± 7.0	0.70

* Adjusted for age, total number of swollen joint counts, functional disability, and educational level. CRP = C-reactive protein; TAS-20 = 20-item Toronto Alexithymia Scale; BDI-II = Beck Depression Inventory-II.

The estimated impacts of CRP level on perceived pain arranged by the presence or absence of depression and alexithymia are shown in Table 4. CRP level was significantly associated with perceived pain severity among those without alexithymia, irrespective of the presence of depression, even after controlling for age, total number of swollen joint counts, functional disability, and educational level. Moreover, among nondepressed patients with alexithymia, the linear association between CRP level and pain severity became insignificant after adjusting for covariates. However, no association was observed between CRP level and pain severity among the group of depressed patients with alexithymia.

DISCUSSION

In a previous study, we reported that perceived pain increased independently in proportion with CRP and depression levels (2). In the present study, we provide additional information regarding these associations. Considering that pain is an unpleasant experience with sensory, affective, and cognitive dimensions (13), it is not surprising that alexithymia, a disorder of affect regulation with a cluster of cognitive and affective characteristics, is substantially associated with pain perception.

We confirmed that RA patients with alexithymia report more severe pain than expected because of inflammation. According to the present results, the severity of perceived pain increased independently in a linear fashion with increased CRP levels and with depression only among those without alexithymia. In contrast, among patients with alexithymia, the association between CRP level and depression was more complicated and differed with respect to the presence of depressive symptoms. If they were depressed, patients with alexithymia tended to report severe pain regardless of the inflammation level. Conversely, nondepressed patients with alexithymia did not report severe pain when they had mild to moderate inflammation. Nondepressed patients with alexithymia reported severe pain only when their CRP levels were high.

Two different types of persistent pain are known to exist: nociceptive (inflammatory) pain and neuropathic pain (32). Nociceptive pain is triggered by inflammation, which stimulates nociceptive receptors at the periphery of the nervous system (33). Therefore, it is natural that perceived pain severity increases linearly with CRP level, reflecting the stimulation of nociceptive pain receptors. The present study indicates the possibility that patients with alexithymia are sensitive to neuropathic pain, but not to nociceptive pain. Thus far, the association between alexithymia and nociceptive pain has never been directly discussed. Considering the characteristics of alexithymia, which include difficulty in distinguishing between emotional feelings and physical states (5), it is understandable that patients with alexithymia may be insensitive to mild to moderate physical stimulation originating from their inner body when they are not under emotional stress. A recent experimental study supports our speculation. Herbert et al examined 155 healthy students who had no or only minimal depressive symptoms (mean ± SD BDI-II score 3.52 ± 3.11) and found that the total TAS-20 score was inversely associated with interoceptive awareness, which was measured by the ability to count one's heartbeat (20). Future studies should confirm the interaction between emotional distress and the strength of internal or external stimuli on symptom perception in patients with alexithymia. The findings of such a study may partly explain unhealthy behaviors, including the delay in health care utilization, low compliance, or other behaviors that can lead to poor health outcomes, including early death, that have been consistently observed in the population with alexithymia (11).

Previous studies have repeatedly suggested the necessity of detecting and managing depression in patients attending rheumatology clinics (34–37). The present results clearly suggest the importance of considering the presence and influences of alexithymia when designing an effective approach to reduce pain in RA. According to our observation, if patients have high CRP levels, treatment focusing on inflammation should be prioritized regardless of the levels of alexithymia and depression. With regard to the patients with low to middle levels of CRP, the patients' alexithymic tendency should be considered when designing the pain control strategy. Patients without alexithymia reported increased pain in response to increasing levels of CRP or depression; therefore, antiinflammatory therapy will be effective for them, but a psychosocial approach should be considered as well, since the more depressed the patients are, the more pain they perceive. Further, with regard to patients with alexithymia, the effects of antiinflammatory therapy seem to be limited, and some psychosocial interventions must be necessary.

How should we approach patients with alexithymia? Treating depression using medication and/or psychotherapy has been reported to be difficult among patients with alexithymia (38–41), and methods to reduce alexithymia have not been established yet (42). Theoretically, supportive psychiatric treatments are recommended for patients with primary alexithymia, whereas modified psychodynamic therapies are considered well suited for those who develop secondary alexithymia as a reaction to stressful situations (43). Two randomized controlled studies demonstrated the effectiveness of 4 months of weekly group psychotherapy, including relaxation and role playing, for patients with coronary heart disease (44) and 5 months of weekly supportive individual psychotherapy for general psychiatric outpatients to reduce alexithymia levels (45). We need a greater accumulation of evidence to identify how to increase the effectiveness of alexithymia treatment. Cognitive–behavioral therapy (CBT) has been an established treatment option for the management of chronic pain (46). A course of therapy that begins with primary individual supportive therapy and continues following a more interpretive approach, focusing on the modification of alexithymic characteristics (45) combined with a CBT program to reduce pain, would be worth trying for patients with severe alexithymia.

A recent systematic review confirmed that psychological interventions in patients with RA had a small but significant beneficial effect (47). According to their comparative analyses, intervention techniques using the self-regulation theory (goal setting, planning, self-monitoring, feedback, and relapse prevention) were more effective in reducing depressive symptoms and anxiety. For individuals with alexithymia, such practical and behavioral approaches seem appropriate; however, the self-monitoring process might need to be modified. Rheumatologists' attention to the psychological problems of each patient and their collaboration with behavioral medicine specialists and expert clinical psychologists are essential to achieve appropriate treatment options (34).

Despite the relatively consistent findings of previous studies demonstrating a positive correlation between alexithymia and CRP level (6–8), we failed to confirm this correlation. Individuals with alexithymia, who are thought to be vulnerable to stressful situations and might have a weakened antiinflammatory buffer capacity, might also tend to have high CRP levels (8). One possible reason for the discrepancy might be the differences in patient characteristics. The subjects of the current study were all patients with RA who experienced chronic inflammation, whereas the previous study subjects were either physically healthy adults (6,7) or subjects randomized from the general population (8). In addition, significant racial/ethnic differences in the distribution of CRP have been known to exist as well (48). Future studies should confirm the differences related to the background of the study population.

There were some limitations to this study. First, we designed this study based on theories derived mainly from observational studies (3,5,9,12,17). Although we believe there were important clinical implications in our study, many issues have yet to be clarified. Recent advances in brain imaging have revealed the uniqueness of alexithymia in the neural response to internal and external stimuli (49), suggesting its possibility in utilizing a biopsychosocial approach in clinical practice (10). Second, the results of this study were based on data measured at a single time point; therefore, we could not assess the direction of the association, and any measurement error may have influenced the findings. Third, our subjects were selected from a group of patients with RA visiting the rheumatology clinic at our university. Although there were no significant differences in the background characteristics of RA patients who did and did not participate in the study, the sample may have differed from the RA patient population as a whole. Finally, we used self-reported measures to evaluate pain and psychological variables. Although the TAS-20 is the most common tool to measure alexithymia internationally, and self-report measures are more acceptable in the clinical setting (34), the use of observer-rated measures has been recommended (25). Future studies should be conducted chronologically along with subjective and objective measures of psychological factors associated with alexithymia.

In conclusion, although there are various interpretive limitations, alexithymia may play a substantial role in pain perception as well as depression. Assessment of alexithymia and the use of biopsychosocial approaches are essential in achieving better pain control in patients with RA.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Masayo Kojima had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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ORIGINAL ARTICLE: SOCIAL RESEARCH, PLANNING AND PRACTICE

Incidence of certified need of care in the long-term care insurance system and its risk factors in the elderly of Japanese population-based cohorts: The ROAD study

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Aim: To examine the incidence of certified need of care in the national long-term care insurance (LTCI) system, and to determine its risk factors in the elderly of Japanese population-based cohorts of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study.

Methods: Of the 3040 participants in the baseline examination of the ROAD study, we enrolled 1773 (699 men, 1074 women) aged 65 years or older who were not certified as in need of care level elderly at baseline. Participants were followed for incident certification of need of care in the LTCI system. Associated factors in the baseline examination with occurrence were determined by multivariate Cox proportional hazards regression analysis. Muscle dysfunction was defined in accordance with the European Working Group on Sarcopenia in Older People algorithm for screening sarcopenia.

Results: A total of 54 men and 115 women were certified as in need of care level elderly during the average 4.0-year follow up. The incidence was 2.0 and 2.5 per 100 person-years in men and women, respectively. Identified risk factors were region, age, body mass index <18.5 or ≥27.5 kg/m^2, grip strength, knee extension torque, usual gait speed, chair stand time and muscle dysfunction.

Conclusions: Both underweight and obesity, as well as low muscle strength and physical ability, are risk factors for certification of need of care. Considering muscle dysfunction is a risk factor for occurrence, screened individuals are recommended to receive early intervention programs regardless of muscle volume. **Geriatr Gerontol Int 2014; 14: 695–701.**

Keywords: activities of daily living, certification of need of care (*youkaigo-nintei*), disability, long-term care insurance system, prospective cohort study.

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 (seven levels, including requiring support [levels 1 and 2] and requiring long-term care [levels 1–5]). The total number of certified in need of care level elderly was reported to be 5 million in 2011.[2]

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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 required to reduce its risk and decrease the number of disabled elderly requiring care in their activities of daily living (ADL). For establishment of an evidence-based prevention strategy, it is critically important to accumulate epidemiological evidence including the incidence of certified need of care and identification of risk factors. However, there have been no studies to clarify the incidence of certified need of care in the LTCI system or its risk factors using large-scale, population-based cohorts.

In 2005, we started a large-scale, population-based cohort study entitled the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study with a total of 3040 participants, which aims to elucidate the environmental and genetic backgrounds of musculoskeletal diseases.[3,4] The present study investigated the incidence of certified need of care in the national LTCI system, and determined its risk factors using a database from the ROAD study.

Methods

Participants

The present 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, we created a baseline database from 2005–2007, which included clinical and genetic information on 3040 residents of Japan (1061 men, 1979 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 participants were randomly drawn from the register database of Itabashi ward residents, with a response rate of 75.6% in the group aged >60 years. Participants in the rural regions in Hidakagawa and Taiji were recruited from resident registration lists, with response rates of 68.4% and 29.3%, respectively, in the groups aged >60 years. Inclusion criteria were the ability to: (i) walk to the survey site; (ii) report data; and (iii) understand and sign an informed consent form. For the present study, we enrolled 1773 participants (699 men, 1074 women; mean age 75.4 years) aged 65 years or older who were not certified as need of care level elderly in the national LTCI system at baseline. All participants provided written informed consent, and the study was carried out with approval from the ethics committees of the University of Tokyo and the Tokyo Metropolitan Institute of Gerontology.

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. Underweight was defined as BMI <18.5 and obesity as BMI ≥27.5, according to the 2004 consensus statement from the WHO regarding appropriate BMI for Asian populations.[6] Grip strength was measured on bilateral sides using a handgrip dynamometer (TOEI LIGHT, Saitama, Japan); the higher measurement was recorded. Isometric peak knee extension torque was measured at a knee flexion angle of 90° using a dynamometer (GT-30; OG GIKEN, Okayama, Japan) twice in participants from the urban regional cohort (Itabashi, Tokyo); the higher measurement was recorded. The time taken to walk 6 m at usual walking speed in a hallway was recorded, and usual gait speed was calculated. Skeletal muscle dysfunction was defined as usual gait speed ≤0.8 m/s or grip strength <30 kg in men and <20 kg in women, according to the algorithm for screening sarcopenia recommended by the European Working Group on Sarcopenia in Older People (EWGSOP).[7,8] The time taken for five consecutive chair rises without the use of hands was recorded in the rural regional cohorts (Hidakagawa and Taiji, Wakayama). Hands were folded in front of the chest with feet flat on the floor. Timing began with the command "Go", and ended when the buttocks contacted the chair on the fifth landing.

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 ADL 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 the 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 ADL. Mental status, including dementia, is also assessed. These data are analyzed to calculate a

Table 1 Baseline characteristics of population at risk for certified need of care in the long-term care insurance system

	Entire cohort		Urban cohort		Rural cohort	
	Men	Women	Men	Women	Men	Women
No. participants	699	1,074	333	486	366	588
Age (years)	75.6 (5.1)	75.2 (5.3)	77.5 (3.7)	77.3 (3.8)	73.8 (5.5)†	73.5 (5.8)†
Height (cm)	160.9 (6.0)	147.9 (6.0)*	161.0 (5.8)	148.2 (5.4)*	160.8 (6.2)	147.7 (6.5)*
Weight (kg)	59.4 (9.1)	50.0 (8.3)*	59.4 (8.2)	49.8 (7.8)*	59.4 (9.9)	50.1 (8.8)*
BMI (kg/m²)	22.9 (2.9)	22.8 (3.4)	22.9 (2.7)	22.7 (3.3)	22.9 (3.1)	22.9 (3.5)
BMI <18.5 (%)	6.2	8.0	6.1	7.9	6.3	8.0
BMI ≥27.5 (%)	5.7	9.3**	3.9	8.5**	7.4	9.9
Grip strength (kg)	30.4 (6.8)	19.4 (4.9)*	28.6 (6.1)	18.2 (4.1)*	31.9 (7.0)†	20.3 (5.2)*†
Knee extension torque (kgm)	–	–	79.6 (27.2)	54.8 (17.0)*	–	–
Usual gait speed (m/s)	1.17 (0.31)	1.10 (0.33)*	1.27 (0.24)	1.22 (0.24)*	1.08 (0.34)†	1.00 (0.36)*†
Chair stand time (s)	–	–	–	–	10.8 (3.7)	12.2 (5.4)*
Muscle dysfunction (%)§	48.7	56.0**	52.6	60.0**	45.2	52.6**‡
Smoking (%)	21.0	3.2**	19.2	3.0**	22.6	3.4**
Alcohol consumption (%)	61.2	23.0**	61.0	28.8**	61.3	18.4**‡

Except where indicated otherwise, values are mean (SD). *$P < 0.05$ versus men in the corresponding group of the same cohort by unpaired Student's *t*-test. **$P < 0.05$ versus men in the corresponding group of the same cohort by χ^2-test. †$P < 0.05$ versus urban cohort in the corresponding group of the same sex by unpaired Student's *t*-test. ‡$P < 0.05$ versus urban cohort in the corresponding group of the same sex by χ^2-test. §Muscle dysfunction was defined as usual gait speed ≤0.8 m/s or grip strength <30 kg in men and <20 kg in women. BMI, body mass index; LTCI, long-term care insurance system.

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 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 level, 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 carried out using STATA statistical software (STATA, College Station, TX, USA). Differences in the values of the parameters between two groups were tested for significance using the non-paired Student's *t*-test and χ^2-test. Factors associated with occurrence of certified need of care were determined using Cox proportional hazards regression analysis; hazard ratios (HR) and 95% confidence intervals (CI) were determined after adjusting for region, age, sex, and BMI.

Results

Of the 1773 participants who were not certified as in need of care level elderly at baseline, information on certification of need of care could be obtained in 1760 (99.3%) during the average 4.0-year follow up. A total of 54 men and 115 women were certified as in need of care level elderly in the national LTCI system; whereas, 1591 remained uncertified during the follow-up period. A total of 126 participants died, and eight moved away.

Table 1 shows the baseline characteristics of the population at risk for occurrence of certified need of care in the LTCI system. Although BMI was not significantly different between men and women in the entire, urban or rural cohorts, prevalence of obesity (BMI ≥27.5) was significantly higher in women than in men in the entire and urban cohorts. The prevalence of underweight was higher in women than in men in the entire,

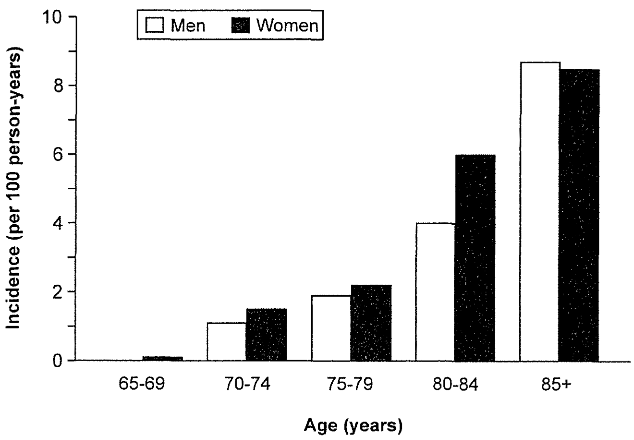

Figure 1 Incidence of certified need of care in the long-term care insurance system in men and women in each age stratum.

urban and rural cohorts; however, there was no significant difference. The prevalence of skeletal muscle dysfunction, determined by gait speed and grip strength, was significantly higher in women than in men in the entire, urban and rural cohorts.

Figure 1 shows sex- and age-distributions of the incidence of certified need of care in the LTCI system. Incidence was 2.3/100 person-years in the overall population of the entire cohort, and 2.0/100 person-years in men and 2.5/100 person-years in women. The incidence was very low in the age-stratum of 65–69 years, whereas, it tended to be markedly higher in the age-strata of 80 years and older in both sexes.

We then determined the risk factors for occurrence of certified need of care in the LTCI system. First, analysis was carried out using region, age, sex and BMI as explanatory variables in the Cox proportional hazards regression model (upper part of Table 2). Rural region and age were found to be risk factors for occurrence of certified need of care in the overall population. Sex and BMI were not significantly different. To further investigate the association between BMI and occurrence, we categorized BMI into three groups. Both underweight (BMI <18.5) and obesity (BMI ≥27.5) were found to be risk factors for occurrence of certified need of care, showing a U-shaped association. As for muscle strength and physical performance, handgrip strength, knee extension torque, usual gait speed, chair stand time and muscle dysfunction were found to be significantly associated with occurrence of certified need of care (lower part of Table 2). We carried out the same analyses in men and women separately (Table 2), and found results similar to those of the overall population.

Discussion

The present study investigated the incidence of certified need of care in the national LTCI system, and

Table 2 Hazard ratios and 95% confidence intervals for occurrence of certified need of care in the long-term care insurance system

	Overall population Crude HR (95% CI)	Overall population Adjusted HR (95% CI)	Men Crude HR (95% CI)	Men Adjusted HR (95% CI)	Women Crude HR (95% CI)	Women Adjusted HR (95% CI)
Region (rural *vs* urban)	1.15 (0.83–1.59)	1.61 (1.17–2.24)[b]	1.13 (0.65–1.96)	1.64 (0.94–2.86)[g]	1.15 (0.77–1.72)	1.59 (1.07–2.38)[g]
Age (+1 year)	1.17 (1.13–1.20)	1.17 (1.14–1.21)[c]	1.19 (1.12–1.26)	1.19 (1.13–1.26)[h]	1.16 (1.12–1.20)	1.16 (1.12–1.21)[h]
Sex (women *vs* men)	1.25 (0.90–1.74)	1.24 (0.89–1.73)[d]	–	–	–	–
BMI (+1 kg/m^2)	0.98 (0.93–1.03)	1.01 (0.96–1.06)[e]	0.93 (0.84–1.02)	0.96 (0.88–1.06)[i]	1.00 (0.94–1.06)	1.02 (0.97–1.08)[i]
≥18.5 or <27.5	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
BMI <18.5	2.10 (1.31–3.38)	1.77 (1.10–2.84)[e]	2.43 (1.09–5.40)	1.69 (0.75–3.82)[i]	1.93 (1.07–3.48)	1.79 (0.99–3.22)[i]
BMI ≥27.5	1.82 (1.13–2.93)	2.12 (1.32–3.43)[e]	1.39 (0.50–3.87)	1.91 (0.68–5.38)[i]	1.92 (1.12–3.29)	2.18 (1.27–3.75)[i]
Grip strength (+1 kg)	0.93 (0.91–0.95)	0.94 (0.91–0.97)[f]	0.91 (0.87–0.95)	0.94 (0.89–0.99)[j]	0.89 (0.85–0.92)	0.94 (0.89–0.98)[j]
Knee extension torque (+1 kgm)	0.97 (0.96–0.99)	0.97 (0.96–0.99)[f]	0.97 (0.95–0.99)	0.97 (0.95–0.99)[j]	0.97 (0.95–0.99)	0.97 (0.95–1.00)[j]
Usual gait speed (+0.1 m/s)	0.80 (0.77–0.85)	0.84 (0.79–0.90)[f]	0.81 (0.74–0.88)	0.83 (0.74–0.92)[j]	0.80 (0.76–0.85)	0.85 (0.78–0.92)[j]
Chair stand time (+1 s)	1.09 (1.07–1.12)	1.06 (1.03–1.10)[f]	1.18 (1.10–1.27)	1.11 (1.03–1.21)[j]	1.09 (1.06–1.11)	1.06 (1.02–1.09)[j]
Muscle dysfunction (yes *vs* no)[a]	2.91 (2.02–4.19)	1.71 (1.16–2.52)[f]	2.60 (1.45–4.68)	1.68 (0.91–3.09)[j]	3.07 (1.92–4.92)	1.72 (1.04–2.85)[j]
Smoking (yes *vs* no)	0.98 (0.58–1.68)	1.39 (0.79–2.43)[f]	1.18 (0.62–2.26)	1.54 (0.79–3.01)[j]	0.95 (0.30–2.99)	1.09 (0.35–3.47)[j]
Alcohol consumption (yes *vs* no)	0.71 (0.50–0.99)	0.83 (0.58–1.21)[f]	0.78 (0.45–1.35)	0.93 (0.53–1.61)[j]	0.70 (0.42–1.16)	0.76 (0.46–1.27)[j]

[a]Muscle dysfunction was defined as usual gait speed ≤0.8 m/s or grip strength <30 kg in men and <20 kg in women. [b]Adjusted for age, sex and body mass index (BMI). [c]Adjusted for region, sex and BMI. [d]Adjusted for region, age and BMI. [e]Adjusted for region, age and sex. [f]Adjusted for region, age, sex and BMI. [g]Adjusted for age and BMI. [h]Adjusted for region and BMI. [i]Adjusted for region and age. [j]Adjusted for region, age and BMI. Urban region and men were used as references. CI, confidence interval; HR, hazard ratio.

determined its risk factors using Japanese population-based cohorts. Identified risk factors were region, age, underweight, obesity, handgrip strength, knee extension torque, usual gait speed, chair stand time and muscle dysfunction (determined by the EWGSOP algorithm for screening sarcopenia).

In the present study, we could not obtain information on causes of certified need of care in the LTCI system. Therefore, we could not analyze the direct association of each causing condition with such factors as anthropometric and physical performance measurements. The Government of Japan reported that the top five leading causes of certified need of care were cerebral stroke, dementia, asthenia as a result of older age, joint disease and fall-related fracture, comprising 71.6% of all causes in 2010.[10] Based on these data, most of the causes of incident certification in the present study are inferred to be among the top five leading conditions.

Both low and high BMI were found to be risk factors for occurrence of certified need of care, showing an overall U-shaped association. This U-shaped association is similar to that between BMI and risk of death.[11,12] The association between risk of death from cardiovascular disease and other causes, and BMI was reported to be U-shaped in East Asians,[11] whereas the risk of all-cause mortality versus BMI was also found to have a U-shaped association in Western European and North American populations.[12] High BMI is an established risk factor for chronic diseases, including hypertension, dyslipidemia and diabetes mellitus, which increase the risk of cerebral stroke.[13] High BMI is also a major risk factor for knee osteoarthritis,[14–17] which can cause ADL disability in the elderly.[18] In contrast, low BMI is an established risk factor for osteoporosis and related fracture.[19] It also might relate to asthenia, a condition of loss or lack of bodily strength as a result of chronic wasting disease. Underweight as a result of malnutrition or sarcopenia is suggested to be included in this category.

Other identified risk factors were handgrip strength, knee extension torque, usual gait speed, chair stand time and muscle dysfunction (determined by the EWGSOP algorithm for screening sarcopenia). Previous studies have reported that low muscle strength and physical performance were predictors of subsequent ADL disability in the elderly.[20–23] The results of the present study are consistent with these previous reports. As many of the performance tests used in the present study are easy to carry out and evaluate, they can be utilized for screening elderly persons at high risk of certified need of care in the LTCI system. Those who were classified as having muscle dysfunction in the present study were at high risk of sarcopenia as well as certified need of care, regardless of muscle volume. Therefore, elderly persons screened by the EWGSOP algorithm are recommended to receive early intervention programs for prevention of ADL disability and subsequent deterioration leading to certified need of care.

The Japanese Orthopedic Association proposed the concept of "locomotive syndrome" in 2007 for the promotion of preventive health care of locomotive organs.[24–26] Locomotive syndrome refers to conditions under which the elderly have been receiving support or long-term care, or high-risk conditions under which they might soon require support or long-term care, that are caused by musculoskeletal disorders.[24–26] Functional declines in locomotive organs, including muscle strength, walking speed and balancing ability, usually progress slowly and gradually. As such, it might be difficult for people to recognize this decline in their daily life. Therefore, it is of particular importance to raise awareness of the growing risk caused by these disorders, and to take action to improve and maintain the health of locomotive organs. Population approaches, including promotion of the concept of locomotive syndrome to both younger and older generations, are important, in addition to high-risk approaches, including identifying those at risk for certified need of care and practicing intervention programs to reduce the risk of certified need of care.

There were some limitations in the present study. As we could not obtain information on causing conditions, we could not determine the risk factors for occurrence of certified need of care with respect to each causing condition. Additional studies are necessary to identify those direct associations. In the present study, the rural region was at higher risk of incident certified need of care compared with the urban region. The reasons for this could include differences in available public and private transportation or delivery services regarding meals and commodities for the elderly. In addition to these, the threshold between certified and non-certified elderly might be different among municipalities, which could lead to regional differences. Although the Certification Committee for Long-term Care Need in each municipality determines certification in accordance with guidelines formulated by the Government, the Committee also has to consider assessment by the applicant's primary physician and objective evaluation results regarding physical and mental status, which could affect the threshold of certification. Another limitation was health bias. Participants at baseline in the present study were those who could walk to the survey site, and could understand and sign an informed consent form. As those who could not were not included in the analyses, the study participants do not truly represent the general population due to health bias. Therefore, incidence of certified need of care was most likely underestimated, which should be taken into consideration when generalizing the results of the present study.

In conclusion, the present study revealed the incidence of certified need of care in the national LTCI system, and determined its risk factors using Japanese population-based cohorts. Both underweight and obesity were found to be risk factors for certified need of care, suggesting that maintenance of intermediate BMI is important for prevention. Low muscle strength and physical ability were also shown to be risk factors for certified need of care. Physical performance measures identified as predictors can be used as screening tools to identify high-risk individuals. Considering muscle dysfunction, screened by the EWGSOP algorithm, was a risk factor for occurrence, screened individuals are recommended to receive early intervention programs regardless of muscle volume. Further studies are necessary to develop intervention programs and to test their effectiveness, along with accumulation of epidemiological evidence, to prevent certified need of care and reduce the social and economic burdens associated with this condition.

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Disclosure statement

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

A 5–22-year follow-up study of stemmed alumina ceramic total elbow arthroplasties with cement fixation for patients with rheumatoid arthritis

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Abstract

Background We determined mid to long-term results of total elbow arthroplasty (TEA) by use of unlinked elbow prostheses with solid alumina ceramic trochleae, and ceramic ulnar stems (stemmed Kyocera type I; SKC-I) for patients with rheumatoid arthritis.

Patients and methods Fifty-four elbows of 39 patients were available for detailed clinical and radiographic review after a follow-up period of at least 5 years. The mean follow-up period was 12.6 years (range 5–22 years). Clinical condition before and after surgery was assessed by use of a modified version of the Mayo Elbow Performance Score (MEPS; 0–100 points) and a Japan Orthopaedic Association Elbow score (JOA score; 0–100 points). The radiographs were reviewed and loosening was defined as a progressive radiolucent line >1 mm wide that was completely circumferential around the prosthesis. Clinical records of post-operative events affecting the elbows were used for survival analysis of the prostheses using the Kaplan–Meier method.

Results The average modified MEPS and JOA scores improved significantly from 39.7 ± 14.3 to 44.7 ± 9.4, respectively, pre-operatively, to 89.7 ± 15.4 and 83.1 ± 12.8, respectively, post-operatively ($P < 0.0001$). The functional assessment score also improved from 4.9 ± 2.8 to 8.5 ± 3.3 points ($P < 0.0001$). With loosening or implant revision defined as end points, the likelihood of survival of the prosthesis for up to 20 years was 92.6 % (95 % confidence interval (CI), 85.6–100.0) or 86.3 % (95 % CI 75.0–97.6), respectively.

Conclusion Satisfactory clinical results were obtained after TEA using SKC-I prostheses, which provided excellent pain relief and functional range of motion. The results of our study reveal the high reliability over a long period of the cemented SKC-I prosthesis with an alumina ceramic component.

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Introduction

The elbow joint is affected in 25–53 % of patients with rheumatoid arthritis (RA) [1]. The mainstay of surgical treatment for RA elbows includes open or arthroscopic synovectomy for early-stage disease, and interposition and total elbow arthroplasty (TEA) for progressive and late-stage disease. TEA is primarily indicated for damaged RA elbows with painful stiffness, painful instability, and ankylosis. The clinical outcomes of TEA for the reconstruction of RA elbows were disappointing in the late 1970s, but modifications and improvements of elbow prostheses during the ensuing three decades has made TEA a reliable procedure with results that rival those of hip and knee arthroplasties [2, 3]. The most successful prostheses identified by long-term follow-up studies have an unlinked (non-constrained) or linked (semi-constrained) design. The former includes Capitellocondylar [4], Souter–Strathclyde [5, 6], and Kudo elbows [7, 8]; the latter includes Coonrad-Morrey [9] and GSB III prostheses [10]. The unlinked design relies on the presence of sufficient bone stock to seat the prosthesis and the ligaments and capsular structures to provide stability of the elbow, whereas the linked design relies on mechanical linkage. Theoretically, the potential for instability or dislocation after a TEA is greater with the unlinked prosthesis, whereas loosening and wear are the major concerns associated with linked prostheses [2].

In 1979, on the basis of a measurement study involving Japanese cadaveric elbows, we developed an unlinked surface replacement prosthesis using polycrystalline alumina ceramic as a solid trochlea on high-density polyethylene (Kyocera type I; KC-I) and used this clinically [11]. The initial design of the KC-I prosthesis did not include the intra-medullary stem, and the results of a 3-year follow-up of prostheses implanted without bone cement in 21 RA elbows were disappointing, with loosening and subsidence of the humeral component caused by inadequate fixation [11]. In 1986, the first model change was made to an unlinked stemmed type (Stemmed Kyocera type I; SKC-I), and this was used in 15 RA elbows [15]. The initial 8 elbows were implanted without cement fixation and early tilt or subsidence of the humeral component was noted; consequently we decided to use cement fixation in all cases from late 1987, resulting in stable clinical outcomes. This retrospective case series reports mid to long-term results from cemented alumina ceramic TEA using an SKC-I prosthesis for reconstruction of RA elbows.

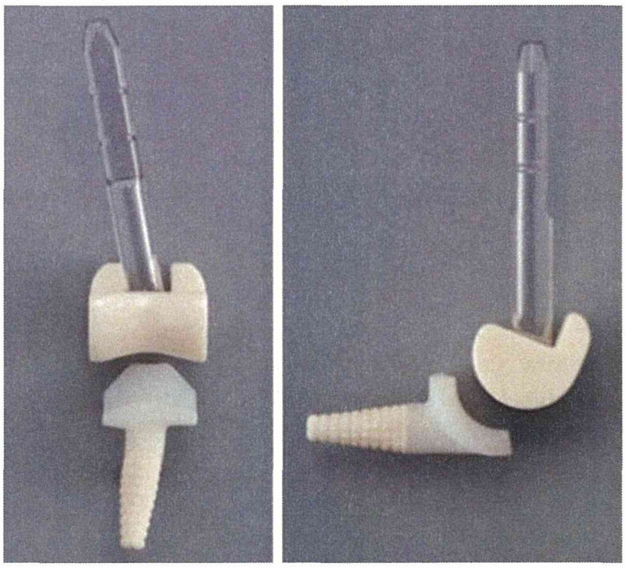

Fig. 1 Photograph of a stemmed Kyocera type I prosthesis (a prosthesis for the left elbow is shown). The humeral component consists of a solid ceramic trochlea and sapphire stem, and the ulnar component consists of a high-density polyethylene and ceramic stem. On the anterior/posterior plane, maximum curvature difference is 0.75 mm (range 0–0.75 mm) at the center of trochlea, and 1.25 mm (range 0.62–1.25 mm) at the lateral edge of trochlea. On the lateral/medial plane, maximum curvature difference is 1 mm (range 0–1 mm)

Patients and methods

In this retrospective study we reviewed clinical and radiographic outcomes of TEA using SKC-I unlinked elbow prostheses (Fig. 1). This study was approved by the Ethics Committee of our institute. The SKC-I prosthesis consists of a humeral component (polycrystalline alumina ceramic trochlea with a sapphire stem) and an ulnar component (high-density polyethylene; HDP) to which a plate is connected with a ceramic stem. The length of the stem was 6 cm for the humeral component and 2.5 cm for the ulnar component. The humeral articular surface was designed with 8° of valgus angulation and 23° of anterior flexion to the stem. The stem of the ulnar component was designed with 7° of valgus angulation to the ulnar articular surface. There was no size variation, but right and left discrimination was present. We used the SKC-I solely for RA elbows with painful flexion contracture of less than 100° or painful instability causing extreme limitation of daily function. Joint destruction should be advanced beyond Larsen's grade IV [12] on radiographs. If either half of the humeral condyle or olecranon was absent with severe lateral or medial instability, a linked elbow prosthesis was indicated (Fig. 2).

We enrolled 83 patients (105 elbows) who underwent primary TEA with SKC-I prostheses using cement fixation between December 1987 and February 1999. All patients met the American Rheumatism Association 1987 revised criteria for RA. One surgeon (H.I.) implanted all of the prostheses. Fourteen patients (14 elbows) were lost to follow-up. Of the remaining 91 elbows in 69 patients, 37 elbows in 32 patients for whom follow-up was <5 years were excluded from survival analysis. Because two patients who underwent bilateral TEA were recorded in both the <5 years and the >5 years follow-up groups, data for 54 elbows in 39 patients were used for the 5-year minimum detailed clinical and radiographic reviews. All elbows were classified as Larsen's grade IV or V. Thirty-seven women and 2 men were enrolled; the patients' ages ranged from 43 to 72 years of age (average 59.0 years) at the time of surgery, with 28 right and 26 left elbow replacements. The average follow-up period was 150.6 months (range 61–269 months). Twelve patients (18 elbows) died; their pre-operative data and records at the final follow-up visit were used for analysis (Table 1). All patient data were

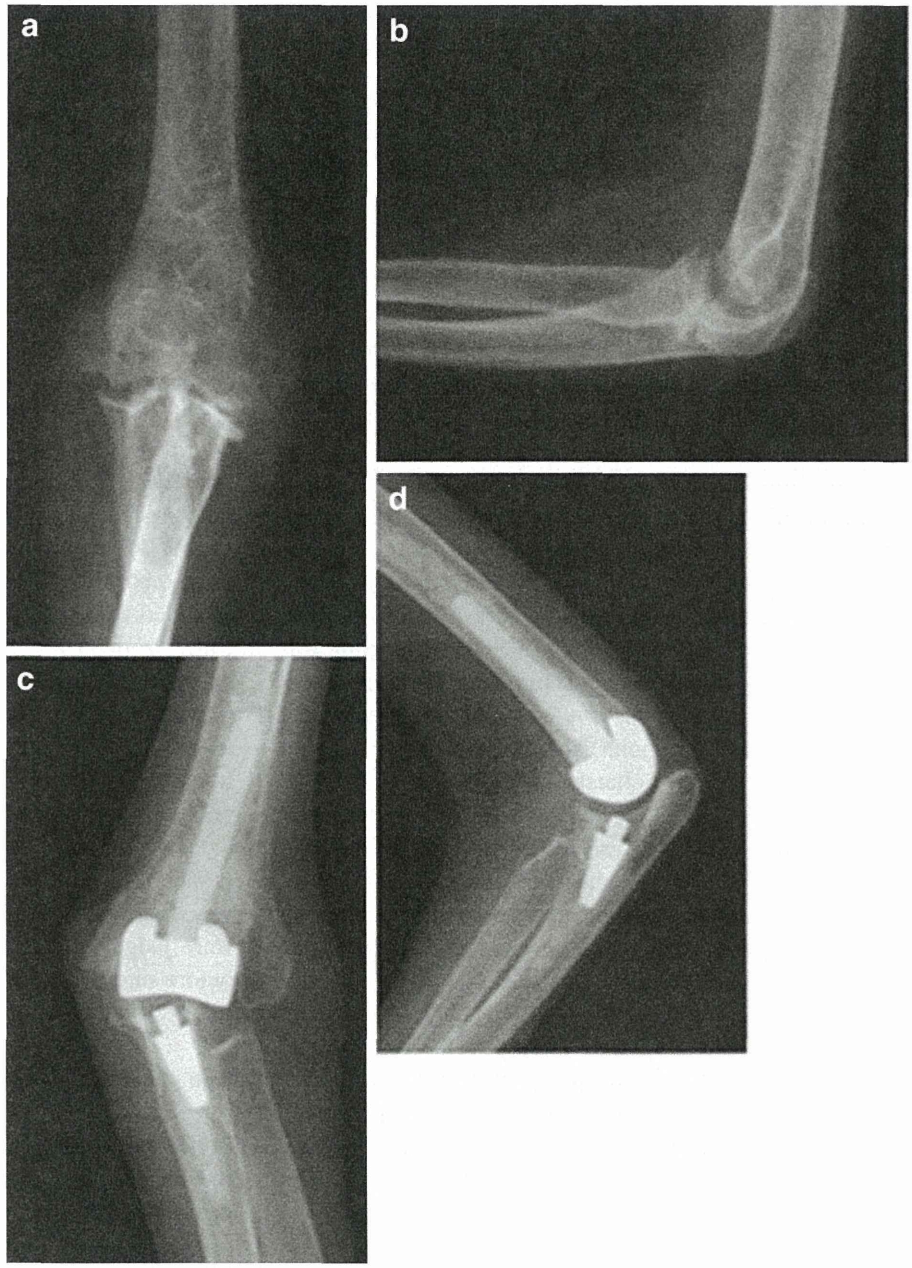

Fig. 2 Pre-operative anteroposterior (**a**) and lateral (**b**) radiographs of the left elbow of a 56-year-old woman (patient no. 9) who had rheumatoid arthritis, with Larsen's grade IV joint destruction. Anteroposterior (**c**) and lateral radiographs (**d**) of the left elbow 268 months after surgery using a stemmed Kyocera type I prosthesis with cement fixation. The Darrach procedure was added simultaneously to the left distal radio-ulnar joint

Table 1 Features of 54 elbows

Number of elbows (patients)	54 (39)
Age at time of surgery (years)	59.0 ± 8.7 (43–72)
Gender (female/male)	37/2
Side (right/left)	28/26
Follow-up period (months)	150.6 ± 59.4 (61–269)
Number of patient deaths during follow-up	12 (18 elbows)

originally recorded using the Japan Orthopaedic Association (JOA) elbow evaluation score [13], and it was difficult to convert our patients' records to the Mayo Elbow Performance Score (MEPS) [9]. Therefore, the clinical condition of each elbow before and after surgery was also assessed according to the modified MEPS for pain (0–60 points), range of motion (ROM; 0–30 points), and stability of the joint (0–10 points) [14]. On the basis of this system, the results were defined as good (75–100), fair (50–74), and poor (<50). Functional impairment was assessed separately using the JOA elbow evaluation score; activities assessed comprised washing the face, eating, fastening buttons (underwear), pouring a glass of water, self-hygiene, and putting on and taking off socks. Each activity was worth a potential 2 points (2: easy, 1: difficult, and 0: unable) giving a total of 12 points. The anteroposterior and lateral radiographs were reviewed carefully, and evaluated for the position of the implant, the cement mantle, radiolucent lines, bone resorption, and osteolysis. Loosening was defined as a progressive radiolucent line >1 mm that was completely circumferential around the prosthesis [5].

Surgical procedure

The patient was placed in the full lateral position with the upper arm horizontal and the forearm hanging vertically. A posterolateral [15] or posterior surgical approach [16] was used. The ulnar nerve was identified and meticulous dissection was carried out proximally and distally to the first motor branch of the flexor carpi ulnaris. The posterior aponeurosis of the triceps tendon was reflected distally, and the deep part of the triceps was divided along the reflection of the musculotendinous expansion from the olecranon. After resection of the radial head, the elbow joint was further flexed and a synovectomy was performed. Resection of the tip of the olecranon gave broader access to the joint. The humeral end was trimmed and intramedullary reaming was performed along the central guide pin. The guide instrument was set and a square bone cut was made to remove the damaged trochlea. The joint was then dislocated without sacrificing the medial collateral ligament (MCL). If the bony spur expanding along the MCL disturbed the dislocation, the bony spur was resected piece-by-piece from the inside of the joint. After the ulnar surface had been cut away with a bone saw, thus making the thickness of the remaining olecranon approximately 10 mm, reaming was performed with a reamer, and a circular rasp was used to create a circular bed for the ulnar component. The humeral and ulnar trial prostheses were positioned to check the stability and mobility of the joint. After irrigation, the humeral and ulnar components were fixed with bone cement. Before closing the wound, the triceps tendon was firmly sutured to the olecranon by use of two drill holes at the olecranon. An ulnar nerve translocation was typically not needed.

Post-operative care

A splint was applied with the elbow at 90° of flexion; this remained in place until post-operative day 14. Passive range of motion (ROM) exercise was started around post-operative day 7, followed by active ROM exercise after post-operative day 14. By post-operative day 21–28, the active range of motion was expected to improve from 30°–125° in extension and flexion. A full range of daily activities was permitted after 6 weeks [17].

Statistical analysis

All continuous measurements are given as mean ± SD. Statistical analysis was performed by one-way analysis of variance. Survival of the prosthesis was analyzed by the Kaplan–Meier method with loosening, and revision with removal of the prosthesis with or without reinsertion of a new implant defined as the end point. All analysis was conducted by use of Prism software (version 5.0a; GraphPad Software, San Diego, CA, USA) with a $P < 0.05$ regarded as significant.

Results

Clinical assessment (Supplemental table)

Pain scores and range of motion (ROM) were markedly improved by surgery. Resection of distal ulnar end (Darrach procedure) was combined in 8 elbows (nos. 8, 11, 13, 19, 39, 44, 45, 46) to improve pain at the distal radio-ulnar joint, and forearm rotation. The average post-operative modified MEPS and JOA scores both improved significantly from 39.7 ± 14.3 and 44.7 ± 9.4, respectively, pre-operatively, to 89.7 ± 15.4 and 83.1 ± 12.8, respectively, post-operatively ($P < 0.0001$; Tables 2, 3). Functional assessment by use of the JOA score revealed significant improvement from 4.9 ± 2.8 pre-operatively to 8.5 ± 3.3 points post-operatively ($P < 0.0001$; Table 4). No clinical data were available for one patient who had suffered a humeral fracture (elbow no. 40) at final follow-up; this was, therefore, rated as a poor result. Of the 54 elbows, 2 were judged to be good, 20 were fair, and 32 were poor before surgery. At the final follow-up visit, 46 elbows were judged to be good, 5 were fair, and 3 were poor (Table 2).

Complications (Table 5)

Sixteen of 54 elbows had minor to major complications, so the incidence of complications was 29.6 %. One patient had persistent post-operative paresthesia in the distribution of the ulnar nerve (elbow no. 14). Intra-operative fractures of the humerus occurred in 2 elbows in 2 patients (elbow nos. 17, 53). A humeral epicondylar fracture (elbow no. 17) was treated by simultaneous Kirschner wire fixation. A fissure fracture occurred at the humeral shaft of elbow no. 53, but the bone fragment was stable after cement fixation of the humeral component and did not require internal fixation. In both elbows, bone union was seen within 3 months after surgery.

Post-operative fractures occurred as a result of trauma for 6 elbows of 6 patients (elbow nos. 2, 3, 4, 26, 40, 53). Four fractures occurred at the ulna and two at the humerus. For one elbow with an olecranon fracture resulting from a fall (elbow no. 2), the ulnar component was lost from the joint. Because the pain at the elbow joint was mild and the patient did not want re-implantation of the prosthesis, the

Table 2 Pre and post-operative clinical assessment by use of the modified version of the Mayo Elbow Performance Score

Criteria	Score (points)	Pre-operative	Post-operative
Pain (max., 60 points)		Number of elbows (%)	
None	60	1 (2)	42 (79)
Mild to occasional, no medication	40	2 (4)	8 (15)
Moderate to occasional, activity limited, medication	20	26 (48)	2 (4)
Severe to incapacitating	0	25 (46)	1 (2)
Motion (max., 30 points)		Number of elbows (%)	
Arc of extension/flexion			
>90	30	30 (56)	48 (91)
60–89	20	14 (26)	5 (9)
30–59	10	7 (13)	0
<30	0	3 (6)	0
Stability (max., 10 points)		Number of elbows (%)	
Effect on function of the elbow			
None or mild (does not limit activity)	10	11 (20)	26 (49)
Moderate (impairs certain functions)	5	25 (46)	15 (28)
Severe (markedly limits activity)	0	18 (33)	12 (23)
Total score (max., 100 points)		39.7	89.7
Overall results (good/fair/poor)		2/20/32	46/5/3

Post-operative clinical data were not available for elbow no. 40 because of humeral fracture

Table 3 Pre and post-operative clinical assessment by use of the Japanese Orthopaedic Association (JOA) Elbow score

Criteria	Pre-operative	Post-operative
Pain (max., 30 points)	8.8	27.8
Function (max., 20 points)	10.0	15.8
Range of motion (max., 30 points)	15.8	25.4
Flexion (°)	118.5	141.6
Extension (°)	−35.6	−18.4
Arc of flexion/extension (°)	82.9	123.2
Pronation (°)	49.6	78.8
Supination (°)	55.6	84.4
Arc of forearm rotation (°)	105.2	163.2
Instability (max., 10 points)	4.4	6.3
Deformity (max., 10 points)	5.8	7.8
Total JOA score (max., 100 points)	44.7	83.1

ulnar component was simply removed, with the cement fragments. This resulted in a fair result at the elbow joint with gross instability that required orthosis. Open reduction and internal fixation was performed for two elbows, one with an olecranon fracture (elbow no. 3) and another with a bi-condylar humeral fracture after loosening (elbow no. 53); both were treated by implant re-implantation with cement fixation. The remaining 3 elbows were treated conservatively. As a result, the outcomes were rated good in 3 cases, fair in one, and poor in 2 at final follow-up.

In this case series, 6 dislocations were noted among 6 patients (elbow nos. 9, 18, 27, 35, 40, 52). Three elbows had severe pre-operative joint destruction rated as Larsen's grade V (elbow nos. 18, 27, 52), one elbow was dislocated with humeral fracture (elbow no. 40), and the causes of dislocation of the remaining two elbows (elbow nos. 9, 35) were unknown. The time of dislocation varied among 4 elbows (1 month, 11 months, 6 years, and 6 years), and was not clear for 2 elbows. MCL repair was performed for 2 elbows (elbow nos. 9, 18), but the remaining 4 patients

Table 4 Pre and post-operative function of the elbow

Function (points)	Pre-operative (n = 44)		Post-operative (n = 51)		P value
	Average	SD	Average	SD	
Washing face (2)	0.7	0.7	1.7	0.7	<0.0001
Eating (2)	0.9	0.6	1.8	0.5	<0.0001
Fastening buttons (underwear) (2)	0.8	0.6	1.4	0.8	<0.0001
Pouring a glass of water (2)	1.0	0.6	1.5	0.8	<0.0001
Self-hygiene care (2)	0.8	0.7	1.4	0.8	0.0003
Putting on and taking off socks(2)	0.8	0.6	0.9	0.8	0.28
Total (12)	4.9	2.8	8.5	3.3	<0.0001

Each function was evaluated and rated as: easy; 2 points, difficult; 1 point, and unable; 0 points, according to the Japanese Orthopaedic Association (JOA) Elbow score. Data were obtained from the records of 44 patients pre-operatively and 51 patients post-operatively

SD standard deviation

P value <0.05 was regarded as significant

Table 5 Complications recorded for 54 elbows

Complications (number of elbows)	Elbow no. in supplemental table
Ulnar neuropathy(1)	14
Intra-op. fracture (2)	17, 53
Post-op. fracture (6)	2, 3, 4, 26, 40, 53
Post-op. implant fracture (1)	11
Dislocation or subdislocation (6)	9,18, 27, 35, 40, 52
Infection (1)	52
Aseptic loosening (4)	12, 19, 40, 53
Revision surgery (3)	3,11, 53
Implant removal (2)	2, 52