ABSTRACT

Background: The epidemiology of primary elbow osteoarthritis (PEOA) remains unknown. We aimed to evaluate the prevalence and associated factors of PEOA in a cross-sectional resident cohort from a municipal registry of a Japanese town.

Methods: A total of 415 residents over 50 years of age were randomly sampled from a Japanese town and were adjusted for age and gender. Those with diseases that could potentially cause a secondary osteoarthritis of the elbow were excluded. The remaining 318 subjects (150 males, 168 females) underwent bidirectional radiography of the elbow. Subjects were diagnosed with PEOA if one of their elbows was Kellgren-Lawrence grade 2 or greater. In addition, motion pain and tenderness at the elbow were examined by orthopedic surgeons. Associated factors for the prevalence of PEOA were statistically analyzed.

Results: The prevalence of PEOA was 25.2% (male, 27.3%; female, 23.2%), and the prevalence of symptomatic PEOA was 0.9%. The age-stratified prevalence of PEOA was as follows: 50-59, 6.2% (male, 5.0%; female, 7.3%); 60-69, 15.4% (male, 17.5%; female, 13.7%); 70-79, 29.5% (male, 35.3%; female, 25.0%); 80-89, 55.9% (male,

55.6%; female, 56.3%). Age and body mass index (BMI) were revealed as factors that increased PEOA.

Conclusions: The prevalence of PEOA in Japanese subjects was 25.2% for those aged 50-89 with a mean age of 69.2 years, most of which were asymptomatic OA without motion pain or tenderness at the elbow. Age and BMI increased the prevalence of PEOA. The prevalence of PEOA increased with age, but the disease was self-accommodated by most people.

Level of Evidence: Level III, Cross-Sectional Design; Epidemiology Study

Keywords: Elbow; osteoarthritis; cohort study; prevalence; risk factors; multivariable analysis; age

Introduction

Elbow osteoarthritis (EOA) may induce elbow pain, restriction of elbow motion, or ulnar neuropathy.[18] EOA can be classified into primary and secondary types. There are various causes of secondary elbow arthritis, including posttraumatic arthritis, septic arthritis, crystal-induced arthritis, hemophilia, ochronosis, and rheumatoid arthritis.[18] Primary EOA (PEOA) is defined as other EOA that excludes secondary EOA. Numerous studies have reported the prevalence of OA in other joints: shoulder, 17.4% in the general population with a mean age of 65.2 years,[10] 16.1% in the general population with a mean age of 71.8 years[16]; hip, 0.7% in subjects who visited the clinic with a mean age of 60 years,[15] 15.7% in the general population with a mean age of 63.9 years[25]; knee, 6.1% in the general population aged 35-74 years,[1] 33.0% in the general population with a mean age of 72.7 years,[4] 63% in the subjects who visited the hospital with a mean age of 61.7 years[24]. To the best of our knowledge, there is only one report that revealed the prevalence of PEOA in a resident cohort with a mean age of 67.2 years.[17] The study reported a prevalence of 52.3% from a resident registry in a Japanese rural community with subjects 40 years or older; however, the study was limited by the

following factors: 1) subjects were not sampled by a randomized method, 2) lateral radiograph of the elbow was not taken and thus OA was determined by anteroposterior radiograph alone.

The aims of the present study were to investigate the prevalence of PEOA assessed by anteroposterior and lateral radiographs of bilateral elbows and to examine associated-factors of PEOA by multivariable analysis in a cross-sectional cohort study of a Japanese town. We randomly sampled subjects aged 50-89 from the basic resident registry to minimize selection bias. All subjects were examined by orthopedic surgeons to determine whether their elbows were symptomatic or asymptomatic.

Materials and Methods

Construction of cohort classified by sex and age groups

This study was one of several projects in "the Obuse study," a cross-sectional cohort to investigate locomotor function and to extend the healthy life expectancy of the Japanese elderly.[6-8,20-22] With a population of 11,326 people (2014), the municipality of Obuse town is located in Nagano prefecture in central Japan.[14] The employment structure of the town was as follows: primary industry workers, 42.4%; secondary industry, 9.6%; tertiary industry, 47.6%. The primary industry provides raw materials to be made into goods as found in farming and mining, the secondary industry use raw materials to make goods, and the tertiary industry is the service sector of a country's economy. Compared to the Japanese population census in 2015 (primary: 4.0%, secondary: 25.0%, tertiary: 71.0%),[13] the proportion of tertiary industries was small, and the proportion of primary industries was large. We defined 8 groups by age (50-59, 60-69, 70-79, and 80-89) and gender (male and female). Each group was planned to consist of approximately 50 participants for a total of at least 400 subjects.

68 We randomly sampled 1,297 individuals from 5,352 people aged between 50 and 89
69 years in the basic resident registry of Obuse town in 2014. Informational materials on
70 the Obuse study were mailed by municipal workers of Obuse along with a request for
71 participation to residents between 50 and 89 years of age who were randomly selected
72 from the town's population registry by using computer generated random numbers.
73 After providing written consent, 415 subjects were enrolled. Prior to the scheduled
74 examination of subjects, interview questionnaires were mailed to collect demographic
75 data, occupational history, sports history, history of trauma, and medical history (Figure
76 1). The interview questionnaires were subsequently evaluated at the day of the
77 examination. The following subjects were excluded: incomplete questionnaires (n=9);
78 prior history of fractures at the shoulder, arm, or wrist (n=52); arthritis, including
79 rheumatoid arthritis and hyperuricemia (n=29); cerebral apoplexy or infarction (n=8).
80 One subject had histories of upper-extremity fracture and diseases causing arthritis.
81 After these exclusions, 318 subjects were ultimately enrolled (Figure 2). There were
82 307 and 11 right- and left-handed subjects, respectively.
83

Evaluation of EOA

All 318 subjects underwent anteroposterior and lateral radiography of the bilateral elbow joints. All radiographic images were assessed by the first author, and the EOA was graded according to the Kellgren-Lawrence (KL) scale.[9] According to previous studies,[17,29] we defined subject with PEOA as subject having KL grade 2 or greater at the either side of the elbow. The radiographic assessment of KL grade 2 was determined by the presence of definite osteophytes at the medial ulnohumeral joint in anteroposterior radiography and either the coronoid process, coronoid fossa, olecranon, or olecranon fossa in lateral radiography (Figure 3).

To check inter and intra- observer reliability of radiographic assessment of KL grade 2, two authors ([redacted]) assessed the bilateral elbows of 40 subjects (80 elbows) according to the KL scale, randomly sampled from the 318 enrolled subjects. These initial radiographic assessments were repeated 1 month later by [redacted]. The inter- and intra-observer reliabilities of the radiographic assessments were calculated by the kappa statistic.

99 All 318 subjects were examined by orthopedic surgeons without prior knowledge of
100 their radiography. Orthopedic surgeons examined subjects about elbow pain during
101 elbow flexion extension motion and checked for tenderness at the humeroradial and
102 humeroulnar joint spaces. Subjects with symptomatic PEOA were defined as those
103 diagnosed as radiographic PEOA with motion pain or tenderness on the same elbow.
104 If the subject exhibited symptomatic PEOA with an asymptomatic contralateral elbow,
105 we categorized the subject as symptomatic PEOA.
106
107 ***Associate factors***
108 The candidates of associated factors were as follows: age, gender, body mass index
109 (BMI), grip strength, smoking history, engagement in heavy manual work, use of
110 vibrating tool, engagement in agricultural labor, and participation in overhead sports
111 (tennis, baseball or softball, badminton, and volleyball). Grip strength (kg) of bilateral
112 hands were evaluated using a Jamar Hand Dynamometer (Sammons Preston Rolyan,
113 Bolingbrook, IL) and mean grip strength of the bilateral hands was used. Smoking
114 history (packs per year × years smoked) was examined. Engagement in heavy manual

115 work, use of vibrating tool, engagement in agricultural labor, and participation in
116 overhead sports were classified by answers of 5 years more history of these
117 questionnaire. If subjects had been engaged in carrying objects 10 kg or more at least 10
118 times a week for more than 5 years, they were defined as heavy manual workers (Figure
119 4).

120

121 ***Statistical analyses***

122 The differences in demographic data between subjects with PEOA and subjects without
123 PEOA were evaluated by the Fisher's exact test or the Welch's t-test. The association
124 between PEOA and age, BMI, grip strength, and smoking history were evaluated using
125 a logistic regression analysis. Subsequently, the relationships between PEOA and
126 gender, heavy manual work, the use of vibrating tool, agricultural labor, and
127 participation in overhead sports were evaluated using the Fisher's exact test. We
128 performed a logistic regression analysis with stepwise method using Akaike's
129 Information Criteria. Statistical analyses were carried out using the JMP®10 (SAS
130 Institute Inc., Cary, NC, USA). The level of significance was set at $P < 0.05$.

131

132 **Results**

133 We examined 318 subject and 636 elbows. PEOA was observed in 80 subjects. PEOA

134 was observed in the right elbow alone for 20 subjects, in the left elbow alone for 21

135 subjects, and in both elbows for 39 subjects. PEOA was observed in the dominant hand

136 for 59 elbows and the non-dominant hand for 69 elbows. The number of elbows with

137 PEOA was 119 (18.7%), and these elbows stratified to KL grade were as follows: 44,

138 KL 2; 45, KL 3; 30, KL 4 (Table 1). The inter- and intra-rater reliabilities for PEOA

139 were 0.79 and 0.83, respectively.

140

141 ***Demographic data***

142 The 8 groups were classified by age and gender. Table 2 shows the demographic data of

143 enrolled subjects.

144

145 ***Prevalence of PEOA***

A total of 80 subjects (25.2%) were classified into the PEOA group. In the PEOA group, there were 41 males (27.3%) and 39 females (23.2%). The distribution of PEOA, stratified by gender and age, is shown in Figure 5. Only 3 out of 80 subjects with PEOA were classified as symptomatic PEOA, all of whom showed tenderness at the radiohumeral joint, and none showed elbow pain on flexion and extension. The remaining 77 subjects with PEOA were classified as asymptomatic PEOA.

Associated factors

The results regarding the candidate associated factors of the PEOA and non-PEOA groups are summarized in Table 3. In univariate analysis, the age, BMI, grip strength, use of vibrating tool and agricultural labor were significant factors for PEOA. In multivariable analysis, the age, BMI, and the smoking were significant factors (Table 4). The prevalence of PEOA increased with age and BMI. On the other hand, the prevalence of PEOA decreased with a longer smoking history.

DISCUSSION

In this study, we evaluated anteroposterior radiographs of the elbow joint in 318 subjects who were randomly selected from residents of a Japanese town aged 50 to 89 years. PEOA was observed in 80 subjects. As a result, the prevalence of PEOA was 25.2%. The associated factors for the prevalence of PEOA were age, BMI, and smoking. The strengths of this research included 1) a randomly selected cohort that was extracted from a basic resident registry with a minimal selection bias, 2) the exclusion of secondary EOA from our questionnaire, and 3) the direct examination of the elbow joint by orthopaedic surgeons to diagnose whether the disease is symptomatic or asymptomatic.

Previous studies on the prevalence of PEOA are scarce. In terms of macroscopic paleopathological survey of the musculoskeletal system, there are reports from excavations in the Czech Republic and Slovenia by Crubezy et al[2] and France by Debono et al.[3] The prevalence of EOA was reported to be approximately 20.0% in the former and 27.0% in the latter, but secondary EOA were not excluded in these studies and thus cannot be compared with this study. To our knowledge, the only study that

177 implements the use of radiographic imaging for a resident cohort is a study by Oya et
178 al.[17] The subjects of their study were elderly Japanese people living in mountainous
179 areas. The mean age of subjects was 67.2 years old in their study, which was
180 comparable to the present study. However, the prevalence of PEOA was 52.3%, which
181 was higher than our results. Oya et al only performed radiographic imaging of the elbow
182 joint in the anteroposterior view. PEOA osteophytes are usually found in the coronoid
183 process and coronoid fossa on lateral view radiographs[12]; therefore, the assessment of
184 lateral view radiographs is essential. Furthermore, Oya et al did not implement
185 randomization of samples for their subjects. Taking account of these differences in
186 study design between the present study and that of Oya et al, the number of PEOA in
187 this study provides a better approximation of its actual measures.
188 In this study, symptomatic PEOA was detected from the presence or absence of
189 motion pain or tenderness under direct examination by an orthopedic surgeon. Three out
190 of 318 subjects (0.9%) were considered symptomatic PEOA. Stanley et al obtained the
191 number of symptomatic EOA with elbow pain or ROM restriction using anteroposterior
192 and lateral radiographs of hospital patients and found that the rate of symptomatic OA

193 in all hospital patients was 2%.[19] Zhang et al evaluated the anteroposterior and lateral
194 radiographs of 7126 individuals aged 16-90 years in Shanxi Province, China. The
195 imaging was examined by physicians, and they reported that symptomatic EOA
196 accounted for 2.9% of the total study population.[29] In all of these studies, the prevalence
197 of symptomatic EOA was less than 3% of all subjects. On the other hand, Oya et al,
198 symptomatic EOA was reported to be 22.6%. Although the 3 other studies including our
199 present study were conducted with direct examinations by physicians, the study by Oya
200 et al relied on subjective patient-reported questionnaires. According to previous projects
201 in "the Obuse study," Isobe et al[8] determined normative values for the QuickDASH
202 questionnaire in the elderly. QuickDASH is a self-administered questionnaire, which
203 consists of a disability/symptom scale of the upper limb. Isobe et al revealed that PEOA
204 was not an associated factor on QuickDASH scores. We believe PEOA was mitigated
205 by self-accommodation of the disease by most people.
206 Age and BMI were associated factors that increased the incidence of PEOA in this
207 study. From a previous study, Soojian et al reported that gender and age were associated
208 factors of PEOA.[1] In our literature search, we found no reports that examined in

209 statistical analysis regarding associated factors of PEOA. Goodfellow et al[5] reported
210 that age changes in the articular cartilage of the elbow joint are presented from necropsy
211 subjects. In other joints, prevalence of OA tended to increase with age.[4,26] BMI has been
212 proved to be an associated factor in OA of metacarpophalangeal, proximal
213 interphalangeal, and distal interphalangeal joints of the hand as well as weight bearing
214 joints, such as hip, knee, and ankle.[27] A possible explanation is that adiponectin is
215 associated with OA.[28] However, it is not clear whether adiponectin is also involved in
216 the relationship between BMI and PEOA.

217 In this study, smoking history was an inhibitory factor of PEOA. It is controversial
218 because there are conflicting reports that on one hand suggest smoking history is an
219 inhibitory factor[11] but on the other hand suggest that it is not an inhibitory factor of
220 OA.[5] Nicotine may suppress cartilage degeneration,[23] and the relationship between the
221 occurrence of OA and nicotine intake should be studied in future investigations.
222 Activities such as overhead sports, the use of vibrating tools, engagement in agricultural
223 labor, and engagement in heavy manual work were small contribution compared to age.

There are several limitations to this research. First, the sample size was small at 318 subjects. Secondly, approximately 1/3 of the selected subjects were enrolled in the study. We did not know the reasons for nonparticipation of subjects in this study, which may have potentially contributed to selection bias. Thirdly, the study is limited to those over 50 years old. Fourthly, the history of trauma, arthritis, cerebrovascular disorders, smoking history, engagement in heavy manual work, use of vibrating tools, engagement in agricultural labor, and participation in overhead sports are based on the results of patient questionnaires; therefore, these evaluations may have involved subjectivity and imprecision to some extent. Fifthly, in determining PEOA, the osteophytes of the olecranon or olecranon fossa may have been overlooked on the lateral view radiographs. Finally, we did not ask participants about symptoms and location of pain. The methods of examination are not uniform in regard to determining the tenderness or motion pain at the elbow joint.

CONCLUSION

The prevalence of PEOA in Japanese subjects was 25.2% for those aged 50-89, most of which were asymptomatic OA without motion pain or tenderness at the elbow. Age and BMI increased the prevalence of PEOA, while a longer smoking history decreased the prevalence of PEOA. The prevalence of PEOA increased with age, but the disease was self-accommodated by most people.

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339

340 **Figure legends**

341 Figure 1. Survey questions regarding activity.

342 Engagement in heavy manual work, use of vibrating tool, engagement in agricultural

343 labor, and participation in overhead sports were classified by answers of 5 years more

344 history of these questionnaire. If subjects had been engaged in carrying objects 10 kg or

345 more at least ten times a week for more than 5 years, they were defined as heavy

346 manual workers.

347

348 Figure 2. Survey questions regarding fractures and joint disorders.

349

350 Figure 3. A flowchart of the subjects enrolled in the study

351 One subject had both a history of an upper-extremity fracture and a disease-causing

352 arthritis. Diseases causing arthritis were hyperuricemia (n=17), rheumatoid arthritis

(n=11), and remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome (n=1).

Figure 4. Radiographs of the elbow assessed as KL grade 2 PEOA.

Definite osteophytes are noted at the medial ulnohumeral joint in anteroposterior view and at the coronoid fossa and coronoid process in lateral view

Figure 5. Distribution of subjects with PEOA, stratified by gender and age

PEOA, primary elbow osteoarthritis.