Factors associated with the increased risk of atlantoaxial osteoarthritis: A retrospective study

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Abstract

Purpose Atlantodens osteoarthritis and atlantoaxial osteoarthritis cause neck pain and suboccipital headaches. Currently, knowledge on the risk factors for atlantoaxial osteoarthritis is lacking. This study aimed to investigate the factors related to the increased risk of atlantoaxial osteoarthritis.

Methods We analyzed computed tomography (CT) images of the upper cervical spine of 1266 adult trauma patients for whom upper cervical spine CT was performed at our hospital between 2014 and 2019. The degree of atlantoaxial osteoarthritis was quantified as none-to-mild (not having osteoarthritis) or moderate-to-severe (having osteoarthritis). Risk factors associated with atlantoaxial osteoarthritis were identified using univariate and multivariable logistic regression analyses.

Results The study group included 69.4% men, and the overall average age of the study population was 54.9 ± 20.4 years. The following factors were independently and significantly associated with atlantoaxial osteoarthritis in the multivariable logistic regression analysis: age in the sixth decade or older (odds ratio [OR], 20.5; 95% confidence interval [CI], 6.2–67.2, $p < 0.001$), having calcific synovitis (OR, 4.9; 95% CI, 2.4–9.9, $p < 0.001$), women sex (OR, 3.3; 95% CI, 1.9–5.7, $p = 0.002$), and not having atlantodens osteoarthritis (OR, 2.1; 95% CI, 1.2–3.8, $p = 0.014$).

Conclusion In the multivariable logistic regression analysis, age in the sixth decade or older, calcification of the transverse ligament, being women, and not having atlantodens osteoarthritis were found to be significantly associated with atlantoaxial osteoarthritis. Delayed diagnosis and treatment can be avoided by focusing on these risk factors.

Keywords

Neck pain, Suboccipital headaches, Atlantoaxial osteoarthritis, Atlantodens joint, Calcification, Transverse ligament

Introduction

Neck pain is a common condition, and its 12-month prevalence is estimated to be within 30%–50% [1]. Most patients with neck pain generally do not require treatment, as it does not have a severe effect on daily life [2]. However, some patients require treatment for prolonged, repetitive symptoms of neck pain and accompanying suboccipital headache. In particular, osteoarthritis (OA) of the atlantoaxial joints is a cause of neck pain and suboccipital headache [3–6]. Pain from atlantoaxial osteoarthritis (AAOA) may predominate on the side affected by severe OA and is worsened by neck rotation and bending toward this side [7, 8].

Conservative treatment is not sufficient to relieve symptoms of AAOA [7]. Initially, the symptoms of AAOA are non-specific and difficult to distinguish. Therefore, the diagnosis of AAOA is often delayed [9]. Recently, surgical treatment has been accepted as an effective therapy. Atlantoaxial fixation surgery is useful in cases of AAOA that are unresponsive to conservative management [7–10].

A few reports have indicated that the prevalence of AAOA increases with age [3, 11-15]. According to those reports, the estimated prevalence of AAOA in the Western population is 4.8%, which increases to 5.4% in the sixth decade and 18.2% in the ninth decade of life [15]. In the clinical setting, we usually obtain anteroposterior and lateral cervical

radiographs of patients with neck pain, but a standard transoral atlas view is often not obtained. As it is difficult to detect AAOA on anteroposterior and lateral cervical radiographs, we need a standard transoral atlas view to detect AAOA. Nevertheless, no clinical studies have clarified the risk factors for AAOA, which raises the question concerning those patients for whom a transoral view should be considered. Therefore, this study aimed to investigate the factors related to the increased risk of AAOA.

Methods

This study was approved by our institution's Ethics Review Board (approval no. 2758). The need for informed consent from the patients was waived considering the retrospective nature of the study.

Individuals eligible for our study were adult patients who were transferred to our emergency and critical care center and required computed tomography (CT) of their cervical spine as part of their diagnostic examination, between January 1, 2014, and December 31, 2019 (n = 1694). Patients with rheumatoid arthritis, those on dialysis, those with a tumor in the cervical spine, those aged < 17 years, and those with a current/prior cervical spinal fracture and previous cervical surgery were excluded. The flow diagram of patient enrolment is presented in Fig. 1. Eventually, 1266 patients met our inclusion

criteria.

The patients were classified into age groups (18–19 years, second decade, third decade, fourth decade, fifth decade, sixth decade, seventh decade, and eighth decade or older) for analysis.

CT measurements

Cervical spine images were obtained using an Optima CT660 scanner (Optima Corp., Tokyo, Japan). Based on sagittal and coronal CT views, we classified OA as atlantodens and atlantoaxial. We used the scoring system reported by Lakshmanan et al. [16], with severity graded as follows: none, mild, moderate, and severe. Based on the method given by Betsch et al. [13], the grades of "none–mild" were classified as "absence of OA,", whereas grades of "moderate" and "severe" were classified as "presence of OA" (Table 1, Fig. 2). An intraosseous cyst within the odontoid process and calcific synovitis were defined as having a lytic defect in the odontoid process and calcification in the transverse ligament, respectively (Fig. 3) [13]. OA grades, presence or absence of intraosseous cysts, and calcific synovitis were evaluated by two raters. Inter-observer reliability was evaluated using the Kappa statistic (κ) for atlantodens OA and AAOA grades and the presence or absence of intraosseous cysts and calcific synovitis.

Statistical analysis

The association of AAOA with the presence or absence of atlantodens OA, age (sixth decade or older, or not), presence or absence of intraosseous cyst, and calcific synovitis were analyzed using a chi-squared test, with the calculation of odds ratios (ORs) and 95% confidence intervals (CIs). A p-value <0.05 was considered significant. The variables that were significantly associated with AAOA in the univariate analysis were included in the multivariate analysis. In this study, we evaluated the relationship of risk factors, such as age, sex, calcific synovitis, intraosseous cyst, and not having atlantodens OA with AAOA by using a multivariable logistic regression analysis. Variables eligible for inclusion in the multivariate models involved those considered associated with an increased risk of AAOA in the literature. After identification of the main effects in the logistic regression models, we checked the models for goodness of fit with the Hosmer–Lemeshow test and tested for co-linearity and residuals to ensure that they fit the data. All analyses were performed using SPSS (version 26; SPSS Inc., Tokyo, Japan).

Results

Demographic data

The age categories of 1266 patients were reported, and the age in our cohort ranged from 18 to 98 (mean, 54.9 ± 20.4) years. This study included 879 men (69.4%) and 387 women

(30.6%). In patients diagnosed with AAOA, the mean age was 75.1 ± 9.5 years, and the proportion of men and women were 39.3% and 60.7%, respectively (Table 2).

Prevalence

Approximately 2.2% of patients had AAOA and their grade distribution was as follows: none-to-mild, 97.8%; moderate, 1.9%; and severe, 0.3% (Table. 3, Fig. 4). Furthermore, the prevalence of AAOA was approximately 2.5%, which increased to 4.5% in the group in the sixth decade and 12.3% in those in the eighth decade or older in this study. Atlantodens OA was present in 33.3% of our patients, and the proportion of each grade was as follows: none-to-mild, 66.7%; moderate, 30.1%; and severe, 3.2% (Fig. 5). The overall prevalence rates of intraosseous cyst and calcific synovitis were 10.8% and 3.6%, respectively. When we included patients diagnosed with AAOA, the prevalence rates of atlantodens OA, intraosseous cysts, and calcific synovitis was 35.7%, 21.4%, and 26.8%, respectively (Table 2). Kappa values indicated strong positive inter-rater agreement (κ = 0.76, κ = 0.86, κ = 0.78, and κ = 0.86, respectively).

Risk factors for AAOA

In the univariate analysis, the following factors were independently and significantly associated with AAOA (Table 4): age in the sixth decade or older ($p < 0.001$), calcific synovitis ($p < 0.001$), women sex ($p < 0.001$), and presence of intraosseous cysts ($p <$

0.001). Overall, no significant association was found between atlantodens OA and AAOA in our cases ($p = 0.702$). However, when we observed cases in the sixth decade or older, the following factors were found to be independently and significantly associated with AAOA: presence of calcific synovitis ($p < 0.001$), not having atlantodens OA ($p = 0.011$), and women sex ($p < 0.001$) (Table 5). Risk factors associated with AAOA in the univariate analysis are presented in Tables 4 (all patients) and 5 (patients in their sixth decade or older).

The results of the multivariate analysis to identify independent risk factors for AAOA are shown in Table 6. The following factors were found to be independently and significantly associated with AAOA: age in the sixth decade or older ($p < 0.001$), calcific synovitis ($p < 0.001$), women sex ($p = 0.002$), and not having atlantodens OA ($p = 0.014$).

Discussion

In this study, we investigated the risk factors associated with AAOA and found that age in the sixth decade or older, presence of calcific synovitis, being women, and not having atlantodens OA were associated with AAOA by using the multivariable logistic regression analysis.

Relationship between age and AAOA

To date, several studies have reported an increased prevalence of AAOA associated with aging [12-15, 17]. Betsch et al. [13] reported a prevalence of 9.5%–9.8% for AAOA. However, another study by Li et al. [12] reported a higher prevalence of AAOA (25%), which may be attributed to the inclusion of patients with neck discomfort in this study.

Few studies have shown the relationship between the prevalence of AAOA and aging. Betsch et al. [13] observed that the prevalence of AAOA is <10% between the age of 18 and 67 years, and it increases to 35%–45% among individuals aged ≥88 years. Zapletal et al. [15] also found an increase in the prevalence of AAOA from 5.4% in the sixth decade to 18.2% in the ninth decade of life. Based on these findings, it can be inferred that head loading (a load carried on the head) for a long time increases the risk for AAOA [3,13]. Therefore, when old patients present with occipital or posterior neck pain, it is important to adopt an appropriate treatment considering the possibility of AAOA.

Relationship between calcific synovitis and AAOA

Calcium pyrophosphate dihydrate deposition (CPPD) is well known to be present in the joints and/or soft tissues and results in pseudogout and crown dens syndrome [18-20]. Joint destruction due to crystal-induced arthritis and pseudogout results from inflammation induced by CPPD deposition within the joints [19, 21]. Kobayashi et al. [20] reported the involvement of the lateral atlantoaxial joint in acute neck pain, and the

presence of calcific synovitis was evaluated using CT.

In our study, calcific synovitis and CPPD crystals were identified in 76.9% of patients in whom the joint fluid could be obtained from the lateral atlantoaxial joint. However, no patient had CPPD crystals in the joint fluid of the lateral atlantoaxial joint in the group without calcific synovitis. Therefore, CPPD arthropathy in the atlantoaxial joint might be caused by the calcification of the transverse ligament of the atlas, which resulted in AAOA.

Relationship between sex and AAOA

In our study, the prevalence of AAOA was significantly higher in women. Kobayashi et al. [20] also reported that women were more likely to be affected by AAOA. Jones et al. [22] observed that men had a 16%–31% higher cartilage volume in the knee. Similarly, the cartilage of the cervical facet joints in women may also be less than that in men. However, in this study, the reason for this difference could not be explained unequivocally because data on the cervical spine were lacking. Further studies are needed on the cartilage of the cervical facet joint.

Relationship between atlantodens OA and AAOA

The atlas and axis are greatly different from other vertebrae in terms of their embryology and anatomy. The atlantodens joint is formed by the insertion of the dens into the ring of

the atlas. The principal role of the atlantodens and atlantoaxial joint is rotation, which contributes to 40%–70% of the total rotation available at the cervical spine [6]. Studies have reported that the increased prevalence of AAOA with age results from this high degree of rotation available at these two segments [4-6, 11].

To our knowledge, only a few studies have shown the relationship between the atlantodens and atlantoaxial joints. Harata et al. [17] reported that AAOA was categorized into three types, namely, the lateral atlanto-axial joint type, atlanto-odontoid joint type, and mixed type, and AAOA could occur separately without atlantodens OA. In other reports, the total cervical range of motion was not affected by aging, but the cervical range of motion of the atlantoaxial joint was decreased in a cadaveric study. This decrease in atlantoaxial motion was likely caused by OA of the atlantodens [16, 23]. We hypothesized that atlantoaxial motion is decreased, the load on the atlantoaxial joint is reduced, and AAOA is inferred. In contrast, the range of motion of the atlantoaxial joint was maintained and AAOA could not be inferred in cases without OA of the atlantodens. Based on these findings, it can be inferred that OA of the atlantodens joint might have suppressed the occurrence of AAOA. However, only a few reports have indicated the relationship between AAOA and the range of motion of the C1/2 rotation. Further studies on these relationships are needed.

Which factors should we consider for taking a transoral atlas view in patients?

In this study, we found four factors associated with AAOA: age (sixth decade or older), calcification of the transverse ligament, being women, and not having the atlantodens OA on anteroposterior and lateral cervical radiographs. Therefore, all these factors must be considered while taking a transoral view in patients with occipital or posterior neck pain.

Study limitations

This study had some limitations. First, selection bias cannot be denied, given the retrospective design of the study. Prospective studies, either longitudinal evaluation of the degenerative changes during individuals' lives or cross-sectional evaluation of randomly selected subjects from the general population, would be ideal. However, the feasibility of such a study could not be justified because of the cost and amount of lifetime radiation exposure of the patients. Second, our study population involved adult patients who were transferred to our emergency and critical care center and, therefore, might not fully reflect the general population. However, our study had the advantage of including a large sample of older patients than in previous reports. Third, information concerning neck and suboccipital pain was not collected. Therefore, we could not clarify the relationship between pain and degenerative changes in AAOA. Finally, we could not evaluate cervical alignment under the influence of gravity, because CT was performed in a supine posture.

Koller et al. [24] reported that altered joint anatomy of C1–2 (deformation and malalignment of C1–2) caused AAOA in patients with C2-fractures. Future studies should evaluate cervical alignment under the influence of gravity in radiographs.

Conclusion

In the multivariable logistic regression analysis, we showed that age (sixth decade or older), calcification of the transverse ligament, being women, and not having atlantodens OA are factors indicating the increased risk of AAOA in our cohort. Therefore, taking a transoral atlas view in radiographs or CT is necessary for patients having these factors and occipital or posterior neck pain. Delayed diagnosis and treatment can be avoided by focusing on these risk factors.

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Figure legends

Fig. 1 Flow diagram of patient enrolment

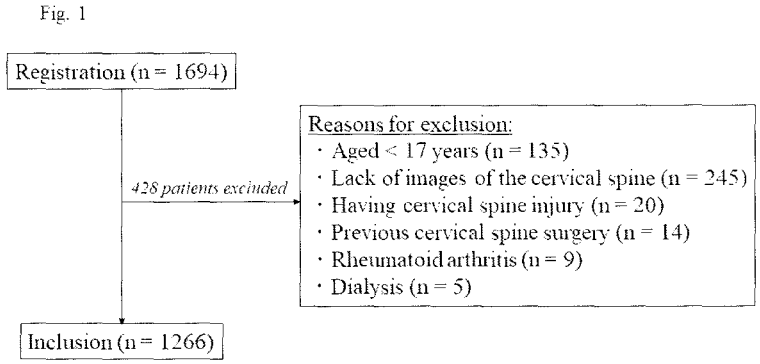

Fig. 2 Evaluation of atlantoaxial osteoarthritis and atlantodens osteoarthritis. Representative computed tomography scans of none-to-mild (left), moderate (middle), and severe (right) cases in the coronal plane

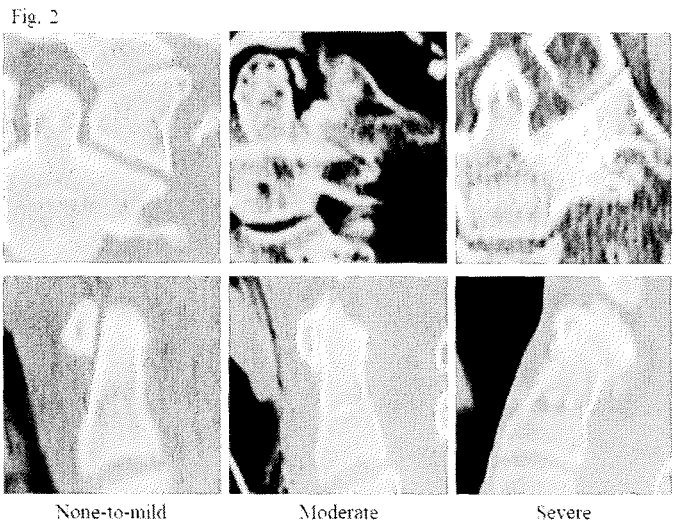

Fig. 3 Evaluation of an intraosseous cyst within the odontoid process and calcific synovitis. Representative computed tomography scans of the odontoid process in the sagittal plane: intraosseous cyst (left) and calcific synovitis (right)

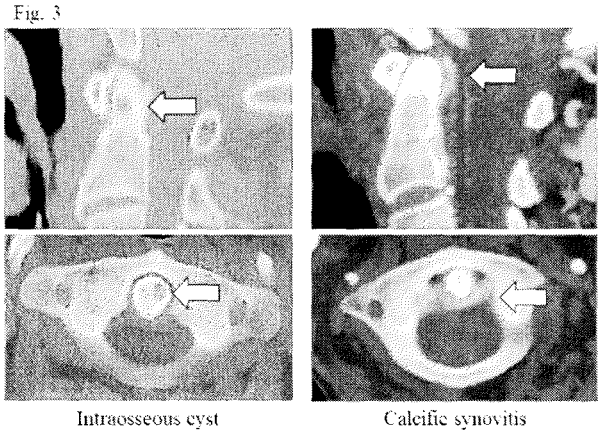

Fig. 4 Prevalence of atlantoaxial osteoarthritis among the age and sex groups. Overall atlantoaxial osteoarthritis was identified in 2.2% of the cases (moderate, 1.9%; severe, 0.3%). The prevalence was significantly higher in women patients aged >70 years than in their men counterparts (* $p < 0.05$, ** $p < 0.01$)

Fig. 4

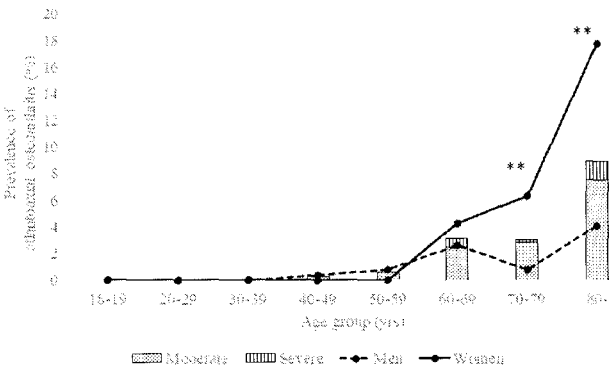

Fig. 5 Prevalence of atlantodens osteoarthritis with age. Overall, atlantodens osteoarthritis was identified in 33.3% of cases (moderate, 30.1%; severe, 3.2%)

Fig. 5

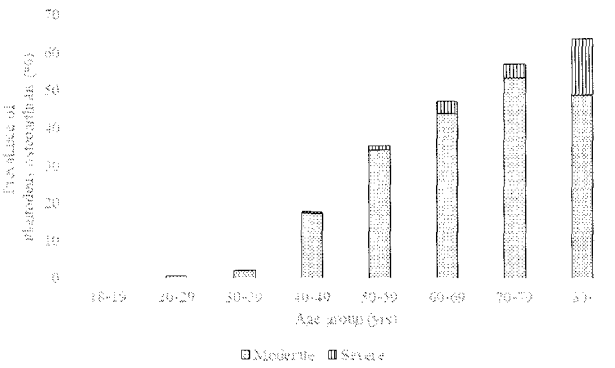

Table 1. Grading of atlantodens and atlantoaxial osteoarthritis

None-to-mild	Normal or narrow joint space with or without minor osteophyte formation
Moderate	Obliterated joint space with or without osteophyte formation
Severe	Ankylosis of the joint with excrescences either in the joint or transverse ligament calcification, or both

Classification was as follows: absence of osteoarthritis, "none" and "mild grades"; presence of osteoarthritis, "moderate" and "severe grades"

Table 2. Summary of patient demographic data

Characteristics	Total	With atlantoaxial osteoarthritis
Age (years)	54.9	75.1
Sex (%) Men	69.4	39.3
Women	30.6	60.7
Atlantodens osteoarthritis (%)	33.3	35.7
Intraosseous cysts (%)	10.8	21.4
Calcific synovitis (%)	3.6	26.8

Table 3. The prevalence of OA in each age group

Prevalence	18-19	20-29	30-39	40-49	50-59	60-69	70-79	80-	total
All	0.0	0.0	0.0	0.3	0.6	3.1	3.0	8.6	2.2
male	0.0	0.0	0.0	0.4	0.8	2.6	0.8	4.1	1.3
female	0.0	0.0	0.0	0.0	0.0	4.3	6.3	17.7	4.4

Table 4. Univariate associations of risk factors and atlantoaxial osteoarthritis in the overall study population

	Odds ratio	95% CI	p-value
Age: sixth decade or older	20.4	6.4–65.7	<0.001
Calcific synovitis	8.2	4.2–16.1	<0.001
Sex: Women	3.6	2.1–6.2	<0.001
Intraosseous cyst	3.1	1.7–5.7	<0.001
Not having atlantodens osteoarthritis	0.9	0.5–1.5	0.702

Table 5. Univariate associations of risk factors and atlantoaxial osteoarthritis in the sixth decade or older

	Odds ratio	95% CI	p-value
Calcific synovitis	4.0	2.0–7.9	<0.001
Sex: Women	3.7	2.1–6.5	<0.001
Not having atlantodens osteoarthritis	2.1	1.2–3.6	0.011
Intraosseous cyst	1.6	0.9–3.0	0.122

Table 6. Multivariate logistic regression model for the development of atlantoaxial osteoarthritis

	Odds ratio	95% CI	p-value
Age: sixth decade or older	20.5	6.2–67.2	<0.001
Calcific synovitis	4.9	2.4–9.9	<0.001
Sex: Women	3.3	1.9–5.7	0.002
Not having atlantodens osteoarthritis	2.1	1.2–3.8	0.014