Rheumatoid vertical and subaxial subluxation can be prevented by atlantoaxial posterior screw fixation

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Abstract

Purpose Literature has described a risk for subsequent vertical subluxation (VS) and subaxial subluxation (SAS) following atlantoaxial subluxation in rheumatoid patients; however, the interaction of each subluxation and the radiographic findings for atlantoaxial fixation has not been described. The purpose of this study was to evaluate the effects of two different posterior atlantoaxial screw fixation on the development of subluxation in patients with rheumatoid atlantoaxial subluxation.

Methods Between 1996 and 2006, rheumatoid patients treated with transarticular fixation and posterior wiring (TA) or C1 lateral mass–C2 pedicle screw fixations (SR) in

the Nagoya Spine Group hospitals, a multicenter cooperative study group, were included in this study. VS, SAS, craniocervical sagittal alignment, and range of motion (ROM) at the atlantoaxial adjacent segments were investigated to determine whether posterior atlantoaxial screw fixation is a prophylactic or a risk factor for the development of VS and SAS.

Results The mean follow-up was 7.2 years (4–12). No statistically significant difference was observed among the patients treated with either of the procedure during the follow-up period. Of 34 patients who underwent posterior atlantoaxial screw fixation, SAS was observed in 26.5 % during the follow-up period; however, VS was not observed. Postoperative C2–7 angle, and Oc–C1 and C2–3 ROM were significantly different between patients with and without postoperative SAS. The incidence of SAS was 38.9 % for TA and 12.5 % for SR; statistically significant differences were observed in the postoperative C1–2 and C2–7 angles, and C2–3 ROM.

Conclusions Atlantoaxial posterior screw fixation may be an appropriate prophylactic intervention for VS and SAS if the atlantoaxial joint develops bony fusion following physiological alignment. Compared to TA, SR provided optimal atlantoaxial angle and prevented lower adjacent segment degeneration, thereby reducing SAS.

Keywords Rheumatoid arthritis · Atlantoaxial subluxation · Vertical subluxation · Subaxial subluxation · Posterior screw fixation

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Abbreviations

RA	Rheumatoid arthritis
AAS	Atlantoaxial subluxation
VS	Vertical subluxation
SAS	Subaxial subluxation

AADI Anterior atlantodental interval
 PADI Posterior atlantodental interval
 ROM Range of motion

Introduction

The three major radiological disorders of rheumatoid arthritis (RA) in the cervical spine are atlantoaxial subluxation (AAS), vertical subluxation (VS), also known as basilar invagination, and subaxial subluxation (SAS). The progression pattern of these subluxations may be influenced by each other and are associated with the natural progression of RA. In the upper cervical region, as a result of the failure in the transverse and alar ligaments, reducible AAS occurs first and irreducible AAS is a sign of the start of VS [1–3], which has a high mortality risk. In subaxial lesions, the occurrence of SAS may be related to not only the state of RA, but also to the development of upper cervical lesion. Although disease-modifying antirheumatic drugs (DMARDs) have had a major impact on the natural history including cervical involvement [4], these subluxations may ultimately cause compression of the brain stem and/or spinal cord leading to myelopathy, and in the worst cases even to quadriplegia or sudden death [5–7]. Therefore, successful timely management of AAS is considered to be important. On this point, atlantoaxial fixation is widely accepted as the most effective option for AAS and potentially may prevent progression of VS and SAS. AA fixation has been proposed as a prophylactic procedure for VS, because the mechanical effect prevents the destruction of the lateral masses of the atlas from the inflammatory process [8]. On the contrary, fused mechanical limitations may occasionally become risk factors for SAS [9–11]. Thus, the question of whether atlantoaxial fusion achieves prophylaxis or leads to development of risk factors for subsequent subluxations has led to some controversy. Few reports have shown the interaction of each subluxation and the radiographic findings for atlantoaxial fixation. In addition, the incidences of VS and SAS after the two recent major types of posterior screw fixations, transarticular [12] and C1–C2 constructs [13, 14], remain unknown. In this investigation, we evaluated VS and SAS after atlantoaxial posterior screw fixation in a consecutive series of patients with RA to determine risk factors for subsequent subluxations.

Methods

Patient demographics

Between January 1996 and December 2006, 14,872 patients registered by the Nagoya Spine Group (NSG),

a multicenter study group for spinal disorders, underwent surgery of the spine. Of these, 64 patients underwent atlantoaxial fixation, including transarticular screw fixation [12], C1 lateral mass–C2 pedicle screw and rod fixation [13, 14], and other types of fixation procedures, for rheumatoid AAS. Patients with RA with previous SAS and/or VS were excluded because occipito-cervical/thoracic fusion was indicated for these patients according to the NSG criteria of our institutions [15] or because of the recommendations of other authors for longer fusions [16, 17]. Fifteen patients who underwent AA fixation only with posterior wiring and strut autograft, 9 who underwent concomitant cervical laminoplasty, and 6 who underwent other types of posterior atlantoaxial fixation were excluded from the study. The remaining 34 patients (18 transarticular screw fixation and 16 C1 lateral mass–C2 pedicle screw fixation) were included in this study. Informed consent was obtained from each patient before enrollment, and the study was approved by the ethics committee of our institutions. There were 12 men and 22 women with a mean age of 63.3 years (45–77 years) at the time of the surgery and the mean follow-up period was 7.2 years (4–12 years). All clinical, radiographic, and surgical reports were reviewed. The indication for AA fixation was mechanical pain and/or cervical myelopathy caused by AAS. A diagnosis of AAS was established if the distance between the anterior aspect of the dens and the posterior aspect of the anterior arch of the atlas (anterior atlantodental interval; AADI) was more than 3 mm in flexion lateral view radiographs. In this study, all patients complained of severe neck pain, all had radiographically confirmed AAS and 21 (61.8 %) presented with myelopathy.

Surgical selection and fashion

The criteria for selecting transarticular screw fixation or C1 lateral mass and C2 pedicle screw fixation depend on the availability of the procedure at the time of operation. The former was implemented earlier than the latter in the series because of its popularity at the time, but the follow-up radiographs for both procedures were obtained at the same time point after the surgery. In both procedures, a posterior midline approach was used, and the semispinalis cervicis muscle was detached once and repaired; however, surgical exposure was greater for transarticular screw fixation compared with C1 lateral mass–C2 pedicle screw fixation because of the screw pathway. For transarticular screw fixation, the screw entry point was just above the C2–C3 facet joint, and the bilateral C1–C2 intervertebral joints were fixed with a transarticular screw at a large sagittal angle. A monocortical bone block was then grafted with sublaminar wiring. In the latter, the C1 lateral mass screw and C2 pedicle screw were independently inserted and

fixed with a rod or a plate, and a cancellous bone graft was implanted on the decorticated posterior surfaces of C1 and C2.

Radiographic evaluation

Radiographs were obtained for all patients in the upright flexion, neutral and extension positions before the surgery and during the follow-up period. Postoperative radiographs were acquired 2 years after the surgery and at the final follow-up. The occurrence of SAS and VS, and the radiographic parameters were analyzed. The radiographic parameters investigated were AADI, posterior atlantodental interval (PADI), the value of Ranawat and Redlund-Johnell [18], C1–2 and C2–7 angles, and the range of motion (ROM) in O–C1 and C2–3. SAS was defined as the presence of a vertebra that moved forward by 3 mm or more toward the lower adjacent vertebra in lateral neutral radiographs. VS was evaluated by Ranawat and Redlund-Johnell methods using lateral radiographs in the neutral position. The Ranawat value was determined as the minimum distance between the line from the center of the anterior arch to that of the posterior arch of the atlas and the center of the pedicles. The Redlund-Johnell value was determined as the minimum distance between the McGregor line [19] and the midpoint of the inferior margin of the body of the axis in the lateral radiographs in the neutral position. For men, VS was defined as a Ranawat value less than 14 mm or a Redlund-Johnell value less than 34 mm, and for women VS was defined as a Ranawat value less than 13 mm or a Redlund-Johnell value less than 28 mm.

Statistical analysis

Pre- and postoperative measurement comparisons were performed using paired *t* tests and between-group comparisons were performed using unpaired *t* tests. Fisher's exact probability test was used for dichotomous variables, including the incidence of SAS and VS. The Pearson's correlation coefficient test was employed to determine the significance of the association between the C1–2 and C2–7 angles. Results with *p* values < 0.05 were considered to be statistically significant, and all values were expressed as mean $\pm$ SDs.

Results

Bony fusion was obtained in all the patients for whom atlantoaxial posterior screw fixation was performed. All patients showed pain relief and neurological improvement immediately after the surgery, but five (14.7 %) showed

cervical myelopathy resulting from the development of SAS. However, no patient required additional surgical treatment at the final follow-up.

AAS and VS after AA posterior screw fixations

AAS was improved in 91.1 % of the patients except for three with AADI > 3 mm after atlantoaxial posterior screw fixations. The mean Ranawat and Redlund-Johnell values in men were 16.50 ± 1.98 mm and 38.42 ± 3.23 mm before the surgery, 16.58 ± 1.51 mm and 38.17 ± 3.04 mm after the surgery, and 16.25 ± 1.60 mm and 38.0 ± 3.28 at the final follow-up, respectively. The mean Ranawat and Redlund-Johnell values in women were 14.95 ± 1.29 mm and 35.22 ± 3.37 mm before the surgery, 15.22 ± 1.34 mm and 35.05 ± 3.36 mm after the surgery, and 15.23 ± 1.34 mm and 35.05 ± 3.36 at the final follow-up, respectively. There were no statistically significant differences in both values before the surgery and at final follow-up between the sexes. VS was prevented in all patients after atlantoaxial posterior screw fixations (Table 1).

C1–2 and C2–7 angles after AA posterior screw fixations

The mean C1–2 angle before and after the surgery was $17.09 \pm 4.96^\circ$ and $26.62 \pm 5.61^\circ$, respectively. There was a significant difference in the C1–2 angles before and after the surgery (*p* < 0.05). At the final follow-up, the C1–2 angle had been maintained at $26.65 \pm 5.63^\circ$. The mean C2–7 angle before and after the surgery was $15.38 \pm 6.25^\circ$ and $6.21 \pm 13.52^\circ$, respectively. There was a significant

Table 1 Radiological characteristics in 34 RA patients treated with posterior atlantoaxial screw fixation

	Preop	Postop	Final f/u
AADI (mm)	7.29 ± 2.26	$2.64 \pm 1.07^*$	2.71 ± 1.03
PADI (mm)	11.32 ± 1.93	$16.94 \pm 2.42^*$	16.94 ± 2.44
Ranawat (mm)	15.50 ± 1.71	15.62 ± 1.54	15.59 ± 1.50
Redlund-Johnell (mm)	36.15 ± 3.61	36.15 ± 3.54	36.09 ± 3.58
C1–2 angle ($^\circ$)	17.09 ± 4.96	$26.62 \pm 5.61^*$	26.65 ± 5.63
C2–7 angle ($^\circ$)	15.38 ± 6.25	$6.21 \pm 13.52^*$	$-4.24 \pm 15.31^{**}$
O–C1 ROM ($^\circ$)	5.09 ± 3.22	6.12 ± 3.71	5.94 ± 3.91
C2–3 ROM ($^\circ$)	3.85 ± 2.16	$2.47 \pm 2.23^*$	2.35 ± 2.25

* There was a significant difference between before and 2 years after surgery (*p* < 0.05)

** There was a significant difference between 2 years after surgery and at the final follow-up (*p* < 0.05)

difference in the C2–7 angles before and 2 years after the surgery ($p < 0.05$). At the final follow-up, the C2–7 angle had decreased to $-4.24 \pm 15.31^\circ$, and there was a significant difference in the C2–7 angles 2 years after the surgery and at the final follow-up ($p < 0.05$).

Correlation between the C1–2 and C2–7 angles

The C1–2 fusion angle and C2–7 angle 2 years after the surgery showed a negative linear correlation ($r = -0.567$, $p < 0.05$), and the C1–2 fusion angle and the extent of the C2–7 change between the C2–7 angle 2 years after surgery and preoperative C2–7 angle showed a negative linear correlation ($r = -0.569$, $p < 0.05$) (Fig. 1). These results showed that hyperlordotic fixation of C1–2 may lead to subaxial kyphosis after AA posterior screw fixations. However, the C1–2 fusion angle and the extent of the C2–7 change between the C2–7 angle at final follow-up and that of 2 years after the surgery showed no correlation ($r = -0.187$, $p = 0.290$) (Fig. 2).

O–C1 and C2–3 ROM after AA posterior screw fixations

The mean O–C1 ROM values before and after the surgery and at the final follow-up were $5.09 \pm 3.22^\circ$, $6.12 \pm 3.71^\circ$, and $5.94 \pm 3.91^\circ$, respectively, but the differences were not statistically significant. The mean C2–3 ROM values before and after the surgery and at the final follow-up were $3.85 \pm 2.16^\circ$, $2.47 \pm 2.23^\circ$, and $2.35 \pm 2.25^\circ$, respectively. There was a significant difference in the C2–3 ROM values before and after the surgery ($p < 0.05$) (Table 1).

SAS after AA posterior screw fixations

SAS was observed in nine patients (26.5 %) after atlanto-axial posterior screw fixations. The radiological mea-

Fig. 1 Correlation between C1–2 fusion angle and the extent of C2–7 change 2 years after surgery. The C1–2 fusion angle and the extent of C2–7 change 2 years after surgery showed a negative linear correlation ($r = -0.569$, $p < 0.05$)

Fig. 2 Correlation between C1–2 fusion angle and the extent of C2–7 change 2 years after surgery. The C1–2 fusion angle and the extent of C2–7 change 2 years after surgery showed no correlation ($r = -0.187$, $p = 0.290$)

surements in patients with or without SAS are presented in Table 2. In the postoperative measurements, there was a statistically significant difference in the C2–7 angle and O–C1 and C2–3 ROM values with and without SAS ($p < 0.05$). SAS was observed 3.79 ± 0.93 years (range 2.0–7.0 years) after the surgery. The incidences of SAS by intervertebral disc level(s) were: C2–C3: 1 (11 %); C3–C4: 5 (56 %); C4–C5: 1 (11 %); and C3–C4 and C4–C5: 2 each (22 %).

Differences in SAS between fixation procedures

SAS was observed in 7 (38.9 %) of 18 patients after transarticular screw fixation and 2 (12.5 %) of 16 after C1 lateral mass–C2 pedicle screw fixation. There was no statistically significant difference in the SAS incidence between the two procedures ($p = 0.087$). There were also no statistically significant differences in the preoperative C1–2 and C2–7 angles

Table 2 Radiological assessment in 34 patients with or without SAS

	SAS+	SAS–	<i>p</i> value
No. of patients	9	25	–
Follow-up (years)	6.22 ± 1.39	6.16 ± 1.68	NS
C1–2 angle (°)			
Preop.	17.78 ± 4.99	16.84 ± 5.02	NS
Postop.	29.0 ± 7.05	25.76 ± 4.88	NS
C2–7 angle (°)			
Preop.	12.89 ± 4.78	16.28 ± 6.55	NS
Postop.	-5.33 ± 15.46	10.36 ± 10.19	0.002
O–C1 ROM (°)			
Preop.	5.56 ± 4.69	4.92 ± 2.61	NS
Postop.	3.44 ± 2.19	7.08 ± 3.70	0.009
C2–3 ROM (°)			
Preop.	4.11 ± 1.96	3.76 ± 2.26	NS
Postop.	1.11 ± 1.76	2.96 ± 2.21	0.031

Table 3 Radiological assessment in 34 patients treated with two different posterior screw fixations

	TA	SR	<i>p</i> value
No. of patients	18	16	–
Follow-up (years)	6.72 ± 1.74	5.63 ± 1.09	NS
Incidence of VS (%)	0	0	NS
Incidence of SAS (%)	38.9	12.5	NS (0.087)
C1–2 angle (°)			
Preop.	16.28 ± 5.31	18.0 ± 4.52	NS
Postop.	29.17 ± 5.06	23.75 ± 4.86	0.003
C2–7 angle (°)			
Preop.	14.17 ± 5.67	16.75 ± 6.76	NS
Postop.	−0.28 ± 12.96	13.50 ± 10.24	0.002
O–C1 ROM (°)			
Preop.	4.61 ± 3.52	5.63 ± 2.87	NS
Postop.	6.17 ± 3.65	6.06 ± 3.89	NS
C2–3 ROM (°)			
Preop.	3.89 ± 1.86	3.81 ± 2.51	NS
Postop.	1.67 ± 1.81	3.38 ± 2.36	0.024

TA Transarticular screw fixation, SR C1-lateral mass, C2 pedicle screw and rod fixation

and the preoperative O–C1 and C2–3 ROM values between the two surgical procedures. On the contrary, there were statistically significant differences in the postoperative C1–2 and C2–7 angles and C2–3 ROM values between the two surgical procedures ($p < 0.05$) (Table 3).

Discussion

There is a gradual degeneration of all the ligaments of the atlantoaxial complex that compromises mechanical stability. The failure in regions of fibrocartilage through autoimmune response in the transverse and alar ligaments subsequently leads to VS [20, 21]. Once VS has occurred, permanent neurological deficit and mortality rate increase drastically, even after adequate surgery has been performed. Surgical consensus for AAS has been established regarding myelopathy or intractable cervical pain, and early atlantoaxial arthrodesis in patients with AAS may potentially prevent progression of VS [8, 9]. However, the question of whether RA patients are at risk for developing VS and/or SAS after AAS treatment is controversial. Several studies have shown that rheumatoid patients have a greater risk of developing SAS after atlantoaxial fixation using wiring systems or transarticular screws [9–11], and the authors emphasized that the risk factor for SAS may be subaxial kyphosis caused by atlantoaxial hyperlordosis. However, the development of SAS is regulated by multiple factors, including not only the

mechanical effect of fixed atlantoaxial angle and secondary subaxial kyphosis, but also disruption of the extensor muscles in addition to a strong effect due to a natural history of RA. Some authors have reported that the incidence of SAS in RA patients not surgically treated was 15–22 % [1, 22, 23] and of AAS was 18–61 % [1, 22]. In patients who were surgically treated, a higher incidence of newly developed SAS and AAS after AA fusion using wiring systems or transarticular screws has been reported (32.7–39 % [9–11] and 100 %, respectively). It is suggested that the higher incidence of SAS after the surgery is probably due to mechanical stress caused by changes in cervical alignment, but there is a significant difference in RA status between patients with and without surgical treatment. The incidence (26.5 %) of SAS in this study may be lower among surgically treated patients and closer to natural status because of strong fixation of the posterior screw constructs.

The presence of subaxial kyphosis was significantly higher in patients with postoperative SAS compared with those without postoperative SAS. It has been reported that the atlantoaxial angle strongly correlated with the C2–7 angle and atlantoaxial fixation for various conditions in hyperextension resulted in the development of subaxial kyphosis [24–26]. Yoshida et al. [26] reported that subaxial kyphosis was 27.8 % in patients with various pathologies 2 years after atlantoaxial posterior screw fixation. In addition, there have been other reports that subaxial kyphosis after atlantoaxial fixation was observed relatively early. However, SAS after atlantoaxial fixation developed relatively late: 2.0–7.0 years after surgery in this study (Figs. 3, 4) and even after 9–24 years in others [9, 11, 16]. Figure 2 indicates that the C1–2 fusion angle may not affect the postoperative subaxial kyphosis during the latter postoperative period. Although it is uncertain whether SAS or subaxial kyphosis occurs first, postoperative atlantoaxial hyperlordosis and subaxial kyphosis probably regulate the development of SAS and are risk factors in the early stage after surgery, but other factors may be closely related to SAS over the long term. We demonstrated that the decrease of ROM in both the O–C1 and C2–3 segments were also risk factors for SAS. In reducible AAS, the C1–2 segment displays hypermobility, and O–C1 ROM decreases reversely. If AAS is improved, the O–C1 segment returns to its original physiological status and its ROM increases [26]; however, the O–C1 ROM decreased in patients with postoperative SAS. C2–3 ROM also significantly decreased in patients with SAS compared with that in patients without SAS. C2–3 facet fusion or decreased ROM may be caused by lower adjacent segment degeneration or injury after surgical intervention. Ishii et al. [11] described that C2–3 spontaneous fusion observed after C1–2 arthrodesis probably occurred because of the extensive exposure of the surgical field following massive bone graft or C2–3

Fig. 3 Radiographs obtained in a 65-year-old female patient with atlantoaxial subluxation following rheumatoid arthritis. She underwent AA fusion with transarticular screws. **a** Preoperative lateral radiograph in flexion position demonstrating severe atlantoaxial subluxation. **b** Lateral radiograph obtained 2 years after surgery. Mild

C4–5 disc height loss was observed. **c** Lateral radiograph obtained 4 years after surgery. SAS of the C4–5 segment was observed. **d** Lateral radiograph obtained 6 years after surgery. Bony union of C4–5 and C5–6 segments and SAS of the C3–4 segment were observed

Fig. 4 Radiographs obtained in a 61-year-old male patient with atlantoaxial subluxation following rheumatoid arthritis. He underwent AA fusion with C1 lateral mass and C2 pedicle screw and rod fixations. **a** Preoperative lateral radiograph in flexion position demonstrating severe atlantoaxial subluxation. **b** Lateral radiograph

obtained 2 years after surgery. Mild C4 anterior slip (1 mm) was observed. **c** Lateral radiograph obtained 3.5 years after surgery. SAS of the C4–5 segment was observed. **d** Lateral radiograph obtained 6 years after surgery. Disc height loss of the C4–5 segment without deterioration of SAS was observed

interlaminar and/or facet damage caused by the insertion of the wire under the C2 lamina or the insertion of C2 transarticular screws. In this study, we found that 33.3 % of the patients (3 of 9 with postoperative SAS) had C2–3 spontaneous fusion, but no patient who had undergone C1 lateral mass–C2 pedicle screw fixation had C2–3 fusion.

We examined the differences in the incidence of SAS between the fixation procedures. There was no statistically significant difference in the incidence of SAS between transarticular and C1–C2 constructs, but there was a statistically significant difference in the postoperative C1–2 and C2–7 angle and C2–3 ROM of the two surgical procedures. In the C1 lateral mass–C2 pedicle screw fixation, a screw is individually implanted in both C1 and C2.

Therefore, reduction of subluxation can be achieved during the surgery by operating on C1 and C2 directly and separately, and the expected atlantoaxial angle can be determined after implanting the screw. Moreover, in this procedure, the lower adjacent segment degeneration was mild compared with the transarticular screw. The C2–3 facet is at risk of being damaged by the use of transarticular screws, because the entry point of the screw is near this facet, which may cause C2–3 fusion or decrease ROM.

The difference in surgical exposure affects postoperative cervical involvement [27]. The differences in the incidence of postoperative SAS may result from differences in the invasion of posterior muscles. Transarticular screw fixation may require more exposure of soft tissues, such as the

nuchal ligament and adjacent muscles below C3 to adjust the angulation for screw insertion, but this exposure can be limited by a stereotactic technique using the image-guidance system [28] or a drill guide [29] for minimally invasive atlantoaxial fusion. In patients with RA, these devices can partially decrease the incidence of postoperative SAS.

This study had several limitations: a retrospective design, an uncontrolled cohort and the radiographic study. To accurately assess the risk factors of SAS, the incidence of subsequent subluxations among patients who have undergone surgery must be compared with the natural incidence of RA in a control cohort. In addition to radiographic analyses, the developing VS or SAS must be evaluated by multimodal factors, including RA subclass, condition of disease, and type of medication. Medications are broadly broken down into nonsteroidal anti-inflammatory drugs, glucocorticoids, and DMARDs (including methotrexate, tumor necrosis factor- α , and interleukin-1 inhibitors), and these drugs are likely to control the progression of subluxations. However, the relationship of these current biological response modifiers to cervical spine surgery for RA has not been studied. Future multidisciplinary prospective studies useful to rheumatologists and spinal surgeons are warranted.

Conclusions

Atlantoaxial posterior screw fixation is an effective surgical procedure that provides rigid initial fixation and successful bone union of C1–2, which provides prophylactic benefits against VS and SAS. C1 lateral mass–C2 pedicle screw fixation maintains physiological alignment of the cervical spine and prevents lower adjacent segment degeneration. As a consequence, subsequent subluxations can be reduced using C1 lateral mass–C2 pedicle screw fixation when compared with transarticular fixation.

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Conflict of interest None.

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