Cervical Spine Surgery in Patients with Rheumatoid Arthritis: Longterm Mortality and Its Determinants

ANTTI RONKAINEN, MINNA NISKANEN, ANU AUVINEN, JUSSI AALTO, and RIITTA LUOSUJÄRVI

ABSTRACT. *Objective.* Atlantoaxial subluxation (AAS) is a frequent manifestation of rheumatoid arthritis (RA). The instability of the craniocervical junction caused by AAS is a potentially fatal condition and may require surgical treatment. Systemic manifestations associated with RA may increase the risk of perioperative complications. We evaluated the longterm mortality and its determinants in RA patients with AAS after cervical spine surgery.

Methods. A retrospective study of consecutive patients treated at Kuopio University Hospital between 1994 and 1998. Preoperative risk factors, neurological impairment using the Ranawat classification, perioperative course, functional outcome, and survival status were evaluated.

Results. During the study period 86 rheumatoid patients with AAS underwent cervical spine surgery. The mean followup time was 7.5 years (range 5.0–9.8). During the followup, 32 patients (37%) died. The mean survival time after surgery was 7.2 years (95% CI 6.7–8.0). Seven patients experienced postoperative complications. Age, AAS other than horizontal, and occurrence of complications were independent predictors of mortality. In two-thirds of the patients there was relief or decrease of pain, and the functional capacity improved. Neurological deficits subsided in 53% of cases.

Conclusion. Patients with RA should be actively studied for AAS or other cervical instability, even when cervical symptoms are minor. Attention should be paid to perioperative management of these patients. Surgical treatment may not decrease the mortality of patients with RA, but it may result in more symptom-free life-years. (J Rheumatol 2006;33:517–22)

Key Indexing Terms:
RHEUMATOID ARTHRITIS   CERVICAL SPINE
SURGICAL TREATMENT   OUTCOME   MORTALITY

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease that affects multiple organ systems. The incidence of RA in Finland is 39/100,000/year, and its prevalence is approximately 0.5%–1.0% in the adult Caucasian population[1]. The life expectancy of patients with RA is shorter than the general population[2-4].

Cervical manifestations of RA that require surgical treatment usually develop in the late phase of the disease[5-7]. Atlantoaxial subluxation (AAS) is a common reason for neck pain and cervical instability. Horizontal subluxation may cause myelopathy, and vertical instability with cranial settling may lead to cranial nerve involvement, vertebrobasilar symptoms, and even death[8,9]. The prevalence of AAS is estimated to be 4%–35%[10,11], and AAS is associated with excess mortality in patients with RA[12]. In a hospital based study, 10% of patients with RA died from medulla compression caused by cervical destruction[13].

Combination antirheumatic therapy retards the progression of rheumatoid AAS[14]. RA patients with AAS benefit from surgical stabilization of the cervical spine[15-17].

The surgical technique is selected based on the degree of instability, neurological symptoms, and findings from the neuroradiological studies. Surgical techniques include posterior C1-C2 fixation, posterior occipitocervical fixation, and combined anterior decompression with densectomy and occipitocervical fixation. C1-C2 fixation results in the loss of 50% of rotation and does not affect flexion extension[18]. Occipitocervical fixation will prevent head movements to a great extent[16]. The perioperative mortality after cervical surgery of patients with RA has been reported to range from 4% to 17%[15]. Systemic manifestations associated with the chronic disease may increase the risk of perioperative complications[19-21]. There are few studies about postoperative morbidity[22,23] and longterm outcome[24] of patients with RA undergoing cervical spine surgery.

Our aim was to examine the postoperative morbidity and longterm mortality and its determinants in patients with RA undergoing posterior fixation for AAS.

MATERIALS AND METHODS

The study population consisted of patients whose diagnosis of RA fulfilled the American College of Rheumatology classification criteria for RA[25], and who were operated on between 1994 and 1998 in Kuopio University Hospital because of craniocervical junction instability, or who had a major revision

after earlier craniocervical fixation. The Department of Neurosurgery of Kuopio University Hospital is the only referral hospital for neurosurgical patients in East Finland, with a catchment area of nearly 900,000 inhabitants. All patients with RA and AAS in East Finland are referred to Kuopio University Hospital for assessment for surgical treatment. Patients were diagnosed as having RA if they fulfilled the American College of Rheumatology classification criteria or if they received prescription drugs for the treatment of RA free of charge through the sickness insurance plan in Finland. The national sickness insurance plan, which also includes RA, covers the entire population of Finland. RA patients with subaxial instability and conservatively treated rheumatoid patients with AAS were not included.

The study was approved by the Ethics Committee of Kuopio University Hospital.

Preoperative assessment and postoperative course. Preoperative neurological impairment was assessed using the Ranawat classification at the time of surgery[26]. The type of RA, medical treatment and clinical symptoms related to RA, duration of RA, and coexisting chronic diseases were recorded by 2 authors (AA and JA). The preoperative condition was assessed using American Society of Anesthesiologists classifications[27]. Information about the perioperative course was collected retrospectively from patient documents (by AA, JA, and MN). The length of hospital stay and the need for admission to the intensive care unit (ICU) were recorded. Complications were considered significant if they affected resource utilization, i.e., prolonged length of hospital stay, unplanned admission to the ICU, or a new operation.

All surgeries took place under general anesthesia. Patients were in a prone position, and their heads were fixed with the Mayfield pin fixation headholder. The fluoroscope was used in every operation to ensure good position of the head and neck and to allow proper instrumentation.

Followup. Data regarding operations were collected from the information system for operative procedures (TOTI[TM], Novo Group Uy, Helsinki, Finland) and from patient documents. The vital status, dates, and causes of death for the patient sample were obtained from the register of causes of death administered by Statistics Finland, which registers all deaths of citizens. The followup time of vital status was defined as the time between the day of operation and August 31, 2003, or until the date of death, whichever came first. The followup of functional status was collected by the independent observer (AA) by reviewing patient documents and by contacting patients or close relatives by telephone. The patients assessed their outcome after surgery by using a 4-grade scale (excellent, good, no change, or poor). Pain, neurological deficit, and functional capacity were assessed separately. If the patient could not be reached or was unable to give the assessment, a close relative was contacted for outcome assessment. The minimum followup time was 12 months.

Statistical methods. Statistical analysis was performed using SPSS 9.0 for Windows (SPSS Inc., Chicago, IL, USA). Normally distributed continuous variables are expressed as means (SD) and non-normally distributed continuous variables as medians and range unless indicated otherwise. Differences between groups were analyzed by Student's unpaired t test for normally distributed data and Mann-Whitney U test for non-normally distributed data. The chi-square test was used for categorical variables. Spearman rank order correlation was used to study the effect of preoperative clinical status on mortality and the correlation between Ranawat class and functional outcome. Kaplan-Meier survival analysis was done to determine the survival time. Cox regression analysis was used to find independent predictors of mortality[28]. In Cox regression analysis, the type of subluxation was divided as purely horizontal and other than horizontal subluxation (vertical, horizontal combined with vertical, or other type of subluxation). A p value < 0.05 was considered significant.

RESULTS

During the study period 86 patients with RA underwent cervical spine surgery. The length of followup was 7.5 years (range 5.0–9.8). During the followup, 32 patients (37%) died; age at the time of death was 68 ± 8.0 years. The mean survival time after surgery was 7.2 years (95% CI 6.7–8.0). The 5-year mortality rate was 30%. Of 18 patients aged 70 years or older, 11 (61.1%) died. One o these patients (5.6%) died within 30 days after surgery.

The demographic characteristics and preoperative conditions among all study patients and separately among survivors and nonsurvivors are presented in Table 1. In univariate analyses, the survivors differed from nonsurvivors only with respect to age, radiological type of AAS, presence of chronic obstructive pulmonary disease, and need for corticosteroid therapy. Surgical techniques are presented in Table 2. The C1-C2 fixations were done either with hooks or wire fixation and extensive occipitocervical fixation with occipital screws and sublaminar hooks. Preoperative neurological status was associated with the type of subluxation. Among 71 patients with preoperative Ranawat class I or II, 61 (85.9%) had purely horizontal subluxation. Correspondingly, among the 15 patients with Ranawat class III, 9 patients (60.0%) had purely horizontal subluxation (p < 0.05).

Perioperative morbidity. Postoperative complications led to increased use of resources in 7 patients (8.1%; Table 3). Two patients died within 30 days after surgery, and postoperative complications contributed to both deaths. In univariate analyses, mortality was higher among patients with perioperative complications than among those without complications (71.4% vs 28.6%; p = 0.05). The tracheas of 80 patients (93.0%) were intubated without difficulties (70 with a laryngoscope and 10 with a fiberoscope). Intubation of 6 (7.0%) patients was difficult. In one case, surgery had to be canceled because of a hematoma in the respiratory tract after an unexpectedly difficult laryngoscopic intubation. This patient was succesfully operated on 3 months later after planned fiberoptic intubation (Table 3).

Determinants of poor outcome. Age, AAS other than horizontal, and the occurrence of a complication were found to be independent predictors of mortality in multivariate analyses (Table 4). The Cox regression analysis was repeated including the preoperative Ranawat class. Ranawat class did not make an independent contribution to mortality.

Functional outcome. Sixty-six patients were contacted for determination of functional outcome. Of the remaining 20 patients that could not be reached, 14 were dead and 6 were lost to followup (Table 5). There was relief or decrease of pain and functional capacity had improved in two-thirds of patients. Neurological deficits subsided in 53% of cases. There was no correlation between preoperative Ranawat class and relief of symptoms. During the followup, 12 (14%) patients underwent additional surgery due to recurrent subluxation in the same segment.

DISCUSSION

There are only a few published reports on the longterm outcome for rheumatoid patients with AAS who have had surgery for cervical spine instability[24,29]. The reason for this could be

Table 1. Demographic characteristics of the study population (n = 86) at the time of surgery.

	Total, n = 86	Alive, n = 54	Deceased, n = 32	p
Age (mean ± SD), yrs	61.8 ± 9.0	59.6 ± 8.9	65.7 ± 8.0	< 0.01
ASA class[27], no. (%)				
1	1 (1.2)	1 (1.9)	0	NS
2	29 (33.7)	20 (37.0)	9 (28.1)	
3	55 (64.0)	33 (61.1)	22 (68.8)	
4	1 (1.2)	0	1 (3.1)	
Coexisting diseases, no. (%)				
Central nervous system	1 (1.2)	1 (1.9)	0	NS
Coronary heart disease	4 (4.7)	3 (5.6)	1 (3.1)	NS
COPD	7 (8.1)	7 (21.9)	0	< 0.05
Diabetes	2 (2.3)	2 (3.7)	4 (12.5)	NS
Cancer	0	1 (3.1)	1 (1.2)	NS
Renal	1 (1.9)	2 (3.7)	3 (9.3)	NS
Psychiatric	2 (2.3)	0	2 (6.3)	NS
Type of RA				
Seropositive	77 (89.5)	50 (92.6)	27 (84.4)	NS
Seronegative	5 (5.8)	2 (3.7)	3 (9.4)	NS
Ankylosing spondylitis	3 (3.5)	1 (1.9)	2 (6.3)	NS
Juvenile	1 (1.2)	1 (1.9)	0	NS
Medical treatment of RA, no. (%)				
NSAID	7 (8.1)	4 (7.4)	3 (9.4)	NS
Hydroxychloroquine	2 (2.3)	1 (1.9)	1 (3.1)	NS
Myochrysine	3 (3.5)	3 (5.6)	0	NS
Penicillamine	4 (4.7)	4 (7.4)	0	NS
Immunosuppressive	27 (31.4)	16 (29.6)	11 (34.4)	NS
Corticosteroids	16 (18.6)	6 (11.1)	10 (31.3)	< 0.05
Sulphasalazine	6 (7.0)	4 (7.4)	2 (6.3)	NS
Combination	21 (24.4)	16 (29.6)	5 (15.6)	NS
Duration of RA, yrs, mean (range)	23.6 (7–47)	22.9 (7–47)	24.8 (8–38)	NS
Clinical symptoms related to AAS, no. (%)				
Headache and neck pain	66 (76.7)	41 (75.9)	25 (78.1)	NS
Neurological deficit	12 (14.0)	7 (13.0)	5 (15.6)	NS
No clinical symptoms	8 (9.3)	6 (11.1)	2 (6.3)	NS
Ranawat classification, no. (%)				
I	24 (27.9)	14 (25.9)	10 (31.3)	NS
II	47 (54.7)	32 (59.3)	15 (46.9)	
IIIA	12 (14.0)	7 (13.0)	5 (15.6)	
IIIB	3 (3.5)	1 (1.9)	2 (1.9)	
Radiological type of AAS, no. (%)				
Horizontal	70 (81.4)	48 (88.9)	22 (68.8)	< 0.05
Vertical	2 (2.3)	1 (1.9)	1 (3.1)	
Horizontal combined with vertical	13 (15.1)	5 (9.2)	8 (25.0)	
Other	1 (1.2)		1 (3.1)	

COPD: chronic obstructive pulmonary disease, NSAID: nonsteroidal antiinflammatory drugs, NS: nonsignificant.

the low number of surgically treated patients in different institutions or the limited possibilities for followup. In Finland, cervical spine operations of patients with RA are centralized to a few departments, and the medical record-keeping is well organized. In our study (mean followup time 7.5 yrs) the mortality rate (37%) was not as high as in a previous study from our country by Santavirta, et al[24], in which the 10-year mortality rate was 47%. In that study, the mean age of operated patients (56 yrs), the duration of RA (17 yrs), and the age at death (62 yrs) were lower than in our study[24]. The patient data

in that study[24] were collected in the 1970s, and the overall evolution of treatment of RA may explain the more favorable outcome among our patients. In another study consisting of 16 patients the 10-year mortality rate was even higher (62%), but the mean age at death (68 yrs) was the same as in our study[29].

The independent predictors of mortality were age, other than horizontal subluxation, and postoperative complications. In a previous study, age was not a risk factor for mortality[24]. This may be due to differences in the age distribution and coexisting diseases, and to the lower number of patients and

older patient population in the previous study[24]. Among patients older than 70 years, the 30-day mortality in our study was lower (5.6%) than reported by Mizutani, *et al* (10%)[15]. Surgical treatment for patients over 70 years old should nonetheless be considered very carefully[15].

In our study, other than horizontal subluxation (vertical, horizontal combined with vertical, or other type) was predictive of mortality. This finding was also reported by Casey, *et al* and Matsunaga, *et al*, who showed that patients with other than horizontal subluxation had a worse outcome than patients with horizontal subluxation[29,30]. Patients with a more complicated type of AAS may have more severe RA manifestations in general, difficult anatomy for intubation, and severely lowered functional capacity, all of which make these patients vulnerable to complications. The incidence of difficult intuba-

tions (7%) in our study was comparable with that in a study by Hakala, *et al*, in which the rate of difficult intubations was 8%–13%[31].

In our study development of postoperative complications was an independent predictor of mortality. This has not previously been established in RA patients undergoing cervical surgery. Two deaths were directly related to surgery. For 3 patients who died during followup, the development of postoperative complications may have been associated with RA or coexisting diseases, reflecting the poor prognosis of RA *per se*. Only a few studies have evaluated the postoperative course of these patients in detail[15,22,23]. The immediate postoperative morbidity associated with surgery (8%) was comparable with a Swedish study (13%)[23] and another Finnish study (11%)[24]. In the study by van Asselt, *et al*, the deaths of patients operated for AAS were not related to the surgery[22], although the mortality within 6 weeks after the operation was higher (6%) than in our study (2.3%). The patient population of the study by van Asselt, *et al* was smaller than ours. In other studies as well the numbers of patients have been too small to allow multivariate analysis, or independent risk factors may not specifically have been sought. The mismatch between demand and supply of healthcare services is increasing. Complications that prolong recovery increase the costs of care and influence the outcome. With meticulous perioperative treatment of these high-risk patients, some of the complications may be preventable.

Tablw 2. Surgical techniques.

	Total, n = 86	Alive, n = 54	Deceased, n = 32
Technique of posterior fixation no. (%)			
C1-C2 posterior fixation	78 (90.7)	49 (90.7)	29 (90.6)
Extensive occipitocervical fixation	3 (3.5)	1 (1.9)	2 (6.2)
Transoral densectomy with posterior fixation	1 (1.2)		1 (3.1)
Revision	4 (4.7)	4 (7.4)	

Table 3. Patients with postoperative complications.

Case	Age, yrs	Sex	Duration of Disease, yrs	Complications	Consequence and Survival Status
1	68	F	18	Inspiratory stridor after extubation in the operating theater. Hypoxemia. Reintubation required	Unplanned admission to ICU immediately after operation. Length of ICU stay 1 day. Death 9 mo after operation
2	70	F	30	Perforation of rectum and peritonitis on postoperative day 4. Septic shock and respiratory failure. Stomatitis and parenteral nutrition. Subphrenic abscess. Laparotomy wound infection. Risk factors: corticosteroid therapy	Emergency operation, resection of colon. ICU admission, prolonged ICU stay (9 days). Prolonged hospital stay (> 2 mo). Alive
3	72	F	30	New hemiparesis. Compression of spinal cord at C1 level	Reoperation during the same hospital stay. Death 4 mo after operation
4	65	M	31	Diarrhea, peritonitis. Risk factors: amyloidosis, uremia, peritoneal dialysis	Prolonged hospital stay. Death on 25th postoperative day due to peritonitis
5	83	F	15	Difficult fiberoptic intubation. ST-segment changes during operation, treated with nitrate fixation. Pulmonary congestion in the recovery room. Risk factor: coronary heart disease	Unplanned ICU admission on postoperative day 2. Length of ICU stay 1 day. Death at 27 mo after operation
6	71	M	30	Difficult intubation. Respiratory arrest in the recovery room and new difficult fiberoptic intubation. ICU stay for 8 days because of upper airway swelling. On postoperative day 9 abdominal pain and dyspnea. Readmission to ICU. Intubation attempts were unsuccessful. Risk factor: corticosteroid therapy	Two emergency admissions to ICU. Death on the 9th postoperative day. Autopsy showed a perforated duodenal ulcer and peritonitis
7	35	M	29	Difficult intubation. At beginning of operation in prone position airway obstruction due to hematoma in intubation tube. Operation cancelled	New operation. Alive

ICU: intensive care unit.

In contrast to the study by Casey, *et al*[30], we found that preoperative neurological deficit (Ranawat class) was not associated with longterm mortality. In the study by Casey, *et al*, there were 79 patients in Ranawat class IIIa and 55 in class IIIb. The mortality was higher in class IIIb (58%) than in class IIIa (26%). In our study, the small number of patients in high Ranawat classes (12 in IIIa and 3 in IIIb) may explain the discrepancy. However, compared with a Swedish patient sample[23], our patients had more severe preoperative neurological deficits. That study did not evaluate longterm mortality. During the followup, 12 (14%) patients underwent reoperation due to recurrent subluxation in the same segment. The number of reoperations is a little higher than those reported by other investigators[7,21]. In our study reoperation did not have any influence on mortality rate.

The proportion of pain-free patients corresponds to previous reports[22,32]. The surgery was less successful in relieving neurological symptoms than in relieving pain, which is in agreement with other studies[22,31,32]. The method we used for outcome assessment has some limitations. It was based on patient's subjective estimation, and a structured and validated questionnaire was not used. Therefore, the results presented in Table 5 should be interpreted critically.

Based on our results, patients with rheumatoid AAS should preferably be treated before the development of severe multiorgan manifestations and more complicated cervical instability. Patients with RA having even minor cervical symptoms should be actively assessed for cervical instability. Attention should be paid to the perioperative management of these patients. Surgical treatment may not decrease the mortality in patients with RA, but it may result in more symptom-free years of life.

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Table 4. Factors contributing to mortality (Cox regression analysis).

Variable (unit)	Relative Risk	95% CI	p
Age (yrs)	1.05	1.00–1.10	< 0.05
Gender (0, 1)	0.74	0.34–1.58	NS
Corticosteroid therapy	1.04	0.46–2.34	NS
Other than horizontal subluxation (0,1)	2.67	1.21–5.86	< 0.05
Perioperative complication (0,1)	4.93	1.75–13.9	< 0.01

Table 5. Functional outcome according to the Ranawat score at time of surgery (n = 66).

	Total, n = 66	Ranawat I, n = 17	Ranawat II, n = 36	Ranawat IIIA, n = 10	Ranawat IIIB, n = 3
Pain					
Excellent result	32 (48.5)	8 (47.0)	20 (55.6)	4 (33.3)	
Good result	15 (22.7)	3 (17.6)	8 (22.2)	3 (25.0)	1 (33.3)
No change	10 (15.2)	3 (17.6)	2 (5.6)	3 (25.0)	2 (66.7)
Poor	9 (13.4)	3 (17.6)	6 (16.7)		
Neurological deficit					
Excellent result	29 (43.9)	5 (29.4)	21 (58.3)	3 (30.0)	
Good result	6 (9.0)	0	4 (11.1)	2 (20.0)	
No change	20 (30.3)	9 (52.9)	6 (16.7)	3 (30.0)	2 (66.7)
Poor	11 (16.6)	3 (17.6)	5 (13.9)	2 (20.0)	1 (33.3)
Functional capacity					
Excellent result	26 (52.0)	9 (52.9)	17 (47.2)	4 (40.0)	
Good result	11 (22.0)	3 (17.6)	9 (25.1)	2 (20.0)	
No change	7 (14.0)	3 (17.6)	3 (8.3)	3 (30.0)	2 (66.7)
Poor	6 (12.0)	2 (11.8)	7 (19.4)	1 (10.0)	1 (33.3)

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