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Original

Clinical Evaluation and Prognosis of Rheumatoid Patients Receiving Cervical Spine Surgery

Mika NAKATSUI, Yoshiharu KATO, Motoya KUBOTA, Koichi KANAYA and **Tatsuo ITOH***

Department of Orthopedic Surgery, Tokyo Women's Medical University
*Department of Orthopedic Surgery, Tokyo Women's Medical University Yachiyo Medical Center

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A retrospective study was performed to examine the risk factors for mortality in patients with rheumatoid arthritis (RA) undergoing cervical spine surgery. RA patients often have multiple complications. Even after successful cervical spine surgery, some patients can still have an unfavorable outcome. Therefore, spinal surgeons need to identify the risk factors that can influence mortality and consider the prognosis before making an appropriate decision about surgery. We reviewed 87 RA patients, and examined the mortality rate, sex, age, type of cervical subluxation, severe systemic complications, type of RA, cause of death, severity of myelopathy, and life expectancy. We compared these factors between patients who survived and those who died. Sixty-one patients survived and 26 died (mortality rate: 29.9%). The average follow-up period was 5.3 years. The mortality rate of men was higher than that of women. Age at surgery, and age at onset of RA were higher in patients who died. Patients who died had a shorter duration of RA. The mortality rate was higher in patients with subaxial subluxation (SAS), severe myelopathy, and severe systemic complications. The most common cause of death was infection. Cervical spine surgery should be performed in RA patients after considering their sex, age, and complications, and provided that the complications can be controlled.

Key words: rheumatoid arthritis, spinal surgery, mortality, prognosis, cause of death

Introduction

Recently, various surgical procedures are being performed to treat rheumatoid cervical spine. Patients with rheumatoid arthritis (RA) can develop various problems, including impaired activities of daily living (ADL) due to poly-arthritis, severe systemic complications, and side effects of steroid therapy. Accordingly, some patients have a poor result of surgery with regard to walking ability and survival time due to such complications. However, there have not been many recent reports about the prognosis of RA patients after cervical spine surgery. There was general reluctance to carry out surgery in RA patients with very severe myelopathy, which patients had objective weakness and long truct sign and were unable to walk (Ranawat class IIIb), but surgical/anesthetic techniques and postoperative management have advanced remarkably in recent years. We reviewed the clinical data of 87 RA patients who underwent cervical spine surgery at Tokyo Women's Medical University (TWMU) to compare the clinical course between each type of cervical subluxation and to study the influence of the severity of myelopathy on the postoperative life expectancy, in order to determine whether or not we should perform cervical spine surgery in RA patients with very severe myelopathy.

Materials and Methods

Eighty-seven patients (male 23, female 64) who underwent cervical spine surgery at TWMU from 1991 to 2003 were reviewed. All patients had been diagnosed with RA according to the 1987 classification criteria by the American Collage of Rheumatol-

Table 1 Demographic characteristic of the study population (n = 87)

	Total n = 87	Alive n = 61	Dead n = 26	p
Sex				< 0.01
Male	23	10	13 (56.5%)	
Female	64	51	13 (20.3%)	
Age at surgery (year)	32-79 (Av.60.1)	32-79 (Av.58.3)	46-79 (Av.64.4)	< 0.05
Duration of RA (year)	1-37 (Av.16.8)	1-13 (Av.18.2)	2-24 (Av.13.1)	< 0.01
Age of onset of RA (year)	18-74 (Av.43.5)	18-64 (Av.40.1)	20-74 (Av.51.6)	< 0.01
Types of cervical subluxation				
Atlanto-axial subluxation (AAS)	31	28	3	
Vertical subluxation subluxation (VS)	1	7	6	
Subaxial subluxation (SAS)	13	0	1	
AAS + VS	8	7	7	
AAS + SAS	16	9	7	
VS + SAS	4	1	3	
AAS + VS + SAS	5	2	3	
CS or OPLL	9	7	2	
(Group of SAS)	35	19	16	< 0.01
(Group of VS)	18	10	8	N.S.
Ranawat's classification (Before surgery)				
Class I	10	8	2	
Class II	14	14	0	
Class IIIa	36	29	7	
Class IIIb	27	10	17 (63%)	< 0.01
Ranawat's classification (After surgery)				
Class I	13	11	2	
Class II	26	22	4	
Class IIIa	37	26	11	
Class IIIb	11	2	9 (89%)	< 0.01
Systematic complications				
Severe complications group	32	14	18	< 0.01
Without severe complications group	55	47	8	
Types of RA				
Mutilans type	40	28	12	N.S.
Other types	47	33	14	

ogy. The follow-up period ranged from 0 month (death within 1 month) to 139 months (11.6 years), and the average time was 63.0 months (5.3 years). The follow-up rate was 88.6%. The age at surgery was 32-79 years (average: 60.1 years), the duration of RA was 1-37 years (average: 16.8 years), and the age at onset of RA was 18-74 years (average: 43.5 years). Other cervical surgery had been performed in 7 patients. Cervical subluxation was classified as atlanto-axial subluxation (AAS) in 31 patients, vertical subluxation (VS) in 1 patient, subaxial subluxation (SAS) in 13 patients, AAS+VS in 8 patients, AAS+SAS in 16 patients, VS+SAS in 4 patients, AAS+VS+SAS in 5 patients, and AAS+cervical spondylosis (CS) or ossification of the posterior longitudinal ligament (OPLL) in 9 patients (Table 1). The surgical methods were C1-2 posterior fusion by the method of Magerl & Brooks (M&B) in 37 patients, subaxial decompression by open door laminoplasty (LP) according to the method of Itoh & Tsuji[1)2)] in 15 patients, occipito-cervical fusion (OCF) with the Luque SSI or Orelude system in 19 patients, anterior body fusion (ABF) in 3 patients, M&B+LP in 5 patients, LP+ABF in 2 patients, posterior spinal fusion (PSF) in 1 patient, M&B+LP+ABF in 2 patients, ABF+laminectomy (Ln) in 1 patient, M&B+PSF in 1 patient, and M&B+PSF+ABF in 1 patient (Table 2).

Ranawat's classification was used to evaluate the severity of myelopathy as follows: Ranawat Class I was no neurological deficit, Class II was subjective weakness with hyperreflexia and dysesthesia, and Class III was objective weakness and long-tract signs (Class IIIa patients were able to walk and

Table 2 Surgical procedures

Procedure	No. of patients
Magerl & Brooks (M&B)	37
laminoplasty (LP)	15
occipito-cervical fusion (OCF)	19
anterior body fusion (ABF)	3
M&B + LP	5
LP + ABF	2
PSF	1
M&B + LP + ABF	2
ABF + laminectomy (Ln)	1
M&B + PSF	1
M&B + PSF + ABF	1
Total	87

Class IIIb patients were unable to walk). Before surgery, 10 patients were in class I, 14 patients were in class II, 36 patients were in class IIIa, and 27 patients were in class IIIb. After surgery, 13 patients were in class I, 26 patients were in class II, 37 patients were in class IIIa, and 11 patients were in class IIIb (Table 1).

We examined the following items.

1. Mortality

Mortality rate, period from surgery to death, age at death, and sex

2. Comparison between surviving and dead patients

1) Age: age at surgery, duration of RA, and age at onset of RA

2) Type of cervical subluxation: AAS, SAS, VS, AAS+SAS, AAS+VS, or AAS+SAS+VS

3) Percentage of patients with severe systemic complications

We divided the patients into two groups based on the severity of systemic complications, i.e., a severe complications group and a group without severe complications. Patients with cardiac, respiratory, or renal dysfunction were defined as having severe complications.

4) Type of RA

Mutilans or not[4)~8)]. The mutilans type of RA was defined as severe joint dysfunction with an opera glass deformity of at least three MP and PIP joints of the fingers or toes and involvement of other joints.

3. Cause of death

4. Severity of myelopathy

1) Relationship to the type of cervical subluxation

2) Relationship with life expectancy: mortality rate and survival rate

For statistical analysis, we adopted student's t-test, the χ^2-test, or analysis of variance (ANOVA), for testing group differences for continuous and categorical variables respectively. Cox Proportional Hazard regression analysis was used to identify possible predictors for survival. Significance was established at $p<0.05$. Analyses were done with Stat View software and SAS (Statistical Analysis System version 9.1.3, SAS Institute, Cary NC).

Results

1. Mortality

Sixty-one patients survived and 26 patients died during the follow-up period. The mortality rate was 29.9%. The period from surgery to death was 0 month (operative death) to 125 months (average: 33.6 months), and the age at death was 48-81 years (average: 67.5 years). The mortality rate for men was 56.5% (13/23), while that for women was only 20.3% (13/64). A significant ($p<0.001$) difference was found between the male and female mortality rates.

2. Comparison between surviving and dead patients

1) Age

(1) Age at surgery: The surviving patients were aged 32-79 years (average: 58.3 years) and the patients who died were aged 46-79 years (average: 64.4 years), with the latter group being significantly older ($p<0.05$).

(2) Duration of RA: For the surviving patients, the duration of disease was 1-33 years (average: 18.2 years), while it was 2-24 years (average: 13.1 years) for those who died. The latter group had a significantly shorter duration of RA ($p<0.01$).

(3) Age of onset: For the surviving patients, the age of onset of RA was 18-64 years (average: 40.1 years), while it was 20-74 years (average: 51.6 years) for those who died. The latter group was significantly ($p<0.01$) older at the onset of RA.

2) Type of cervical subluxation

The mortality rate at final follow up was 9.7% (n=

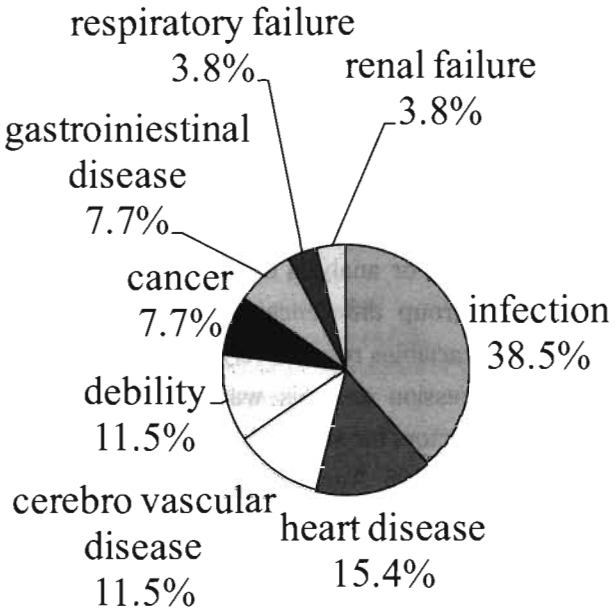

Fig. 1 Causes of death
The most common cause of death was infection.

3) for patients undergoing AAS only, while it was 44.4% (8/18 patients) on average for those undergoing VS (VS only: 100%, VS+AAS: 12.5%, VS+SAS: 75%, VS+AAS+SAS: 60%). In patient receiving SAS, it was 55.3% (21/38 patients) on average (SAS only: 46.2%, SAS+AAS: 56.2%, SAS+VS: 75%, SAS+AAS+VS: 60%). The SAS group had a higher mortality rate than the other groups.

3) Patients with severe complications

Among the surviving patients, 26.4% (n=14) had severe systemic complications, while the rate among patients who died was 72.0% (n=18). A significantly ($p<0.01$) higher incidence of severe complications was observed in the latter group.

4) Type of RA

Patients with mutilans RA accounted for 45.9% (n=28) of the survivors (n=61) and 46.2% (n=12) of the dead patients (n=26), with no significant difference between the two groups.

3. Cause of death

The cause of death was infection (pneumonia) in 10 (38.5%) of the 26 patients who died, followed by, heart disease in 4 (15.4%), cerebrovascular disease (bleeding or infarction) in 3 (11.5%), debility in 3 (11.5%), cancer in 2 (7.7%), gastrointestinal disease in 2 (7.7%), respiratory failure in 1 (3.8%), and renal failure in 1 (3.8%) (Fig. 1).

In the 3 patients who died within one month postoperatively, death was due to renal failure, pneumonia, and cerebral infarction. All deaths from infection were due to pneumonia; 4 patients had RA-related interstitial pneumonia before surgery. 3 patients developed pneumonia after surgery (cervical spine surgery in 1, the other surgery in 2), and 1 patient had pancytopenia due to treatment with methotrexate. The cause of death was thought to be related to RA (infection, interstitial pneumonia, renal failure, side effect of medication, debility due to impaired ADL, and postoperative cerebral infarction) in 18 patients (69%), while it was unrelated to RA (cancer in 2, multiple cerebral infarcts in 1, and myocardial infarction in 1) in 4 patients and unclear in 4 patients.

4. Severity of myelopathy

1) Type of cervical subluxation

According to Ranawat's classification (preoperative), type IIIb patients accounted for 3.2% (1/31 patients) of the group having AAS only, 50% (9/18 patients) of the VS group (VS only, VS+AAS, VS+SAS, and VS+AAS+SAS), and 62.9% (22/35 patients) of the SAS group (SAS only, SAS+AAS, SAS+VS, and SAS+AAS+VS). There was a higher percentage of patients with severe myelopathy in the SAS group (Fig. 2).

2) Survival time

(1) Mortality: There was a higher mortality rate for Ranawat's IIIb patients both before surgery (63%, $p>0.005$) and after surgery (89%, $p>0.005$) (Table 1).

(2) Survival rate: Kaplan-Meier analysis showed that both short-term and long-term survival were significantly lower in class IIIb patients according to the preoperative Ranawat's classification (Fig. 3a). The postoperative Ranawat's classification (Fig. 3b) indicated that long-term survival was the same in class IIIa and IIIb, but short-term survival was better in class IIIa. Furthermore, the average survival time was significantly ($p>0.05$) longer in class IIIa (46.9 months) than class IIIb (6.6 months), and most of the deaths in class IIIb occurred within 1 year.

In univariate analysis, sex, age at surgery, dura-

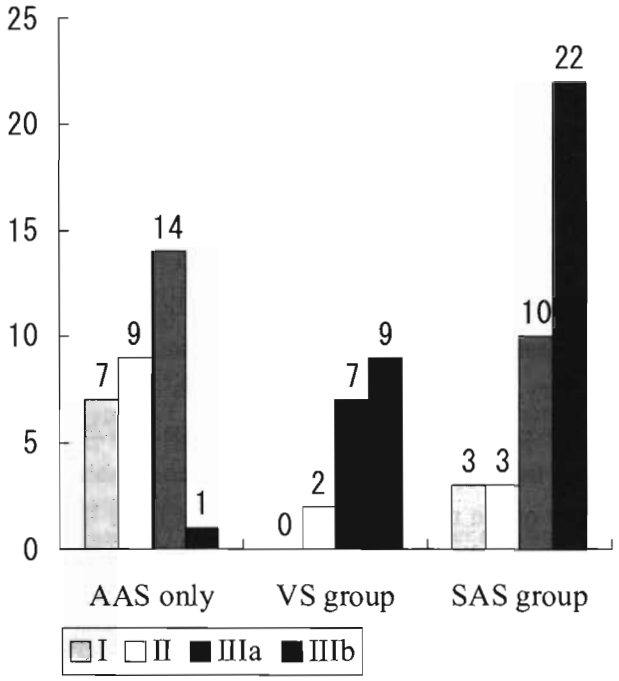

Fig. 2 Relationship between the type of cervical subluxation and the severity of myelopathy (Ranawat's classification before surgery)
Class IIIb patients accounted for 3.2% of AAS only, 50% of the VS group (VS only, VS + AAS, VS + SAS, and VS + AAS + SAS), and 57.9% of the SAS group (SAS only, SAS + AAS, SAS + VS, and SAS + AAS + VS). There was a significantly higher percentage of patients with severe myelopathy in the SAS group.

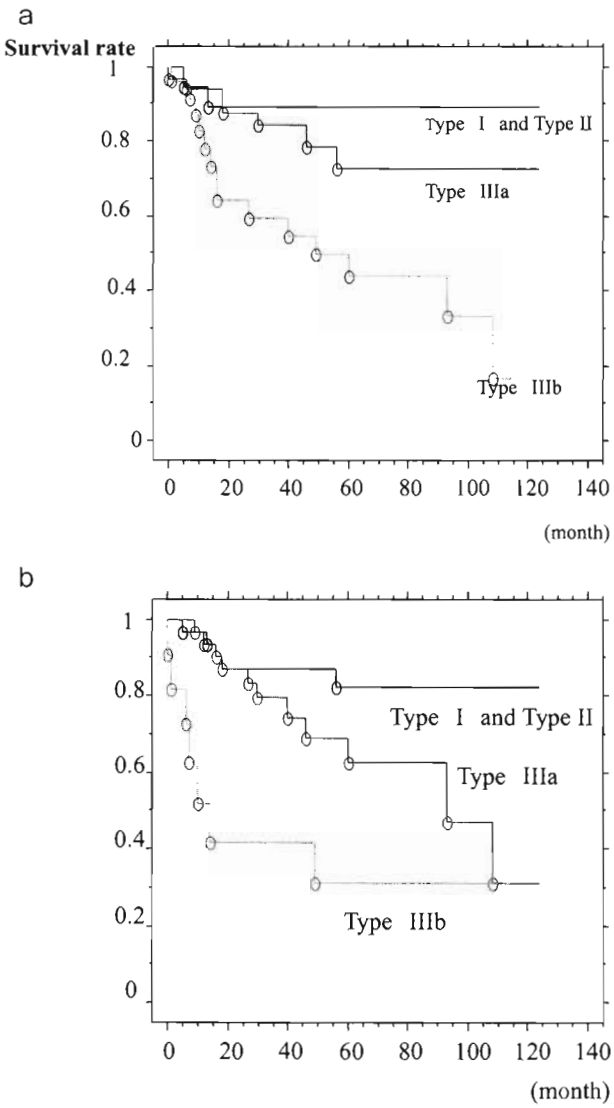

Fig. 3 Kaplan-Meier survival curves based on the clinical
a: Preoperative, Ranawat's classification. Ranawat class IIIb patients had a higher mortality rate.
b: Postoperative, Ranawat's classification. The average survival time was longer for class IIIa patients than class IIIb patients.

tion of RA, age of onset of RA, SAS group, having severe systemic complications. Ranawat IIIb (both before and after surgery) had significant differences (Table 1). But in multiple Cox regression, only Ranawat IIIb (both before and after surgery) and age of onset of RA were strongly affected to the life expectancy (Table 3).

Discussion

In this study, we characterized the outcome, cause of death, and prognostic factors for RA patients undergoing cervical spine surgery. Recently, these issues have been discussed[9)~12)], but there have been few reports about the question of whether or not cervical spine surgery should be performed in RA patients with very severe myelopathy. In addition, it is unclear whether cervical spine surgery is able to improve not only the ADL but also the life expectancy. According to our results, severe myelopathy certainly affects the outcome, mortality and the survival time, and we conclude that surgery should be done if it is possible to control the patient's complications.

Several studies[13)~15)] have already evaluated the mortality rate and prognosis of RA patients receiving cervical spine surgery. According to the results of these studies, the average age at death was 64.8 years, the average age at onset of RA was 48.8 years, and the average duration of disease was 15.6 years, but these studies only assessed patients who died after surgery. In other words, little is known about the differences between surviving patients

Table 3 Cox proportional hazard ratio regression for survival (stepwise method)

Parameter	Probability	Hazard Ratio
Ranawat IIIb (beforesurgery)	0.0376	0.363
Ranawat IIIb (after surgery)	0.0171	0.309
Age of onset of RA	0.0051	1.058

and dead patients. In our study, the patients who died were older at the onset of RA and had a shorter duration of disease compared with the surviving patients. The reason may be that myelopathy became more severe because RA lesions were superimposed on cervical spines affected by osteoporosis and spondylosis, while a decrease of ADL due to joint dysfunction and cardiopulmonary dysfunction increased the mortality rate. Lower cervical lesions (SAS) had more influence on the severity of myelopathy than upper cervical lesions (AAS) because of the narrower spinal canal at this level.

We also assessed the causes of death in the patients who underwent spinal surgery. Most of the previous reports[16)~18)] have concentrated on patients having surgical treatment. In particular, there have been few reports about the causes of death in patients receiving spinal surgery. When we compared our results with those of the other authors, infection was the most common cause of death in every series, but there was a higher rate of infection in our postoperative patients (36%) compared with conservative series (18-23%). Cancer showed a lower prevalence (about 10%) in our study and the other studies compared with the national average in Japan, and the reason for this may be that the average life expectancy of RA patients is shorter (about 65 years) than that of the general population. Respiratory and renal dysfunction were less common (4%) compared with other series of patients having conservative treatment (11-21%). Because our patients all had to be fit for surgery, they presumably did not include any subjects with very severe dysfunction.

When survival was assessed by Kaplan-Meier analysis for each level of myelopathy (Figs. 3a, 3b), both the preoperative and postoperative curves showed that survival was lower for the severe myelopathy patients (IIIb). When preoperative and postoperative survival curves were compared, the survival time of patients who could advance to class IIIa from class IIIb after surgery was clearly improved versus those who did not.

Even if the long-term survival of class IIIa and IIIb was similar after surgery, the average survival time was markedly longer in class IIIa, and most of the class IIIb deaths occurred within 1 year after surgery. Thus, we consider that it is important to improve IIIb patients to IIIa by surgery (72%), because this will allow longer survival, and also the severity of the myelopathy was proved to be the factor of mortality statistically (Table 3). In addition, it is worthwhile for bed-ridden patients to undergo surgery in order to be able to use a wheelchair or for wheelchair-bound patients to have surgery and become ambulant.

Conclusion

We reviewed RA patients who had undergone cervical spine surgery. Factors that contributed to a poor prognosis included male, sex, comparatively old age of the onset of RA, advanced SAS with severe myelopathy, and severe systemic complications. Infection was the most common cause of death after surgery. In conclusion, cervical spine surgery should be performed in RA patients whose complications can be controlled in order to improve ADL and prolong survival.

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関節リウマチの頸椎手術例の術後評価と生命予後の検討

東京女子医科大学整形外科
*東京女子医科大学八千代医療センター整形外科
中津井美佳（ナカツイミカ）・加藤　義治（カトウヨシハル）・久保田元也（クボタモトヤ）・金谷　幸一（カナヤコウイチ）・伊藤　達雄（イトウタツオ）*

関節リウマチ（RA）の頸椎病変に対する手術療法においては良好な短期成績が得られる反面，全身合併症，ステロイド使用の合併症，多関節病変による日常生活動作（ADL）の低下などのために期待した長期成績が得られない場合も少なくない．またRA患者では生命予後も短いため手術後の生存期間も問題となる．今回我々は自験例の長期手術成績，死亡率などより，年齢，性差，脊髄症状の重症度などが手術患者の生命予後に与えるか否かその影響を検討した．

対象は1991～2003年に東京女子医科大学整形外科において，頸椎手術を受けたRA患者87例（男性23例，女性64例）であった．追跡時，生存61例，死亡26例で死亡率29.9%，平均観察期間は5.3年，追跡率は88.6%であった．男性の死亡率は女性よりも有意に高く，手術時年齢，RA発症年齢は死亡群で有意に高く，RA罹病期間では死亡群が有意に短かった．下位頸椎亜脱臼（SAS）を有する群，重症脊髄症，重篤な全身合併症を有する群の死亡率が高かった．死亡群の死因では感染症（肺炎38.5%）が最も多かった．重篤な脊髄症を有し，術前歩行不能であった群のうち，術後歩行可能に改善した群は，術後も歩行不能のままであった群より有意に術後生存期間が長かった．

これまでRA頸椎にて手術を受けた患者の長期成績，特に生命予後を検討した論文は少ない．さらにRA患者は全身状態が悪く手術の危険性も高いため，かつてはRA頸椎の手術には消極的な意見も多かった．しかし近年，手術手技や麻酔技術の向上から周術期管理も改善し，患者自身のQOL向上に対する希望も強いため，積極的に手術を行う傾向にある．今回の検討から，男性，手術時およびRA発症年齢が高い，RA罹病期間が短い，SAS，重症脊髄症，重篤な全身合併症があることが生命予後の危険因子として認められた．さらに手術で歩行機能・麻痺が改善すれば予後が良くなることより危険因子に注意し，全身状態のコントロールがつくならば，積極的に手術を行うべきと考えている．