Pooled data analysis on anterior versus posterior approach for rheumatoid arthritis at the craniovertebral junction

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OBJECT Rheumatoid arthritis (RA) is one of the most debilitating autoimmune diseases affecting the craniovertebral junction (CVJ). Patients predominantly present with myelopathic symptoms and intractable neck pain. The surgical approach traditionally has been either a combined anterior and posterior approach or a posterior-only approach. In this article, the authors review pooled data from the literature and discuss the benefits of the two types of approaches.

METHODS A search of the PubMed database was conducted using key words that describe spine deformities in RA and specific spinal interventions. The authors evaluated the neurological outcomes based on the Ranawat scale in both the groups through chi-square analysis. Multiple logistic regression was carried out to further examine for potential confounders. Any adverse sequelae resulting from either approach were also documented. Because all the procedures performed via a transoral approach in the analyzed articles also involved posterior fixation, for convenience of comparison, the combined procedures are referred to as “anterior approach” or “anterior-posterior” in the present study.

RESULTS The search yielded 233 articles, of which 11 described anterior approaches and 14 evaluated posterior approaches. The statistical analysis showed that patients treated with a posterior approach fared better than those treated with an anterior (combined) approach. It was noted that those patients in whom the cervical subluxations were reducible on traction predominantly underwent posterior approaches.

CONCLUSIONS CVJ instability is a serious complication of RA that requires surgical intervention. Although the anterior-posterior combined approach can provide direct decompression, it is associated with morbidity, and the analysis showed no statistically significant benefit to patients. In contrast, the posterior approach has been shown to provide statistically significant superiority with respect to stabilization and subsequent pannus reduction. Surgical approaches are undertaken based on the reducibility of subluxations with traction and the vector of compressive force. However, the choice of surgical approach should be based on the individual patient's pathology.

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KEY WORDS atlantoaxial subluxation; cranial settling; basilar invagination; rheumatoid arthritis

RHEUMATOID arthritis (RA) is a debilitating systemic autoimmune disease that predominantly affects synovial joints. Craniovertebral junction (CVJ) involvement is seen in 36%–88% of patients.^{1,2,4,13,22,32,40} The pathophysiology of the inflammatory disorder often starts with synovitis, followed by formation of a pannus, which is characterized by inflammatory infiltrate (T cells, B cells, and cytokines) and digestive enzymes (matrix metalloproteinases, collagenases). Given the erosive and

bulky nature of the pannus and its dangerous location at CVJ, the probability of potential fatal complications such as cervical spine instability, blockage of vertebral arteries, and direct spinal cord compression is likely to increase as the disease progresses. A number of spinal deformities have been associated with RA. Atlantoaxial (C1–2) instability is the most common clinical manifestation, and it may lead to atlantoaxial subluxation or basilar invagination/cranial settling.

ABBREVIATIONS AADI = anterior atlantodental interval; CVJ = craniovertebral junction; PADI = posterior atlantodental interval; RA = rheumatoid arthritis.

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Spinal surgery is often indicated when patients present with intractable neck pain or progressive neurological symptoms. The surgical procedures are generally categorized into two groups: 1) combined anterior and posterior approaches and 2) posterior-only approach. The principle behind the anterior approach is to achieve direct decompression of the anterior cervical pathology, and the goal of the posterior approach is to stabilize the alignment of the vertebral column with immobilization to reduce pannus formation.¹⁴ Direct decompression via C-1 laminectomy may also be carried out if the vector of pressure is greater posteriorly. To date, there is no general consensus on which approach is the best for patients with RA. In this review, we aim to provide an overview of different spinal interventions and attempt to derive a surgical management algorithm that is tailored specifically to rheumatoid abnormalities at the CVJ.

Methods

A comprehensive search of the English-language literature for the years 1975–2014 was performed on PubMed using combinations of the following phrases that describe spine deformities (“atlantoaxial subluxation”, “basilar invagination”, “cranial settling”, “subaxial subluxation”, “rheumatoid arthritis”) and spinal interventions (“spine surgery”, “anterior approach”, “posterior approach, transoral”, “fusion”, “fixation”). Additional articles were located by cross-referencing articles encountered initially through the PubMed searches. Each index article was analyzed in detail, specifically focusing on the clinical outcome following either anterior or posterior approach. Since all the transoral procedures being done were complemented with posterior fixation, the combined approach is referred to in this paper, for convenience of comparison, as “anterior approach” or “anterior-posterior approach.” Inclusion criteria comprised articles (case reports, case series, meta-analyses, clinical trials, literature reviews, molecular studies, animal models, and guidelines) originating from peer-reviewed literature and discussing the surgical management, outcomes, and complications of RA at the CVJ. Analyses were performed with SPSS 22.0 software. A chi-square test was used in simple comparison of approaches (anterior vs posterior) with respect to neurological outcome, while multivariate logistic regression was performed to assess the influence of confounding factors.

Results

Study Selection

Our PubMed search yielded 233 articles for screening and with the application of our inclusion criteria we narrowed the results to 25 articles (11 primarily on combined anterior-posterior approach and 14 on posterior-only approach). Of these 25 articles, 17 met the criteria for inclusion in our pooled data analysis. The detailed study selection flowchart is shown in Fig. 1.

Study Characteristics

The 11 combined anterior-posterior approach manuscripts included 674 patients (Table 1) and the 14 posterior-

FIG. 1. Flow diagram representing the search criteria for selecting the articles. Out of 489 articles identified in the PubMed database and evaluated for this study, only 17 met the criteria for inclusion in the pooled data analysis.

only manuscripts included 592 patients (Table 2). Anterior approaches consisted primarily of transoral approaches while posterior approaches comprised occipitocervical, atlantoaxial, and subaxial fusion with laminectomy. The transoral approach was always supplemented with posterior fixation in the studies included in this analysis. For the convenience of categorizing the approaches, the combined anterior-posterior approach will be referred as “anterior approach” and posterior-only fusion as “posterior approach” for the rest of the paper.

Neurological Outcome

Neurological outcome was assessed based on the Ranawat classification. Improvement in neurological outcome was defined as improvement of at least 1 Ranawat

TABLE 1. Characteristics of studies describing an anterior approach*

Authors & Year	Type of Study	No. of Pts	Mean Age in Yrs (range)	Female/Male	FU (mos)	Type of Surgery†	Diagnosis
Menezes et al., 1985	Retrospective	45	—	—	—	Transoral in 7; posterior fixation in 38	BI, AAS, SAS
Crockard et al., 1986	Retrospective	14	57.8 (19–78)	11:3	18	Transoral	AAS
Spetzler et al., 1988	Retrospective	13	—	—	—	Transoral	BI
Hadley et al., 1989	Retrospective	21	54	—	24	Transoral	BI
Crockard et al., 1990	Retrospective	68	—	—	—	Transoral	AAS
Casey et al., 1996 [‡]	Prospective	134	62.9 (22–82)	110:24	—	Transoral in 91; posterior fixation in 43	BI
Casey et al., 1996 [‡]	Prospective	55	64.7	44:11	—	Transoral & posterior fixation	BI
Casey et al., 1997 [‡]	Prospective	116	62.3 (60.6–63.9)	92:24	45.3	Transoral in 67; posterior fixation in 49	BI (71 irreducible)
Kerschbaumer et al, 2000	Retrospective	15	61.6 (31–82)	12:3	50.7	Transoral	BI in 8 (coexisting pannus in 3; odontoid fracture in 1); pannus compression in 5 (coexisting pannus compression in 1); odontoid fracture alone in 1
Nannapaneni et al., 2005	Retrospective	32	66.81 (36–85)	25:7	39	Transoral in 21; posterior fixation in 11	AAS (coexisting BI in 6; BI & SAS in 3; SAS in 5)
Choi & Crockard, 2013	Retrospective & prospective	533 (216 w/ RA)	46.3	43%:57%	62.1	Transoral	BI, congenital malformation, chordoma

AAS = atlantoaxial subluxation; BI = basilar invagination; FU = follow-up; pts = patients; SAS = subaxial subluxation; — = data unavailable.

* Gray shading indicates studies that were included in the pooled data analysis.

† The transoral approach was always supplemented with posterior fixation in the studies included in this analysis.

‡ Similar studies by same authors and based on same database.

class above the preoperative assessment. Among the 25 articles that discussed the use of anterior or posterior approaches, 4 anterior approach articles and 11 posterior approach articles reported Ranawat classification data; 68% of patients treated with an anterior approach demonstrated neurological improvement, whereas 98% of patients treated with a posterior approach showed neurological improvement. When anterior versus posterior approach was the sole factor considered, the odds ratio for neurological improvement was 0.579 (95% CI 0.379–0.886) as summarized in Fig. 2. In our multivariate analysis, when anterior versus posterior approach was adjusted for factors such as sex, mean age, preoperative neurological status, and length of follow-up, there was no significant correlation with neurological outcome. The pooled data describing the percent change in postoperative Ranawat classification from preoperative Ranawat classification were also analyzed, as shown in Figs. 3 and 4.

Complications following an anterior or a posterior approach are described in Table 3 and Table 4, respectively.

Nonsurgical Predictors of Neurological Improvement

Several preoperative factors, including sex, use of corticosteroids, and duration of myelopathy, were found to be not strongly associated with outcome.^{30,33} In our review, a multivariate analysis of the effect of age, sex, surgical technique, and follow-up period was performed to analyze the influence of these factors on neurological improvement (Table 5). Despite the significant finding in the pre-

vious univariate analysis, we found that the surgical techniques were no longer significantly correlated with outcome when the mentioned factors were added. This was probably due to the smaller sample size ($n = 121$) available for the analysis and possible influence of confounding factors. Interestingly, sex and follow-up period were found to be potential confounders. Female sex had a significant effect on neurological outcome ($p = 0.001$). It is well known that female sex is associated with a higher susceptibility to most autoimmune diseases, including RA. Meanwhile, it is logical that the longer the follow-up, the greater the chance for recovery in terms of neurological status ($p = 0.003$).

In consideration of demographic factors, elderly age is significantly correlated with poor outcome.^{5,34} This should prompt careful selection of elderly surgical candidates and also might suggest the beneficial effect of early surgical intervention. On the other hand, high Ranawat class, especially Class IIIB (with long tract dysfunction) typically is associated with slow recovery and a high mortality rate.^{33,34} Casey et al.,⁵ in their multivariate analysis, demonstrated a high predictive value of preoperative spinal cord cross-sectional area for improvement of neurological outcome ($p = 0.026$). In other words, the smaller the spinal cord cross-sectional area, the worse the outcome. The spinal cord atrophy due to chronic compression and trauma most likely explains this observed phenomenon. Indeed, this led to more investigations focusing on different radiographic parameters: anterior atlantodental inter-

TABLE 2. Characteristics of studies describing a posterior approach*

Authors & Year	Type of Study	No. of Pts	Mean Age in Yrs (range)	Female/Male	FU (mos)	Type of Surgery	Diagnosis
Ranawat et al., 1979	Retrospective	33	62 (42–85)	21:12	54 (12–96)	Posterior fusion (occipitocervical in 12; atlantoaxial in 13); anterior fusion in 5	AAS in 13; BI in 1; SAS in 7; AAS & SAS in 7; SAS & BI in 3
Thompson & Meyer, 1985	Retrospective	12	53 (25–68)	10:2	36 (7–84)	Posterior fusion (occipitocervical in 2; atlantoaxial in 10)	AAS
Larsson & Toolanen, 1986	Retrospective	34	54 (29–72)	20:9	36	Posterior fusion (occipitocervical in 6; atlantoaxial in 28)	AAS in 28; BI in 6
Clark et al., 1989	Retrospective	41	57 (34–82)	36:5	40 (23–74)	Posterior fusion (occipitocervical in 16; atlantoaxial in 20); transoral in 2; anterior cervical vertebrectomy in 1	AAS in 20; BI in 5; SAS in 4
Santavirta et al., 1991	Retrospective	38	56 (35–77)	30:8	—	Posterior fusion	AAS in 27; BI in 2; SAS in 10
Chan et al., 1992	Retrospective	19	54.2	14:5	60	Posterior fusion (occipitocervical in 16; atlantoaxial in 20)	AAS
Eyres et al., 1998	Retrospective	26	64.5	21:5	—	Posterior fusion	AAS in 13; SAS in 7; BI in 6; AAS & SAS in 4
Christensson et al., 2000	Retrospective	82	65 (36–81)	61:21	7	Posterior fusion (atlantoaxial in 53 & occipitocervical in 19)	AAS in 66; SAS in 27; BI in 10
Omura et al., 2002	Retrospective	11	61.5 (46–74)	11:0	39.8 (14–62)	Posterior fusion (occipitocervical)	AAS in 1; SAS in 1; AAS, SAS & BI in 3
Tanaka et al., 2005	Retrospective	26	53	6:20	—	Posterior fusion (atlantoaxial)	AAS
Clarke et al., 2006	Retrospective	51	61	40:11	96	Posterior fusion (atlantoaxial in 31; subaxial in 17; occipitocervical in 3)	AAS in 33; SAS in 8; BI in 2
Ronkainen et al., 2006	Retrospective	86	61.8	—	90 (60–120)	Posterior fusion (atlantoaxial in 78; occipitocervical in 3)	AAS
Kotil, 2012	Retrospective	15	57.4	6:9	—	Posterior fusion	AAS in 2; SAS in 8; AAS & BI in 5
Miyamoto et al., 2013	Retrospective	118	61.0	86:32	64 (1–180)	Posterior fusion (atlantoaxial in 28; occipitocervical in 41); anterior fusion in 5	BI, AAS, BI

* Gray shading indicates studies that were included in the pooled data analysis.

val (AADI) and posterior atlantodental interval (PADI). AADI and PADI measure the space available between spinal cord and the vertebra ventrally and posteriorly. Boden et al., have observed that a PADI of at least 10 mm always resulted in improvement of 1 neurological class,³ and hence many spine experts have advocated surgery when PADI is less than 14 mm in atlantoaxial subluxation. In the same report, PADI was proven superior as both a diagnostic and a prognostic parameter when AADI failed to be as useful as PADI. On the other hand, subaxial canal diameter, which is the space available for the spinal cord below the axis, was shown to have similar finding (< 14 mm) as a useful prognostic factor in subaxial subluxation. Furthermore, vertical subluxation, as in basilar invagination, has a worse prognosis and poor motor recovery compared with horizontal subluxation. Despite the high rate of morbidity resulting from surgery, the fear of potentially life-threatening events eventually prompts most spinal surgeons to perform surgery.

Discussion

The optimal surgical approach in the treatment of the rheumatoid spine remains a controversy in spine surgery. To our knowledge, there have been only 2 studies that included analyses of type of spine surgery (anterior vs posterior) in RA patients.^{7,30} Casey et al.⁷ reported the results of a prospective study involving 116 patients with vertical translocation, a Ranawat neurological classification of at least Class II, and a mean postoperative follow-up of 62.3 months. The choice of anterior-posterior combination vs posterior-only surgery was made based on whether the compression was predominantly anterior or posterior and if the translocation was reducible with traction. A transoral procedure was carried out in 67 cases (57.8%). Neurological improvement was seen in 46% of the patients treated with a posterior approach group and 44% of those treated with an anterior approach group. However, the difference of 2 percentage points was not statistically significant. In

FIG. 2. Bar diagram summarizing the comparative neurological improvement in patients treated with anterior versus posterior approaches. About 68% of patients who underwent an anterior approach demonstrated neurological improvement in comparison with 98% of patients who underwent a posterior approach. Neuro = neurological.

the same study, the authors also showed higher incidence of chest infection in the anterior-approach group, but the association was not statistically significant. Nannapaneni and colleagues³⁰ examined surgical outcome in patients with very poor preoperative neurological status (Ranawat Class IIIB) and a mean follow-up of 39 months. All the patients underwent halo placement before surgery, and if their subluxation was reducible, they had the posterior-only surgery. However, only 2 of the patients with reduc-

ible subluxations had basilar invagination. The influence of different surgical approaches on clinical outcome was not found to be statistically significant. Several articles have shown that pannus regression is also possible with posterior stabilization despite anterior location of the pannus.^{20,23,24,37,41,42}

Transoral

Fang and Ong were among the first to use a transoral

FIG. 3. Analysis of the pooled data demonstrating the neurological outcome based on the Ranawat criteria for the anterior approach. It is easily appreciated that the more severe the disease is, the less is the possibility of improvement.

FIG. 4. Analysis of the pooled data demonstrating the neurological outcome based on the Ranawat criteria for the posterior approach. Ranawat scores have shown better improvement in the posterior approach.

approach in treating atlantoaxial instability.¹⁷ It can be categorized into 3 different types: 1) transoral-transpalatal approach, 2) transoral-transpharyngeal or standard transoral, and 3) transmandibular with split. The standard transoral approach provides exposure from the lower third of the clivus to C-2. Due to the common rheumatoid spine pathology at CVJ, the standard transoral approach has been mainly employed in direct ventral decompression from the mass effect exerted by the pannus and odontoid peg compression on the spinal cord at the CVJ. The decompression is achieved mainly via odontoidectomy, and posterior fixation is carried out on the same day to correct the cranio-cervical instability resulting from the procedure. Choi et al.⁹ described a decreasing trend in the use of transoral procedures in a series of 479 patients over 3 decades. This might be explained by the evolution of medical treatment (i.e., disease-modifying antirheumatic drugs) and the advancement of surgical approaches, especially the dorsal route of fixation and fusion.

Endoscopy

More recently, endoscopic transnasal procedures have gained popularity for odontoid resection. These minimally invasive techniques address various limitations of open transoral approaches. Avoidance of a transmaxillary procedure is probably the major advantage, as the splitting of the palate is known to be associated with a high incidence of morbidity.⁹ However, Choi et al. pointed out the relatively high incidence of CSF leak associated with the endoscopic technique (22%–25%) compared with the conventional one (1.3%).

Atlantoaxial Fusion

Historically, a posterior fusion mainly comprised of various wiring construct techniques, which include Galie, Brooks, and Sonntag-Dickman techniques. During the 1st decades of the 21st century, there has been a trend of increasing use of transarticular screws in correcting atlan-

TABLE 3. Complications following an anterior approach

Authors & Year	Sepsis	Respiratory*	Cervical Infection	Cardiac Failure/MI	Dysphagia	CSF Leak	Pseudarthrosis	SAS/ASD
Ranawat et al., 1979	7.1%	7.1%	NR	NR	NR	NR	4/28	14.3
Thompson & Meyer, 1985	NR	8.3%	NR	NR	NR	NR	8.3%	NR
Larsson & Toolanen, 1986	NR	2.9%	NR	NR	NR	NR	14%	NR
Clark et al., 1989	NR	7.3%	7.3%	2.4%	NR	NR	NR	NR
Santavirta et al., 1991	5.3%	2.6%	2.6%	7.9%	NR	NR	NR	NR
Chan et al., 1992	5.3%	5.3%	5.3%	5.3%	5.3%	NR	NR	NR
Eyres et al., 1998	NR	NR	3.8%	NR	NR	NR	NR	NR
Christensen et al., 2000	NR	NR	3.7%	1.2%	NR	1.2%	NR	NR
Omura et al., 2002	NR	NR	9.1%	NR	NR	NR	NR	NR
Tanaka et al., 2005	NR	0	7.7%	NR	NR	NR	NR	NR
Clarke et al., 2006	NR	NR	NR	NR	NR	NR	NR	39.3%
Ronkainen et al., 2006	NR	2.3%	NR	NR	NR	NR	NR	NR
Miyamoto et al., 2013	NR	NR	NR	NR	NR	NR	4.3%	NR

ASD = adjacent segment disease; MI = myocardial infarction; NR = not reported.

* Pneumonia, respiratory insufficiency.

TABLE 4. Complications following a posterior approach

Author & Year	Pharyngeal Infection	Cervical Wound Infection	VA Occlusion w/ Brainstem Stroke	Respiratory*	CSF Leak	Meningitis	Septicemia
Menezes et al., 1985	0	NR	NR	NR	NR	NR	NR
Crockard et al., 1986	0	NR	NR	NR	NR	NR	NR
Menezes & VanGilder, 1988	7.0%	NR	NR	NR	NR	NR	NR
Spetzler et al., 1988	NR	NR	7.7%	7.7%	NR	NR	NR
Hadley et al., 1989	NR	4.7%	4.7%	9.5%	0	NR	NR
Crockard et al., 1990	NR	NR	NR	5.9%	8.8%	2.9%	1.4%
Casey et al., 1997	4.3%	0.9%	NR	19.8%	NR	2.6%	NR
Nannapaneni et al., 2005			3.1%	12.5%			
Choi & Crockard, 2013	0	2.1%	NR	10.8%	0	0.5%	1.1%

VA = vertebral artery.

* Pneumonia, pulmonary embolus, atelectasis.

TABLE 5. Results of multivariate analysis*

Variable	Adjusted OR for Neurological Improvement	p Value
Anterior vs posterior	0.584	0.445
Sex (female)	21.250	0.001
Age (>70 yrs)	1.563	0.445
Preop Ranawat class (Class III)	1.471	0.391
Follow-up (>5 yrs)	13.106	0.003

* Odd ratios for neurological improvement, estimated significance for anterior versus posterior, sex, mean age, preoperative neurological status, and length of follow-up in the 121 cases included in the pooled data analysis.

toaxial subluxation. Unlike the conventional wiring techniques, the placement of transarticular screws from the pars interarticularis of C-2 into the lateral mass of C-1 can provide immediate rigid internal fixation.

Occipitocervical Fusion

Extension of fusion or fixation to the occipital bone is commonly carried out in patients with basilar invagination. This is the type of fusion that has always been employed following anterior odontoidectomy to correct the secondary instability.

Limitations of This Study

The major limitation of our analysis was the small number of qualifying studies that included long-term follow-up. In addition, our analysis was based almost entirely on

FIG. 5. Treatment algorithm of Menezes et al., which assists the surgeon in decision making depending on the physical examination and radiological findings and the reducibility of the deformity. Decompr. = decompression; 1° = primary. From Menezes et al.²⁸ Published with permission.

retrospective studies. It included only 1 prospective study, and we did not find any randomized clinical trial in the current literature.

Conclusions

Numerous factors, including reducibility of the deformity, the direction of greatest compression, preoperative neurological status, and the patient's age, need to be considered before deciding to carry out either approach. In 1980, Menezes et al. proposed an algorithm (Fig. 5) for surgical treatment of CVJ pathology based on most of the factors mentioned.²⁸ Our findings reinforced the principle of management as illustrated in the algorithm and also added several extra factors (i.e., preoperative neurological status) for consideration when choosing either approach.

In our analysis, we showed that 66% of those with Class IIIB myelopathy improved to at least 1 class above in the anterior-approach group during postoperative follow-up while compared with 46% in the posterior-approach group. There was no case in either group in which a patient's condition improved to Class I. Patients with a Ranawat Class IIIB score have the worst prognosis and outcome.

As far as neurological improvement is concerned, overall, statistics demonstrated the superiority of the posterior approach in patients whose subluxation is reducible. Hence, it would be best to avoid an anterior approach unless it is indicated, as in those cases in which a subluxation is not reducible, even with traction. We recommend that surgical decision making in managing CVJ complications of RA should be based on the correlation between the clinical picture and radiological findings in individual patients, and we hope that our results will be helpful in that process.

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Conception and design: Madhavan. Acquisition of data: Chieng. Analysis and interpretation of data: Madhavan, Chieng. Drafting the article: Chieng. Critically revising the article: Madhavan. Reviewed submitted version of manuscript: Vanni. Statistical analysis: Madhavan. Administrative/technical/material support: Vanni. Study supervision: Madhavan, Vanni.

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