Rheumatoid Arthritis of the Cervical Spine
Clinical Considerations

Bradley R. Wasserman, M.D., Ronald Moskovich, M.D., F.R.C.S., and Afshin E. Razi, M.D.

Abstract

Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder affecting multiple organ systems, joints, ligaments, and bones. Although clinical findings can be confounded by the severity of multifocal joint and systemic involvement, a careful history is critical to identify symptoms of cervical disease; serial physical examination is the best noninvasive diagnostic tool. Thorough physical and neurologic examinations should be performed in all patients and serial functional assessments charted. Radiographs of the cervical spine with lateral flexion-extension dynamic views should be obtained periodically and used to “clear” the cervical spine before elective surgery requiring general anesthesia. Advanced imaging, such as magnetic resonance imaging (MRI) or myelography and computed tomography (CT), may be necessary to evaluate the neuraxis. Early initiation of pharmacotherapy may slow progression of rheumatoid cervical disease. Operative intervention before the onset of advanced myelopathy results in improved outcomes compared to the surgical stabilization of patients whose conditions are more advanced. A multidisciplinary approach involving rheumatology, surgery, and rehabilitation is beneficial to optimize outcomes.

Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder affecting multiple organ systems, joints, ligaments, and bones. The extra-articular involvement may involve the skin, the eye, the larynx, and the pulmonary, cardiovascular, hematologic, renal, neurologic, and lymphatic systems. Although there are periods when RA flares and times when it is quiescent, it frequently results in a proliferative and erosive synovitis that progresses to destruction of articular cartilage. RA is the most common inflammatory disorder affecting the cervical spine, an involvement that is second only to RA in the metatarsophalangeal joints. The course of the disease is unpredictable. For some patients, it manifests as a benign process, while in others, a progressive pattern of instability develops. In 1890, Garrod reported involvement of the cervical spine in 178 (36%) of 500 patients with RA.1 In 1951, Davis and Markley2 were the first to describe medullary compression from atlantoaxial subluxation. In 1952, Kornblum and colleagues3 were the first to recognize the relationship between RA and cervical spine instability, the knowledge of which has deepened our understanding of the effects of RA on the cervical spine. More recent literature has documented involvement of the cervical spine early in the course of RA,4 often within the first 2 years after diagnosis.4,5 Craniovascular complications arise in 30% to 50% of patients who have had RA more than 7 years, while atlantoaxial subluxation with myelopathy develops in 2.5 percent of those with RA for more than 14 years.5

Bradley R. Wasserman, M.D., was a Chief Resident, Department of Orthopaedic Surgery, and is currently a fellow in the Department of Sports Medicine, University of Pittsburgh Medical Center, Pennsylvania. Ronald Moskovich, M.D., F.R.C.S., is Assistant Professor, New York University School of Medicine, and within the Division of Spine Surgery, Department of Orthopaedic Surgery. Afshin E. Razi, M.D., is Clinical Assistant Professor, NYU School of Medicine, and within the Division of Spine Surgery, Department of Orthopaedic Surgery, NYU Hospital for Joint Diseases, NYU Langone Medical Center, New York, New York.

Correspondence: Ronald Moskovich, M.D., NYU Hospital for Joint Diseases, 301 East 17th Street, New York, New York 10003; ronald.moskovich@nyumc.org.
Although the exact etiology is uncertain, RA is multifactorial and currently believed to be triggered by exposure of an immunogenetically susceptible host to an arthritogenic microbial antigen. It is an immunologically mediated disorder that can affect the articular and non-articular organ systems. The articular involvement is a symmetrical peripheral joint disease affecting large and small joints and axial involvement predominantly of the upper cervical spine.

Following the expression of the new antigen, these synovial cells stimulate the body to produce immunoglobulins (IgM) against autologous IgG, the so-called rheumatoid factor. An inflammatory response is initiated by the activated CD4+ helper T cells, stimulating the release of monocytes, macrophages, and synovial fibroblasts to produce the proinflammatory cytokines interleukin-1, interleukin-6, and TNF-α and to secrete matrix metalloproteinases through cell-surface signaling by means of CD69 and CD11, as well as through the release of soluble mediators such as interferon-γ and interleukin-17; this ultimately results in synovitis and pannus formation. The sequelae of this process can lead to destruction or incompetence of the involved ligaments, bones, or joints, or any combination thereof. Early initiation of pharmacotherapy using disease modifying anti-rheumatic drugs (DMARDS) in combination with the introduction of newer immunological mediators, such as TNF-α blockers, slows progression of the disease. Initiation of aggressive therapy prior to cartilage destruction may actually prevent or significantly mitigate joint damage, usually caused by rheumatoid pannus. It is also important to identify patients who are at risk of developing irreversible neurologic deficit and to intervene surgically before neurologic deterioration compromises their already limited functional ability.

**Anatomy**

The anatomy and the dynamic forces exerted on the cervical spine make it especially vulnerable to the effects of RA. There are numerous synovial joints, including the atlanto-occipital, atlantoaxial, and facet (apophyseal) joints. The neurocentral joints of Luschka and the intervertebral disks are also functional components of the subaxial motion segments. The occipit-C1 and C1-C2 articulations are the only segments in the spine without intervertebral disks. These two segments consist exclusively of synovial joints and, thus, do not benefit from the protection afforded by the more stable cartilaginous intervertebral joints. Even the transverse ligament of the atlas (C1) articulates with the posterior aspect of the dens via a synovial joint.7 The unique characteristics of the atlas and axis permit increased motion of the cervical spine. The atlas lacks a vertebral body and supports the head by lateral articulations with the occipital condyles, resulting in greater than 50% of the total cervical spine flexion and extension at the occiput-C1 articulation. The odontoid process of the axis articulates with the atlas-transverse ligaments. This unique articulation accounts for approximately 50% of all cervical spine rotation. The dynamic forces on the cervical spine are increased by its range of motion and its location between the stiffer thoracic spine and the weight of the head.

The stability of the atlantoaxial complex depends primarily on the integrity of the transverse ligament. The alar ligament is a secondary stabilizer located between the odontoid process and the occiput. The apical ligaments provide additional support for the occiput-atlanto-axial articulation. Because the C1-C2 facets are primarily oriented in the axial plane, compared to the lower cervical spine, there is no bony structure interlocking the atlas and axis to prevent subluxation.8 Fielding and coworkers demonstrated that the integrity of the transverse ligament is an important factor in preventing anterior subluxation of the atlas, especially during neck flexion.7,8 In RA, the transverse ligament is frequently targeted and becomes incompetent, due to involvement or spread of inflammation from the synovial articulation of the dens. Complete rupture of the transverse ligament allows only 4 to 5 mm of anterior subluxation of the atlas if the secondary stabilizers are intact. Involvement of the secondary stabilizers in RA results in progressive loss of stability of the atlantoaxial joint. The synovial inflammation at the base of the dens can result in erosion of the odontoid process, further compromising stability. The lack of osteophyte formation in the face of hypermobility, a unique characteristic of RA, fails to provide compensatory stability. The dynamic forces generated by the weight of the head and relative stability of the thoracic spine exacerbate the situation and may result in incompetence of the ligamentous stabilizers or fracture of the weakened dens, or a combination of the two. The lower medulla is approximately 11 mm in AP diameter. At the foramen magnum, the spinal diameter is 10 mm and distally 8 to 10 mm. The space available for cord (SAC) is 14 mm at the foramen magnum, 14 mm at C2, and 12 to 14.5 mm in the subaxial spine.6

**Pathophysiology**

The role of mediators of inflammation, such as cytokines, growth factors, and metalloproteinases has been described in the progression of RA. These factors attract and activate cells from the peripheral blood and enhance proliferation and activation of synoviocytes. The proteases can then invade and destroy articular cartilage, subchondral bone, tendons, and ligaments. The histologic picture of a joint affected by RA typically consists of a hypervascular layer of synovium infiltrated with giant cells and other inflammatory cells. There is a high population of lymphocytes in the acute phase. Fibrin is seen as a sheet within the joint cavity. The hyaline cartilage is damaged, and reactive bone formation is seen in the subchondral regions. The ligaments are also involved via disruption of collagen, multiple micro-tears, and fibrous tissue repair. This destructive synovitis progresses to bone erosion and ligamentous laxity, ultimately leading to instabil-
ity and subluxation of the cervical spine. The most common presentations of cervical spine involvement include: atlantoaxial subluxation (65%), cranial settling (20%), subaxial subluxation (15%), or a combination thereof.

Anterior atlantoaxial subluxation (AAS) is the most common deformity and results from laxity of the primary and secondary ligamentous restraints, as described. Anterior subluxation greater than 10 to 12 mm implies destruction of the entire ligamentous complex. The SAC decreases as the anterior atlantodental interval (AADI) increases and the posterior atlantodental interval (PADI) decreases. Rheumatoid pannus, formed by granulation tissue within the synovium due to collagenases and proteolytic enzymes that destroy other ligaments, cartilage, tendons, and bones, has a propensity for the periodontoid region. The pannus itself may further decrease the PADI, resulting in additional injury to the cord. Subluxation may ultimately lead to cord compression, resulting in myelopathy.

Posterior atlantoaxial subluxation occurs less frequently than anterior AAS, accounting for approximately 7% of cases. Posterior subluxation is usually due to erosion or fracture of the dens, and it may carry a higher risk of cord compression than AAS. Lateral subluxation usually occurs with rotational deformity and is seen in as many as 20% of cases.

Cranial settling results from occipito-atlanto-axial erosion that usually follows atlantoaxial subluxation. Other terms describing this deformity include basilar invagination, translocation of the dens, atlantoaxial impaction, superior migration of the odontoid, and vertical settling. However, “basilar invagination” and “basilar impression” are terms usually used to describe actual deformity of the skull base, such as occurs in osteogenesis imperfecta. El-Khoury and associates observed that symmetrical rheumatoid destruction of the occipito-atlanto and atlantoaxial joints allows the cranium to settle on the cervical spine and for the dens to enter the foramen magnum. However, another investigation observed that if only one lateral mass is involved, fixed rotational tilt of the head may result. Superior migration of the dens can lead to brain stem compression. Cranial settling often results in reduction of the atlantoaxial interval due to the conical shape of the dens and reduced motion, giving a false impression of anatomic improvement known as “pseudostabilization.”

Subaxial cervical subluxation occurs secondary to combined destruction of the discovertebral and the facet joints. Subluxation can appear as an isolated deformity or can affect multiple spinal levels, producing a “staircase” deformity. Kudo and Iwano have described anterior soft tissue masses, posterior ligamentous thickening, and bony subluxation. These changes may cause osteophyte formation, ankylosis, bone collapse, and kyphosis. Crockard further postulated that laxity of the atlantoaxial ligaments and subaxial post-inflammatory ankylosis are the two main deforming factors in RA of the cervical spine, with the laxity of the atlantoaxial ligaments playing the predominant role in early RA.

Autopsy reports of patients with RA most likely underestimate the true frequency of death due to rheumatoid cervical changes and spinal cord compression. Mikulowski and colleagues found that of 104 autopsies of RA patients, 11 had AAS with cord compression; seven of these 11 patients had died suddenly. This study revealed a 10% rate of fatal cord compression in patients dying with RA.

In a postmortem study of nine patients with RA and myelopathy, Henderson and coworkers noted that the cord pathology occurred mostly in the dorsal white matter of the spinal cord and was characterized by axonal degeneration, central chromatolysis, and axonal retraction. The cord pathology usually included subaxial degeneration, indicating diffuse injury throughout the cervical spine. Their results concluded that the effects of compression, stretch, and movement were the likely causes of myelopathy, rather than ischemia. However, in another autopsy study of 11 patients with paralysis secondary to RA, Delamarter and Bohlman suggested that the paralysis could be due to either mechanical neural compression or vascular impairment, or both.

The fibers in the pyramidal decussation to the upper limbs are more superior and ventral and more medial than the lower limb fibers, which are located inferior and laterally at the cervicomedullary junction. Atlanto-axial subluxation may result in cruciate paralysis, which is a symmetric upper extremity paralysis with less lower extremity involvement.

**Epidemiology and Natural History**

Complete understanding of the natural history of rheumatoid cervical spine remains deficient, due in part to therapeutic intervention. Reports of the prevalence of cervical spine abnormality associated with RA (17% to 88%) and neurologic complications (11% to 70%) vary widely in the literature. According to one study, approximately 1% of adults in Europe and the United States (2.2 million) are affected by RA, 220,000 (10%) of whom have cervical spine involvement; 62,700 individuals would benefit from surgical stabilization.

There is a wide variation in the prevalence of AAS in RA patients, depending on the length of follow-up. The variations reported in different studies may be due to different populations studied and different criteria (i.e., neurologic or radiographic evaluation or both). Sharp and Purser performed a large general population survey, reviewing 1,478 single lateral cervical films; 78 (5.3%) patients had clinical evidence of RA and, of those, 6.4% (5/78) displayed atlantoaxial subluxation. Of another 79 RA patients admitted to the hospital, 14 (18%) were noted to have atlantoaxial subluxation. Among 241 patients with RA, Riise and associates documented a mean observation time from the diagnosis of RA to AAS of 3.9 years. The prevalence of AAS has been reported to be as high as 12% within 2 years after the onset of RA. Pellici and col-
leagues\textsuperscript{39} reported on the outpatient records of 106 patients from a comprehensive arthritis program at one institution. They reported that 46 (43\%) of their patients already had radiographic evidence of rheumatoid involvement of the cervical spine at the start of their study. Of these 46, AAS was observed in 28 (61\%), AAS combined with subaxial subluxation in 9 (20\%), and subaxial subluxation alone in 5 (11\%). Two years later, Winfield and coworkers\textsuperscript{26} concluded that cervical subluxation was more likely to occur in patients with erosions of the hands and feet, which had a propensity to deteriorate progressively over time. They also noted that the timing and severity of cervical subluxation coincided with the progression of peripheral erosive disease in 26 (76.5\%) of the 34 patients in their case series.

The consequences of the development of AAS can be dire. In 1997, Sunahara and associates\textsuperscript{40} published their follow-up on 21 patients with RA and myelopathy secondary to AAS. All patients were recommended for surgery but refused. No patient showed any sign of improvement, while 16 (76\%) had evidence of deterioration during follow-up. All patients became bedridden within 3 years of the onset of myelopathy. The cumulative probability of survival was 0\% 7 years following the onset of myelopathy. In 2001, Riise and colleagues\textsuperscript{38} reported that patients with AAS had a mortality rate eight-times that of patients without AAS.

Untreated AAS can have very poor outcomes. Once myelopathy has occurred, death is a common sequela. Even with all of the literature that is available on rheumatoid cervical spine, it is still impossible to predict which patient will progress radiographically or which patient will experience neurologic deficits. Hence, the best results of operative stabilization have been reported in patients who were treated before any myelopathic signs were present. There have been several reports stating that the severity of cervical spine involvement in RA correlates to the severity of extant peripheral joint disease, rheumatoid nodules, high seropositivity, vasculitis, high-dose steroid therapy, and male gender.\textsuperscript{9,33,36,38,41-44}

Boden and coworkers\textsuperscript{45} investigated the radiographic and clinical course of 73 patients with rheumatoid involvement of the cervical spine over an average of 7.1 years; 58\% (42/73) became paralyzed. Seven patients with paralysis were treated nonoperatively. None of these individuals improved, and six patients had worsening of their neurologic deficits. Three of the patients died within 1 month after the onset of paralysis, two from compression of the spinal cord. The other four patients died within 4 years of the diagnosis; three died secondary to cord compression, while one passed away from cardiac disease. All seven patients treated nonoperatively died within 4 years, five (71\%) from cord compression; three died within 1 month from the onset of paralysis. Forty-eight percent (35/73) had operative treatment; 71\% (25/35) of those treated operatively for paralysis had neurologic improvement, while only two of these patients (6\%) worsened one neurological level. They also noted that the initial neurologic class was related to neurologic recovery. Rana\textsuperscript{46} reviewed a series of 41 patients with AAS during a 12-year period. Radiographically, 12\% improved, 61\% were unchanged, and 27\% had progression of instability. With disease progression, the occipitoatlantal complex involvement becomes significant and cranial settling develops. The prevalence of cranial settling has been reported to be between 5\% and 38\%.\textsuperscript{21,37,46,47} and progresses in 35\% to 50\% of patients.\textsuperscript{19}

Subaxial subluxation develops in 10\% to 20\% of patients with late stage RA.\textsuperscript{21,25,37} It may also develop in patients who were treated with an arthrodesis. In 1991, Kraus and associates\textsuperscript{14} reported on a series of 79 patients with generalized RA and prior occipito-cervical fusions. Thirty-six percent developed subaxial subluxation an average of 2.6 years following their fusion; however, only 5.5\% of patients treated with an atlantoaxial fusion developed subaxial subluxation an average of 9 years after their fusion. This case series suggests that monosegmental atlantoaxial (C1-C2) arthrodesis is preferable to occiput-C2 fusion, if possible, and also that consideration be given to extending fusion levels in patients with early subaxial subluxation and to monitoring patients with occipitocervical fusion for development of subsequent subaxial subluxation.

**Clinical Manifestations**

A careful history is critical in identifying symptoms of cervical disease. Neurologic findings are difficult to define, because of multifocal involvement associated with muscle wasting, joint arthropathy, decreased range of motion, joint pain, and neuropathy. Many patients may be asymptomatic, even with severe instability, due to the silent nature of this condition. Marks and colleagues\textsuperscript{38} showed a 31-week delay in diagnosis from the first signs of cervical myelopathy. Once myelopathy has occurred, progression is almost a certainty.

A thorough physical examination should be performed in all patients, even though findings can be confounded by the severity of multifocal involvement. Serial physical examinations are the best noninvasive diagnostic tool. Certain findings should arouse suspicion for further work-up, including but not limited to an increase in

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Ranawat Grading System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>No neural deficit</td>
</tr>
<tr>
<td>Class II</td>
<td>Subjective weakness with hyperreflexia and dysesthesia</td>
</tr>
<tr>
<td>Class III</td>
<td>Objective weakness and long tract signs</td>
</tr>
<tr>
<td>Class IIIA</td>
<td>Ambulatory</td>
</tr>
<tr>
<td>Class IIIB</td>
<td>Nonambulatory</td>
</tr>
</tbody>
</table>

\begin{table}
\centering
\caption{Ranawat Grading System}
\begin{tabular}{|c|}
\hline
Class I & No neural deficit \\
Class II & Subjective weakness with hyperreflexia and dysesthesia \\
Class III & Objective weakness and long tract signs \\
Class IIIA & Ambulatory \\
Class IIIB & Nonambulatory \\
\hline
\end{tabular}
\end{table}
pain or weakness, spasticity of the extremities, a change in ambulatory status, bowel or bladder disturbance (or both), Babinski’s sign, loss of proprioception, and hyperreflexia. Plantar reflexes may be difficult to elicit or interpret in patients with forefoot deformities or after foot surgery. Entrapment neuropathies, which are associated with RA, can adversely affect the sensory examination of the upper extremity.

Traditional grading and classification systems for neurologic deficits of RA patients are difficult to apply because of the comorbidities expressed and the multiple joint deficiencies that occur. By nature of the disease itself, disability is multifactorial (with a combination of arthropathy, deformity, compressive neuropathy, and radiculopathies, as well as myelopathy), as previously discussed. Any one of these variables may adversely affect grading. The Ranawat grading system, used commonly in the literature, is a valuable method for evaluating patients’ baseline neurologic function, planning surgery, and examining postoperative outcome (Table 1). Other common classifications are that of the American Rheumatological Association, which is the functional equivalent of the Steinbrocker classification (Table 2). Other grading scales in the literature are described but have not been frequently applied.

Neck pain is the most common complaint, present in 40% to 80% of patients, and located mostly at the craniocervical junction. It is usually associated with occipital headaches. Occipital neuralgia, facial pain, and ear pain can occur from compression of the greater occipital nerve (C2), the nucleus of the spinal trigeminal tract, and the greater auricular nerve, respectively. Pain in the suboccipital region can also occur due to irritation of the lesser occipital nerve (C1). Patients may describe a feeling of their head falling forward with flexion and with a clunking sensation. They may also describe myelopathic symptoms with cord and medullary compression, as well as upper or lower motor neuron signs, or both. Patients may report weakness, loss of endurance, loss of dexterity, gait disturbance, and paresthesias. Neck motion, especially flexion, may cause electric shock sensation of the torso and extremities (Lhermitte’s sign), or either alone. Symptoms of tinnitus, vertigo, visual disturbances, loss of equilibrium, diplopia, and dysphagia can occur due to either verteobasilar insufficiency or mechanical compression of the cervicomедullary junction.

Occipital pain with radiation to the vertex is one of the most common symptoms in patients with cranial settling. Menezes and coworkers documented 100% prevalence in 45 patients evaluated with RA and cranial settling. The investigators also noted myelopathy in 36/45 patients (80%) with cranial settling. Brain stem dysfunction was also higher in patients with cranial settling. The cranial nerve involvement included the glossopharyngeal, hypoglossal, and trigeminal nerves.

Urinary retention and later incontinence or rectal disturbances, or both, are symptoms of more severe disease and occur late in the progression. A patient who has been using crutches or a walker for ambulation and progresses to the use of a wheelchair should raise the suspicion of cervical pathology. Other clinical manifestations reported in the literature include amnestic episodes, brain stem signs, and lower cranial nerve palsies, as well as signs consistent with Brown-Sequard syndrome. However, a study by Rogers and associates suggested that cranial nerve palsies, nystagmus, and other select brain stem dysfunctions are more accurately attributed to the co-morbidities associated with RA, rather than the direct mechanical effects of rheumatoid craniocervical deformities. These investigators reported a low incidence of such problems in 235 RA patients with craniocervical involvement.

### Diagnostic Evaluation

#### Plain Films

Radiographic evaluation of the cervical spine in patients with RA should be performed routinely, as well as preoperatively, even in asymptomatic patients. This should include lateral, anteroposterior (AP), open-mouth odontoid views, and lateral flexion-extension dynamic views. Radiographic changes representing early cervical involvement include odontoid erosion, disc narrowing, and atlantoaxial and subaxial subluxation. Precise evaluation of plain radiographs is often difficult, due to osteopenia, anatomic variation, bony overlap, and most commonly, odontoid erosions. In a retrospective review of 113 RA patients undergoing elective total hip or knee replacement, Collins and colleagues noted 69 individuals (61%) had evidence of cervical abnormalities on preoperative cervical radiographs. These abnormalities included AAS, cranial settling, and subaxial subluxation. They also noted that 35/69 (50%) of patients with abnormal radiographs were asymptomatic.

#### Cervical Instability

As discussed, the four common patterns of cervical instability in rheumatoid disease are 1. isolated AAS; 2. cranial settling associated with AAS; 3. subaxial subluxation; and 4. a combination of AAS, cranial settling, and subaxial subluxation, or a combination of AAS with cranial settling or subaxial subluxation. One should attempt to identify...
critical landmarks on the lateral cervical plain radiograph to facilitate serial diagnostic and prognostic measurements. These include the opisthion (the dorsal border of the foramen magnum), clivus, hard palate, atlas, pedicle of axis, and tip of the odontoid process.

The AADI or ADI is measured from the posterior aspect of the ring of atlas to the anterior aspect of the odontoid process, as measured along the transverse axis of the ring of the atlas. The normal value in an adult is less than 3 mm. AAS is defined as a pre-odontoid interval greater than 3 mm and not fixed in dynamic flexion and extension views. Typically, the AADI is inversely related to the PADI or SAC and is used because of the ease and reliability of measurement. Commonly, the AADI has been utilized in following patients with RA, and many studies have recommended surgical intervention based on measures above 8, 9, or 10 mm. However, more recent studies have questioned the utility of AADI and have shown that AADI is not a reliable parameter in distinguishing patients with neurologic deficit from those who are neurologically intact. With progression of instability, the odontoid process migrates superiorly within the ring of the atlas. With continued cranial settling, the AADI may paradoxically decrease, and even become fixed, resulting in pseudostabilization (Fig. 1), as previously described. More recently, the PADI has been reported as a more reliable predictor of neurologic compromise. The PADI is measured from the posterior aspect of the odontoid process to the anterior edge of the posterior ring of the atlas (as measured along the transverse axis of the ring of the atlas).

Table 3 Indices of Cranial Settling

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Description</th>
<th>Diagnostic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>McGregor’s line</td>
<td>Posterior tip of the hard palate to the most caudal (lowest) cortical margin of the occiput.</td>
<td>Cranial settling is diagnosed when the apex of the dens rises more than 4.5 mm above this line.</td>
</tr>
<tr>
<td>McRae’s line</td>
<td>Foramen magnum, from the basion to the opisthion (posterior rim of foramen magnum).</td>
<td>Protrusion of the tip of the dens above this line indicates cranial settling.</td>
</tr>
<tr>
<td>Chamberlain’s line</td>
<td>Posterior aspect of the hard palate to the opisthion.</td>
<td>Protrusion of the tip of the dens more than 3 mm above this line indicates cranial settling.</td>
</tr>
<tr>
<td>Wackenheim’s line</td>
<td>Drawn along the superior surface of the clivus.</td>
<td>Protrusion of the dens posterior to the projection of this line indicates settling.</td>
</tr>
<tr>
<td>Fischgold-Metzger’s line</td>
<td>Drawn between the tips of mastoid processes on the anteroposterior open-mouth odontoid view.</td>
<td>Protrusion of the tip of the dens above this line indicates cranial settling.</td>
</tr>
<tr>
<td>Ranawat index</td>
<td>Center of the C2 pedicle to the transverse axis of the atlas.</td>
<td>(Normal range: Males: 17 ± 2 mm; Females: 15 ± 2 mm.) Measurement decreases as C1-C2 vertical subluxation occurs.</td>
</tr>
<tr>
<td>Redlund-Johnell measurement</td>
<td>McGregor’s line to the midpoint of the caudal margin of the C2 body.</td>
<td>(Normal: Males ≥ 34 mm; Females ≥ 29 mm). Measurement decreases as C1-C2 vertical subluxation occurs.</td>
</tr>
<tr>
<td>Clark and colleagues</td>
<td>Dividing the odontoid process into three equal parts, or stations, from superior to inferior. Assess which station of the odontoid process is adjacent to the anterior ring of the atlas.</td>
<td>Station I: Anterior ring of atlas is level with superior third of odontoid process (normal). Station II: The anterior ring of atlas is adjacent to the middle third of the dens (mild). Station III: The anterior ring of atlas is adjacent to the caudal third of the dens (severe).</td>
</tr>
</tbody>
</table>

Figure 1 Midsagittal MRI of a 67-year-old female with long-standing RA. The image demonstrates marked vertical subluxation of the dens. The tip of the dens impinges on the medulla and significantly reduces the functional cervicomedullary angle (normal range: 135° to 175°). The ADI paradoxically decreases and may fall into the “normal” range.
noted 60% (19/32) of patients who had AAS and paralysis had an AADI that was less than 9 mm. This weak correlation between AADI and paralysis may be due to variations in the diameter of the atlas as well as in pannus formation behind the odontoid process. Ninety-six percent (23/24) of patients with AAS and a Ranawat class III neurological deficit had a PADI of less than or equal to 13 mm; patients in their series who had a Ranawat class II (n = 11) or a class I rating (n = 31) had mean PADIs of 13 and 15 mm, respectively. A PADI of 14 mm or less yielded 97% sensitivity and 52% specificity for detecting patients with paralysis, compared to an AADI of greater than 8 mm with a 59% sensitivity, 58% specificity, and 56% negative predictive value; patients with a PADI of greater than 14 mm had no neurologic deficits.

Cranial Settling and AAS
Cranial settling can be evaluated with a variety of measurements on plain films, such as the relationship of the tip of the dens to McGregor’s line, McRae’s line, and Chamberlain’s line, among others (Table 3). Measurements may be difficult to obtain when there is erosion of the dens and the overlying mastoid air cells degrade the view of the dens on a lateral radiograph (Figs. 2A and 2B), or either of these situations exist singly. Two common measurements are the Ranawat index and the Redlund-Johnell values (Table 3). The anatomic landmarks used for these measurements are usually clearly seen on lateral films (Figs. 3 and 4). The abnormal Ranawat index most likely represents a settling at the C1-C2 level and the Redlund-Johnell value reflects...
occiput-C2 changes. In 1989, Clark and associates described a method by defining three equidistant stations of the odontoid process of the axis (Fig. 5). Normally, the superior third of the odontoid is level with or adjacent to the anterior ring of the atlas. With mild cranial settling, the middle third of the odontoid process is level with the anterior ring of the atlas (station II). With severe cranial settling, the inferior third of the odontoid process is level with the anterior ring of the atlas (station III).

In 2001, Riew and colleagues published a review of 131 patients with rheumatoid cervical spine. They evaluated the interobserver and intraobserver reliabilities, sensitivity, specificity, and negative and positive predictive values for several measurements used to diagnose cranial settling. The most easily identified landmarks were the hard palate, “definitely visible” on 93% (62/67) of radiographs, and the atlas, which was “definitely seen” on 88% (59/67) of radiographs. The tip of the odontoid process was the least clearly identifiable landmark, having been “definitely seen” on only 34% (22/67) of radiographs, and was completely unidentifiable in 19% (13/67). Of the remaining 31 radiographs (46%), the tip of the dens could only be “guessed.” No single test had a sensitivity or negative predictive value greater than 90% or a reasonable specificity or positive predictive value. However, the combination of Clark’s stations, the Ranawat index, and the Redlund-Johnell value had a sensitivity of 94% and a negative predictive value of 91% for diagnosing cranial settling if any of the three were positive. Consequently, only 6% of patients with cranial settling were improperly diagnosed as not having this manifestation. The investigators recommended that if any of these values are suggestive of cranial settling, a tomograph or MRI should be performed, or, alternatively, whenever there is clinical suspicion of cervicomедullary or brainstem dysfunction in the setting of negative measurements for cranial settling after reviewing plain radiographs.

**Subaxial Subluxation and AAS**

Lower, or subaxial, cervical spine lesions occur with changes in apophyseal joints, the joints of Luschka, interspinous ligaments, and intervertebral discs. As per White and coworkers, the criterion for diagnosing subaxial subluxation is 3.5 mm or more of motion. Boden and associates noted that subluxation with a SAC of 14 mm or less represents a more accurate measurement for risk of neurologic dysfunction, as well as postoperative recovery. Yonezawa and colleagues evaluated 58 RA patients neurologically and radiographically after 5 to 10 years of follow-up. Progression of myelopathy correlated with anterior subluxation (>2 mm) and axial shortening, accompanied by progression of disc collapse, apophyseal joint erosion, and spinous process destruction. These parameters progressed in 50% of patients. One-fourth to one-third of patients who had radiographic progression had a potential for myelopathic changes. Progression of radiographic lesions and deterioration of myelopathy was mainly correlated with a higher dose of corticosteroids, higher stage (or class) of RA, younger patients, and those with longer duration of disease. The findings of this study were also correlated with the results of a study done by Klein and coworkers.

**Advanced Imaging**

Advanced radiographic imaging technology is utilized to evaluate the presence of cord compression, to determine the presence of multilevel disease, and to help predict impending paralysis. Tomograms are particularly useful in determining the amount of cranial settling and to measure SAC or AADI values. Cervical myelography, polytomography, and computed tomography (CT) with intrathecal contrast have all been used to evaluate rheumatoid cervical spine pathologies. Magnetic resonance imaging (MRI) and CT scans, providing both sagittal and coronal views, have largely replaced these studies. CT scans can contribute detailed osseous information and have been shown to have a higher correlation with neurologic deficits than that of AADI assessment. Raskin and associates noted a significant increase in the AADI in 19 patients; however, CT scan showed cord compression in 11, and an absence of compression in the other eight patients. These investigators also noted that absent superficial abdominal reflexes and a history of bladder dysfunction correlated highly with cord compression on CT. Furthermore, CT myelography is useful in patients who have contraindications to MRI scanning.

MRI provides explicit information of soft tissue lesions, the neuraxis, and epidural tissues and continues to be the imaging modality of choice in determining neural compression. The main advantage of an MRI over other imaging procedures is that anatomic structures can be visualized in all planes, without bone artifact or beam hardening effects.
An MRI should be obtained in any patient with a neurologic deficit or abnormalities on plain films. A strong correlation has been found between MRI and myelography, with respect to the diagnosis of compressive cervical spine and clinical evidence of cervical myelopathy in RA patients. MRI can demonstrate cord compression due to bone as well as soft tissue mass, such as the peri-odontoid pannus (Fig. 6). Dvorak and colleagues reported two-thirds of patients (22/34) with AAS had more than 3 mm of pannus; furthermore, a cord diameter of 6 mm in flexion was highly consistent with neurological deficits. Bundschuh and coworkers described the cervicomedullary angle as the angle between a line drawn along the anterior aspects of the cervical cord and another line along the medulla. The normal angle is between 135° and 175° (Fig. 1). Patients with a cervicomedullary angle of less than 135° had cranial settling and clinical signs of C2 root pain, neural compression, or myelopathy. Reijnierse and associates evaluated 42 patients with RA to assess the changes in radiologic measurements between neutral and flexion MRI views. They reported that the cervicomedullary angle changed from 126° to 165° (median, 145°) in neutral position to 118° to 165° (median, 140°) in the flexed position. However, there was no significant change in compression of the brainstem between images obtained in the flexed and neutral positions. They suggested that the distance of the dens to McRae’s line and the amount of pannus were independent determinants of the cervicomedullary angle. These investigators also found that flexion MRI can demonstrate statistically significant subarachnoid space narrowing relative to the neutral position at the atlantoaxial level and below C2. This narrowing significantly affected cord compression at the atlantoaxial level if there was some encroachment on neutral MRI images. Other studies have also highlighted the usefulness and clinical application of dynamic flexion-extension MRI scanning in evaluating RA involvement of the cervical spine. Allmann and colleagues performed dynamic MR imaging of the cervical spine and observed 12% of patients with subarachnoid encroachment in flexion that was not evident on neutral MRI. In a more recent prospective study, Reijnierse and coworkers observed a five-fold increased risk of neurologic dysfunction when MRI revealed atlas erosion and cranial settling, as evidenced by a decreased distance of the dens to McRae’s line. Furthermore, subarachnoid space encroachment was associated with a 12-fold increased risk of neurologic dysfunction. They also associated muscle weakness with a 10-fold increased risk of neurologic dysfunction.

**Electrophysiologic Modalities**

Evaluation of neurologic signs and symptoms may be difficult in patients with advanced rheumatoid deformities or following surgical treatment. Electrophysiologic modalities can serve as additional adjunctive tests in diagnosing and following myelopathy in this patient population. They also can differentiate between radicular and spinal cord involvement. Toolanen and colleagues observed abnormal somatosensory evoked potentials (SSEPs) in 22% (4/18) of patients with subluxation. Lachiewicz and coworkers demonstrated that all patients with reducible atlantoaxial or subaxial subluxation had normal SSEPs. However, 58% (7/12) of those with irreducible AAS or cranial settling, or both, had abnormal SSEPs. In another study, SSEPs have been shown to have a sensitivity of 58% and a specificity of 90% in detecting AAS in patients with RA. Motor evoked potentials also have been used to evaluate cervical spine disease; 67% of 55 patients with RA had an abnormal delay in the latency of the central motor evoked potentials consistent with neural element compression.

In summary, the radiographic predictors of paralysis are as follows: a PADI of less than 14 mm, any combination of AAS with cranial settling, a subaxial canal diameter of less than 14 mm, MRI findings of either a cervicomedullary angle of less than 135°, a cord diameter in flexion of less than 6 mm, or a SAC measure of less than 13 mm. Other recent predictors of paralysis noted in the literature include subaxial anterior subluxation (≥ 2 mm) and axial shortening, accompanied by progressive disc collapse, apophyseal joint erosion, spinal process destruction, and subarachnoid narrowing on MRI.

**Predictors of Neurologic Recovery**

As discussed earlier, Pellicci and colleagues reviewed 106 patients followed over a 5-year period, with 46 (43%)
having cervical spine involvement at the start of the study. Eighty percent had radiographic, while 36% had neurologic progression (most by one grade). Mortality rate was 17%, compared to 9% for the same age group without RA. In 1987, Santavirta and coworkers noted in their review of 34 patients with rheumatoid cervical spine that only one of 16 patients treated nonoperatively had an improvement in pain. Neurologic function diminished in all patients treated nonoperatively. Marks and Sharp reviewed 31 patients with RA and cervical myelopathy. They noted that 19 patients died, with 15 deaths (48%) occurring within 6 months. They also reported that all nonoperatively treated patients and half of those treated with collars died. In this historical paper, four patients were treated with occipitocervical fusion and the three who developed successful fusions survived and had excellent outcomes. These results were similar to that of Meijers and associates, who reported that 9 patients with myelopathy who were treated nonoperatively all died within 1 year, with four deaths arising from cord compression.

Certain clinical and radiographic parameters have been shown to be associated with a poor neurologic recovery after operative stabilization with or without decompression: 1. patients with a more severe preoperative neurologic dysfunction have less chance of an uneventful postoperative recovery; 2. the location of pathology, e.g., cranial settling, especially in combination with AAS, has a significantly worse prognosis than isolated atlantoaxial or subaxial subluxation; and 3. the Ranawat grading system provides a rough estimate of neurological recovery, with a progressively worsening prognosis in patients with stage III compared to stage II, and IIIb compared to IIIa. Casey and colleagues evaluated 134 patients who underwent surgery for rheumatoid involvement of the cervical spine after development of objective signs of myelopathy. Fifty-eight percent of the ambulatory patients (IIIa) attained Ranawat neurological grades I or II as compared with only 20% of the nonambulatory patients (IIIB). They also observed that those patients with Ranawat index IIIB also fared worse in regard to postoperative complication rate, length of hospital stay, functional outcome, and ultimately survival when compared to patients with Ranawat IIIA. Peppelman and coworkers reviewed the results of 90 patients with rheumatoid deformities of the cervical spine with objective neurologic deficits and who were surgically treated. Seventy-eight (86.7%) had improvement of at least one Ranawat class postoperatively. Fifty-eight patients had objective signs of paresis before surgery (IIIa, IIIB); 49 (84.4%) of these individuals obtained resolution of the paresis after surgery. Among the patients with AAS and neurologic findings without cranial settling, 94.8% of patients in their series improved at least one class. Seventy-six percent of patients with neurologic deficits in the setting of AAS and cranial settling improved one class, whereas 71% of patients with neurologic findings with combined AAS, cranial settling, and subaxial subluxation improved at least one class. Furthermore, in their cohort, 15 patients had worsening or recurrence of their neurologic findings; thirteen (86.7%) were caused by later subaxial subluxation.

Several studies have demonstrated that preoperative SAC and postoperative subaxial canal diameter are important specific predictors of neurologic recovery. Patients with isolated AAS and a PADI of more than 14 mm have a better chance of recovery. However, those with a PADI of less than 10 mm prior to surgery have a poor prognosis for functional recovery. Furthermore, patients with combined AAS and cranial settling are expected to have a better neurologic recovery if their PADIs are at least 13 mm. Patients suffering from subaxial subluxation with a postoperative canal diameter less than 14 mm will have less neurologic recovery after surgical intervention. However, patients with a spinal cord area of 44 mm or greater have been shown to have a good prognosis postoperatively. Patient factors that do not appear to correlate with neurologic recovery after operative treatment for rheumatoid cervical spine include gender, age, duration of disease and paralysis before surgery, percent of preoperative subaxial vertebral subluxation, and preoperative anterior atlantoaxial interval.

The manifold rationale for performing C1-C2 fusions (Fig. 7) when significant anterior instability is identified are: 1. earlier performance of a monosegmental atlantoaxial fu-
sion can decrease the development of superior migration of the odontoid; 2. the increase in stress on the subaxial spine will also be reduced compared to having an occiput-to-C2 fusion, that would be indicated to manage more advanced vertical atlantoaxial subluxation; and 3. surgical intervention in patients with Ranawat class IIIA findings may also aid in preventing subsequent irreversible cord damage.

**Conclusion**

RA is a chronic, systemic inflammatory disorder of unknown etiology. It is an immunologically mediated disorder that can affect the articular and non-articular organ systems. Axial involvement predominantly affects the upper cervical spine. The morbidity of the disorder can have profound effects on an individual’s activities of daily living as a consequence of deformity, pain, and neurological dysfunction. Early initiation of pharmacotherapy using DMARDS in combination with newer immunological mediators reduces the inflammatory components of RA. Indeed, initiation of aggressive therapy prior to cartilage destruction may actually prevent or significantly mitigate destabilizing cervical joint damage and reduce the need for surgical intervention. Radiographs of the cervical spine should be performed initially and within 2 years after diagnosis of RA, and periodically thereafter. Dynamic cervical images should be taken prior to any elective operation to rule out instability. Operative intervention before the onset of advanced myelopathy results in improved outcomes, compared to the stabilization of patients whose conditions are more advanced. A multidisciplinary approach involving medical, surgical, and rehabilitation disciplines is necessary to optimize outcomes.

**Disclosure Statement**

None of the authors have financial or proprietary interest in the subject matter or materials discussed, including, but not limited to, employment, consultancies, stock ownership, honoraria, and paid expert testimony.

**References**


64. Wackenheim A. Disostosi chiro-lombare. Disostosi stenotica dell’impressione basilaire. Radiologica Medica. 1979;65:21-6. [Italian].


