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Review

The impact of rheumatoid arthritis on atlantoaxial stability and its relevant complications

Nikolaos Perisynakis[1], Dimitrios S. Evangelopoulos[1,2,3], Paris A. Velitsikakis[4], Elias Vasiliadis[1,3], Spyridon Pneumaticos[1,3]

[1]*Postgraduate Training Program, KAT Hospital, National and Kapodistrian University of Athens School of Medicine, KAT Hospital, Athens, Greece*

[2] *Department of Metabolic Bone Diseases, National and Kapodistrian University of Athens School of Medicine, KAT Hospital, Athens, Greece*

[3] *Third Department of Orthopaedic Surgery, National and Kapodistrian University of Athens, School of Medicine, KAT Hospital, Athens, Greece*

[4] *First Department of Orthopaedic Surgery, National and Kapodistrian University of Athens, School of Medicine, Attiko University Hospital, Chaidari, Athens, Greece*

Abstract

Rheumatoid arthritis (RA) is chronic, symmetric, inflammatory, peripheral polyarthritis of unknown etiology, typically leading to joint destruction through bony and cartilaginous erosions. Cervical spine is commonly engaged in the clinical frame of rheumatoid arthritis, regarding almost exclusively the upper third of it. Electronic databases PubMed, Scopus, and Google Scholar were searched using the following keywords: "rheumatoid arthritis," "cervical spine," "pathophysiology," and "treatment," with the logical operator 'AND' utilized between search terms. Additionally, phrases such as "rheumatoid arthritis in cervical spine" and "rheumatoid arthritis pathophysiology" were used for the search. Supplementary searches were performed to identify any additional pertinent articles not covered in the initial search. Through this review we intend to enlighten the presence of cervical myelopathy as part of rheumatoid arthritis, describing clinical features, imaging techniques and laboratorial examinations as well as treatment options available for this group of patients.

Keywords

Rheumatoid arthritis; cervical spine; pathophysiology and treatment

Corresponding author

Nikolaos Perisynakis
email: nperisynakis@hotmail.com

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by systemic inflammation, primarily affecting the synovial joints. It stands as one of the most prevalent autoimmune diseases worldwide, affecting approximately 1% of the global population. Although its exact etiology remains unknown, environmental factors, genetic predisposition, and immunological dysregulation contribute to its development. Females are disproportionately affected by RA, with a female-to-male ratio of approximately 3:1 **(1)**. Furthermore, the onset of RA typically occurs between the ages of 30 and 50, although it can manifest at any age, including childhood and late adulthood. While commonly recognized for its debilitating effects on the hands, wrists, and knees, RA can also have profound implications in the upper cervical spine, particularly regarding atlantoaxial instability (AAI) and its associated complications. Significant advancements in rheumatoid arthritis research occurred during the 20th century, particularly with the discovery of disease-modifying antirheumatic drugs (DMARDs) and biologic agents. These therapeutic breakthroughs revolutionized the management of RA, offering patients improved symptom control and disease modification. **(2)** The pathophysiology of rheumatoid arthritis involves a complex interplay of genetic susceptibility, environmental triggers, and immune dysregulation. In RA, the immune system mistakenly targets the synovial membrane lining the joints, leading to chronic inflammation, synovial hyperplasia, and joint destruction. Autoantibodies such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs) play pivotal roles in the pathogenesis of RA, contributing to the formation of immune complexes and perpetuating the inflammatory cascade **(3).**

Within the context of the upper cervical spine, rheumatoid arthritis can result in atlantoaxial instability (AAI), a potentially life-threatening complication characterized by abnormal movement between the atlas (C1) and axis (C2) vertebrae. Instability in this region can lead to spinal cord compression, vertebral artery compromise, and neurological deficits, underscoring the critical importance of early detection and intervention **(4)**. In summary, rheumatoid arthritis represents a multifaceted autoimmune disease with diverse clinical manifestations, including upper cervical spine involvement.

A literature search was conducted to identify all relevant articles pertaining to the topic, associated with the specified search criteria. The electronic databases utilized included PubMed, Scopus, and Google Scholar. The literature search was conducted using predetermined keywords carefully chosen to encompass all facets of the subject under investigation. The keywords employed were "rheumatoid arthritis," "cervical spine," "pathophysiology," and "treatment," with the logical operator 'AND' utilized between search terms. Additionally, phrases such as "rheumatoid arthritis in cervical spine" and "rheumatoid arthritis pathophysiology" were used for the search. Supplementary searches were performed to identify any additional pertinent articles not covered in the initial search. The design and execution of this review adhered to the PRISMA guidelines.

Study selection

Two independent authors conducted the study selection process, engaging in a thorough abstract screening to eliminate articles not pertinent to the investigated subject. Subsequently, the same two authors reviewed the full text of the identified articles, with a focus on inclusion criteria such as English language and full-text availability. Specifically, this review encompassed all relevant studies exploring the influence of rheumatoid arthritis on the upper cervical spine, particularly with regard to atlantoaxial instability and associated complications.

Discussion

Clinical Features

The clinical appearance of cervical disorders in RA is not a typical initial manifestation due to the fact that such findings regarding local neck pain, stiffness, decreased range of motion and compressive myelopathy tend to appear later on as the primary disease leads further into more advanced conditions and severe complications. At the same time,

it is important to keep in mind that asymptomatic cervical spine involvement meets up to 33% - 50% of the RA patients **(5-7)**. Given that, it is necessary to keep a high suspicion about cervical spine complications in RA patients as a well-timed recognition may offer proper management and treatment.

High neck pain, specifically in the craniocervical joint, is the most common symptom in these cases, followed by occipital headaches. Additionally, many patients complain about crepitations in this anatomical region as well as a sensation that their head is "falling forward" when bending over, finding that can be reproduced with appropriate physical examination.

In general, symptoms related to the upper cervical spine depend on the pathophysiology behind each particular phase of the disease. Synovitis and oedema are the initial disorders causing pain and stiffness in this anatomical region, while afterwards a new stage of the disease comes forward including bony erosions, destruction of the articular surfaces and thus joint instability progressively leading to spinal stenosis and myelopathy. Regarding the later, atlantoaxial instability and subluxation is the commonest deformity (AAI) met in half of these patients. Suboccipital pain, typically a consequence of C2 nerve root involvement, is associated with AA (C1-C2) subluxation, causing C2 radicular pain, which is the commonest radiculopathy that occurs in RA (8,9). The other half suffers from various subaxial deformities leading to subluxations (SAS) giving the impression of a stepladder deformity.

The neurological deficit caused by myelopathy is of critical importance to be noticed as the mortality and morbidity rate that follows is very high. Weakness, muscle atrophy, numbness, bowel-bladder disorders, paresthesia, loss of proprioception, spasticity, hyperreflexia and abnormal reflexes such as plantar reflexes or Hoffman's reflex may occur and therefore raise the suspicion regarding the cervical spine involvement. Particularly patients with spinal compression from the upper third of the cervical spine may present Lhermitte's sign, also known as "barber's chair phenomenon", which is a sensation of a transient electric chock that runs downwards from the cervical to the lumbar spine and the extremities upon neck flexion. Moreover, patients with severe compression may suffer from symptoms related to joint-instability-induced nerve compression, such as dysphagia due to compression of the vagus and glossopharyngeal nerves but also dysarthria due to compression of the hypoglossal nerve. Other neurological deficits include symptoms related to compression of the trigeminal tract resulting to facial dysesthesia and/or facial pain, syringomyelia, locked-in syndrome and even sudden death (1,10,11). There are several classifications and score-systems related to cervical myelopathy (Ranawat, Nurick, Japanese Orthopaedic Association, European Myelopathy Score). The Ranawat classification is the commonest in use at present.

Imaging Techniques

Radiological imaging has a fundamental role in the diagnosis of cervical spine pathologies, with classic radiography being a first-line approach. Magnetic resonance imaging (MRI) and computer tomography (CT) are used for more precise evaluation of soft tissues and bones respectively. MRI has the possibility to show early inflammatory changes such as effusions, synovitis, bone marrow edema (BME), and the relation of spinal lesions to brain stem, spinal cord, and nerve roots, whereas CT is the most precise technique for complex bone anatomy.

Plain Radiography: Plain radiographs are still in use regarding screening techniques about cervical spine involvement in RA. AAI accounts for approximately 65% of the total subluxations of the spine (1,12). Measurement of the anterior atlanto-dental interval (AADI) is defined as the distance from the posterior margin of the anterior ring of C1 to the anterior surface of the odontoid. Posterior atlanto-dental interval (PADI) reflects the distance from the posterior aspect of the odontoid to the anterior margin of the lamina of C1 are used to evaluate the AAI using lateral fluoroscopy. The normal value of AADI in adults should be less than 3 mm (13), while AADI > 5 mm is an indicator of clinically significant AAS instability. It is important to note that the reliability of AADI as an indicator of atlantoaxial instability is limited in patients with cranial settling. In this case, AADI might be mistakenly regarded as decreased

when in fact the patient suffers from severe instability (14). PADI on the other hand is a good measurement of the available space for the spinal cord in relation to its bony elements. The PADI is most accurately assessed with CT imaging in the subluxed, usually flexed, position. The space available for the cord may be less than the PADI as assessed on plain films or CT because soft tissue pannus may also contribute to cord compression (15).

There are several measurements that try to quantify the vertical subluxation of the odontoid. Though not a single one high sensitivity or specificity. Combination of measurements seem to have the greatest predictive power (16). The four commonest measurements are those of McRae, McGregor, Chamberlain, and Redlund-Johnell (15).

Computed Tomography: Computed tomography enhances the understanding of the complex anatomy of the cranio-cervical junction, including the atlanto-occipital joint, atlantoaxial joint, intervertebral joints, uncovertebral (Luschka) joints, and apophyseal joints. Multiplanar CT is optimal for the detailed visualization of anatomical variants, cysts, erosions, dens fractures, and subluxations, including the most challenging for radiography, the atlanto-axial level. Although CT is superior in the assessment of bony and soft tissue involvement when compared to plain radiography, it is still confined in comparison to MRI, mostly regarding the spinal cord and nerve-root imaging.

Magnetic Resonance Imaging: MRI is considered the gold standard for spinal cord and nerve-root imaging. Fluid-sensitive sequences with fat saturation are preferred for visualizing bone marrow oedema. Typical MRI protocols include sagittal T1- and T2-weighted sequences, T2 STIR and axial T2-weighted images. Optionally, the coronal T2-weighted sequence can be used, primarily to evaluate lateral subluxation. Furthermore, sagittal post-contrast T1-weighted images can be used to assess active inflammatory lesions, mainly synovitis. MRI shows cysts, erosions of the dens or spinous processes, or vertebral endplates and spinal cord involvement in the C-spine. Functional MRI of the C-spine that includes flexion, extension, and neutral positions is possible, but it is not used in routine practice (17,18).

Treatment

Indications: The indications for surgery in patients with rheumatoid arthritis get modified as the research progresses. Nowadays, the AO Spine Foundation recommends that surgery should be considered in patients presenting with myelopathy, C1-C2 subluxation with mobility between both vertebrae, progressive neurological deficit, instability with the risk of neural element compression, and chronic intractable pain unresponsive to analgesics. Surgical intervention can lead to significant improvement in symptoms, particularly in pain reduction (19-27). An older study by van Asselt KM et al recommended surgery for patients with Ranawat classes IIIA and B, as neural improvement is possible and may result in improved mobility (28).

Surgical goal: The primary goals of surgery are to relieve neurologic compression and eradicate instability, preventing further neurologic decline (27,29). According to a more recent model proposed by Goel, the primary pathogenesis point causing lateral mass collapse and buckling of the posterior longitudinal ligament, resulting in the formation of a pannus, is instability manifested at the facets. In rheumatoid arthritis (RA), addressing the retro-odontoid pannus directly may not be necessary, and surgical efforts should be focused on the atlantoaxial instability (AAI) (20,30). The primary goal of cervical reconstruction surgery in RA patients is to eliminate instability by achieving both immediate and long-term stability. Many studies have shown that pedicle screw fixation and C1/2 transarticular screw fixation are biomechanically superior to other conventional procedures involving wiring or clamping (31-35). Restoring anatomical craniovertebral alignment in atlantoaxial dislocation patients can be achieved by manually distracting the facets of the atlas and the axis and placing bone graft or metal spacers within the joint, coupled with atlantoaxial screw fixation (20,36,37). In C1–C2 vertical instability, decompression of the spinal cord is achieved either directly by resecting the odontoid

process or indirectly through reduction of the deformity with C1–C2 facet spacers. For subaxial instability, long instrumentations are preferred over short ones, with pedicle screws at the cranial and caudal points of the fixation (e.g., C2 to Th2–3) (20).

MacDowall et al studied the results of surgery on a national cohort of 176 patients with cervical manifestation of RA. Regarding electromyostimulation (EMS), the only group that showed improvement one year after surgery was the C1–C2 horizontal instability group. The C1–C2 vertical instability group improved two years after surgery but regressed to baseline values at five years of follow-up. Reasons for reoperations included pseudarthrosis or implant failure, infection, chronic implant-related pain, residual or restenosis, and postoperative bleeding. Implant failures caused by laminar hooks were identified as the most dangerous. All groups exhibited improvement in pain and quality of life after fusion surgery, but successful management of myelopathy was achieved only within the C1–C2 horizontal instability group. Despite recommended treatment methods for C1–C2 vertical instability, 63% of patients in the Swespine registry underwent posterior fusion only, even though these results are known to be unsatisfactory. This high percentage of posterior fusion as the chosen treatment method is likely why the C1–C2 vertical instability group did not experience improvement in myelopathy after surgery (20,38). A study by van Asselt KM et al observed over a two-year follow-up period the clinical effects of cervical spine surgery for occipital neuralgia in patients with rheumatoid arthritis (RA). The available data on the percentages of patients achieving pain relief through surgery were limited, but generally, operations were successful in most patients, ranging from 78% to 92%. The study emphasizes the importance of observing the effects of neck surgery over an extended period. After two years, 82% of surviving patients with occipital neuralgia alone remained free of pain, supporting the argument for performing neck surgery in RA patients with this specific condition. However, in patients with occipital neuralgia combined with cord compression, only 78% and 50% were pain-free three months and two years postoperatively, respectively, indicating that the pain-relieving effect of surgery is less evident in patients with more extensive disease. This observation may be related, among other factors, to the progression of the underlying disease. The study suggests that surgery may be particularly useful for pain relief in patients with occipital neuralgia alone. Nonetheless, the study acknowledges the relatively small number of studies for patients with cervical myelopathy, the percentage of patients with neurological improvement varied from 44% to 89%. In this study, postoperative neurological improvement was observed in 73% and 67% of surviving patients with cervical myelopathy (with or without occipital neuralgia) three months and two years after surgery (28). Atlantoaxial stabilization can be approached either anteriorly or posteriorly, depending on factors such as the site of compression and the surgeon's preference (39). Sunahara et al. emphasized the vital role of cervical spine surgery in a study involving 21 RA patients not treated surgically; 16 of them experienced deterioration, and the chance of surviving 7 years after myelopathy onset was 0% (40). Surgery has also been effective in addressing pannus regression, an inflammatory complication of RA. Bydon et al. demonstrated a 44% decrease in the mean volume of pannus in patients undergoing posterior fusion, with or without decompression (13,41). Patients undergoing surgery for RA are frequently on various rheumatoid medications, including nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, methotrexate, and biological agents (tumor necrosis factor-α and interleukin-1 antagonists), which can hinder fusion success. Discontinuing these medications is often impractical due to the risk of flare-ups. However, corticosteroids have been shown to impair bone and wound healing (42), methotrexate may affect bone healing (43), and biologics increase the risk of opportunistic infections (44). Previous studies indicate that surgical outcomes are more favorable in patients with less preoperative impairment and that the outcomes of surgery for the rheumatoid cervical spine vary based on different diagnoses (27,45). Analyses stratified by dichotomous preoperative variables revealed that the presence of steroids, methotrexate, biologics, and prednisone dosage less than 7.5 mg did not

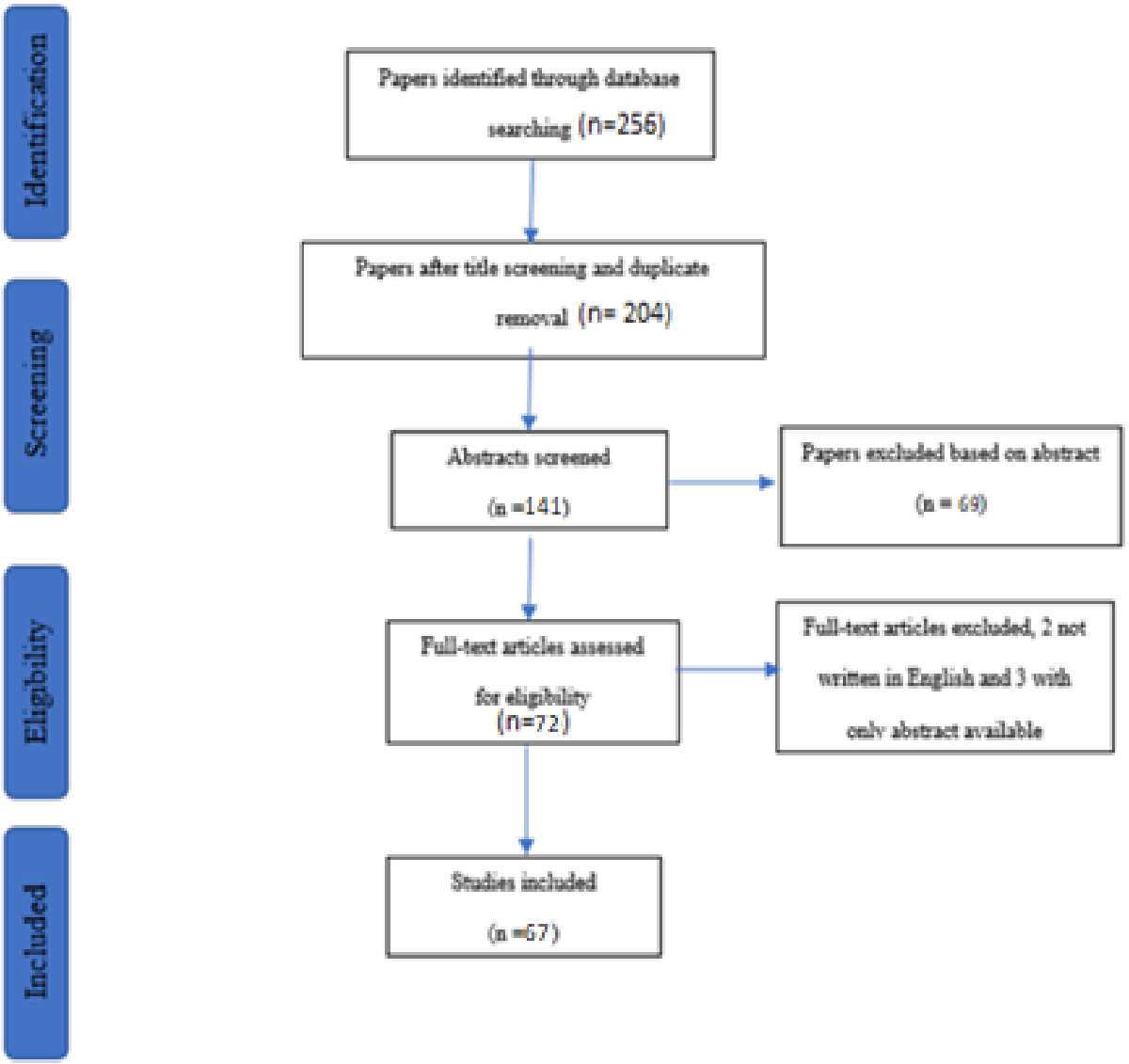

Figure 1.Prisma Flow Chart

significantly affect outcomes. However, prednisone dosages ≥7.5 mg were associated with significantly smaller improvements in Nurick score compared to patients not on steroids or those on prednisone dosages <7.5 mg (0.40 vs. 1.36, p=0.042). Similarly, patients on biologics showed significantly smaller improvements in Nurick score compared to patients not on biologics (0.27 vs. 1.16, P = 0.038) (46). Studies also showed that early intervention before cranial settling decreases the risk of future instability (27,47). Although surgical treatment may offer potential benefits, further studies are needed to establish their role in managing rheumatoid patients. Generally, better surgical outcomes are observed in patients with less preoperative impairment. Prognostic factors include Ranawat classification, spinal

cord area, PADI, advanced age, atlantoaxial instability, and postoperative complications (23,47-51).

Complications

The study of van Asselt KM et al (2001) suggests that the causes of death were mostly not related to surgery or due to the aggregation of myelopathy, making the best-case value more likely to be closer to the true value (28). A recent trial (2022) demonstrated similar outcomes following anterior and posterior surgical approaches, with higher complication rates for the former, primarily due to postoperative dysphagia and dysphonia (52). Concerns about the safety profile of surgery in patients with RA or AS are raised, considering the potential impact of medical treatments on surgical outcomes and an increased risk of complications. The study notes that patients with RA or AS had an elevated risk of complications after surgery, emphasizing the importance of clear communication with patients about these risks before undergoing surgery (53). Fortunately, life-threatening complications and early reoperations were rare. Another study aimed to identify risk factors for complications in patients with RA undergoing various cervical spine surgeries. The prevalence of complications was 20.1% in this study. It was newly found that short height, high ASA-PS, short disease duration of RA, and long fusion procedures could be risk factors for perioperative complications (54-56). Moreover, for severe complications, administration of high-dose prednisolone, existence of SAS, OC fusions and long fusions were suggested as risk factors. However, there have been only a few reports that shorter patients were at higher risk for perioperative complications, as shown in coronal and carotid endarterectomy (57). A study by Sakuraba et al showed that the mean value of ASA-PS was significantly higher in patients with perioperative complications than in patients with no complications (58). Physical constitution could affect perioperative complications and anesthesia management, such as have a direct impact on issues related to surgery as the surgical field can be limited, knowing that height and BSA have been shown to correlate with the diameter of the common carotid artery, and additionally studies show that obesity correlates with comorbidities in patients with RA and perioperative complications after various surgeries (59-65). A series of studies show that the duration of RA may affect the incidence of perioperative complications. More specifically they show that a shorter duration of RA may correlate with higher incidence of perioperative complications than in patients with longer duration. However, the mean disease duration of RA at the time of cervical spine surgery was 17.6 years in the complication group and 20.2 years in the no-complication group. It is challenging to determine the clinical significance of this 2.5-year difference over such a long disease duration. A possible reason might be related to the features of cervical spine lesions in patients with RA. Most studies have reported that cervical spine lesions are a feature of longstanding rather than early disease, generally becoming apparent ten years into the natural history of RA (58,66-67). Another study recommended that the use of laminar hooks should be avoided with the exception of atlas claws, which showed no complication rate of loosening or dislocating, because they were found to have the most dangerous postoperative complications, exposing patients to higher risks than those associated with pseudarthrosis after screw fixation (20).

Conclusion

In conclusion, the recognition of cervical symptoms in rheumatoid arthritis (RA) patients, despite their often-late onset, is crucial due to the high prevalence of asymptomatic cervical spine involvement. Understanding the pathophysiological phases of RA aids in identifying symptoms and employing timely interventions. Neurological deficits demand prompt recognition, with diagnostic imaging playing a pivotal role in identifying cervical pathologies, despite certain limitations. While surgical interventions offer potential benefits for RA patients with cervical manifestations, challenges exist, including implant failures and medication impacts on fusion success. Further research is warranted to elucidate optimal treatment strategies and mitigate perioperative risks in RA patients with cervical disorders.

References

1. Nguyen H. V., Ludwig S. C., Silber J., et al. Rheumatoid arthritis of the cervical spine. Spine Journal. 2004;4(3):329–334. doi: 10.1016/j.spinee.2003.10.006.
2. Wasserman B. R., Moskovich R., Razi A. E. Rheumatoid arthritis of the cervical spine—clinical considerations. Bulletin of the NYU Hospital for Joint Diseases. 2011;69(2):136–148.
3. Shah A., St. Clair E. Rheumatoid arthritis. In: Longo D. L., Fauci A. S., Kasper D. L., Hauser S. L., Jameson J., Loscalzo J., editors. Harrison's Principles of Internal Medicine. 18th. chapter 321. New York, NY, USA: McGraw-Hill; 2012.
4. Delamarter RB, Bohlman HH. Postmortem osseous and neuropathologic analysis of the rheumatoid cervical spine. Spine. 1994;19(20):2267–74. doi: 10.1097/00007632-199410150-00004.
5. Neva MH, Häkkinen A, Mäkinen H, Hannonen P, Kauppi M, Sokka T. High prevalence of asymptomatic cervical spine subluxation in patients with rheumatoid arthritis waiting for orthopaedic surgery. Annals of the Rheumatic Diseases 2006;65:884-88. doi.org/10.1136/ard.2005.042135
6. Oda T, Fujiwara K, Yonenobu K, et al. Natural course of cervical spine lesions in rheumatoid arthritis. Spine (Phila Pa 1976) 1995;20:1128–35.
7. Paus AC, Steen H, Røislien J, Mowinckel P, Teigland High mortality rate in rheumatoid arthritis with subluxation of the cervical spine: a cohort study of operated and nonoperated patients. J.Spine (Phila Pa 1976). 2008 Oct 1;33(21):2278-83. doi: 10.1097/BRS.0b013e31817f1a17. PMID:18784629
8. A. W. B. Heywood, I. D. Learmonth, and M. Thomas, "Cervical spine instability in rheumatoid arthritis," JBJS—Series B, 1988;70(5):702–07.
9. Lipson SJ. "Rheumatoid arthritis in the cervical spine," Clinical Orthopaedics and Related Research, 1989;239:121–27.
10. B. R. Wasserman, R. Moskovich, and A. E. Razi, "Rheumatoid arthritis of the cervical spine—clinical considerations," Bulletin of the NYU Hospital for Joint Diseases, vol. 69, no. 2, pp. 136–148, 2011.
11. W. E. Krauss, J. M. Bledsoe, M. J. Clarke, E. W. Nottmeier, and M. A. Pichelmann, "Rheumatoid arthritis of the craniovertebral junction," Neurosurgery 2010;66(3):A83-A95.
12. Shen FH, Samartzis D, Jenis LG, An HS. Rheumatoid arthritis: evaluation and surgical management of the cervical spine. Spine J 2004;4:689-700. https://doi.org/10.1016/j.spinee.2004.05.001
13. Siempis T, Tsakiris Ch, Zikou A, George A. Alexiou GA, Voulgaris S, Argyropoulou MI. Radiological assessment and surgical management of cervical spine involvement in patients with rheumatoid arthritis. Rheumatol Int. 2023;43(2):195-208. doi: 10.1007/s00296-022-05239-5 PMCID: PMC9898347
14. Casey ATH, Crockard HA, Geddes JF, Stevens J. Vertical translocation: the enigma of the disappearing atlantodens interval in patients with myelopathy and rheumatoid arthritis. Part I. Clinical, radiological, and neuropathological features. J Neurosurg 1997;87:856-862.https://doi.org/10.3171/jns.1997.87.6.085
15. Mukerji N, Todd NV. Cervical Myelopathy in Rheumatoid Arthritis Neurol Res Int. 2011; 2011:153628. Published online 2011 Nov 22. doi: 10.1155/2011/153628 PMCID: PMC3238417
16. Riew KD, Hilibrand AS, Palumbo MA, Sethi N, Bohlman HH. "Diagnosing basilar invagination in the rheumatoid patient: the reliability of radiographic criteria," JBJS-Series A, 2001;83(2):194-200.
17. Kotecki M, Gasik R, Głuszko P, Sudoł-Szopińska I. Radiological Evaluation of Cervical Spine Involvement in Rheumatoid Arthritis: A Cross-Sectional Retrospective Study. J Clin Med. 2021;10(19):4587. Published online 2021 Oct 5. doi: 10.3390/jcm10194587 PMCID:PMC8509796
18. Kotecki M, Sotniczuk M, Gietka P, Gasik R, Sudoł-Szopińska I. Imaging of cervical spine involvement in inflammatory arthropathies: a review. Pol J Radiol. 2021;86:e620–e629. Published online 2021 Nov 20. doi: 10.5114/pjr.2021.111363 PMCID: PMC8652349
19. Bouchaud-Chabot A, Lioté F. Cervical spine in-

volvement in rheumatoid arthritis. A review. Joint Bone Spine 2002;69(2):141-54. doi: 10.1016/s1297-319x(02)00361-5.
20. MacDowall A, Barany L Bodon G. Surgical treatment outcome on a national cohort of 176 patients with cervical manifestation of rheumatoid arthritis. J Craniovertebr Junction Spine. 2021;12(3):248–56. Published online 2021 Sep 8. doi:10.4103/jcvjs.jcvjs_200_20 PMCID: PMC8501822
21. Lorber A Pearson CM, Rene RM. Osteolytic vertebral lesions as a manifestation of rheumatoid arthritis and related disorders. Arthritis Rheum 1961;4:514-532
22. Grob D, Würsch R, Grauer W, Sturzenegger J, Dvorak J. Atlantoaxial fusion and retrodental pannus in rheumatoid arthritis. Spine (Phila Pa 1976) 1997; 22:1580-84
23. Boden SD, Dodge LD, Bohlman HH, Rechtine GR. Rheumatoid arthritis of the cervical spine. Alongterm analysis with predictors of paralysis and recovery. J Bone Joint Surg Am 1993;75:1282-97
24. Nakano KK, Schoene WC, Baker RA, Dawson DM. The cervical myelopathy associated with rheumatoid arthritis: analysis of patients, with 2 postmortem cases. Ann Neurol 1978;3:144-151
25. Santavirta S, Slätis P, Kankaanpää U, Sandelin J, Laasonen E. Treatment of the cervical spine in rheumatoid arthritis. J Bone Joint Surg Am 1988;70:658-67
26. Crockard HA. Surgical management of cervical rheumatoid problems. Spine (Phila Pa 1976) 1995;20: 2584-90
27. Mallory GW, Halasz SR, Clarke MJ. Advances in the treatment of cervical rheumatoid: Less surgery and less morbidity. World J Orthop 2014;5(3): 292-303
28. van Asselt KM, Lems W, Bongartz E, Hamburger H, Drossaers-Bakker K, Bijkmans, van Soesbergen RM. Outcome of cervical spine surgery in patients with rheumatoid arthritis. Ann Rheum Dis. 2001;60(5):448–452. doi: 10.1136/ard.60.5.448 PMCID: PMC1753638
29. Menezes AH, Van Gilder JC, Clark CR, el-Khoury G. Odontoid upward migration in rheumatoid arthritis. An analysis of 45 patients with "cranial settling". J Neurosurg 1985; 63:500-09
30. Goel A. Retro-odontoid mass: An evidence of craniovertebral instability. J Craniovert Junc Spine 2015;6:6-7
31. Abumi K, Kaneda K, Shono Y, Fujiya M One-stage posterior decompression and reconstruction of the cervical spine by using pedicle screw fixation systems. J Neurosurg (Spine 1) 1999;90:19-26
32. Grob D, Crisco JJ 3rd, Panjabi MM, Wang P, Dvorak J. Biomechanical evaluation of four different posterior atrantoaxial fixation techniques. Spine 1992;17:480–90
33. Kotani Y, Cunningham BW, Abumi K, McAfee PC. Biomechanical analysis of cervical stabilization systems: an assessment of transpedicular screw fixation in the cervical spine. Spine 1994;17:2529-39
34. Magerl F, Seemann PS. Stable posterior fusion of the atlas and axis by transarticular screw fixation. In: Kehr P, Weidner A (eds) Cervical spine I. Springer, Berlin Heidelberg New York, 1997;322–327
35. Takahashi J, Shono Y, Nakamura I, Hirabayashi H, Kamimura M, Ebara S, Kato H. Computer-assisted screw insertion for cervical disorders in rheumatoid arthritis. Eur Spine J. 2007;16(4):485-94
36. Goel A, Sharma P. Craniovertebral realignment for basilar invagination and atlantoaxial dislocation secondary to rheumatoid arthritis. Neurol India 2004;52:338-41
37. Goel A, Pareikh S, Sharma P. Atlantoaxial joint distraction for treatment of basilar invagination secondary to rheumatoid arthritis. Neurol India 2005;53:238-40
38. Hamblen D. Surgical management of rheumatoid arthritis: The cervical spine. In: Postgraduate Textbook of Clinical Orthopaedics. Bristol: Wright;1983
39. John L. Gillick, John Wainwright, Kaushik Das. Rheumatoid Arthritis and the Cervical Spine: A Review on the Role of Surgery Int J Rheumatol.

2015; 2015: 252456. doi: 10.1155/2015/252456 PMCID: PMC4553335
40. Sunahara N, Matsunaga S, Mori T, Ijiri K, Sakou T. Clinical course of conservatively managed rheumatoid arthritis patients with myelopathy. Spine 1997;22:2603-07
41. Bydon M, Macki M, Qadi M, De la Garza-Ramos R, Kosztowski TA, Sciubba DM, Wolinsky JP, Witham TF, Gokaslan ZL, Bydon A. Regression of an atlantoaxial rheumatoid pannus following posterior instrumented fusion. Clin Neurol Neurosurg 2015;137:28-33
42. Howe CR, Gardner GC, Kadel NJ. Perioperative medication management for the patient with rheumatoid arthritis. J Am Acad Orthop Surg 2006;14:544-51
43. Gerster JC, Bossy R, Dudler J. Bone non-union after osteotomy in patients treated withmethotrexate. J Rheumatol 1999;26:2695-97
44. Giles JT, Bartlett SJ, Gelber AC, Nanda S, Fontaine K, Ruffing V et al. Tumor necrosis factor inhibitor therapy and risk of serious postoperative orthopedic infection in rheumatoid arthritis. Arthritis Rheum 2006;55:333-37
45. Miyamoto H, Sumi M, Uno K. Outcome of surgery for rheumatoid cervical spine at one institute over three decades. Spine J 2013;13:1477-84
46. Ryan Khanna, Brian J. Dlouhy, Zachary A. Smith, Sandi K. Lam, Tyler R. Koski, Nader S. Dahdaleh J. The impact of steroids, methotrexate, and biologics on clinical and radiographic outcomes in patients with rheumatoid arthritis undergoing fusions at the craniovertebral junction. Craniovertebr Junction Spine. 2015;6(2):60–64. doi: 10.4103/0974-8237.156044 PMCID: PMC4426523
47. Clarke MJ, Cohen-Gadol AA, Ebersold MJ, Cabanela ME. Long-term incidence of subaxial cervical spine instability following cervical arthrodesis surgery in patients with rheumatoid arthritis. Surg Neurol 2006;66:136-40.
48. Schmitt-Sody M, Kirchhoff C, Buhmann S, Metz P, Birkenmaier C, Troullier H, Jansson V, Veihelmann A. Timing of cervical spine stabilization and outcome in patients with rheumatoid arthritis. Int Orthop 2008;32:511-51
49. Ranawat CS, O'Leary P, Pellicci P, Tsairis P, Marchisello P, Dorr L. Cervical spine fusion in rheumatoid arthritis. J Bone Joint Surg Am 1979;61:1003-10
50. Ronkainen A, Niskanen M, Auvinen A, Aalto J, Luosujärvi R. Cervical spine surgery in patients with rheumatoid arthritis: longterm mortality and its determinants. J Rheumatol 2006;33:517-22
51. Agarwal AK, Peppelman WC, Kraus DR, Pollock BH, Stolzer BL, Eisenbeis CH, Donaldson WF. Recurrence of cervical spine instability in rheumatoid arthritis following previous fusion: can disease progression be prevented by early surgery? J Rheumatol 1992;19:1364-70
52. Siril T. Holmberg, Agnete M. Gulati, Tonje Okkenhaug Johansen, Øyvind O. Salvesen, Vetle Vangen Lønne, Tore K. Solberg, Erling A. Tronvik, Øystein P. Nygaard, Sasha Gulati. Surgery for degenerative cervical myelopathy in patients with rheumatoid arthritis and ankylosing spondylitis: a nationwide registry-based study with patient-reported outcomes. Acta Neurochir (Wien)2022;164(12):3165-71.doi: 10.1007/s00701-022-05382-9 PMCID: PMC9705458
53. Bernstein DN, Kurucan E, Menga EN, Molinari RW, Rubery PT, Mesfin A. Comparison of adult spinal deformity patients with and without rheumatoid arthritis undergoing primary non-cervical spinal fusion surgery: a nationwide analysis of 52,818 patients. Spine J. 2018;18:1861-66
54. Umekawa M, Takai K, Taniguchi M. Complications of spine surgery in elderly Japanese patients: implications for future of world population aging. Neurospine. 2019;16:780-88
55. Wolters U, Wolf T, Stützer H, Schröder T. ASA classification and perioperative variables as predictors of postoperative outcome. Br J Anaesth. 1996;77:217–22
56. Somani S, di Capua J, Kim JS, Phan K, Lee NJ, Kothari P, et al. ASA classification as a risk stratification tool in adult spinal deformity surgery: a study of 5805 patients. Glob Spine J. 2017;7:719-26
57. Messé SR, Kasner SE, Mehta Z, Warlow CP, Roth-

well PM, European Carotid Surgery Trialists. Effect of body size on operative risk of carotid endarterectomy. J Neurol Neurosurg Psychiatry. 2004;75:1759-61
58. Sakuraba K, Omori Y, Kai K, Terada K, Kobara N, Kamura S, Fujimura K, Bekki H, Ohta M, Miyahara HA, Fukushi JI. Risk factor analysis of perioperative complications in patients with rheumatoid arthritis undergoing primary cervical spine surgery. Arthritis Res Ther. 2022;24(1):79
59. de Resende Guimarães MFB, Rodrigues CEM, Gomes KWP, Machado CJ, Brenol CV, Krampe SF, et al. High prevalence of obesity in rheumatoid arthritis patients: association with disease activity, hypertension, dyslipidemia and diabetes, a multi-center study. Adv Rheumatol. 2019;59:44
60. Dindo D, Muller MK, Weber M, Clavien P-A. Obesity in general elective surgery. Lancet (London, England). 2003;361:2032–35
61. Houdek MT, Wagner ER, Watts CD, Osmon DR, Hanssen AD, Lewallen DG, et al. Morbid obesity: a significant risk factor for failure of two stage revision total hip arthroplasty for infection. J Bone Joint Surg Am. 2015;97:326–32
62. Jiang J, Teng Y, Fan Z, Khan S, Xia Y. Does obesity affect the surgical outcome and complication rates of spinal surgery? A meta-analysis. Clin Orthop Relat Res. 2014;472:968–75
63. García AM, Durántez DF, Guzmán CC, Torres PMC, Parra MGR, Fernández Jiménez PE. Is obesity a risk factor for complications, hospital admissions, and surgical cancellations in ambulatory surgery? Rev Esp Anestesiol Reanim. 2015;62:125–32
64. Gurunathan U, Myles PS. Limitations of body mass index as an obesity measure of perioperative risk. Br J Anaesth. 2016;116:319–21
65. Mortensen JD, Talbot S, Burkart JA. Cross-sectional internal diameters of human cervical and femoral blood vessels: relationship to subject's sex, age, body size. Anat Rec. 1990;226:115–24
66. Hagenow A, Seifert J, Zeissig A, Conrad K, Kleymann A, Aringer M. Relevant incidence of cervical arthritis in patients with erosive seropositive rheumatoid arthritis even today. Clin Exp Rheumatol. 2013;31:213–38
67. Dreyer SJ, Boden SD. Natural history of rheumatoid arthritis of the cervical spine. Clin OrthopRelat Res. 1999:98–106

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