

# An Overview on the Role of Surgical Management in Ankylosing Spondylitis

Abdullah Saeed A Alahmari<sup>1</sup>, Suhaila Kamal Qari<sup>2</sup>, Reaah Ibrahim Asiri<sup>3</sup>, Turki Ali Almohammadi<sup>4</sup>, Mohammed Ali M Alqarni<sup>1</sup>, Hala Mohammed Aljahdali<sup>4</sup>, Ali Hamad Alnasser<sup>5</sup>, Fares Aqeel Alaqeel<sup>6</sup>, Omar Adel Kazim<sup>7</sup>, Halimah Ahmed Othman Qasem<sup>8</sup>, Hadeel hamad Albraik<sup>9</sup>

<sup>1</sup>Faculty of Medicine, Bisha University, Bisha, KSA. <sup>2</sup>Department of ENT, Al Noor specialist hospital, Makkah, KSA. <sup>3</sup>Department of Surgery, Ahad Rofaidah General Hospital, Khamis Mushait, KSA. <sup>4</sup>Faculty of Medicine, Ibn Sina National College of Medicine, Jeddah, KSA. <sup>5</sup>Faculty of Medicine, King Saud University, Riyadh, KSA. <sup>6</sup>Department of orthopedic, King Fahad Specialist Hospital, Buraidah, KSA. <sup>7</sup>Faculty of Medicine, King Abdulaziz University, Jeddah, KSA. <sup>8</sup>Department of Internal Medicine, King Fahad Central Hospital, Jazan, KSA. <sup>9</sup>MBBS, Emergency Department, King Khalid hospital, Alkharj, KSA.

## Abstract

Ankylosing spondylitis is a chronic illness affecting the spine/pelvic limb joints and the sacroiliac, resulting in ankylosis and deformity of joints and the spine. Hip joints can be affected on both sides, making them more susceptible and prone to more significant injury than other joints. Even though novel biological therapies have drastically altered the management of this illness, surgical intervention is still necessary in some cases. To evaluate the role of surgical treatment in ankylosing spondylitis and provide a good review of the different surgical options suggested for different situations. For articles selection, the PubMed database was utilized, and the following keys were used in the Mesh (“ankylosing spondylitis” [Mesh]) AND (“surgical management” [Mesh]) OR (“evaluation” [Mesh])). Patients with ankylosing spondylitis are commonly susceptible to developing severe structural and functional complications to the hip and the spine, such as severe kyphosis, severe hip arthritis, heterotopic ossification, and a spinal fracture. In such cases, surgical intervention is mostly needed. However, there are a lot of controversies surrounding surgical intervention in different situations of ankylosing spondylitis.

**Keywords:** Ankylosing spondylitis, Surgical management, Evaluation, Prognosis

## INTRODUCTION

Ankylosing spondylitis is a chronic illness affecting the sacroiliac and spine/pelvic limb joints, resulting in ankylosis and deformity of joints and the spine [1]. The illness most commonly affects the shoulder and hip joints, and surgical treatment is necessary if significant joint contracture is discovered [2]. Given that 1/3 of patients have hip symptoms, an accurate hip range of motion evaluation is important to understand disease progression better. Hip joints can be affected on both sides, making them more susceptible and prone to more significant injury comparing other joints. The hip joint's flexion contracture, most common in the advanced stages of the illness, causes a stiff stride that requires flexion of the knee joint to keep a standing position [3]. Even though novel biological therapies have drastically altered the management of this illness, surgical intervention is still necessary in some cases. This paper aims to evaluate the role of surgical treatment in ankylosing spondylitis and provide a good review of the different surgical options that are suggested for different situations.

## MATERIALS AND METHODS

For articles selection, the PubMed database was utilized, and the following keys were used in the Mesh (“ankylosing

spondylitis” [Mesh]) AND (“surgical management” [Mesh]) OR (“evaluation” [Mesh])).

Regarding the inclusion criteria, the papers were chosen according to one of the following topics: ankylosing spondylitis, evaluation, and surgical management.

Exclusion criteria were all other articles without one of these topics as their primary endpoint.

## RESULTS AND DISCUSSION

**Address for correspondence:** Reaah Ibrahim Asiri, Department of Surgery, Ahad Rofaidah General Hospital, Khamis Mushait, KSA. rero9559@gmail.com

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 3.0 License, which allows others to remix, tweak, and build upon the work non commercially, as long as the author is credited and the new creations are licensed under the identical terms.

**How to cite this article:** Alahmari A S A, Qari S K, Asiri R I, Almohammadi T A, Alqarni M A M, Aljahdali H M, et al. An Overview on the Role of Surgical Management in Ankylosing Spondylitis. Arch. Pharm. Pract. 2021;12(2):106-11. <https://doi.org/10.51847/9AZbv4ZIT>

Ankylosing spondylitis, on the other hand, impairs patients' quality of life by causing uveitis (25-40%), inflammatory bowel disease (26%), dactylitis (25-50%), and psoriasis (10%) [4]. Although the cause of the disease is unknown, Human Leukocyte Antigen (HLA) B27 is one of the most critical variables; the frequency of HLA-B27-positive individuals varies from 0.4% to 1.4% based on the patients' ethnicity [5]. This illness affects most people between 20 and 30, although it can take up to six years to diagnose [3].

Ankylosing spondylitis is a kind of spondyloarthritis persistent immune-mediated inflammatory arthritis. It most commonly affects males in their thirties and mostly impacts the sacroiliac joints and axial skeleton [6]. Even though Galen first described the condition, it was not until the 19<sup>th</sup> century that it might be correctly identified thanks to accounts by Bekhterev, Strümpell, and Marie. Although the HLA-B27 variant is recognized to have a significant link to the disease, additional genes have a role in its formation [7].

Identifying numerous inflammatory pathways brought in the age of biological treatments, resulting in a new era in ankylosing spondylitis treatment and prognosis. TNF inhibitors were the first to be authorized, but the interleukin-17 (IL-17)/IL-23 axis has gained importance in recent years, culminating in the approval of novel biological disease-modifying antirheumatic medicines that block IL-17. Despite these advancements, the disease processes underlying the condition remain unknown, and new knowledge about novel therapies' etiology, triggers, and outcomes continues to emerge [6].

### Diagnosis

The utmost widely applied criteria for ankylosing spondylitis classification were established in 1966 and modified in 1984 [8-10].

They are as follows:

1. Inflammatory low back pain has been present for at least three months, which improves by exercise and does not get relieved by rest.
2. Motion limitation of the lumbar spine in the sagittal and frontal planes.
3. Reduced chest expansion (relative to normal values for sex and age).
4. Grade 2 or greater bilateral sacroiliitis. Grade 3 or greater unilateral sacroiliitis. When the fourth or fifth criterion is present with any clinical criteria, definitive ankylosing spondylitis is considered to be present [8]. Nevertheless, radiographic sacroiliitis may not manifest for many years. Therefore, additional modalities like Magnetic Resonance Imaging (MRI) have been recommended to provide further diagnostic validation in individuals with early illness [5, 11].

### Clinical Approach

Inflammatory back pain is a significant point in a patient's history. Stiffness, low back pain, and early onset that is worse early in the morning or follows rest lasts at least 30 minutes and improves with movement are the most common symptoms of ankylosing spondylitis [5]. Sacroiliitis is accompanied by a vague unilateral or bilateral hip pain that might radiate into the upper posterior thigh. Pain in the cervical or thoracic regions may be experienced. Moreover, patients may experience synovitis or enthesitis in the peripheral joints (including plantar fasciitis or Achilles enthesitis). Sleep deprivation and tiredness during the day are frequent. Ankylosing spondylitis can be confused with other spondyloarthropathies, such as enteropathic arthropathy, reactive arthritis, and psoriatic arthritis that can be hard to differentiate among them in the early stages. In patients with inflammatory back pain with a background of psoriasis, iritis, infection, or inflammatory bowel illness, clinicians must have a high suspicion index [8].

Initially, especially in mild cases, clinical symptoms are mostly minimal. Forward lumbar flexion (Schober's test, >5 cm flexion is normal), lateral lumbar flexion, and chest expansion should all be measured, as well as palpating and pressuring the sacroiliac joints. Synovitis or enthesitis should be checked in the peripheral joints as well. Possible extra-articular manifestations of ankylosing spondylitis, such as aortic incompetence, cardiac conduction abnormalities, anterior uveitis (which affects up to 40% of patients), and pulmonary fibrosis, should also be evaluated [5, 10].

### Investigations

The HLA-B27 is found in 90-95 percent of white western European patients with ankylosing spondylitis, compared to about 8% in the general population. However, the incidence varies by population [9]. Because there are numerous subtypes of HLA-B27, not all are pathogenic, and other non-HLA-B27 genes have a role. Thus, the link is complicated. In genetically susceptible individuals, the condition is probably triggered by an unknown environmental trigger. It is important to note that most people who have HLA-B27 will never develop ankylosing spondylitis [8, 11].

Erythrocyte Sedimentation Rates (ESR) and C-reactive Protein (CRP) will be increased in most individuals with ankylosing spondylitis. Inflammatory marker levels in ankylosing spondylitis are less helpful for controlling disease activity than other inflammatory diseases like rheumatoid arthritis. They can be more related to disease activity in peripheral joints than axial disease. Normocytic normochromic anemia may be observed [8].

The disease's hallmark is sacroiliitis, and Changes in the lower third of the sacroiliac joints are common. The joint may appear unclear and blurry at first, followed by sclerosis, bone erosions, and apparent joint expansion. Long-term illness can lead to complete bony fusion [5]. Squaring of the vertebral bodies, marginal vertebral body erosions, and the

development of bone bridges or syndesmophytes between neighboring vertebrae are all seen on radiographs of the spine. Moreover, spinal ligament ossification is possible, and spinal osteopenia is frequent. Almost complete fusion of the vertebral column can happen in severe long-term illness. This radiographic manifestation is called the bamboo spine [8]. As mentioned earlier, plain radiographs may be normal in the initial phases of ankylosing spondylitis, but further imaging, particularly MRI, is critical in diagnosing ankylosing spondylitis. In detecting sacroiliitis, magnetic resonance imaging of the sacroiliac joints is more sensitive than either conventional radiography or computed tomography. Thus, MRI should be considered in individuals with typical symptoms of inflammatory back pain but normal plain radiographs, especially if they are HLA-B27 seropositive. In individuals with active ankylosing spondylitis, MRI can be utilized to track their progress. However, enthesitis can be diagnosed with the aid of musculoskeletal ultrasound screening [12, 13].

Ankylosing spondylitis is related to fractures and osteoporosis. Because of new bone development, dual-energy x-ray absorptiometry can underestimate the fracture risk in ankylosing spondylitis, especially in the spine. Biochemical markers of bone resorption have been utilized in ankylosing spondylitis research and may have therapeutic utility in the future. Fractures at the thoracolumbar and cervicothoracic connections are the most frequent, and they can happen even with minor trauma. While approaching patients with previously stable ankylosing spondylitis with sudden consistent spine pain, the physicians must have a low threshold of suspicion for fracture [12-15].

### Management

Even though novel biological therapies have drastically altered the management of this illness, surgical intervention is still necessary in some cases. Indeed, in ankylosing spondylitis patients who develop the illness at a young age, hip involvement is high, and hip involvement is common, ranging from 25 to 50%, with bilateral involvement being prevalent [16-19].

### Total Hip Replacement

Total hip replacement is the most frequent surgical surgery in ankylosing spondylitis patients. It is usually recommended for refractory pain and disability and structural deterioration to the hip [20]. For optimal outcomes, a multidisciplinary approach is recommended. It should be led by a rheumatologist, customized to the specific patient profile, and using a mix of medicinal and non-medicinal therapy [21]. However, surgical therapy of a chronic inflammatory illness necessitates caution. The overall approach, from preoperative considerations to intraoperative challenges and consideration of potential surgical complications, is critical. Total hip replacement is a very simple procedure in some cases. However, it may be challenging in individuals with ankylosing spondylitis. A careful approach to preoperative

preparation is essential. To decrease the surgical risk, it is critical to understand the disease's activity and severity. Complete blood work is required to detect inflammation using markers like CRP and ESR and complete blood count. A physical examination is necessary to determine limb length discrepancies, spinal involvement and associated limitations, and hip range of motion [17]. Before undergoing total hip replacement surgery, a thorough examination of the sciatic and femoral nerves and their vascular condition should be performed. Furthermore, a pulmonary functional evaluation should be performed because the condition is usually exacerbated by respiratory involvement, particularly in the late stages of the illness. Moreover, a similar strategy for cardiovascular involvement must be applied because of the common aortic problem in ankylosing spondylitis patients.

As a result of the increased rigidity or osteoporosis in ankylosing spondylitis patients, they tend to have a significant rate of spinal instability. When spinal instability occurs, it can increase the chance of a spinal fracture or dislocation, resulting in serious neurological damage. Finally, the severity of the spinal illness can make it difficult to position patients for total hip replacement. Therefore a thorough preoperative anesthesiologist examination is recommended, especially for those with significant cervical involvement. Regional anesthesia is often recommended to minimize the problem of a difficult airway, even though other dangers like epidural hematoma and complete spinal anesthesia may be raised in some situations. After the total hip replacement, several studies indicated an improvement in function and a reduction in discomfort [21]. After ten years, the prostheses had a survival rate of around 90%, dropping to 65% after 20 years. Approximately 1% of total hip replacements fail, and some require modification within the first 5–10 years due to aseptic loosening [22]. Only 5% of total hip replacement cemented failures are commonly reported, but the uncemented failure rate is significantly greater (28%). The justification for using uncemented total hip replacement in the last few years has been based on the younger age of ankylosing spondylitis patients and the easier feasibility of a surgical revision compared to uncemented ones [22].

### Heterotopic Ossification

Heterotopic ossification is a possible complication of total hip replacement, and there are currently no particular guidelines for this critical disease. Heterotopic ossification is the abnormal growth of bone in the non-skeletal tissues, including tendons, muscle, or other soft tissue. When heterotopic ossification is formed, new bone grows at three times the normal rate, resulting in painful, jagged joints. Up to 40% of ankylosing spondylitis patients develop heterotopic ossification, and the majority of the time, they are asymptomatic. This issue's severity might limit the range of motion in certain people. However, comparing other bone diseases, including Paget's disease and diffuse idiopathic skeletal hyperostosis, the risk of heterotopic ossification in

ankylosing spondylitis patients is lower. When ankylosing spondylitis patients require several surgical procedures, suffer postoperative infectious complications, and have an active illness, the risk of heterotopic ossification rises [23]. In a cohort of 20 ankylosing spondylitis patients, heterotopic ossification was found in 30% of them, related to a high level of CRP [24].

### Corrective Osteotomy and Stabilization

In severe cases of ankylosing spondylitis, spinal surgery is another therapeutic option considered in the recent guidelines. The most common surgical treatment recommended is corrective osteotomy and stabilization. Corrective osteotomy is recommended in functional, clinical, and radiological circumstances of severe ankylosing spondylitis like in adults with severe kyphosis or severe hip arthritis. This surgery has three surgical procedures types: open, closed, and poly-segmental osteotomy has been proposed [25, 26].

Stabilization and corrective osteotomy procedures are most frequently indicated in some patients, like in adults with severe hip arthritis or severe kyphosis. This surgery has a 4% perioperative fatality rate and a 5% incidence of irreversible neuropathic complications. This operation has been shown to improve the prevention of progressive deformity, the reduction of pain caused by muscular tiredness, the improvement of disability, the recovery of global balance and horizontal axis of view, and the improvement of digestive and respiratory function [27].

Closing- vs. Opening Wedge Osteotomy (CWO/OWO) techniques are fundamentally distinct among osteotomy methods for treating kyphotic deformity. OWO was initially developed in 1945, and several surgeons have since improved it. This technique creates a space in the spinous and laminae processes, necessitating manual extension of the lumbar spine to correct the kyphotic deformity. The procedure's high complication risk is related to the procedure's steep lordotic angle and extension of the anterior column, which can result in significant vascular and neurological damage [28].

Therefore, Poly-segmental Wedge Osteotomy (PWO) was proposed in 1949 to fix this issue; it was updated in the 1980s. Multiple CWOs in the posterior lumbar spine were used to produce a more harmonic opening of the anterior disc spaces with moderate posterior shortening spanning. In contrast to the previous technique, PWO was recommended by internal fixation utilizing Harrington rods, laminar hooks, and eventually transpedicular screws. However, implant failure has been reported in >40% of patients due to restricted intervertebral disc flexibility and a significant influence on the instrumentation. As a result, the postoperative satisfaction rates were significantly lower than predicted [29].

Later, monosegmental CWO was introduced and improved afterward. In this operation, the posterior wedge of the

vertebral body and the posterior components of one vertebra is removed to accomplish lumbar spine correction by passive extension. Internal fixation, like in PWO, is required to improve immediate stability. Correction is accomplished using this method. Therefore, CWO appears to have higher postoperative satisfaction and complication rates than OWO or PWO.

According to these three surgical processes, surgical methods for treating kyphosis have been continually developed. Closing-opening-wedge osteotomy (COWO), which is especially useful in cervical spine surgery, was proposed to overcome some restrictions and combine the benefits of CWO and OWO at the same time. The posterior column is excised the same way CWO, with the wedge tip at the vertebral midsagittal position. The anterior cortex is shattered, and the anterior column is opened during osteotomy closure, or a plane is osteotomized anteriorly parallel to the endplates. At 2.2- to 7.5-year follow-ups, this treatment decreased localized kyphosis from an average of 67–18°. Moreover, according to several studies, aorta lengthening and spinal cord shortening were well tolerated in all patients [29-32].

### Spinal Fracture in Ankylosing Spondylitis (Cervical and Thoracolumbar)

The ankylosed spine's associated spinal immobility, along with the disease's poor bone mineral density, makes the spine vulnerable to fractures [33]. The thoracolumbar spine and subaxial cervical spine are the most often observed vertebral fractures in ankylosing spondylitis patients. In such cases, surgical intervention is still controversial. Patients with ankylosing spondylitis are more susceptible to perioperative morbidity and death due to their enhanced risk of cardiac conduction and pulmonary complications abnormalities. The typical approach used to be nonoperative treatment, including traction, bed rest, and immobilization/bracing. Nonoperative treatment of these vertebral fractures in ankylosing spondylitis patients, on the other hand, can often result in poor fracture healing and pseudarthrosis. According to recent research, individuals who receive surgical therapy have superior clinical results [25, 34, 35].

One of the most serious complications of ankylosing spondylitis is atlantooccipital subluxation. Pain (72.7%) was the most frequent symptom, followed by neurological impairment and occipito-cervical deformity. The most frequent presenting symptom was sensory abnormalities (62.5%), followed by cranial neuropathy and weakness. Involvement of the cranial-vertebral junction (CVJ) in ankylosing spondylitis is most probably due to subaxial fusion, which increases the load on the atlantoaxial and atlantooccipital joints, making them more prone to fracture and dislocation. According to reports, atlantoaxial subluxation affects between 0.5 and 32% of ankylosing spondylitis patients with a male predominance [29, 36].

Conservative treatment may be appropriate for asymptomatic patients or those with pain but no neurologic complaints. External immobilization using a crown halovest or a hard orthosis can be explored in these rare situations. However, there is a significant risk of disease development. Surgery is required for symptomatic individuals since one-third of these patients will experience disease progression if not treated [37].

Dorsal decompression and fusion is the recommended therapy for such patients. It is usually done by deploying iliac crest autografts extending from the occiput to the upper cervical lamina and spinous procedures. Then, postoperative tension is needed until the graft is integrated. Surgical treatment of CVJ injuries due to SA has been demonstrated to enhance patient outcomes. However, the outcome of these difficult surgeries is probable to depend on the surgeon's technical skill.

Managing subaxial spinal injuries in ankylosing spondylitis patients is particularly difficult due to the high morbidity and death rates. Even a low-velocity collision can cause significant neurological damage in these individuals, and in one-third of cases, cervical fractures in patients with ankylosing spondylitis are fatal. The cervical-thoracic junction or the lower cervical spine is the most often fractured region [38]. The diagnosis is frequently missed or delayed because the patients are commonly on corticosteroid medication. The fractures are difficult to see on traditional X-rays of the kyphotic cervical and thoracic spine [36].

Treatment for cervical spine fractures in people with ankylosing spondylitis is still debatable. While some surgeons have observed a greater risk of problems following surgery, others recommend surgical fixation over conservative therapy since it avoids the dangers of conservative treatment. Conservative therapy has always been the gold standard for treating cervical spine fractures in ankylosing spondylitis patients. Bed rest, traction, and immobilization with a halo vest are all part of the treatment. However, bed rest is typically not suggested for them because these patients are at a higher risk of developing decubitus and pulmonary problems. Even though conservative treatment is often regarded as the gold standard, the negative consequences of not operating on these fractures cannot be underestimated. These consequences include increasing regional kyphosis with loss of reduction, risk of non-union due to continuous shearing pressures on the fracture site, and risk of neurologic aggravation. Surgical therapy (isolated posterior decompression) is becoming more common. A posterior approach or a combination of techniques is being utilized. Long segment posterior fixation with screws and plates/rods alone, with or without a posterior bone transplant, has been documented most frequently [39].

Regarding postoperative care, most surgeons believe that a halo brace is not required because bone union usually

happens within three months. Instead, a molded cervical collar might be utilized.

AS patients are also more likely to suffer from thoracolumbar spine fractures. Compared to typical spine fractures, ankylosed thoracolumbar spine fractures are extremely unstable. Following thoracic and lumbar fractures, the prevalence of neurologic sequelae is also greater in ankylosing spondylitis patients, with more than half of patients suffering post-injury neurologic impairments.

Because of the increased risk of complications in ankylosing spondylitis patients, treating thoracolumbar fractures is still debatable. While early research suggested that nonsurgical therapy might be a safe option, more current investigations have shown that operational treatment had better clinical outcomes. Improvements in surgical methods and instruments are most likely to blame for these results. Conservative therapy has been demonstrated to frequently result in poor fracture healing, which leads to chronic discomfort and, eventually, pseudoarthrosis, making surgical intervention more challenging.

Caron *et al.* examined a significant number of individuals with ankylosing spinal diseases and spine fractures in a retrospective study [25]. Seventy-five individuals received surgical repair in their study, and 37 were treated conservatively. Surgical patients had a reduced mortality rate (23% vs. 51%). These findings show that surgical treatment is superior for ankylosing spondylitis patients. Lu *et al.* recently published a study on 25 ankylosing spondylitis patients with thoracolumbar fractures, demonstrating that surgical therapy can result in solid fusion and improved neurological status. Still, conservative treatment leads to pseudoarthrosis and progressive neurologic impairment. Pedicle screw fixation of the posterior long segment is commonly used [40]. So, Surgical therapy for thoracolumbar fractures is becoming more common, but it remains the same for cervical fractures in ankylosing spondylitis patients [36].

## CONCLUSION

Patients with ankylosing spondylitis are commonly susceptible to developing severe structural and functional complications to the hip and the spine, such as severe kyphosis, severe hip arthritis, heterotopic ossification, and a spinal fracture. In such cases, surgical intervention is mostly needed. However, there are a lot of controversies surrounding surgical intervention in different situations of ankylosing spondylitis.

ACKNOWLEDGMENTS: None  
 CONFLICT OF INTEREST: None  
 FINANCIAL SUPPORT: None  
 ETHICS STATEMENT: None

## REFERENCES

1. van Royen BJ, Dijkmans BA, editors. Ankylosing spondylitis: diagnosis and management. CRC Press; 2006. doi:10.3109/9780849374463.
2. Alenazi SM, Aljhdali AF, Alwakil AI, Alghafari MA, Alshahrani AA, Almansouri FA, et al. An overview of abdominoplasty surgical approach: a literature review. *Pharmacophore*. 2020;11(6):48-51
3. Moon KH, Kim YT. Medical treatment of ankylosing spondylitis. *Hip Pelvis*. 2014;26(3):129-35. doi:10.5371/hp.2014.26.3.129.
4. Zochling J, Maxwell L, Beardmore J, Boonen A. Tnf-Alpha Inhibitors for Ankylosing Spondylitis. *Cochrane Database Syst Rev*. 2005. doi:10.1002/14651858.cd005468.
5. Khan MA. Update on spondyloarthropathies. *Ann Intern Med*. 2002;136(12):896-907. doi:10.7326/0003-4819-136-12-200206180-00011.
6. Garcia-Montoya L, Gul H, Emery P. Recent advances in ankylosing spondylitis: understanding the disease and management. *F1000Res*. 2018;7:1512. doi:10.12688/f1000research.14956.1.
7. Chen B, Li J, He C, Li D, Tong W, Zou Y, et al. Role of HLA-B27 in the pathogenesis of ankylosing spondylitis. *Mol Med Rep*. 2017;15(4):1943-51. doi:10.3892/mmr.2017.6248.
8. McVeigh CM, Cairns AP. Diagnosis and management of ankylosing spondylitis. *BMJ*. 2006;333(7568):581-5. doi:10.1136/bmj.38954.689583.de.
9. Linden SV, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. *Arthritis Rheum*. 1984;27(4):361-8. doi:10.1002/art.1780270401.
10. Moll JM, Wright V. New York clinical criteria for ankylosing spondylitis. A statistical evaluation. *Ann Rheum Dis*. 1973 Jul;32(4):354-63. doi:10.1136/ard.32.4.354.
11. Rudwaleit M, Khan MA, Sieper J. The challenge of diagnosis and classification in early ankylosing spondylitis: do we need new criteria?. *Arthritis Rheum*. 2005;52(4):1000-8. doi:10.1002/art.20990.
12. Braun J, Landewé R, Hermann KG, Han J, Yan S, Williamson P, et al. Major reduction in spinal inflammation in patients with ankylosing spondylitis after treatment with infliximab: results of a multicenter, randomized, double-blind, placebo-controlled magnetic resonance imaging study. *Arthritis Rheum*: Off J Am Coll Rheumatol. 2006;54(5):1646-52. doi:10.1002/art.21790.
13. Baraliakos X, Brandt J, Listing J, Haibel H, Sörensen H, Rudwaleit M, et al. Outcome of patients with active ankylosing spondylitis after two years of therapy with etanercept: clinical and magnetic resonance imaging data. *Arthritis Care Res*: Off J Am Coll Rheumatol. 2005;53(6):856-63. doi:10.1002/art.21588.
14. Cairns AP, Wright SA, Taggart AJ, Coward SM, Wright GD. An open study of pulse pamidronate treatment in severe ankylosing spondylitis, and its effect on biochemical markers of bone turnover. *Ann Rheum Dis*. 2005;64(2):338-9. doi:10.1136/ard.2004.022871.
15. van den Berg R, Baraliakos X, Braun J, van der Heijde D. First update of the current evidence for the management of ankylosing spondylitis with non-pharmacological treatment and non-biologic drugs: a systematic literature review for the ASAS/EULAR management recommendations in ankylosing spondylitis. *Rheumatology*. 2012;51(8):1388-96. doi:10.1093/rheumatology/kes066.
16. Dagfinrud H, Hagen KB, Kvien TK. Physiotherapy interventions for ankylosing spondylitis. *Cochrane Database Syst Rev*. 2008;2008(1):CD002822. doi:10.1002/14651858.cd002822.pub3.
17. Lubrano E, Astorri D, Taddeo M, Salzmann A, Cesarano E, Brunese L, et al. Rehabilitation and surgical management of ankylosing spondylitis. *Musculoskelet Surg*. 2013;97(2):191-5. doi:10.1007/s12306-013-0285-9.
18. Cooksey R, Brophy S, Husain MJ, Irvine E, Davies H, Siebert S. The information needs of people living with ankylosing spondylitis: a questionnaire survey. *BMC Musculoskelet Disord*. 2012;13(1):1-8. doi:10.1186/1471-2474-13-243.
19. Vander Cruyssen B, Muñoz-Gomariz E, Font P, Mulero J, De Vlam K, Boonen A, et al. Hip involvement in ankylosing spondylitis: epidemiology and risk factors associated with hip replacement surgery. *Rheumatology*. 2010;49(1):73-81. doi:10.1093/rheumatology/kep174.
20. Braun JV, Van Den Berg R, Baraliakos X, Boehm H, Burgos-Vargas R, Collantes-Estevez E, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis*. 2011;70(6):896-904. doi:10.1136/ard.2011.151027.
21. Batra YK, Sharma A, Rajeev S. Total spinal anaesthesia following epidural test dose in an ankylosing spondylitic patient with anticipated difficult airway undergoing total hip replacement. *Eur J Anaesthesiol*. 2006;23(10):897-8. doi:10.1017/s0265021506251378.
22. Valle-Onate R, Ward MM, Kerr GS, Deodhar A, Clegg D. Physical therapy and surgery. *Am J Med Sci*. 2012;343(5):353-6. doi:10.1097/maj.0b013e3182514080.
23. Tang WM, Chiu KY. Primary total hip arthroplasty in patients with ankylosing spondylitis. *J Arthroplasty*. 2000;15(1):52-8. doi:10.1016/s0883-5403(00)91155-0.
24. Schwarzkopf R, Cohn RM, Skoda EC, Walsh M, Jaffe F. The predictive power of preoperative hip range of motion for the development of heterotopic ossification. *Orthopedics*. 2011;34(3):169. doi:10.3928/01477447-20110124-10.
25. Caron T, Bransford R, Nguyen Q, Agel J, Chapman J, Bellabarba C. Spine fractures in patients with ankylosing spinal disorders. *Spine*. 2010;35(11):E458-64. doi:10.1097/brs.0b013e3181cc764f.
26. Zhu W, He X, Cheng K, Zhang L, Chen D, Wang X, et al. Ankylosing spondylitis: etiology, pathogenesis, and treatments. *Bone Res*. 2019;7(1):1-6. doi:10.1038/s41413-019-0057-8.
27. Kubiak EN, Moskovich R, Errico TJ, Di Cesare PE. Orthopaedic management of ankylosing spondylitis. *J Am Acad Orthop Surg*. 2005;13(4):267-78. doi:10.5435/00124635-200507000-00006.
28. Qian BP, Mao SH, Jiang J, Wang B, Qiu Y. Mechanisms, predisposing factors, and prognosis of intraoperative vertebral subluxation during pedicle subtraction osteotomy in surgical correction of thoracolumbar kyphosis secondary to ankylosing spondylitis. *Spine*. 2017;42(16):E983-90. doi:10.1097/brs.0000000000002015.
29. He A, Xie D, Cai X, Qu B, Kong Q, Xu C, et al. One-stage surgical treatment of cervical spine fracture-dislocation in patients with ankylosing spondylitis via the combined anterior-posterior approach. *Medicine*. 2017;96(27). doi:10.1097/md.00000000000007432.
30. Lin B, Zhang B, Li ZM, Li QS. Corrective surgery for deformity of the upper cervical spine due to ankylosing spondylitis. *Indian J Orthop*. 2014;48(2):211-5. doi:10.4103/0019-5413.128771.
31. Koller H, Koller J, Mayer M, Hempfing A, Hitzl W. Osteotomies in ankylosing spondylitis: where, how many, and how much?. *Eur Spine J*. 2018;27(1):70-100. doi:10.1007/s00586-017-5421-z.
32. Bourghli A, Boissière L, Vital JM, Bourghli MA, Almusrea K, Khoury G, et al. Modified closing-opening wedge osteotomy for the treatment of sagittal malalignment in thoracolumbar fractures malunion. *Spine J*. 2015;15(12):2574-82. doi:10.1016/j.spinee.2015.08.062.
33. Weiss RJ, Wick MC, Ackermann PW, Montgomery SM. Increased fracture risk in patients with rheumatic disorders and other inflammatory diseases—a case-control study with 53,108 patients with fracture. *J Rheumatol*. 2010;37(11):2247-50. doi:10.3899/jrheum.100363.
34. Westerveld L, Verlaan JJ, Oner FC. Spinal fractures in patients with ankylosing spinal disorders: a systematic review of the literature on treatment, neurological status and complications. *Eur Spine J*. 2009;18(2):145-56. doi:10.1007/s00586-008-0764-0.
35. Kurucan E, Bernstein DN, Mesfin A. Surgical management of spinal fractures in ankylosing spondylitis. *J Spine Surg*. 2018;4(3):501-8. doi:10.21037/jss.2018.06.15.
36. El Tecle NE, Abode-Iyamah KO, Hitchon PW, Dahdaleh NS. Management of spinal fractures in patients with ankylosing spondylitis. *Clin Neurol Neurosurg*. 2015;139:177-82. doi:10.1016/j.clineuro.2015.10.014.
37. Ramos-Remus C, Gomez-Vargas A, Hernandez-Chavez A, Gamez-Nava JI, Gonzalez-Lopez L, Russell AS. Two-year follow-up of anterior and vertical atlantoaxial subluxation in ankylosing spondylitis. *J Rheumatol*. 1997;24(3):507-10. PMID: 9058657.
38. Hunter T. The spinal complications of ankylosing spondylitis. *In Seminars in Arthritis Rheum*. 1989;19(3):172-82. doi:10.1016/0049-0172(89)90030-9.
39. Harrop JS, Sharan A, Anderson G, Hillibrand AS, Albert TJ, Flanders A, et al. Failure of standard imaging to detect a cervical fracture in a patient with ankylosing spondylitis. *Spine*. 2005;30(14):E417-9. doi:10.1097/01.brs.0000170594.45021.67.
40. Lu ML, Tsai TT, Lai PL, Fu TS, Niu CC, Chen LH, et al. A retrospective study of treating thoracolumbar spine fractures in ankylosing spondylitis. *Eur J Orthop Surg Traumatol*. 2014;24(1):117-23. doi:10.1007/s00590-013-1375-y.