Review Article

Thoracic manifestations and respiratory function alterations in axial spondyloarthritis and newest possibilities of ultrasound to detect changes in diaphragm—a narrative review

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Background and Objective: Axial spondyloarthritis (axSpA) includes thoracic manifestations and changes in respiratory function that require a comprehensive understanding for effective treatment. This review aims to investigate these manifestations and evaluate the role of ultrasound in detecting diaphragmatic changes to provide insights for improved diagnosis and treatment strategies in axSpA patients.

Methods: A systematic search was conducted in Index Medicus and Scopus from 2003 to 2023. Inclusion criteria included primary and secondary publications, with a focus on high-quality evidence such as randomised controlled trials and systematic reviews with or without meta-analysis. Keywords spondyloarthritis, respiratory, chest, thoracic, diaphragm and ultrasound were used in the search. A total of 22 articles were identified after duplicates, and inadequate papers were removed.

Key Content and Findings: The review included the prevalence, classification and extra-articular manifestations of axSpA, highlighting the impact on respiratory function. Thoracic manifestations and the potential impact of pharmacological interventions were detailed, and various conditions affecting respiratory dynamics were discussed. In addition, the utility of ultrasonography in assessing diaphragmatic function was explained and the techniques, parameters and measurements used to assess diaphragmatic movement, muscle thickness and respiratory mobility were described. The results illustrate the changes in diaphragmatic function in axSpA patients and their correlation with disease activity.

Conclusions: This narrative review highlights the intricate relationship between axSpA and respiratory manifestations and emphasises the significant impact on thoracic function and diaphragmatic dynamics. The utility of ultrasound in assessing diaphragmatic function offers a promising avenue for objective evaluation that provides insight into disease activity and potential therapeutic responses. This review emphasises the critical role of early diagnosis and vigilant monitoring, and advocates a multidisciplinary approach that integrates non-pharmacological interventions, particularly tailored physical activity, to maintain and improve respiratory function in axSpA patients. Increased research initiatives and awareness of pulmonary complications in axSpA are essential to optimise medical care and improve treatment outcomes in this patient group.

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Introduction

Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease predominantly affecting the spine and sacroiliac joints. The clinical picture is characterised by pain, stiffness and limited mobility with a resulting restriction of functional capacity. In 2009, the Assessment of SpondyloArthritis International Society (ASAS) proposed classification criteria for axSpA (1). Taking into account the presence of changes on native radiograph or magnetic resonance only, the nomenclature distinguishes between radiographic axSpA (r-axSpA), including ankylosing spondylitis (AS), and non-radiographic axSpA (nr-axSpA) (2). The estimated prevalence of axSpA is 0.36% to 0.70% and AS between 0.20% and 0.25% (3,4).

In axSpA, there are often extra-articular manifestations of the disease that are part of the SpA concept, but also those that are not. Considering the organ system affected, they can be divided into: ocular manifestations (uveitis—mostly unilateral, acute, anterior uveitis) (5), gastrointestinal (inflammatory bowel disease) (6,7), skin (psoriasis) (8), bone (osteoporosis and associated low energy vertebral fractures) (9), cardiovascular (conduction disorders, valvular heart disease, cardiomyopathy, atherosclerosis, thrombosis, aortitis, pericarditis, vasculitis) (10-13), renal disease (IgA glomerulonephritis, amyloid deposition, microhaematuria, microalbuminuria, impaired renal function) (14) and pulmonary manifestations, described in detail later.

Disease assessment in people with axSpA is a comprehensive and multi-layered process that includes dimensions such as disease activity, functional status, pain perception, stiffness, fatigue, mobility and quality of life. The ASAS/OMERACT (Outcome Measures in Rheumatology) consortium has provided recommendations for assessing outcomes in this context (15).

Treatment modalities include both pharmacological and non-pharmacological interventions. Despite the remarkable progress made by the widespread use of biologics, which have significantly improved outcomes in this group, a subgroup of patients show suboptimal response or intolerance to these therapies (16). For all patients, especially this subgroup, it is of utmost importance to achieve positive treatment outcomes through lifestyle modifications. The European Alliance of Associations for Rheumatology (EULAR), along with most national rheumatology societies, advocates the inclusion of regular physical activity as it is associated with reduced disease activity, slowing of disease progression, attenuation of functional impairment, improved thoracic and spinal mobility, improved cardiorespiratory function and overall improvement in well-being (17,18).

Assessment of physical function is recognised as a critical aspect within the ASAS/OMERACT core collection of outcome measures. However, despite the need for a holistic approach to the treatment of axSpA, involving a harmonious integration of pharmacological and non-pharmacological approaches, the latter interventions are often undervalued and neglected. This dilemma presents a particular challenge, as empirical clinical research undeniably highlights the limited capacity for physical activity in individuals with axSpA (19-21). We present this article in accordance with the Narrative Review reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1936/rc).

Methods

The aim of this paper is to review the thoracic manifestations and changes in respiratory function in axSpA, and to gain insight into the latest ultrasound capabilities to detect changes in the diaphragm in these patients that may potentially impact early diagnosis and treatment outcomes.

To this end, we conducted a review of the existing literature in two major databases, Index Medicus and Scopus, from 2003 to 2023. Our search included secondary and tertiary publications, focusing on the highest ranked articles according to the evidence-based medicine hierarchy, randomised controlled trials and systematic literature reviews with or without meta-analysis. Using the keywords spondyloarthritis, respiratory, chest, thoracic, diaphragm and ultrasound, we initially found 242 articles. After subtracting duplicates and papers that do not match thematically, there were 22 that are included in this

Table 1 The search strategy summary

Items	Specification
Date of search	8th June 2023
Databases searched	Scopus, Index Medicus
Search terms used	spondyloarthritis, respiratory, chest, thoracic, diaphragm and ultrasound
Timeframe	2003–2023
Inclusion and exclusion criteria	Inclusion criteria: study type: cross-sectional studies, comparative studies, randomised controlled trials, systematic literature reviews with or without meta-analysis; language: English, German
	Exclusion criteria: case reports, case series, articles that do not match thematically despite the search parameters
Selection process	The literature search was conducted independently by two researchers who also performed the initial literature screening
	A third researcher independently conducted an additional screening of the literature
	The final selection of literature was made by consensus of all researchers, which was thematically and qualitatively consistent with the research

narrative review. An overview of the database research strategy is presented in *Table 1*.

Thoracic manifestations and respiratory function alterations in axSpA

The first descriptions of lung and pleural involvement in individuals with spondyloarthritis date back to 1941 and 1949 (22). Although changes in lung function and ventilatory disturbances are often due to changes in the stiffness and elasticity of the thorax and thoracic spine, it is important to highlight the conditions stemming from pulmonary parenchymal changes, as well as those that occur as potential consequences of pharmacological interventions in axSpA. The predominant clinical conditions that lead to impaired respiratory function in axSpA patients include chest discomfort, restrictive chest disorders, interstitial lung disease, apical fibrosis (apical fibrobulous disease), pulmonary superinfection, spontaneous pneumothorax, obstructive sleep apnoea, bronchiolitis obliterans, bronchiocentric granulomatosis, cricoarytenoid arthritis and iatrogenic reactivation of latent tuberculosis (23,24).

In addition to reactivation of latent tuberculosis [often associated with anti-tumor necrosis factor (TNF)-α drugs], pneumonitis (associated with methotrexate, leflunomide and gold salts), DRESS (drug reaction with eosinophilia and systemic symptoms) associated with sulfasalazine, asthma, triggered by nonsteroidal anti-inflammatory drugs (NSAIDs), and rare cases of new-onset, and progression of interstitial lung disease (reported with anti-TNF-α drugs) are possible side effects of pharmacological interventions for inflammatory rheumatological diseases (25). Pleuritis and lupus-like syndrome (associated with anti-TNF-α drugs) further expand the spectrum of lung involvement (25). In addition, the prevalence of chronic obstructive pulmonary disease (COPD) is significantly higher in people with psoriatic arthritis and AS (26).

Inflammatory changes in the joints and entheses, coupled with ossification and fusion of the thoracic spine, costovertebral joints and occasionally costosternal joints, sternoclavicular joints and manubriosternal synchondrosis contribute to a reduction in chest mobility. These changes culminate in the development of thoracic kyphosis, inflexibility of the thorax, formation of syndesmophytes and further decrease in spinal and thoracic mobility during the respiratory cycle (27). The persistent stiffness of the rib cage exacerbates atrophy of the intercostal muscles, which increases the workload on the diaphragm as the main inspiratory muscle. All these factors contribute to a reduction in lung volume and capacity compared to the healthy population (28-30).

Fibrocystic changes in the upper lobe of the lung are thought to result from thickening of the apical portion of the pleura due to decreased ventilation of the upper lobes of the lung as a result of chest stiffness (31). Although these changes are predominantly asymptomatic, they can lead to superinfections with mycobacteria or fungi, especially *Aspergillus fumigatus*. Furthermore, they can occasionally lead to unilateral or, rarely, bilateral spontaneous pneumothorax (occurring in about 0.29% of patients), which requires immediate medical attention (32).

The gold standard for diagnosing restrictive lung disease is measurement of total lung capacity (TLC) by plethysmography. However, due to its limited availability in certain healthcare settings, spirometry is recommended as a reliable screening tool to identify a restrictive pattern in respiratory dysfunction with a sensitivity of about 60% (29,33,34).

In individuals affected by AS, the decline in lung function typically manifests as a restrictive pattern, with a prevalence of 20–57% (35). This phenomenon is primarily due to restricted chest mobility, which is present in almost all individuals with advanced disease, and to a lesser extent, interstitial lung disease (24,36-40).

Although restrictive pulmonary changes in axSpA are often asymptomatic, their impact on functionality and quality of life is undeniable (41). Studies have revealed a negative correlation between chest mobility and forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) values (28,41-43). A characteristic phenomenon is the maintenance or even enhancement of gas exchange across the alveolar-capillary membrane, which suggests extrapulmonary limitation rather than primary pulmonary dysfunction (25).

Comparative study by Berdal *et al.* found a relationship between spinal and thoracic mobility and changes in the percentage of expected FVC in individuals with AS. Of note, the authors found no significant correlations between lung function and measures of disease activity, physical function, smoking and cardiorespiratory functional capacity during physical activity (40). A study by Romagnoli *et al.* demonstrated an increased workload of the diaphragm and abdominal muscles in AS patients that compensates for limited chest mobility (44). In individuals with AS and kyphotic deformities of the thoracic spine, changes in the direction of movement of the diaphragm and a shortened anterior abdominal wall adversely affect the respiratory process. Liu *et al.* also confirmed that AS patients with kyphotic deformities experience sagittal axial rotation of the diaphragm, which can reduce both vital capacity and FVC (45).

This underlines the importance of preserving spinal mobility in patients while emphasising that the prevention of radiological progression, starting with the immediate initiation of adequate treatment, must be a top priority.

Ultrasound assessment of diaphragm function and its significance in people with axSpA

The diaphragm, a vital respiratory muscle, has a dome-shaped form and can be anatomically divided into two main segments: the central portion, which consists of a tendon, and the outer muscular portion. Functionally, this muscular part is further divided into two components: the crural segment, located medially and originating from the lumbar vertebrae (L2–L4), and the larger costal segment, located laterally and connected to the inner surfaces of the six lower ribs, thus forming the zone of apposition (ZOA) (46,47).

During breathing, contraction of the muscle fibres in the ZOA causes the diaphragm to move craniocaudally, resulting in an increase in intrathoracic volume and a subsequent decrease in intrathoracic pressure. This mechanism facilitates the inflow of air into the lungs. At the same time, the muscle fibres in the costal portion of the diaphragm elevate the lower chest, contributing to its expansion. In the exhalation phase, the diaphragm relaxes and its upward displacement results from the elastic recoil of the lungs. For sustained, rhythmic and uninterrupted breathing, it is essential that the muscle fibres of the diaphragm have some endurance against fatigue. In the adult human diaphragm, the composition of muscle fibres is 55% type I fibres (which are slow fatigue resistant), 21% type IIA fibres (fast oxidative fibres with intermediate fatigue resistance) and 24% type IIB fibres (fast glycolytic fibres with low fatigue resistance) (48). Ultrasound is used as a means to assess diaphragmatic function by measuring muscle thickening and respiratory mobility. Two acoustic windows are used in this assessment: the subcostal area (SCA) and the ZOA.

During a diaphragmatic contraction, ultrasound examinations through the SCA window provide insights into the cranio-caudal excursion of the diaphragm. To acquire these images, a low frequency phased array or curved array probe (2–5 MHz) is strategically placed just below the costal arch along the midclavicular and anterior axillary line (for anterior subcostal view) or along the mid and posterior axillary line (for posterior subcostal view). The ultrasound probe is tilted cranially and aligned perpendicular to the diaphragmatic dome. The diaphragm is visualised as a hyperechoic line extending over the liver and spleen, which serve as acoustic windows. During the inspiration phase, the diaphragm should move in the direction of the probe. The examination is performed during different breathing patterns, including quiet breathing, deep breathing and the sniffing manoeuvre (49-52).

At the same time, ZOA window is used to observe muscle thickness and thickening fraction (TF). In the intercostal approach, a 10–15 MHz linear array transducer

is placed in cranio-caudal alignment and perpendicular to the skin, typically between the mid-axillary line or the antero-axillary line within the 8th to 11th intercostal spaces. The diaphragm appears as a three-layered structure lying between the pleural and peritoneal membranes. Measurements of the diaphragm are taken in either B or M mode using callipers, with recordings at the end of expiration (expressing functional residual capacity—FRC) and at the end of inspiration (expressing TLC) during deep breathing (49,53,54).

Boussuges *et al.* have demonstrated, in their reproducibility and a repeability study, a high degree of reproducibility by the same examiner (96–94%) and between examiners (95–91%) when measuring the movement of both hemidiaphragms during quiet breathing (50). In addition, measurement of diaphragm thickness fration in M-mode and B-mode has been shown to be reproducible in a group of 66 healthy subjects with a repeatability coefficient of 0.10–0.15 for M-mode and 0.16–0.26 for B-mode. A repeatability coefficient ≤0.3 was considered acceptable. For less experienced users, ultrasound examination with M-mode is more accurate (55,56).

The respiratory mobility of the diaphragm is determined by the maximum distance the diaphragm travels between forced inspiration and expiration (in millimetres). Normal values of diaphragmatic mobility depend on the patient's sex, position, positioning and orientation of the ultrasound probe, the side of the hemidiaphragm and the type of inspiration (quiet breathing or deep breathing).

During deep breathing in the supine position, the measurements are as follows:

- Right hemidiaphragm: 4.7±1.0 cm (female) *vs.* 5.3±1.1 cm (male);
- Left hemidiaphragm: 4.8±0.3 cm (female) *vs.* 5.4±1.3 cm (male).

For comparison, in standing position, the values are:

- Right hemidiaphragm: 5.7±1.0 cm (female); 7.0±1.1 cm (male);
- Left hemidiaphragm: 6.4±1.0 cm (female); 7.5±0.9 cm (male).

During quiet breathing, the sex- and position-related differences are significantly smaller, with the following values:

- Right hemidiaphragm: 1.6±0.3 cm (female); 1.8±0.3 cm (male);
- Left hemidiaphragm: 1.6±0.4 cm (female); 1.8±0.4 cm (male) (50,56).

Diagnosis of diaphragmatic weakness is established by observing decreased mobility during deep breathing, with or without paradoxical movement during the sniffing manoeuvre (57).

Assessment of the trophicity and contractile efficiency of the diaphragm involves evaluation of the thickness of the diaphragm (Tdi), the ratio of thickening at the end of inspiration and expiration (TdTLC/TdFRC), and the fraction of diaphragmatic thickening (TF) at the end of forced inspiration (Tdi-insp) and forced expiration (Tdi-exp) [(Dtf) = (tdiTLC – tdiFRC)/tdiFRC] in both hemidiaphragms (54,58).

Tdi-exp provides information about the trophicity of the diaphragm. Reference values for healthy individuals, based on a cross-sectional study of 109 healthy subjects with an average age of 25.8±6.5 years, are 0.14±0.03 cm for women and 0.19±0.04 cm for men (59).

The lower limit of acceptable diaphragmatic thickness at FRC is 0.15 cm, and an increase in diaphragmatic thickness from FRC to TLC of at least 20% is considered physiological. A difference in thickness from sides at FRC of >0.33 cm is abnormal (60).

The TF is calculated using the following formula: TF = [(Tdi-insp – Tdi-exp)/Tdi-exp] × 100. Cardenas *et al.* conducted a study on a sample of 64 healthy participants and determined an average physiological TF of (169±43)% in women and (204±61)% in men (52).

The diaphragm is expected to thicken by at least 20% during maximal inspiration, with minimal side-to-side variation (61). It has been found that the displacement of the diaphragm is greater in supination than in standing or sitting, considering the same volume of inspiration (62). According to Boussuges *et al.* study on the 410 healthy volunteers the mean value and lower limit of normal diaphragmatic displacement during quiet breathing and the sniffing manoeuvre are comparable to the values for people in a standing position. However, the mean and lower limits of diaphragmatic displacement during deep breathing in the seated position were lower than in the standing position (50). A technical report by Houston *et al.* found that the normal right-to-left ratio of maximum diaphragmatic displacements during deep breathing was in the range of 0.5 to 1.6 (63).

Diagnosis of diaphragmatic dysfunction includes ultrasound values of TF <20–29% and diaphragmatic excursion of less than 1 cm. Reduced, absent or paradoxical diaphragmatic motility supports the diagnosis of diaphragmatic palsy. Reduced Tdi-exp (<0.11 cm) and reduced TF (<20%) support a diagnosis of chronic diaphragmatic palsy, while reduced, absent or paradoxical

mobility and reduced TF <20% support a diagnosis of acute diaphragmatic palsy (56).

Studies have not demonstrated a relationship between diaphragmatic thickness and body mass index (BMI), respiratory index or chest circumference (59). In contrast to these findings, research by Kantarci *et al.* on 164 healthy subjects indicates that BMI <18.5 kg/m^2 and >40 kg/m^2 is associated with statistically lower diaphragmatic motility in healthy subjects (64). Diaphragmatic thickness and contractility are only slightly influenced by age, sex or smoking status (60).

In people with axSpA, changes in the diaphragm may be seen on ultrasound, indicating muscle dysfunction that could be associated with respiratory symptoms. Ünlü *et al.* conducted a comparative study with 33 subjects with axSpA and observed a non-significant reduction in diaphragmatic mobility compared to a control group using ultrasound. In addition, their study found a positive correlation between diaphragmatic mobility and the occiput to wall distance and a negative correlation with cervical spine rotation and the modified Schober test. These results suggest a correlation between limited axial mobility and diaphragmatic movement (65). A cross-sectional study by Dhahri *et al.* studied diaphragm and respiratory function with ultrasound in 50 people with axSpA. Their study showed a decrease in diaphragm thickness and a correlation between diaphragm thickness and lung function parameters. This was confirmed by the results of spirometry from the same study, which indicated restrictive disorders in 32% of the subjects and pathological values of chest motility in 72%. Diaphragmatic thickness was found to correlate with FVC and supine FVC, further confirming the correlation between ultrasound diaphragmatic assessment and spirometry results (66).

In a cross-sectional study of 50 patients diagnosed with AS by Mejri Ep Ajili *et al.*, 54% of the subjects were found to have decreased right hemidiaphragm motility and 48% were found to have decreased left hemidiaphragm motility. In addition, decreased diaphragmatic thickening was found in the right hemidiaphragm in 56% of the subjects and in the left hemidiaphragm in 60%. The study also showed a correlation between right hemidiaphragm inspiratory thickness and FVC and FVC in the supine position (67).

In a cross-sectional study by Güneş *et al.* of 49 patients diagnosed with axSpA, a negative correlation was found between the erythrocyte sedimentation score and the diaphragmatic thickness ratio during the respiratory cycle (dtr), which assesses the thickness ratio at maximum inspiration (TLC) and expiration (FRC). This suggests a possible relationship between disease activity and changes in diaphragmatic function. The authors suggested that assessment of dtr could complement pulmonary function tests (PFTs) and emphasised the importance of early interventions, such as specific exercises to improve diaphragmatic function, in people with axial SpA (68).

Inspiratory muscle training leads to an improvement in inspiratory muscle strength, targeting the diaphragm muscles in particular, thereby increasing functional capacity. This programme also serves to increase chest expansion, which increases its benefit by exerting a positive influence on mitigating disease activity in patients with axSpA (69).

Conclusions

A thorough understanding of the pulmonary manifestations in people with axSpA is essential for accurate diagnosis and targeted treatment strategies.

A comprehensive, multidisciplinary therapeutic approach that includes careful monitoring of pulmonary changes plays a fundamental role in improving patient outcomes and quality of life.

The use of ultrasound measurements to quantify diaphragm thickness, which, given its central role as the main inspiratory muscle, combined with an assessment of its respiratory mobility, provides objective insights into its functional dynamics. Insufficient diaphragmatic mobility can lead to a reduction in lung volume and capacity, which in turn affects the patient. By detecting inadequate diaphragmatic mobility, ultrasound can alert the physician to a possible reduction in lung volume and capacity so that appropriate measures can be taken to optimise respiratory function. In contrast, the observation of increased diaphragmatic mobility during follow-up examinations can indicate improved disease control and a better response to therapy, so that treatment strategies can be targeted towards a better outcome for the patient. A nuanced understanding of these adaptive changes is essential for ongoing monitoring of the condition of axSpA patients to facilitate therapeutic interventions to optimise respiratory function.

Promoting further research initiatives and raising awareness of pulmonary complications has the potential to improve the efficiency of medical care and treatment outcomes for patients with axSpA.

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Footnote

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References

1. Rudwaleit M, van der Heijde D, Landewé R, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis 2009;68:777-83.
2. Michelena X, López-Medina C, Marzo-Ortega H. Non-radiographic versus radiographic axSpA: what's in a name? Rheumatology (Oxford) 2020;59:iv18-24.
3. Sieper J, Poddubnyy D. Axial spondyloarthritis. Lancet 2017;390:73-84.
4. Dean LE, Jones GT, MacDonald AG, et al. Global prevalence of ankylosing spondylitis. Rheumatology (Oxford) 2014;53:650-7.
5. Zeboulon N, Dougados M, Gossec L. Prevalence and characteristics of uveitis in the spondyloarthropathies: a systematic literature review. Ann Rheum Dis 2008;67:955-9.
6. Rudwaleit M, Baeten D. Ankylosing spondylitis and bowel disease. Best Pract Res Clin Rheumatol 2006;20:451-71.
7. De Keyser F, Mielants H. The gut in ankylosing spondylitis and other spondyloarthropathies: inflammation beneath the surface. J Rheumatol 2003;30:2306-7.
8. Umezawa Y. Psoriatic arthritis. J Dermatol 2021;48:741-9.
9. El Maghraoui A. Osteoporosis and ankylosing spondylitis. Joint Bone Spine 2004;71:291-5.
10. Roldan CA. Valvular and coronary heart disease in systemic inflammatory diseases: Systemic Disorders in heart disease. Heart 2008;94:1089-101.
11. Brunner F, Kunz A, Weber U, et al. Ankylosing spondylitis and heart abnormalities: do cardiac conduction disorders, valve regurgitation and diastolic dysfunction occur more often in male patients with diagnosed ankylosing spondylitis for over 15 years than in the normal population? Clin Rheumatol 2006;25:24-9.
12. Sari I, Okan T, Akar S, et al. Impaired endothelial function in patients with ankylosing spondylitis. Rheumatology (Oxford) 2006;45:283-6.
13. Tanoue LT. Pulmonary involvement in collagen vascular disease: a review of the pulmonary manifestations of the Marfan syndrome, ankylosing spondylitis, Sjögren's syndrome, and relapsing polychondritis. J Thorac Imaging 1992;7:62-77.
14. Rodrigues AC, Marques JC, Reis M, et al. Kidney Disease in Ankylosing Spondylitis: a case series and review of the literature. J Bras Nefrol 2023;45:36-44.
15. Navarro-Compán V, Boel A, Boonen A, et al. Instrument selection for the ASAS core outcome set for axial spondyloarthritis. Ann Rheum Dis 2023;82:763-72.
16. Webers C, Ortolan A, Sepriano A, et al. Efficacy and safety of biological DMARDs: a systematic literature review informing the 2022 update of the ASAS-EULAR recommendations for the management of axial spondyloarthritis. Ann Rheum Dis 2023;82:130-41.
17. Regel A, Sepriano A, Baraliakos X, et al. Efficacy and safety of non-pharmacological and non-biological pharmacological treatment: a systematic literature review informing the 2016 update of the ASAS/EULAR recommendations for the management of axial spondyloarthritis. RMD Open 2017;3:e000397.
18. O'Dwyer T, O'Shea F, Wilson F. Exercise therapy for spondyloarthritis: a systematic review. Rheumatol Int 2014;34:887-902.
19. Hsieh LF, Wei JC, Lee HY, et al. Aerobic capacity and its correlates in patients with ankylosing spondylitis. Int J Rheum Dis 2016;19:490-9.
20. Ozdem Yr O, Inanici F, Hasçelik Z. Reduced vital capacity

leads to exercise intolerance in patients with ankylosing spondylitis. Eur J Phys Rehabil Med 2011;47:391-7.
21. van der Esch M, van 't Hul AJ, Heijmans M, et al. Respiratory muscle performance as a possible determinant of exercise capacity in patients with ankylosing spondylitis. Aust J Physiother 2004;50:41-5.
22. HAMILTON KA. Pulmonary disease manifestations of ankylosing spondylarthritis. Ann Intern Med 1949;31:216-27.
23. Danve A. Thoracic Manifestations of Ankylosing Spondylitis, Inflammatory Bowel Disease, and Relapsing Polychondritis. Clin Chest Med 2019;40:599-608.
24. Kanathur N, Lee-Chiong T. Pulmonary manifestations of ankylosing spondylitis. Clin Chest Med 2010;31:547-54.
25. Kelly C, Iqbal K, Iman-Gutierrez L, et al. Lung involvement in inflammatory rheumatic diseases. Best Pract Res Clin Rheumatol 2016;30:870-88.
26. Gergianaki I, Tsiligianni I. Chronic obstructive pulmonary disease and rheumatic diseases: A systematic review on a neglected comorbidity. J Comorb 2019;9:2235042X18820209.
27. Fisher LR, Cawley MI, Holgate ST. Relation between chest expansion, pulmonary function, and exercise tolerance in patients with ankylosing spondylitis. Ann Rheum Dis 1990;49:921-5.
28. Seçkin U, Bölükbasi N, Gürsel G, et al. Relationship between pulmonary function and exercise tolerance in patients with ankylosing spondylitis. Clin Exp Rheumatol 2000;18:503-6.
29. Feltelius N, Hedenström H, Hillerdal G, et al. Pulmonary involvement in ankylosing spondylitis. Ann Rheum Dis 1986;45:736-40.
30. El Maghraoui A. Pleuropulmonary involvement in ankylosing spondylitis. Joint Bone Spine 2005;72:496-502.
31. Campbell AH, Macdonald CB. Upper lobe fibrosis associated with ankylosing spondylitis. Br J Dis Chest 1965;59:90-101.
32. Lee CC, Lee SH, Chang IJ, et al. Spontaneous pneumothorax associated with ankylosing spondylitis. Rheumatology (Oxford) 2005;44:1538-41.
33. Cerrahoglu L, Unlu Z, Can M, et al. Lumbar stiffness but not thoracic radiographic changes relate to alteration of lung function tests in ankylosing spondylitis. Clin Rheumatol 2002;21:275-9.
34. Aaron SD, Dales RE, Cardinal P. How accurate is spirometry at predicting restrictive pulmonary impairment? Chest 1999;115:869-73.
35. Drăgoi RG, Amaricai E, Drăgoi M, et al. Inspiratory muscle training improves aerobic capacity and pulmonary function in patients with ankylosing spondylitis: a randomized controlled study. Clin Rehabil 2016;30:340-6.
36. Baser S, Cubukcu S, Ozkurt S, et al. Pulmonary involvement starts in early stage ankylosing spondylitis. Scand J Rheumatol 2006;35:325-7.
37. Altin R, Ozdolap S, Savranlar A, et al. Comparison of early and late pleuropulmonary findings of ankylosing spondylitis by high-resolution computed tomography and effects on patients' daily life. Clin Rheumatol 2005;24:22-8.
38. Sampaio-Barros PD, Cerqueira EM, Rezende SM, et al. Pulmonary involvement in ankylosing spondylitis. Clin Rheumatol 2007;26:225-30.
39. Ayhan-Ardic FF, Oken O, Yorgancioglu ZR, et al. Pulmonary involvement in lifelong non-smoking patients with rheumatoid arthritis and ankylosing spondylitis without respiratory symptoms. Clin Rheumatol 2006;25:213-8.
40. Berdal G, Halvorsen S, van der Heijde D, et al. Restrictive pulmonary function is more prevalent in patients with ankylosing spondylitis than in matched population controls and is associated with impaired spinal mobility: a comparative study. Arthritis Res Ther 2012;14:R19.
41. Dincer U, Cakar E, Kiralp MZ, et al. The pulmonary involvement in rheumatic diseases: pulmonary effects of ankylosing spondylitis and its impact on functionality and quality of life. Tohoku J Exp Med 2007;212:423-30.
42. Sahin G, Calikoğlu M, Ozge C, et al. Respiratory muscle strength but not BASFI score relates to diminished chest expansion in ankylosing spondylitis. Clin Rheumatol 2004;23:199-202.
43. Durmuş D, Altay F, Uzun O, et al. Ankilozan Spondilitte Klinik ve Pulmoner Fonksiyonlar Arasındaki İlişki. Arch Rheumatol 2009;24:178-82.
44. Romagnoli I, Gigliotti F, Galarducci A, et al. Chest wall kinematics and respiratory muscle action in ankylosing spondylitis patients. Eur Respir J 2004;24:453-60.
45. Liu C, Wu B, Guo Y, et al. Correlation between diaphragmatic sagittal rotation and pulmonary dysfunction in patients with ankylosing spondylitis accompanied by kyphosis. J Int Med Res 2019;47:1877-83.
46. Green M, Moxham J. The respiratory muscles. Clin Sci (Lond) 1985;68:1-10.
47. Roussos C. Function and fatigue of respiratory muscles. Chest 1985;88:124S-32S.
48. Gransee HM, Mantilla CB, Sieck GC. Respiratory muscle plasticity. Compr Physiol 2012;2:1441-62.

49. Tuinman PR, Jonkman AH, Dres M, et al. Respiratory muscle ultrasonography: methodology, basic and advanced principles and clinical applications in ICU and ED patients-a narrative review. Intensive Care Med 2020;46:594-605.
50. Boussuges A, Finance J, Chaumet G, et al. Diaphragmatic motion recorded by M-mode ultrasonography: limits of normality. ERJ Open Res 2021;7:00714-2020.
51. Testa A, Soldati G, Giannuzzi R, et al. Ultrasound M-mode assessment of diaphragmatic kinetics by anterior transverse scanning in healthy subjects. Ultrasound Med Biol 2011;37:44-52.
52. Cardenas LZ, Santana PV, Caruso P, et al. Diaphragmatic Ultrasound Correlates with Inspiratory Muscle Strength and Pulmonary Function in Healthy Subjects. Ultrasound Med Biol 2018;44:786-93.
53. Ueki J, De Bruin PF, Pride NB. In vivo assessment of diaphragm contraction by ultrasound in normal subjects. Thorax 1995;50:1157-61.
54. Cohn D, Benditt JO, Eveloff S, et al. Diaphragm thickening during inspiration. J Appl Physiol (1985) 1997;83:291-6.
55. Cappellini I, Picciafuochi F, Bartolucci M, et al. Evaluation of diaphragm thickening by diaphragm ultrasonography: a reproducibility and a repeatability study. J Ultrasound 2021;24:411-6.
56. Santana PV, Cardenas LZ, Albuquerque ALP, et al. Diaphragmatic ultrasound: a review of its methodological aspects and clinical uses. J Bras Pneumol 2020;46:e20200064.
57. Gerscovich EO, Cronan M, McGahan JP, et al. Ultrasonographic evaluation of diaphragmatic motion. J Ultrasound Med 2001;20:597-604.
58. Gottesman E, McCool FD. Ultrasound evaluation of the paralyzed diaphragm. Am J Respir Crit Care Med 1997;155:1570-4.
59. Carrillo-Esper R, Pérez-Calatayud ÁA, Arch-Tirado E, et al. Standardization of Sonographic Diaphragm Thickness Evaluations in Healthy Volunteers. Respir Care 2016;61:920-4.
60. Boon AJ, Harper CJ, Ghahfarokhi LS, et al. Two-dimensional ultrasound imaging of the diaphragm: quantitative values in normal subjects. Muscle Nerve 2013;47:884-9.
61. Boussuges A, Rives S, Finance J, et al. Assessment of diaphragmatic function by ultrasonography: Current approach and perspectives. World J Clin Cases 2020;8:2408-24.
62. Houston JG, Angus RM, Cowan MD, et al. Ultrasound assessment of normal hemidiaphragmatic movement: relation to inspiratory volume. Thorax 1994;49:500-3.
63. Houston JG, Morris AD, Howie CA, et al. Technical report: quantitative assessment of diaphragmatic movement--a reproducible method using ultrasound. Clin Radiol 1992;46:405-7.
64. Kantarci F, Mihmanli I, Demirel MK, et al. Normal diaphragmatic motion and the effects of body composition: determination with M-mode sonography. J Ultrasound Med 2004;23:255-60.
65. Ünlü E, Pamuk ÖN, Erer B, et al. Diaphragmatic movements in ankylosing spondylitis patients and their association with clinical factors: an ultrasonographic study. Rheumatol Int 2012;32:435-7.
66. Dhahri R, Mejri I, Ghram A, et al. Assessment Tools for Pulmonary Involvement in Patients with Ankylosing Spondylitis: Is Diaphragmatic Ultrasonography Correlated to Spirometry? J Multidiscip Healthc 2023;16:51-61.
67. Mejri Ep Ajili I, Dghaies A, Dhahri R, et al. Diaphragm ultrasound in spondyloarthritis: assessment of diaphragmatic motion and respiratory function. Eur Respir J 2022;60:4229.
68. Güneş S, Genç A, Sunar İ, et al. SAT0330 Value of Diaphragmatic Assessment in Relation to Pulmonary Functions and Disease Activity in Axial Spondyloarthropathies: Preliminary Report. Annals of the Rheumatic Diseases 2019;78:1244.
69. Verep U, Çiçek E, Özyürek S. The Role of Core Stability and Core Muscles in Ankylosing Spondylitis: A Review of Functional and Clinical Importance. Journal of Basic and Clinical Health Sciences 2023;7:545-52.

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