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REVIEW ARTICLE

A Review of Machine Learning Methods for Classification of Ankylosing Spondylitis Data

Fadhaa O. Sameer*
Tropical-Biological Research Unit, College of Science, University of Baghdad, Baghdad, Iraq

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Corresponding Author:
Fadhaa Othman Sameer
fadhaa.sameer@sc.uobaghdad.edu.iq, 07902173201
ORCHID:
https//orcid.org/0000-0001-8758-6195

ABSTRACT

Ankylosing Spondylitis (AS) is a chronic inflammatory disease that primarily affects the spine and sacroiliac joints. Early diagnosis and treatment are crucial to preventing irreversible damage and improving patient outcomes. Early diagnosis of AS is critical yet difficult. Delays in diagnosis are widespread, typically lasting many years after symptoms first appear, due to the non-specific nature of early indicators and a lack of understanding among healthcare practitioners. Machine learning (ML) methods have shown great potential in classifying AS data, aiding in early detection and personalized treatment strategies. This paper aims to review the current literature on ML methods for AS classification, highlighting trends, challenges, and future directions in the field. It provides researchers with the latest insights into ML applications and encourages new ideas by analyzing image processing techniques utilized by these methods. In this systematic review, 43 articles are analyzed, focusing on the application of deep learning and machine learning techniques in diagnosing Ankylosing Spondylitis. The findings emphasize that ML methods significantly enhance segmentation accuracy and improve case classification for various rheumatologic diseases, including AS.

INTRODUCTION

Machine learning (ML) is a branch of artificial intelligence (AI) which focuses in statistics and computer science. Machine learning (ML) employs sample data or prior knowledge to improve a performance criterion and works on learning relationships from datasets gathered by computer algorithms(Dhall, Vaish, and Vaishya 2024).

In order to minimize the generalization error of the prediction for a given dataset, machine learning is an area of computer science that works with algorithms that estimate the ideal values for the parameters of statistical models (Koo et al. 2024). In addition to finding more complicated relationships between variables, machine learning models outperform classical methods in predicting the values of a qualitative or quantitative variable in various groups of individuals(Calvo Pascual, Castro Corredor, and Garrido Merchán 2024).

Machine learning and deep learning (DL) are increasingly used in biomedical research and healthcare for image labeling, annotation, segmentation, data harmonization, cancer diagnosis, and gene expression analysis(Kennedy et al. 2023). Machine learning systems are increasingly used in rheumatologist studies and have received a lot of interest lately because to their advantageous properties (Fernández-Gutiérrez et al. 2021a).

Over the past ten years, there has been a growing use of machine learning (ML) and deep learning (DL) approaches for the classification of Ankylosing Spondylitis (AS). Many machine learning algorithms have been used.

Ankylosing spondylitis (AS) is a long-term, inflammatory immune-mediated condition affecting the axial skeleton and peripheral joints. The pathophysiology of AS is not fully known, however activation of the innate and adaptive immune responses, strong genetic predisposition factors, and the participation of cytokines mostly produced by T helper 17 cells and macrophages are important (Koo et al. 2024).

Surgery and treatment for other joint locations may become essential if AS is discovered in its advanced stages. Thus, research conducted over the past ten years has stressed the importance of using computational methods to identify AS early on(Walsh et al. 2019). From this vantage point, the treatment process will be extensive if radiological imaging fails to reveal portions of the development-oriented axis(Cooksey et al. 2021). If AS is discovered after joint function has been lost, treatment for the disorder must last a lifetime. Currently, identifying AS through non-intrusive examination of the patient data analyzed by the created technologies bears a significant responsibility(Koo et al. 2023).

The developed diagnostic system will methodically abstract these data, thus the integration will yield holistic information that might not have been discovered

from visual screening. As a result, population-based research can be disseminated, and created mechanisms can increase the stability of the results.

Several studies have looked into classifying AS data using machine learning techniques. These approaches typically entail the use of algorithms for data analysis, including genetic, clinical, and imaging data, such as support vector machines, random forests, neural networks, and deep learning techniques. These research have shown how machine learning (ML) may be used to find patterns and biomarkers linked to AS, which can help with the disease's diagnosis and prognosis. This review aims to provide researchers in rheumatology with up-to-date information on the usage of DL and ML, inspiring them to produce new research ideas by assessing classification using AI approaches. This paper covers current classifying AS data using machine learning techniques and includes a table of data and system attributes. Several topics, like "Do we need ML for classifying AS data?", "Is it beneficial to use ML in classifying AS data?", and "What kind of ML technologies do we need?" were addressed.

MATERIAL AND METHODS

Several significant citation databases, including the National Library of Medicine, Scopus, Web of Science, IEEE Explore, ELSEVIER, Springer, and Science Direct, were used to find sources for this systematic literature review. First, the AND command was used in a variety of combinations to combine the terms Artificial Intelligence, Machine Learning, features selection, Ankylosing Spondylitis, and classification. The sources employed for the review that is being given have the most recent dates of release available, ranging from 2015 to 2024 research.

Details of the 200 publications that were accessed here are displayed along with the analysis and filtering processes. According to the review, the following qualifications were met:

- The study must be conducted in English and published no earlier than 2015.
- Ankylosing spondylitis (AS) patients should use machine learning algorithm technique.
- Research aiming to target Ankylosing spondylitis disease should use medical pictures to discover anatomical structures.
- The main goal of the literature review should be furthered by research, and it should have an influence on linked fields of inquiry.

The followings were the justifications for exclusions:

1. The research was only offered as an abstract.
2. its primary topic was ineligible for the review that was presented.
3. it only addressed theoretical concepts.
4. it was not possible to access the full text.
5. it did not provide specific details about the applied method.

The ways that Ankylosing Spondylitis (AS) is treated with machine learning (ML)

There are three distinct approaches to apply machine learning (ML) techniques for Ankylosing Spondylitis (AS).

1. Identification and Diagnosis of Diseases
2. Forecast of Disease Development and Specific Therapy Actions
3. Identification of Images.

Early Diagnosis and Biomarker Identification

Machine learning algorithms have improved the diagnosis and treatment of Ankylosing Spondylitis (AS) by evaluating large datasets and identifying promising biomarkers. These algorithms can anticipate common illnesses, death, and timely treatment, transforming healthcare by recognizing biomarkers such as Granulysin and IL2RB.

Forecast of Disease Development and Specific Therapy Actions

Machine learning (ML) models are increasingly being used to predict disease progression and guide therapy for Ankylosing Spondylitis (AS). These models improve diagnostic accuracy and enable tailored treatment techniques, thereby tackling the complications of AS. ML models can combine a variety of clinical data to predict therapy outcomes, hence optimizing therapeutic decisions.

Identification of Images.

The most specific examination for ankylosing spondylitis is magnetic resonance imaging (MRI), which generates signals using energy from a powerful magnet and results in a series of cross-sectional images. A computer analyzes these photos, or "slices," to construct an image of the joint. An MRI can assist in diagnosing ankylosing spondylitis in the early stages of the disease.

RESULTS AND DISCUSSION

Selected publications were reviewed in this section. Additionally, Table 1 lists similar studies in order of publication date and provides a summary of their contents. Studies on Ankylosing Spondylitis (AS) could be categorized as shown in Figure 1. After the eligibility phase was finished, 47 studies were found to be worthy of examination. Results distribution by year after studies were filtered in Figure 2. Table 2 also included the data source for the studies that had been filtered.

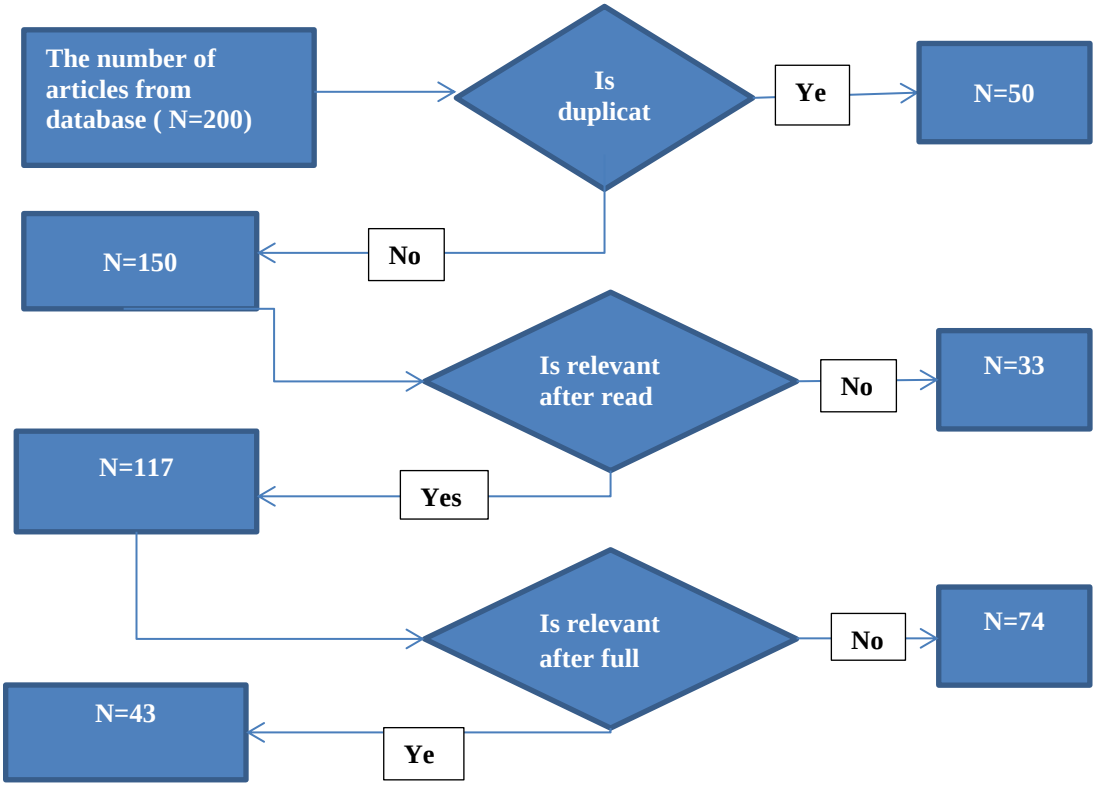

Fig. 1: The technique used in the present review

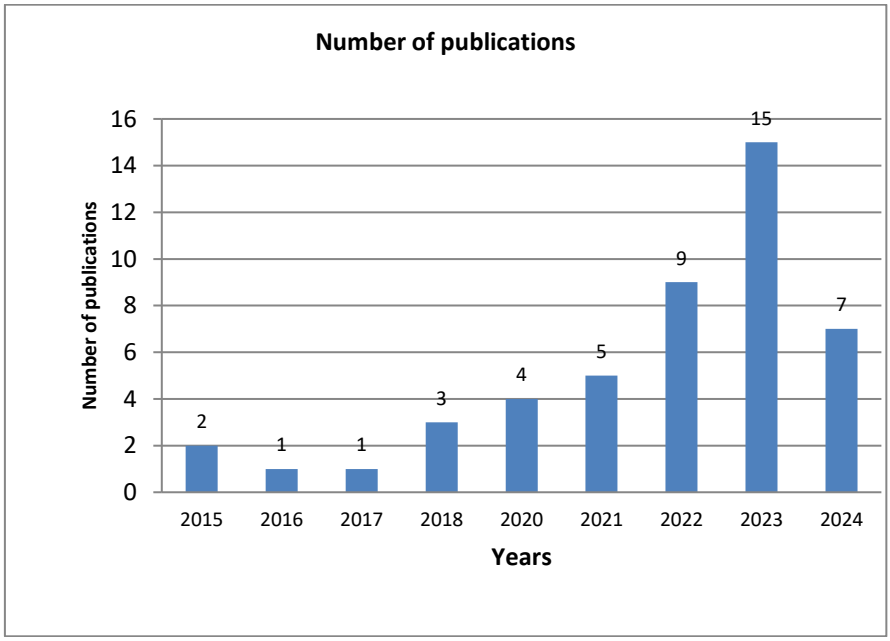

Fig. 2: Distribution of studies after filtering by year

Table 1: Lists similar studies in order of publication date and provides a summary of their contents.

Ref.	Title of paper	Type	Objective	Input	Study based on	Machine Learning method	Results
(A Cortes, W P Maksymowych, B P Wordsworth, R D Inman, P Danoy, P Rahman, M A Stone, M Corr, Lianne S Gensler, D Gladman, A Morgan, H Marzo-Ortega, M M Ward, T J Learch, J D Reveille, M A Brown, M H Weisman Cortes, W P Maks 2015)	Association study of genes related to bone formation and resorption and the extent of radiographic change in ankylosing spondylitis	Research Article	Identify genetic associations with radiographic damage severity in ankylosing spondylitis Investigate variants in genes related to bone pathways in AS	A total of 1537 AS cases of European heritage were examined.	Genetic associations with radiographic severity in ankylosing spondylitis. Roles of bone resorption and prostaglandins pathways in AS.	Genotyped 498 SNPs in 74 genes in phase 1. Tested 15 SNPs in phase 2 for association.	Association with SNP rs8092336 in RANK gene Association with SNP rs1236913 in PTGS1 gene
(Huscher et al. 2015)	Trends in treatment and outcomes of ankylosing spondylitis in outpatient rheumatological care in Germany between 2000 and 2012. Dörte Huscher	Research Article	Describe changes in drug treatment for ankylosing spondylitis (AS) Compare clinical outcomes and quality of life indicators over time	German database collects clinical data on inflammatory rheumatic diseases. AS patients' data from 2000 to 2012 analyzed.	the study is based on a robust national database that tracks treatment and outcomes for AS patients over a significant period, allowing for a detailed analysis of trends and their implications for clinical practice in rheumatology.	Prospective study using German Collaborative Arthritis Centres database Data from 2000 to 2012 analyzed for AS treatment trends	Increased use of NSAIDs and TNF inhibitors in AS treatment. Improved clinical outcomes, quality of life, and employment rates.
(Dubreuil 2016)	validity of ankylosing spondylitis diagnoses in The Health Improvement Network.	Research Article	The study examines the validity of ankylosing spondylitis (AS) diagnoses in the UK's The Health Improvement Network (THIN) and evaluates the reliability of algorithms used to identify AS cases, a crucial aspect for future research.	In 2014, a questionnaire was sent to GPs regarding 100 adults diagnosed with AS. The study focused on determining the positive predictive value (PPV) of AS diagnostic codes compared to the GP's clinical impression,	The study involved sending questionnaires to GPs regarding patients diagnosed with AS. The responses were used to calculate the positive predictive value (PPV) of various diagnostic algorithms, comparing them to the GP's clinical impression as the gold standard	Questionnaire to GPs for AS diagnosis validation. AS identification algorithm with two codes >7 days apart.	72% PPV for AS diagnosis with GP confirmation Algorithm of 2 AS codes >7 days had highest PPV
(Mlcoch et al. 2017)	Mapping the relationship between clinical and quality-of-life outcomes in patients with ankylosing spondylitis.	Research Article	Explore predictors of quality of life in ankylosing spondylitis patients. Map relationship between clinical parameters and quality of life outcomes.	Prospective multicenter exploratory research without intervention Ankylosing spondylitis patients in 3 specialized clinical centers	Ankylosing spondylitis (AS) prospectively multicenter non-interventional observation research collected data about QoL and clinical outcomes on the initial and four subsequent visits	Prospective multicenter non-interventional observation study Employed simple linear regression and fixed/random effect models	BASFI and ASDAS-CRP predict QoL in AS patients. Sex, invalidity, and activity impairment also influence QoL.
(Gu, Liu, and Wei 2018)	Predicting pathway cross-talks in ankylosing spondylitis through investigating the interactions among pathways.	Research Article	Detect pathway cross-talks in ankylosing spondylitis. Identify pathways to reveal disease pathogenesis.	Microarray data analysis of AS pathways using Monte Carlo cross-validation. Identified top 10 pathway pairs with highest AUC values.	Pathway cross-talk interactions Random forest classification model	Monte Carlo cross-validation method with 50 iterations Random forest classification model for pathway screening	Antigen presentation pathway and fMLP signaling distinguish AS patients accurately. SAPK/JNK signaling and mitochondrial dysfunction pathways also distinguish AS.
(Wang et al. 2018)	Proposal of a New Treatment-Oriented Classification System for Spinal Deformity in Ankylosing Spondylitis.	Research Article	Describe and apply optimal classification system for AS management Guide surgical decision making for AS kyphosis	Classification system for AS kyphosis based on radiographic findings. Surgical decision making guided by the new classification	Classification system for ankylosing spondylitis kyphosis based on radiographic findings. Surgical decision making guided by the new	Classification based on radiographic findings Criteria include location of apex, lumbar modifier, kyphosis severity modifier	AS kyphosis classified into 4 types based on apex location. Types II and III further divided into subtypes for severity.

Ref.	Title of paper	Type	Objective	Input	Study based on	Machine Learning method	Results
				system	classification system		
(Yuan, Li, and Zhang 2018)	Identification of differential modules in ankylosing spondylitis using systemic module inference and the attract method.	Research Article	Identify differential modules in ankylosing spondylitis (AS). Provide insights for AS target therapy and future researc	Gene expression data used for module inference and analysis. Protein-protein interaction networks utilized for network analysis.	Gene set enrichment analysis-analysis of variance model Module level data investigation for differential modules	Network analysis, module inference, attract method Clique-merging algorithm, gene set enrichment analysis-ANOVA model	Identified one differential module for AS using the attract method. Six seed modules with Jaccard score ≥0.5 were detected.
(Deodhar et al. 2020)	Use of machine learning techniques in the development and refinement of a predictive model for early diagnosis of ankylosing spondylitis.	Research Article	Using the medical and pharmaceutical claim histories of patients with and without ankylosing spondylitis (AS), create a predictive mathematical model for the early detection of AS.	claims information from October 2015 to February 2018 and January 2006 to September 2015 from Truven databases.	Machine learning techniques used in predictive model development. Claims data from Truven databases analyzed for early AS diagnosis.	Model A/B fared better than both the clinical and linear regression models.	In contrast to a clinical model (PPV, 1.29%) that used characteristics of spondyloarthritis to predict AS in the Assessment of SpondyloArthritis international society categorization criteria, Model A/B's diagnostic accuracy fared better. A reduced PPV (2.55%) was obtained from a streamlined linear regression model designed to evaluate the practicability of Model A/B. In conclusion In predicting an AS diagnosis among patients in a sizable claims database, Model A/B outperformed a clinically based model; its application may help in the early detection of AS and prompt diagnosis.
(Castro-Zunti et al. 2020)	Early detection of ankylosing spondylitis using texture features and statistical machine learning, and deep learning, with some patient age analysis.	Research Article	Employing computed tomography (CT) data analysis, suggest a statistical ML and DL-based classification technique for preliminary Ankylosing Spondylitis indicators prediction: disintegration	681 JPG grayscale imagery, every displaying a solitary sacroiliac joint	Texture features, statistical machine learning, deep learning used for detection. Patient age analysis conducted in the study.	Local binary structures and gray-level ccurrence matrices (GLCM) are used to create features for input for InceptionV3 CNN InceptionV3 backboned DL Model and k-NN machine learning methods.	Random forest classifiers outperform k-NN classifiers in accuracy, recall, and ROC AUC after 8 rounds of cross-validation. These results are 96.0% for younger control individuals and 82.4% for young control patients. A DL predictor outperforms all control patients, with cross-validation accuracy, recall, and ROC AUC of 99.0%, 97.5%, and 0.97 respectively.
(Navarini et al. 2020)	Cardiovascular Risk Prediction in Ankylosing Spondylitis: From Traditional Scores to Machine Learning Assessment.	Research Article	Evaluate cardiovascular risk algorithms in ankylosing spondylitis patients. Compare traditional predictors with machine learning for CV risk assessment.	Baseline medical data used for CV risk calculation in AS patients. ML techniques used: SVM, RF, KNN for CV risk assessment.	Traditional cardiovascular risk algorithms and machine learning techniques. Feature analysis using random forest's importance ranking.	Retrospective analysis of prospectively collected data Comparison of traditional cardiovascular risk predictors with machine learning algorithms	18 CV events occurred in 133 AS patients. Traditional CV risk algorithms had poor discriminative ability.
(S. Lee et al. 2020)	Machine learning to predict early TNF inhibitor users in patients with ankylosing spondylitis.	Scientifc Reports	In patients with kylosing spondylitis, create an artificial neural network (ANN) model to predict early TNF inhibitor users.	Patients who visited the rheumatology clinic at Samsung Medical Center between December 2003 and September 2018 had their baseline laboratory and demographic	Baseline demographics and laboratory data. Machine learning methods: ANN, SVM, RF, XGBoost.	models such as random forest, logistic regression, support vector machines, and XGBoost.	The ANN model outperformed logistic regression, support vector machine, random forest, and XGBoost in predicting early-TNF users, with CRP and ESR being the most significant baseline factors.

Ref.	Title of paper	Type	Objective	Input	Study based on	Machine Learning method	Results
				data examined.			
(S. Lee et al. 2021)	Machine learning-based prediction model for responses of bDMARDs in patients with rheumatoid arthritis and ankylosing spondylitis.	Research Article	Compare machine learning with logistic regression for bDMARD response prediction. Identify important clinical factors affecting bDMARD responses using machine learning.	Clinical data matrix used for training prediction models. Data included demographics, disease activity, medication, and laboratory findings.	Techniques for machine learning, such as logistic regression and random forests Patient self-reporting scales: PtGA in RA, BASFI in AS	RFor prediction models, use logistic regression and andom forest (RF-method). Feature importance analysis using Gini importance for RF-method.	RF-method outperformed logistic regression in predicting bDMARD responses in RA. In AS, the performance of logistic regression and machine learning was comparable.
(Gou et al. 2021)	Automatic segmentation and grading of ankylosing spondylitis on MR images via lightweight hybrid multi-scale convolutional neural network with reinforcement learning.	Research Article	Automatic segmentation and grading of ankylosing spondylitis on MR images. Integration of lesion segmentation and grading in a pipeline	AS MRI dataset with 100 subjects used for evaluation. Performance metrics include DSC, surface distance, HD95, volume, sensitivity.	Lightweight hybrid multi-scale convolutional neural network Reinforcement learning-based data augmentation module	Lightweight hybrid multi-scale CNN with reinforcement learning Voxel constraint strategy for incomplete segmentation results	On the AS dataset, the average DSC of LHR-Net was 0.71, and 31 out of 38 subjects were appropriately graded using LHR-Net.
(Zheng et al. 2021)	Identification of immune related cells and crucial genes in the peripheral blood of ankylosing spondylitis by integrated bioinformatics analysis.	Research Article	Identify key genes and inflammation states in ankylosing spondylitis. Analyze immune cell subpopulations in peripheral blood samples.	Transcriptome profiles from GSE25101 and GSE73754 datasets were merged. Identified 334 DEGs related to immune response in ankylosing spondylitis.	DEGs and immune cell proportions Hub genes validated for ROC curve analysis	Transcriptome analysis from GSE25101 and GSE73754 datasets Bioinformatics tools: Limma, clusterProfiler, GSEA, CIBERSORT, STRING, Cytoscape	334 DEGs identified, involved in immune response and cytotoxicity. Higher CD8+ T cells, naive CD4+ T cells in AS.
(Fernández-Gutiérrez et al. 2021b)	Mining Primary Care Electronic Health Records for Automatic Disease Phenotyping: A Transparent Machine Learning Framework	Research Article	The study proposes a transparent data-driven methodology, identifies influential clinical signals with minimal variables, and uses a cost-sensitive machine-learning framework to address imbalance in clinical diagnostic data, despite its high dimensionality and difficulty in dimensionality.	The imbalance of clinical diagnostic data is a typical but ignored issue while using the framework suggested to apply cost-sensitive machine-learning techniques to the linked dataset of 9657 individuals with 1484 cases of RA and 204 instances of AS.	using a limited set of features, people with a condition from electronic health records (EHRs).	Decision trees, including C5.0 trees, Classification and Regression Trees (CARTs), and Conditional Inference (CI) trees, were used in an automatic data-driven model to address class imbalance and achieve strong generalization.	Classification and Regression Trees (CARTs), Conditional Inference (CI) trees, and C5.0 trees were the three different decision tree algorithms used in the system.
(M. C. Hwang et al. 2022)	Identifying Trajectories of Radiographic Spinal Disease in Ankylosing Spondylitis: A 15-year follow up study of the PSOAS Cohort.	Research Article	Determine the several ways that ankylosing spondylitis progresses as a spinal condition. Study associated clinical factors influencing spinal disease burden groups.	Analyzed data from 561 AS patients with 1618 radiographs. Utilizing GBTM, four unique patterns of spinal illness development were found.	Trajectory modeling based on groups (GBTM) Clinical and sociodemographic covariables	Group-based trajectory modeling (GBTM) to classify longitudinal mSASSS patterns. +G9	Four distinct patterns of spinal disease progression identified using GBTM. Baseline predictors for higher spinal disease burden groups identified. Identify distinct patterns of spinal disease
(Zhu et al. 2022)	Development and Validation of a Machine Learning-Based Nomogram for Prediction of Ankylosing Spondylitis	Research Article	using machine learning models rather than traditional techniques that just relied on ICD codes to predict the radiographic development of individuals with chronic	A study at Guangxi Medical University tested 348 AS patients using various tests. Time-series data on baseline characteristics, test outcomes,	The classification could be based on various clinical and demographic factors that are relevant to ankylosing spondylitis, such as age, gender, genetic markers,routine	The study utilized machine learning algorithms like random forest, LASSO, and SVM-RFE to predict AS likelihood, eliminating false positives and generating a final risk score, Model	The random forest model demonstrated the best accuracy in predicting radiographic progression in AS, a long-term inflammatory arthritis resulting in spinal ankylosis, using machine learning

Ref.	Title of paper	Type	Objective	Input	Study based on	Machine Learning method	Results
			inflammatory arthritis and treatment strategies for AS	medication administration, and the adjusted Stoke Ankylosing Spondylitis Spine Score were collected from 1,123 patients over 18 years.	blood, liver, and kidney testing. and clinical symptoms.	AB.	models.
(Koo et al. 2022)	A pilot study on deep learning-based grading of corners of vertebral bodies for assessment of radiographic progression in patients with ankylosing spondylitis	Research Article	Develop deep learning model for grading vertebral body corners. Create computer-aided tool for assessing radiographic progression in AS.	1280 patients with AS, 5,083 cervical, 5245 lumbar radiographs reviewed. 119,414 corners measured, 110,088 in training, 9326 in validation set.	Deep learning model Convolutional neural network model	By using Models A and B sequentially, the research employed machine learning methods to estimate the likelihood of AS. As a result, erroneous positives were removed, and Model AB, the final risk score, was generated.	For mSASSS scoring, the average accuracy, sensitivity, and specificity are 0.91604, 0.80288, and 0.94244. created a deep learning model with outstanding performance for assessing the vertebral body corners.
(Alber et al. 2022)	Single Cell Transcriptome and Surface Epitope Analysis of Ankylosing Spondylitis Facilitates Disease Classification by Machine Learning	Research Article	Identification of molecular features associated with ankylosing spondylitis (AS) Development of machine learning models for AS classification with high accuracy	SNP data was examined using Plink and Analysis Power Tools. Michigan Imputation Server was used to impute additional sites.	machine learning models that used CITE-seq data.	Single cell CITE-seq technology Machine learning models for classification of AS patients	In RNA and surface protein expression, AS patients have overexpression of CD52. Finding surface proteins and genes linked to AS in particular cell populations AUC > 0.95 was attained by machine learning models that used CITE-seq data.
(Zhang et al. 2022)	Immune mechanism of low bone mineral density caused by ankylosing spondylitis based on bioinformatics and machine learning	Research Article	Determine the immunological genes that play a major role in poor BMD.Create diagnostic models utilizing important genes.	study using open-source data from the GEO database.Jilin Provincial Health Technology Innovation Program is the source of funding.	Key immune-related genes (I-DEGs) Machine learning methods	DEG analysis, immune gene identification, correlation calculation, machine learning models Enrichment analysis, gene network construction, immune infiltration analysis	It was discovered that 19 immune-related genes are essential for low bone mineral density (LBMD) in people with ankylosing spondylitis (AS). These significant genes can be used as biomarkers to estimate the probability of LBMD in AS patients.
(J. Wen, Wan, and Dong 2022a)	Diagnostic Biomarkers Screened by Machine Learning Algorithms in Ankylosing Spondilytis	Research Article	Identify diagnostic biomarkers for ankylosing spondylitis Establish a predictive model for early diagnosis	GSE73754 GSE25101	Machine learning algorithms Common differential expressed genes in AS patients	Machine learning algorithms used: Decision curve analyses, functional analysis. Hubgenes IL2RB and ZDHHC18 identified as potential biomarkers.	ZDHHC18 and IL2RB are possible blood biomarkers for AS. In many cohorts, the diagnostic model demonstrated high prediction accuracy.
(Kang et al. 2022)	Prediction of radiographic progression pattern in patients with ankylosing spondylitis using group-based trajectory modeling and decision trees	Research Article	Identify radiographic progression trajectories in ankylosing spondylitis patients. Develop a prediction model based on clinical factors for AS patients.	Data from 1,125 AS patients analyzed for radiographic progression. Factors like sex, age, ocular, and joint involvement associated.	Clinical factors and decision trees. Prediction of radiographic progression in AS patients.	Group-based trajectory modeling for radiographic progression patterns Decision tree analysis for predicting disease progression trajectories	Three trajectory classes were identified: class 1, which had an increasing slope, class 2, which had a low slope, and class 3, which had the highest slope.
(Han et al. 2022)	Identification of diagnostic mRNA biomarkers in whole blood for ankylosing spondylitis using WGCNA and machine learning feature selection	Research Article	Identify diagnostic mRNA biomarkers for ankylosing spondylitis in blood. Develop novel diagnostic markers for ankylosing spondylitis.	Whole blood mRNA expression data from 72 subjects (52 AS, 20 controls) 13 key mRNAs identified for AS diagnosis and severity correlation	GCNA, machine learning feature selection, gene set enrichment analysis mRNA expression profile analysis, protein-protein interaction network, qPCR verification	Weighted gene co-expression network analysis SVM-RFE machine learning feature selection	Identified 13 key feature mRNAs for AS diagnosis. Cxcr6, IL17RA, Lrrfip1 correlated with severity of AS symptoms.

Ref.	Title of paper	Type	Objective	Input	Study based on	Machine Learning method	Results
(J. Wen, Wan, and Dong 2022b)	Novel peripheral blood diagnostic biomarkers screened by machine learning algorithms in ankylosing spondylitis	Research Article	Machine learning techniques were used to screen for common differentially expressed genes in GSE73754 and GSE25101 between normal individuals and AS patients. The hub genes that were evaluated led to the establishment of a diagnostic model. Subsequently, the model was verified across other datasets.	The study utilized data sets from the Gene Expression Omnibus database, including whole-blood RNA expression data from AS patients and normal individuals, to further explore three suitable genes.	First attempt to classify AS using machine learning and single-cell data.	machine learning algorithms: the least absolute shrinkage and selection operator (LASSO), logistic regression , a support vector machine recursive feature elimination (SVMRFE) and random forest (RF)	Machine learning models were developed to predict AS using IL2RB and ZDHHC18. Results showed increased risk with ZDHHC18 expression, but opposite for IL2RB in vivo. The model had good prediction accuracy in both training and validation populations.
(H. Li et al. 2023)	Comprehensive AI-assisted tool for ankylosing spondylitis based on multicenter research outperforms human experts	Research Article	generate an ensemble deep learning (DL) model for AS diagnosis. The model's respective scores in GSE73754, GSE25101, GSE18781, and GSE11886 were 0.86, 0.84, 0.85, and 0.89.	thorough clinical and imaging information on 356 AS patients from Guangxi Medical University's First Affiliated Hospital. There were 284 patients in the training set and 72 patients in the external test set.	Ensemble deep learning model Pelvic radiographs (PXRs)	five CNN models that yielded the ensemble model's output for the final inference and fared the best during internal validation.	The ensemble DL model outperformed human experts in a multicenter external test set, with precision, recall, and area under the receiver operating characteristic curve values of 0.90, 0.89, and 0.96 respectively, significantly increasing diagnostic precision.
(Koo et al. 2023)	Machine learning models with time-series clinical features to predict radiographic progression in patients with ankylosing spondylitis	Research Article	Predict radiographic progression in ankylosing spondylitis patients Identify important features contributing to radiographic progression	EMR data from 1,123 AS patients Time-series clinical features from first, second, and third visits	Time-series clinical features from electronic medical records (EMRs) Machine learning techniques: high gradient boosting, random forest, and logistic regression	Selection operation and least absolute shrinkage in logistic regression Extreme gradient boosting and random forest methods	When it came to radiographic progression prediction, the random forest model performed best. 73.73% was the mean accuracy, while 0.79 was the AUC.
(D. Li et al. 2023)	Identification of potential biomarkers for ankylosing spondylitis based on bioinformatics analysis		The purpose of this work is to use thorough bioinformatics analysis to look for important genes associated with ankylosing spondylitis.	Researchers used publicly available gene expression datasets from the Gene Expression Omnibus database, specifically GSE73754 and GSE11886, to integrate expression matrices and identify differentially expressed genes associated with AS.	the classification in this study is based on biomarker identification, gene expression analysis, immune cell infiltration levels, functional enrichment, and network analysis, all of which contribute to understanding the pathogenesis of ankylosing spondylitis.	The study utilized bioinformatics methods, including weighted correlation network analysis (WGCNA) and immune infiltration analysis, to identify key genes associated with ankylosing spondylitis classification.	The discovered indicators may be very important in the immunological milieu of AS and are strongly associated with immune cell infiltration. This study may facilitate the clinical diagnosis and management of AS and stimulate additional research in this field.
(Kennedy et al. 2023)	Predicting a diagnosis of ankylosing spondylitis using primary care health records – a machine learning approach	Research Article	to create a profile of the traits of individuals who are most likely to receive an AS diagnosis in the future using machine learning techniques in early identification of AS patients.	The research utilized the Secure Anonymised Information Linkage (SAIL) databank, a vast collection of routine health data, to identify patterns and characteristics linked to ankylosing spondylitis.	After symptoms appear, a diagnosis may take ten years to confirm (by x-rays)	Principal component analysis and feature/variable selection were used in the model's development to create decision trees.	The model validates lower back pain, uveitis, and NSAID use under age 20 as associated with AS development in men, suggesting multiple models may improve predictive value and reduce diagnosis time.

Ref.	Title of paper	Type	Objective	Input	Study based on	Machine Learning method	Results
(Tas et al. 2023)	ASNET: A Novel AI Framework for Accurate Ankylosing Spondylitis Diagnosis from MRI	Research Article	The purpose of this work is to use magnetic resonance imaging (MRI) and a pre-trained hybrid model to diagnose AS.	This study introduced a new dataset from Elazı g Fethi Sekin City Hospital. 2018 saw the use of the Philips Multiva 1.5 Tesla MRI equipment, which is manufactured in the Netherlands. The hospital administration system provided the clinical records of the patients from 2018 to 2023.	Pretrained convolutional neural networks (CNNs): DenseNet201, ResNet50, ShuffleNet Deep feature engineering model utilizing transfer learning approach	A new deep feature engineering paradigm uses three popular pretrained CNNs: ShuffleNet, ResNet50, and DenseNet201, creating deep features using transfer learning and employing three feature selectors and k-nearest neighbors classifier for classification.	The suggested strategy achieved high accuracy, recall, precision, and F1-score values in axial, coronal, and contrast-enhanced images, with accuracy rates of 99.80%, 99.60%, 100%, and 99.80%, respectively, for the axial dataset.
(Taş et al. 2023)	Global Shapley Explanations and LIME on HLA-B27 Positivity in Ankylosing Spondylitis Patients	Research Article	edict HLA-B27 gene presence in AS patients. Evaluate health parameters' association with HLA-B27.	This study utilized 17 Ankylosing Spondylitis (AS) patient data from Erzurum City Hospital for three months, with the ethics committee's approval. XAI Research estimated HLA-B27 using health factors and demographic features.	Health parameters and genetic predisposition of Ankylosing Spondylitis patients. XAI techniques used to explain RFC model predictions.	To find the most effective method for predicting HLA-B27 positive, a number of classification models were assessed. Based on evaluation metrics, it was determined that the Random Forest Classifier (RFC) was the highest performing model among the others.	The study's findings not only showed how well the RFC model predicted HLA-B27 positive, but they also emphasized the significance of the health indicators linked to this genetic marker and the value of ethical research methods.
(Dong 2023)	Machine learning-based characterization of cuprotosis-related biomarkers and immune infiltration in Ankylosing spondylitis	Research Article	Identify cuprotosis-related biomarkers in ankylosing spondylitis Explore immune infiltration and correlation with immune function	Gene expression profiles from the datasets GSE18781, GSE25101, and GSE73754. The GSE18781 external dataset was utilized to confirm the prediction capacity.	The examination of biomarkers and machine learning methods. immune cell infiltration and genes associated with cuprotosis.	Three algorithms for machine learning: SVM-RFE, random forest, and LASSO Classification of specimens with ankylosing spondylitis using consensus clustering technique	Six distinct cuprotosis-related genes (CRGs) associated with ankylosing spondylitis have been identified. SLC31A1 and PDHB, two important genes, were discovered to be connected to immune infiltration in AS.
(Gao et al. 2023)	A Predictive Disease Risk Model for Ankylosing Spondylitis: Based on Integrated Bioinformatic Analysis and Identification of Potential Biomarkers Most Related to Immunity	Research Article	Identify early biomarkers for AS diagnosis. Develop predictive disease risk model for AS.	Differential expression analysis identified 4 DEGs related to immunity. 36 and 163 DEGs found in datasets GSE25101 and GSE73754.	genes connected to the immune system Analysis of the weighted gene coexpression network in AS with immune infiltration.	WGCNA used to create gene coexpression network in AS. Immune data scored using ssGSEA for immune-related genes.	discovered putative immunological indicators for the early detection of AS. created a model to predict the probability of developing ankylosing spondylitis.
(Sun et al. 2023)	Identification of clinical heterogeneity and construction of a novel subtype predictive model in patients with ankylosing spondylitis: An unsupervised machine learning study.	Research Article	Determine whether ankylosing spondylitis patients exhibit clinical heterogeneity. Create a fresh disease subtype prediction model.	patients with ankylosing spondylitis. Discovering clinical heterogeneity and developing a new subtype prediction model.	Clinical heterogeneity Unsupervised machine learning techniques	Unsupervised machine learning Finding the subtype prediction model and clinical heterogeneity identification	Researchers identified various subtypes of ankylosing spondylitis patients using clustering analysis, revealing a wide range in disease presentation and progression. This highlights clinical heterogeneity, impacting care strategies and treatment decisions. A unique predictive model was created to categorize patients into subgroups.
(Mo et al. 2023)	Towards Automatic Scoring of Spinal X-ray for Ankylosing Spondylitis	Research Article	Validate machine learning for fundoscopy analysis in autoimmune diseases. Use deep learning to diagnose	n-house dataset of lateral cervical and lumbar X-ray images Axial spondylarthritis patients were	VertXGradeNet predicts mSASSS scores for cervical and lumbar VUs. Evaluated on lateral X-ray images for axial spondylarthritis	VertXGradeNet: 2-step auto-grading pipeline for mSASSS prediction. Utilizes VUs from VertXNet for mSASSS predictio	Balanced accuracy of 0.56 and 0.51 for 4 mSASSS scores. VertXGradeNet predicts mSASSS scores for cervical and lumbar VUs.

Ref.	Title of paper	Type	Objective	Input	Study based on	Machine Learning method	Results
			ankylosing spondylitis, psoriatic arthritis, psoriasis.	included in the datasets	patients.		
(M. Hwang et al. 2023)	Quantitative proteomic screening uncovers candidate diagnostic and monitoring serum biomarkers of ankylosing spondylitis	Research Article	sought to discover serum biomarkers of ankylosing spondylitis (AS) for diagnosis and monitoring disease activity	examined the serum of healthy control (HC) and AS patients who had not received biologic therapy. Eighty samples of AS patients with active disease and inactive disease were matched 1:1:1 by age, gender, and race.	use the Ingenuity Pathway Analysis (IPA) tool for upstream regulators and the Cytoscape Molecular Complex Detection (MCODE) plugin to find clusters in protein-protein interaction networks.	Lasso regression was utilized in the study to identify a 13-protein model for diagnosing ankylosing spondylitis, showcasing machine learning's role in early detection and classification.	Using a thorough proteome search, several putative AS diagnostic and disease activity monitoring serum biomarkers were identified. Enrichment analysis revealed important routes for AS surveillance and diagnosis. Using lasso regression, a multi-protein panel with a moderate degree of predictive power was found.
(Vodencarevic et al. 2023)	OP0058 Prediction of low disease activity in patients with Ankylosing spondylitis treated with secukinumab in real world data fromthe german aquila study.	Research Article	the The primary goals were to: (1) use machine learning techniques to predict low disease activity (LDA) in individual AS patients receiving Secukinumab (SEC); and (2) use explainable artificial intelligence (XAI) to identify the most significant variables and their impact on the prediction.	The AQUILA study's 580 AS patients' data were utilised. To create prediction models, thirty-two baseline (BL) demographic, clinical, and treatment factors were used as input data.	To create prediction models, thirty-three baseline (BL) demographic, clinical, and treatment factors were used as input data.	Ten different prediction models were applied and contrasted. The probability that a randomly selected patient with LDA will have a higher tendency than a patient with moderate to high disease activity to achieve LDA is represented by the area under the receiver operating characteristic curve (AUROC).	The most significant predictor at BL was the BASDAI, which was followed by the quantity of biologic pretreatments, C-reactive protein (CRP), the evaluation of the ASAS-HI (the international society health index for spondyloarthritis), patient height, and CRP.
(Calvo Pascual, Castro Corredor, and Garrido Merchán 2024)	Machine learning classification of vitamin D levels in spondyloarthritis patients	Research Article	Estimate whether a patient with spondyloarthritis has a low, medium, or high 25 dihydroxy 20 epi vitamin D3 level.	115 patients' information was gathered. Out of 32 variables in total	the 25 dihydroxy 20 epi vitamin d3 level (low, medium, or high) in spondyloarthritis patients.	interpretable decision trees and an integrated strategy which makes use of 10-fold cross-validation and Bayesian optimization techniques	Established an accessible tree of decisions and a combination that improved predicted precision across a prepared dataset through the application of 10-fold cross-validation and Bayesian optimization.
(Jia et al. 2024)	Ankylosing spondylitis prediction using fuzzy K-nearest neighbor classifier assisted by modified JAYA optimizer.	Research Article	Enhance JAYA algorithm with SCJAYA for optimization. Develop bSCJAYA-FKNN model for AS diagnosis and prognosis.	bSCJAYA-FKNN model achieved 99.23% accuracy in diagnosing AS. SCJAYA surpasses other algorithms in convergence speed and solution precision.	SCJAYA optimization algorithm enhances JAYA with salp swarm behavior. bSCJAYA-FKNN model improves AS diagnosis accuracy using feature selection.	SCJAYA optimization algorithm with salp swarm and predation strategies bSCJAYA-FKNN classifier using binary SCJAYA for feature selection	Specificity: 99.52%, MCC: 0.9906, F-measure: 99.41%, accuracy rate: 99.23% Time spent computing: 7.2800 seconds
(H. Liu and Peng 2024)	Identification of a Novel Gene Expression Signature Associated with Amino Acid Metabolism (AAM) in Ankylosing Spondylitis (AS)	Research Article	Determine important genes linked to AAM for the diagnosis and prognosis of AS. Examine the possible biomarkers' and diagnostic genes' functional pathways.	AAM-related genes identified for AS diagnosis and prediction. Three key AAM-related genes: TP53INP1, TUBB, RBM47.	Important genes linked to AAM are identified for the diagnosis of AS. Ankylosing Spondylitis (AS): An analysis of AAM metabolism.	DEGs identification in the GSE25101 and GSE73754 datasets WGCNA for the identification of genes linked to AS and AAM scores	TUBB, RBM47, and TP53INP1 have been discovered as putative AS biomarkers. Value as a diagnostic tool for AS, rich in pathways that activate neutrophils
(Shi et al. 2024)	Prediction of the activity of early ankylosing spondylitis using radiomics texture analysis on STIR.	Research Article	In order to assess the activity of bone marrow oedema of the sacroiliac joints in early AS, the study sought to investigate the utility of textural analysis of radiomics based on the short tau inversion recovery (STIR) sequence.	43 patients with early AS whose data were randomly divided into the training cohort (n=116) and verification cohort (n=56) according to the ratio of 7:3	Texture study of radiomics on STIR sequence Assessment of bone marrow edema in early AS	These texture feature parameters were used to create the final prediction model and derive the Radscore, and the best feature subsets were found by the Mann-Whitney U-test, the minimum-Redundancy Maximum-Relevancy (mRMR),	Radiomics texture analysis predicts bone marrow oedema activity in AS. Radscore, SPARCC, and ADC show good differentiation between active and stable groups.

Ref.	Title of paper	Type	Objective	Input	Study based on	Machine Learning method	Results
						and lastly the least absolute shrinkage and selection operator (LASSO).	
(Ma et al. 2024)	Exploring the common mechanisms and biomarker ST8SIA4 of atherosclerosis and ankylosing spondylitis through bioinformatics analysis and machine learning	Research Article	Determine shared biomarkers and pathways between ankylosing spondylitis and AS. Examine ST8SIA4 as a gene for shared diagnosis.	GSE100927, GSE28829, GSE155512 for AS GSE73754, GSE25101 for ankylosing spondylitis	This study employs bioinformatics approaches to identify common biomarkers and pathways between AS and ankylosing spondylitis.	Bioinformatics analysis with gene expression datasets Machine learning algorithm SVM-RFE for biomarker identification	T8SIA4 identified as common diagnostic marker for AS and ankylosing spondylitis. Lysosomal pathway involvement in both conditions explored.
(P. Wen et al. 2024)	Identification of necroptosis-related genes in ankylosing spondylitis by bioinformatics and experimental validation	Research Article	Identify necroptosis-related genes in ankylosing spondylitis. Investigate FASLG and TARDBP as potential therapeutic targets.	Gene Expression Omnibus database External datasets for validation	The identification of necroptosis-related genes in ankylosing spondylitis (AS) was primarily based on gene expression analysis. Researchers compared gene expressions between AS patients and healthy controls using the Gene Expression Omnibus database.	Machine learning algorithms: LASSO, SVM-RFE, random forest Cellular experiments for gene validation	Identified 18 differentially expressed necroptosis-related genes in ankylosing spondylitis. FASLG and TARDBP are hub genes with diagnostic potential for AS.
(Shuai et al. 2024)	Rapid diagnosis of Rheumatoid arthritis and Ankylosing spondylitis based on Fourier transform infrared spectroscopy and deep learning.	Research Article	Early diagnosis of rheumatoid arthritis and ankylosing spondylitis Utilize FTIR spectroscopy and deep learning for accurate diagnosi	l81 samples from each of the following: rheumatoid arthritis, ankylosing spondylitis, and healthy controls	Using deep learning models, this study used Fourier transform infrared (FTIR) spectroscopy on dried serum samples to diagnose rheumatoid arthritis and ankylosing spondylitis early.	Using dried serum samples, Fourier transform infrared spectroscopy Deep learning model using multi-scale convolutional neural network (MSCNN)	The MSCNN model's AUC for diagnosis was 0.99. FTIR spectroscopy has the ability to diagnose rheumatism quickly.

In addition, the study by (A Cortes, W P Maksymowych, B P Wordsworth, R D Inman, P Danoy, P Rahman, M A Stone, M Corr, Lianne S Gensler, D Gladman, A Morgan, H Marzo-Ortega, M M Ward, T J Learch, J D Reveille, M A Brown, M H Weisman Cortes, W P Maks 2015)identified genetic associations with radiographic damage severity in ankylosing spondylitis. Investigate variants in genes related to bone pathways in AS. A total of 1537 AS cases of European heritage were examined; all met the modified New York criteria. Radiographic severity was determined using the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) using digitized lateral radiographs of the cervical and lumbar spines. The study discovered a relationship between SNP rs8092336 in RANK and SNP rs1236913 in PTGS1, but no link was detected between radiographic severity and HLA-B*27. The study (Huscher et al. 2015), The study reveals that non-steroidal anti-inflammatory drugs (NSAIDs) have become the primary treatment for ankylosing spondylitis (AS) in Germany, with 67% of patients prescribed in 2012. Currently, almost half of AS patients are treated with tumor necrosis factor inhibitors (TNFi). Combinations of NSAIDs and sDMARDs are common, with 10% of patients receiving NSAID or sDMARD monotherapy. Improvements in disease control and patient outcomes have been observed over the years.

The study by (Dubreuil 2016) examined the validity of ankylosing spondylitis (AS) diagnoses in the UK's THIN database and the reliability of case-identification algorithms. The research involved sending questionnaires to 100 AS patients and testing various algorithms. The study found that out of 85 submitted questionnaires, 61 confirmed AS, resulting in an overall PPV of 72%. The highest PPV (89%) was obtained with two algorithms. The study highlights the importance of accurate diagnosis and reliable algorithms in diagnosing AS.

The study of (Mlcoch et al. 2017) is a prospective multicenter observational study aimed to map health-related quality of life (QoL) in patients with ankylosing spondylitis (AS) using clinical parameters like the Bath Ankylosing Spondylitis Functional Index (BASFI) and the Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS-CRP). The study collected data on QoL and clinical outcomes over multiple visits. The findings showed that BASFI and ASDAS-CRP were strong predictors of QoL, along with factors like sex, invalidity, and activity impairment. The fixed effect

model was suggested as a viable alternative for analyzing longitudinal data. Also, the study (Gu, Liu, and Wei 2018) explored the pathogenesis of ankylosing spondylitis (AS) by identifying functional pathway cross-talks. Researchers used microarray profiles and a Monte Carlo cross-validation approach to identify differentially expressed genes (DEGs) between AS patients and normal controls. A discriminating score was created for each pathway pair, and a random forest classification model was used to identify the top ten pathway pairs with the highest AUC values. The best identified pathway pair was the antigen presentation pathway and fMLP signaling in neutrophils, with a flawless AUC of 1.000.

The research of (Wang et al. 2018) introduced a new classification system for managing ankylosing spondylitis (AS) using radiographic data. The system categorizes AS kyphosis into four types based on apex position, lumbar modifier (A), and thoracic/thoracolumbar kyphosis severity. This aids in preoperative surgery planning and identifies osteotomy locations and levels. However, further validation is recommended to ensure accurate classification and improve surgical decision-making.

The attract approach and network analysis were used in this study (Yuan, Li, and Zhang 2018) to find differential modules in ankylosing spondylitis (AS). It consisted of four steps: network inference, module discovery, seed module evaluation, and differential module identification. The study found 5,301 nodes and 28,176 interactions in both networks, including 20 modules for AS and 21 for healthy controls. Six seed modules were discovered, one of which had the highest differential MCD of 0.077. This revealed one distinct module as a possible marker for AS target treatment.

A study of (Deodhar et al. 2020) aimed to develop a predictive mathematical model for early identification of ankylosing spondylitis (AS) using medical and pharmacy claims history. The model was trained using Truven databases from 2006 to 2018 and used machine learning to identify features distinguishing AS patients from controls. The model predicted 1923 patients in Segment 1 without AS history, and 120 patients in Segment 2 received an AS diagnosis, with a positive predictive value of 6.24%. The model's diagnostic accuracy compared favorably with a clinical model, with a simplified linear regression model yielding a lower PPV of 2.55%.

The study by (Castro-Zunti et al. 2020) described the first use of machine learning and deep learning-based classifiers to detect erosion, an early AS symptom, on computed tomography (CT) images. The authors employed gray-level co-occurrence matrices and local binary patterns to produce input features for machine learning techniques such as k-nearest neighbors and random forest. Deep learning solutions were built and tested, and random forest classifiers outperformed k-NN classifiers in terms of accuracy, recall, and ROC AUC. The findings point to the possibility of machine and deep learning for AS diagnosis.

A study of (Navarini et al. 2020) evaluated the performance of seven cardiovascular risk algorithms in a metacentric cohort of ankylosing spondylitis (AS) patients. Traditional CV predictors were compared with machine learning (ML) techniques. The primary outcome was the first CV event. Out of 133 AS patients, 18 had a CV event. The discriminatory ability of the algorithms was evaluated using the area under the receiver operating characteristic (ROC) curve. The ML algorithms had the highest importance for C-reactive protein (CRP), while SBP and hypertension treatment had lower importance.

The study of (S. Lee et al. 2020)aimed to develop an artificial neural network (ANN) model to predict early TNF inhibitor users in patients with ankylosing spondylitis. The data was analyzed from Dec. 2003 to Sep. 2018, and patients were divided into early-TNF and non-early-TNF users. The ANN model performed better than logistic regression, support vector machine, random forest, and XGBoost models in predicting early-TNF users. Feature importance analysis revealed CRP and ESR as the top significant baseline characteristics for predicting early-TNF users. The model demonstrated the potential of machine learning in predicting treatment response in various rheumatologic diseases.

The study of (S. Lee et al. 2021) used machine learning to predict bDMARD responses in RA and AS patients. Data was sourced from the Korean College of Rheumatology Biologics therapy registry, with 625 and 611 patients in the training dataset and independent test datasets. Baseline clinical characteristics were used as input features. Multiple machine learning methods, including random forest (RF-method), were used to generate models and compared with the logistic regression model. The RF-method model showed superior prediction performance in RA patients, with an accuracy of 0.726 compared to 0.689. However, machine learning and logistic regression showed similar performance in AS patients. The most important features in both diseases were patient self-reporting scales, such as patient global assessment of disease activity (PtGA) in RA and Bath Ankylosing Spondylitis Functional Index (BASFI) in AS.

The study of (Gou et al. 2021) presented an automatic AS grading method that integrates lesion segmentation and grading in a pipeline. The lightweight hybrid multi-scale convolutional neural network with reinforcement learning (LHR-Net) is proposed for AS lesion segmentation, equipped with a hybrid multi-scale module and a reinforcement learning-based data augmentation module. A voxel constraint strategy is proposed to resolve incomplete segmentation results

caused by inhomogeneous intensity distributions in MR images. The performance of the proposed LHR-Net was evaluated on a clinically collected AS MRI dataset, with the average DSC reaching 0.71 on the test set. With accurately segmented lesions, 31 subjects in the test set (38 subjects) were correctly graded, demonstrating the potential of the proposed LHR-Net for reproducible computer-assisted diagnosis of AS grading.

The study published by (Zheng et al. 2021) used bioinformatics analysis to identify key genes and inflammation states in ankylosing spondylitis (AS). The transcriptome profiles of GSE25101 and GSE73754 were combined, and differentially expressed genes (DEGs) were identified using Limma and threshold values. Functional enrichment and pathway enrichment analyses were performed using the clusterProfiler package and Gene Set Enrichment Analysis (GSEA). A total of 334 DEGs were identified, primarily involved in immune response, autophagy, and natural killer cell-mediated cytotoxicity. Nine genes with AUC > 0.70 were considered AS hub genes. The validated hub genes may provide new insights into the molecular mechanisms of AS.

A study developed a machine-learning framework to automatically identify patients with specific conditions using electronic health records (EHRs). Researchers linked various EHR sources, including 918 million primary care and 40 million secondary care records, to form a unique dataset. They developed a disease-phenotyping framework that included patient representation, feature selection, and algorithm development. The framework was tested on a dataset of 9,657 patients, identifying 1,484 cases of rheumatoid arthritis (RA) and 204 cases of ankylosing spondylitis (AS). It achieved an accuracy of 86.19% and a positive predictive value of 88.46% for RA and 99.23% for AS(Fernández-Gutiérrez et al. 2021b) .

The study of (M. C. Hwang et al. 2022) aimed to identify distinct patterns of vertebral involvement change over time and study associated clinical factors. Data from the Prospective Study of Outcomes in Ankylosing Spondylitis (PSOAS) observational cohort was analyzed, identifying four distinct trajectory groups: non-progressors, late-progresses, early-progressors, and rapid-progressors. Baseline predictors associated with higher spinal disease burden groups included baseline mSASSS, male gender, longer disease duration, elevated CRP, and smoking history. Time-varying anti-TNF use per year was associated with decreased mSASSS progression only in the rapid-progressor group. The study concluded that independent confirmation in other AS cohorts is needed to confirm these radiographic patterns.

A study by(Zhu et al. 2022) aimed to develop machine learning models to improve diagnosis using routine blood tests and liver and kidney function tests. Researchers screened 348 patients using three machine learning methods: LASSO, random forest, and support vector machine recursive feature elimination. Seven key diagnostic features were identified for the nomogram model: erythrocyte sedimentation rate, red blood cell count, mean platelet volume, albumin, aspartate aminotransferase, and creatinine. The developed nomogram can assist orthopedic surgeons in creating personalized treatment strategies for AS patients, enhancing diagnostic efficiency.

In study of (Koo et al. 2022) a deep learning model was developed to grade the corners of cervical and lumbar vertebral bodies for detecting mSASSS. The model used digital radiographic examinations and a key-point detection deep learning model to identify disk points between vertebral bodies. The study reviewed 119,414 radiographs from 1280 AS patients, achieving a mean accuracy of 91.6%, sensitivity of 80.3%, and specificity of 94.2% for mSASSS scoring in one corner. This high-performance model suggests potential for future computer-aided tools.

The study by (Alber et al. 2022) reveled that certain cell types, including CD52, CD16+ monocytes, CD8+ TEM cells, and natural killer cells, overexpress genes associated with cytotoxicity in patients with As. Tregs under express CD39, suggesting reduced functionality. An overrepresented NK cell subset in AS overexpresses CD16, CD161, and CD38, as well as cytotoxic genes and pathways. Machine learning models were developed using CITE-seq data to classify AS, achieving an AUROC curve of > 0.95.

The study by (Zhang et al. 2022)identified key immune genes and mechanisms of low bone mineral density (LBMD) in ankylosing spondylitis (AS) patients. Using AS and LBMD datasets, differential expression gene analysis was performed, and immuno-related genes (IRGs) were obtained. Key I-DEGs were identified, with IFNAR1, PIK3CG, PTGER2, TNF, and CCL3 being the key I-DEGs. These genes had a good relationship with key modules' hub genes. Multiple machine learning methods showed that key I-DEGs had excellent diagnostic performance in both AS and LBMD. They may affect neutrophil infiltration and NETs formation, influencing bone remodeling in AS.

A study using machine learning algorithms screened differentially expressed genes between normal people and AS patients in GSE73754 and GSE25101. The model was established by IL2RB and ZDHHC18, which showed high prediction accuracy and high net benefit. The genes were mainly clustered in immune response-related processes, and their expression was found to be linked to the risk of AS. This study provides valuable insights into the pathogenesis of AS and could potentially aid early diagnosis (J. Wen, Wan, and Dong 2022a).

The study of (Kang et al. 2022) aimed to identify trajectories of spine radiographic progression over time and use them, along with clinical factors, to develop a

prediction model for patients with ankylosing spondylitis (AS). Data from medical records of AS patients was extracted between 2001 and 2018, and Modified Stoke Ankylosing Spondylitis Spinal Scores (mSASSS) were estimated. Three trajectory classes were identified: class 1, which had an increasing slope, class 2, which had a low slope, and class 3, which had the highest slope.

The study by(Han et al. 2022) analyzed mRNA biomarkers in the whole blood of AS patients using a Gene Expression Omnibus dataset. It identified three mRNA modules associated with AS and functional annotations of these modules, revealing immune biological processes. Machine learning-based feature selection methods, SVM-RFE, were used to screen out 13 key feature mRNAs. IL17RA, Sqstm1, Picalm, Eif4e, Srrt, Lrrfip1, Synj1, and Cxcr6 were found to be significant for AS diagnosis, with Cxcr6, IL17RA, and Lrrfip1 correlated with AS symptoms severity.

The study of (J. Wen, Wan, and Dong 2022b)explored the potential of IL2RB and ZDHHC18 as blood biomarkers for early diagnosis of Aspergillosis (AS). Machine learning algorithms were used to screen common differentially expressed genes between normal people and AS patients. The model showed high prediction accuracy and high net benefit. Functional analyses revealed that these genes were mainly clustered in immune response-related processes. The study provides insights into the pathogenesis of AS and suggests that these biomarkers could supplement existing diagnostic methods.

The study by (Koo et al. 2023) used machine learning models to predict radiographic progression in Ankylosing Spondylitis (AS) patients using time-series data from electronic medical records (EMRs). The data was collected from 1,123 AS patients between January 2001 and December 2018 at a single center. The study used three machine learning methods: logistic regression, random forest, and extreme gradient boosting algorithms. The random forest model was found to be the best predictor of radiographic progression, with a mean accuracy of 73.73% and an area under the curves of 0.79. The most important variables for predicting progression were total mSASSS, age, and alkaline phosphatase.

The study by(D. Li et al. 2023) used bioinformatics to screen differentially expressed genes and perform functional enrichment analysis to identify biological functions and signaling pathways associated with AS. Key genes were identified using WGCNA and CIBERSORT algorithms, and pathogenic regions were identified using GWAS data. Seven potential biomarkers were identified, with T cell, CD4 naïve cell, and neutrophil levels significantly higher in the disease group. Drugs like ibuprofen, forskolin, bongkrek-acid, and cimaterol showed a negative correlation with disease perturbations.

In study of (Li et al. 2023) a comprehensive AI tool was developed to diagnose and predict the course of Aspergillosis (AS) using a dataset of 5389 pelvic radiographs. The model demonstrated impressive performance, surpassing human experts' accuracy and improving diagnostic accuracy. The model also accurately categorizes patients into high- and low-risk groups, providing a strong foundation for individualized care. Clinical prediction models were developed and validated using clinical data from 356 patients.

The study of (D. Li et al. 2023) aimed to identify key genes in ankylosing spondylitis (AS) using bioinformatics analysis. Gene expression profiles were collected from Gene Expression Omnibus and two microarray datasets were downloaded. A bioinformatic approach was used to screen differentially expressed genes and perform functional enrichment analysis. Weighted correlation network analysis (WGCNA) was used to identify key genes and pathogenic regions. Seven potential biomarkers were identified, with T cell, CD4 naïve cell, and neutrophil levels significantly higher in the disease group. The study suggests these biomarkers may help in AS diagnosis and treatment and provide new ideas for further research.

The study of (Kennedy et al. 2023) used machine learning to create a profile of individuals likely to be diagnosed with ankylosing spondylitis (AS). The Secure Anonymised Information Linkage databank was used, and data was analyzed for both men and women. The model showed that lower back pain, uveitis, and NSAID use under age 20 are associated with AS development. However, in a low prevalence population, the positive predictive value is very low. Multiple models may be needed to improve predictive value and reduce the time to diagnosis.

This study by(Tas et al. 2023) aims to diagnose Aspergillosis (AS) using a pre-trained hybrid model using magnetic resonance imaging (MRI). The researchers collected a new MRI dataset with three cases and introduced a novel deep feature engineering model using three renowned pretrained convolutional neural networks (CNNs): DenseNet201, ResNet50, and ShuffleNet. The model generated deep features using the transfer learning approach, with two feature vectors generated from an MRI. The k-nearest neighbors classifier was used in the classification phase, and the iterative majority voting algorithm was applied in the information phase. The model achieved high accuracy, recall, precision, and F1-score for axial images and coronal images, and achieved high accuracy, recall, precision, and F1-score for contrast-enhanced images. The study's success in diagnosing AS disease using axial images without contrast-enhanced MRI is significant in healthcare and economic terms.

The study by (Taş et al. 2023) aimed to understand the genetic predisposition of Aspergillosis (AS) and the potential of X-Analytical Intelligence (XAI) techniques

in medical diagnosis. It evaluated various classification models and selected the best-performing RFC model. The model's predictions were explained using XAI techniques like SHAP and LIME. WBC, Hematocrit, uric acid, and gender showed the strongest association with HLA-B-27. The study's strengths include comprehensive model evaluation, explainability of model decisions, and revealing the relationship between health parameters and HLA-B-27.

The study by(Zhou et al. 2023) aimed to identify shared biomarkers and pathways of Asthma and Urexia nervosa (US) and Urexia nervosa (UC) using integrated bioinformatics. Gene expression data was obtained from the GEO database, and weighted gene co-expression network analysis was used to identify AS and UC-related gene modules. Machine learning was used to screen hub genes, and gene set enrichment analysis was used to analyze pathway-level changes. The study identified KCNJ15 as a common diagnostic gene for both AS and UC, providing potential diagnostic biomarkers and insights into AS-related UC mechanisms.

The study by(Dong 2023) aimed to identify new biomarkers for ankylosing spondylitis (AS) using gene expression profiles from GSE73754, GSE25101, and GSE18781 datasets. Machine learning algorithms were used to screen cuprotosis-related genes (CRGs) and classify AS specimens. Key genes were identified through difference analysis, clustering, and spearman correlation analysis. A nomogram model was established, and the accuracy of cuprotosis-related genes in predicting AS disease was verified using external data sets. The study found that PDHB had the strongest positive correlation with T cells CD8, followed by T cells CD4 memory resting, and the strongest negative correlation with Neutrophils. SLC31A1 had the strongest positive correlation with NK cells resting and the strongest negative correlation with T cells CD8.

The study of (Gao et al. 2023) aimed to identify early biomarkers related to immunity in Aspergillosis (AS) and develop a predictive disease risk model using bioinformatic methods and the Gene Expression Omnibus database. The researchers used GEO datasets to identify differentially expressed genes and created a gene coexpression network between AS and healthy samples. They identified central genes related to immunity, key immune cells, pathways, gene modules, and the coexpression network in AS. The AS disease risk model can guide clinical diagnosis and treatment, potentially aiding in personalized immunotherapy.

The study of (Sun et al. 2023) used unsupervised machine learning (UML) to classify patients with Aspergillosis (AS) based on clinical characteristics. A novel subtype predictive model was constructed using C-reactive protein (CRP), absolute value of neutrophils (NEU), and absolute value of monocytes (MONO). The model was validated using routine blood tests from 3671 AS patients and 5720 non-AS patients. The results showed that FTO expression was negatively correlated with both NEU and MONO, and immunohistochemistry analysis confirmed the downregulated expression of FTO. The study concluded that UML provides a remarkable classification of a heterogeneous cohort of AS patients, and FTO expression was correlated with immune cell infiltration in AS patients.

The study of (Mo et al. 2023) presentd VertXGradeNet, a 2-step auto-grading pipeline that predicts mSASSS scores for cervical and lumbar vertebral units in X-ray spinal imaging. It uses VUs from a previous VU extraction pipeline and achieves balanced accuracy of 0.56 and 0.51 for four different mSASSS scores on two test datasets, potentially streamlining spinal radiograph readings and reducing clinical trial costs.

The study by (M. Hwang et al. 2023) aimed to identify serum biomarkers for diagnosing and monitoring ankylosing spondylitis (AS) using biologic-treatment-naïve AS and healthy control patients' sera. Eighty samples were analyzed using SOMAscan.. T-tests were performed to identify differentially expressed proteins (DEPs) in AS patients and healthy control patients. The Cytoscape Molecular Complex Detection plugin and Ingenuity Pathway Analysis were used to identify clusters in protein-protein interaction networks. Lasso regression analysis identified a Diagnostic 13-protein model predictive of AS, with a sensitivity of 0.75, specificity of 0.90, a kappa of 0.59, and overall accuracy of 0.80.

A study done by (Vodencarevic et al. 2023) using real-world data from the AQUILA study aimed to predict LDA in AS patients treated with spinal cord injury (SEC) using machine learning methods and explainable artificial intelligence (XAI). The study used data from 580 AS patients and identified 32 demographic, clinical, and treatment parameters at baseline. The most influencing predictor was BASDAI at baseline, followed by the number of pretreatments with biologics, C-reactive protein, assessment of spondyloarthritis international society health index (ASAS-HI), and patient height. The best performing prediction model had an AUROC of 0.84, with sensitivity and specificity of 0.87 and 0.67, respectively. The study concluded that XAI can provide valuable clinical insights into patient-individual predictions, potentially guiding future AS treatment decisions.

The study by (Calvo Pascual, Castro Corredor, and Garrido Merchán 2024) predicts vitamin D3 levels in spondyloarthritis patients using observational, descriptive, and cross-sectional methods. Data was collected from 115 patients and two classification models were estimated using machine learning. The study also identified new variables like age and post-treatment.

The study of (Shuai et al. 2024) used Fourier transform infrared (FTIR) spectroscopy on dried serum samples to diagnose rheumatoid arthritis and ankylosing spondylitis using deep learning models. The researchers collected 243 samples from ankylosing spondylitis, rheumatoid arthritis, and healthy controls. Three multi-scale convolutional modules were designed using the multi-scale convolutional neural network (MSCNN) to fuse local features and enhance the model's generalization ability. The FTIR was combined with the MSCNN model to achieve a non-invasive, fast, and accurate diagnosis. The study found that the MSCNN model had a diagnostic AUC value of 0.99 and an accuracy rate of 0.93, making it a superior method for distinguishing rheumatism from other diseases.

The study by (H. Liu and Peng 2024)identified key AAM-related genes (AAMRGs) for the diagnosis and prediction of Aspergillosis (AS). Differentially expressed genes (DEGs) were compared between AS and normal groups, and common DEGs (Co-DEGs) were identified. AAM-related DEGs (AAMR DEGs) were acquired by intersection of Co-DEGs and AS-AAMSRGs. The study found that three AAMR DEGs had diagnostic value for AS and significantly enriched to neutrophil activation and degranulation. The study also found that three miRNAs could regulate TP53INP1 and TUBB, while only one could regulate RBM47.

This study by(Ma et al. 2024) used bioinformatics to identify common biomarkers and pathways between Asthma and Ankylosing Spontylitis (AS). Gene expression datasets were obtained from the Gene Expression Omnibus (GEO), and differential expression genes (DEGs) and module genes were identified using the Limma R package and WGCNA techniques. The machine learning algorithm SVM-RFE was applied to identify promising biomarkers, which were validated in terms of their expression levels and diagnostic efficacy. The interaction of the key biomarker with the immune microenvironment was investigated via the CIBERSORT algorithm. The study found that ST8SIA4 is a common diagnostic marker for both AS and spondylitis, upregulated in samples from both diseases. The findings may yield potential diagnostic biomarkers and offer new insights into the shared pathogenic mechanisms underlying these conditions. The study by (P. Wen et al. 2024) compared gene expressions between AS patients and healthy controls, identifying 18 differentially expressed necroptosis-related genes (DENRGs). Two hub genes, FASLG and TARDBP, were identified as hub genes with high specificity and sensitivity for AS diagnosis. Immune cell infiltration analysis suggested that high FASLG expression led to significant infiltration of CD8+ T cells, memory-activated CD4+ T cells, and resting NK cells, while high TARDBP expression enhanced infiltration of naïve CD4+ T cells and M0 macrophages. The study by (Jia et al. 2024)introduced SCJAYA, an enhanced optimization algorithm that incorporates salp swarm foraging behavior and cooperative predation strategies to improve convergence speed and solution quality. SCJAYA has been evaluated against conventional and state-of-the-art meta-heuristic algorithms, showing superior convergence speed and solution precision. The bSCJAYA-FKNN classifier, an advanced model, was proposed to improve accuracy in diagnosing and prognosticating Aspergillosis (AS) using SCJAYA binary version for feature selection.

The study by (Shi et al. 2024) used short tau inversion recovery (STIR) sequence texture analysis to evaluate bone marrow oedema in sacroiliac joints in early AS patients. The study involved 43 patients divided into a training and verification cohort. The optimal feature subsets were obtained using these texture parameters, and the final prediction model was constructed. The results showed that STIR texture analysis is a good prediction method for evaluating bone marrow oedema activity in sacroiliac joints, making it a new, non-invasive, and objective evaluation method for AS activity.

When the datasets utilized in the studies were evaluated, it was found that the majority of them chose to use clinical datasets. However, it has been discovered that some studies prefer datasets that are accessible to other researchers (Table 2). Among the online datasets studied, the GEO database was the most liked. The most used machine learning algorithms of Ankylosing Spondylitis (AS) among them was support vector machine with percent 17% after that decision tree with 15% and CNN with percent 13% (Figure 3).

Table 2: Data sources used in selected studies

Dataset	Number of Studies	Studies Reference
Clinical data	36	(A Cortes1 et al., 2015) (Huscher et al. 2015) (Dubreuil 2016) (Mlcoch et al. 2017) S. Lee et al. 2021) (S. Lee et al. 2020) (**Fernández**-Gutiérrez et al. 2021) (Jia et al. 2024) (Shi et al. 2024) (Shuai et al. 2024) (Yuan, Li, and Zhang 2018) (Koo et al. 2023) (Koo et al. 2022) (Dong 2023) (Mo et al. 2023) (Navarini et al. 2020) (Gu, Liu, and Wei 2018) (Joo et al. 2021) (Tas et al. 2023) (Castro-Zunti et al. 2020) (Han et al. 2022) (Deodhar et al. 2020) (Zhu et al. 2022) (M. Hwang et al. 2023 (Calvo Pascual, Castro Corredor, and Garrido Merchán 2024) (Wang et al. 2018) (J. Wen, Wan, and Dong 2022) (Kang et al. 2022) Jonathan Kennedy,2023 M. C. Hwang et al. 2022) (Castro-Zunti et al. 2020) (P. Wen et al. 2024) (Sun et al. 2023) (Taş et al. 2023 (Hao Li et al. 2023)
Datasets obtained from the GEO database, which includes clinical data.	8	(Ma et al. 2024) (Zheng et al. 2021) (Gao et al. 2023) (J. Wen, Wan, and Dong 2022) (Zhang et al. 2022) (Zhou et al. 2023) (D. Li et al. 2023) (Hua Li and Yang 2023)
Single Cell Transcriptome and Surface Epitope Analysis of Ankylosing Spondylitis	1	(Alber et al. 2022)
Gene expression data obtained from the ArrayExpress database, which includes samples from AS patients and healthy controls.	1	(Yuan, Li, and Zhang 2018)

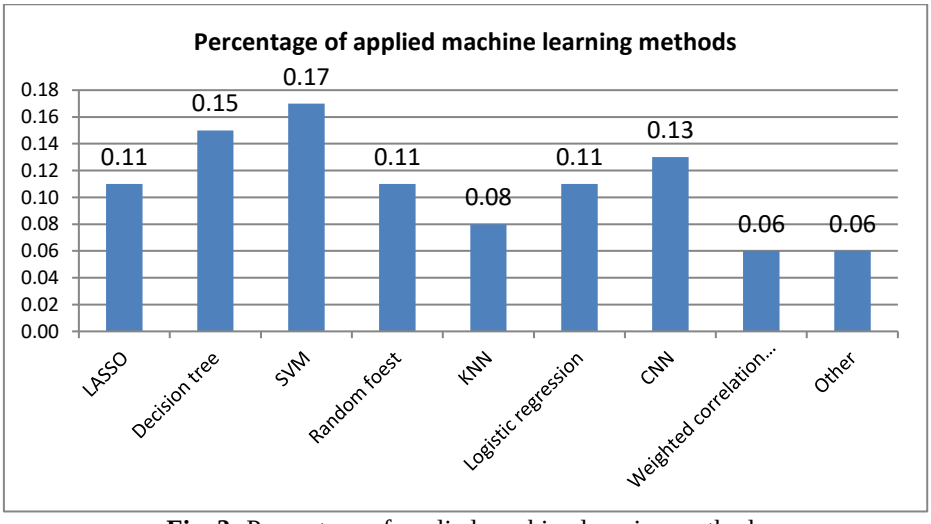

Fig. 3: Percentage of applied machine learning methods

Diagnosing benefits of using Machine Learning in Ankylosing Spondylitis

Early diagnosis enables early treatment of the illness. As a result, people can be shielded from the negative impacts of these circumstances, and their standard of life will rise. Socioeconomic effects of AS disorders are also felt by the patient, the healthcare system, and society at large. According to(Gao et al. 2023), these illnesses have negative clinical and financial repercussions. (Alotaibi, Albarrak, and Alammari 2024) found that people with ankylosing spondylitis are also worried about their ability to work, interact with others, and maintain a family life. From an economic perspective, the most important cost factor is decreased physical function (Castro-Zunti et al. 2020),(Kennedy et al. 2023)(Dubreuil 2016).

Machine vs. Human

Machine learning systems have a critical collaborative potential to support rheumatology professionals, as highlighted in the evaluated works(Mo et al. 2023). What, therefore, makes these cutting-edge systems significant for this area of use? First of all, machine learning based systems can swiftly build links between various types of data that are challenging for humans to comprehend with the introduction of electronic healthcare databases for medical images, reports, and electronic health records (Mlcoch et al. 2017). The statistical foundations and caliber of the data used to train the pertinent systems determine how well the results turn out. Their strongest point is this feature, which enables professionals to offer distinctive knowledge to help with decision-making. In contrast, the decisions made by machine learning (ML) technologies are solely based on the narrow range of application areas that they are intended to support, unlike medical professionals. Because of this, even though the produced systems outperform the experts, the diversity of the data set they are trained on is the single factor limiting their performance (Nick et al. 2015). Machine learning technologies can improve illness identification accuracy, especially in complex cases like cancer and chronic diseases. Medical education should integrate ML to equip healthcare professionals (C. C. Lee, Park, and Hsu 2024). Machine learning has potential diagnostic applications, but issues like data protection, ethical concerns, and specialized training need to be addressed. AutoML democratizes access to these technologies (Badhoutiya et al. 2023). Automated machine learning systems can process vast datasets, identifying patterns that may evade human interpretation, enabling timely interventions. Integrating ML with human expertise improves diagnostic accuracy, reduces errors, and reduces costs. However, challenges like extensive training data and medical imaging variability remain(Choudhury 2024). That being said, even though artificial intelligence systems achieving favorable outcomes, it is clear that the choices they make on their own should only serve to supplement the judgments made by medical specialists.

CONCLUSION

One of the aims of this review was to inform about the latest trends in using machine learning ML methods for the classification of AS data and identify trends, challenges, and future directions in this field. This review provides researchers with the latest information on the use of machine learning and inspires them to generate new ideas in their research by analyzing. The ways three that Ankylosing Spondylitis (AS) is treated with machine learning (ML): Identification and Diagnosis of Diseases, Forecast of disease development with specific therapy actions and. identification of images. However, the number of studies on diseases that negatively affect the quality of life of patients such as Ankylosing Spondylitis, especially in its advanced stages, is quite limited. Examining the studies on the most used machine learning algorithms of Ankylosing Spondylitis (AS) among them was support vector machine with percent 17% after that decision tree with 15% and CNN with percent 13% and these methods were more effective than other approaches.

Although some ML-based diagnosing systems achieved human-level performance results one of the fundamental reasons machine learning technologies cannot find a place in clinical use is that experts do not know precisely what the system has learned, especially in machine learning based systems. There is no definite consensus on how these developed models reach the relevant conclusion during Moreover, professionals' conditioning about human social behavior and the capabilities of inherent, underlying science and technology might be regarded as the basis for their opposition to exploiting the potential of ML in health. As a result, a new way is required to adequately represent how ML models develop their outputs and decision-making processes.

Finally, in rheumatology, it would be incorrect to predict that AI technologies will only bring innovations in Ankylosing Spondylitis (ALTIKARDEŞ, CANAYAZ, and ÜNSAL 2023). In particular, there are ML applied in other rheumatologic disease like Rheumatoid Arthritis(Fung et al. 2023), Osteoarthritis(Pedoia 2019) , Axial Spondyloarthritis (Bressem et al. 2021), Cartilage Lesion (F. Liu et al. 2018) and Scleroderma (Schaefer et al. 2013).

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