Axia SCIENTIFIC PUBLISHING

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Axia Journal of Radiology

# The Assessment of Spinal Cord for Patients with Multiple Sclerosis using Magnetic Resonance Imaging: A Systematic Review

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**Review**

**Received:** 28 November, 2025
**Accepted:** 11 December, 2025
**Published:** 12 December, 2025

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**Citation:** Alhadi Hasan Abd. The Assessment of Spinal Cord for Patients with Multiple Sclerosis

## Abstract

**Background:** Magnetic resonance imaging of the spinal cord is important in multiple sclerosis diagnosis and management, providing information on detection of lesions, progression of the disease and clinical disability. This systematic review aimed to assess the MRI diagnostic performance in identification of spinal cord lesions in patients with MS.

**Methodology:** The current systematic was carried out based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. PubMed, Scopus, Cochrane Library, and Google Scholar databases were accessed. Based on a rigorous screening process, studies that met the inclusion criteria were selected for data extraction and assessed for potential risk of bias. We reviewed studies examining CSA measurement techniques, particularly using Magnetic Resonance Imaging (MRI), and their ability to track spinal cord atrophy in MS. Key outcome measures included reproducibility and reliability, image quality (signal-to-noise ratio and contrast-to-noise ratio), and comparative CSA analysis between MS patients at different disease stages and healthy controls.

**Results:** A 98 studies were identified from the database search. After screening, 7 studies met the inclusion criteria and were included in the systematic review. CSA measurements are reproducible and reliable when high-quality imaging protocols, such as Active Surface Model (ASM) combined with Phase-Sensitive Inversion Recovery (PSIR), are used. High-field MRI (3T) improves image quality, significantly enhancing lesion detection and CSA measurement accuracy. CSA reductions were most pronounced in Secondary Progressive MS (SPMS) and Primary Progressive MS (PPMS) patients, with strong correlations to clinical disability measures (EDSS). CSA was consistently smaller in MS patients compared to healthy controls, particularly in progressive MS forms, highlighting its potential as a biomarker for disease progression.

**Conclusion:** CSA is a valuable and reliable biomarker for spinal cord atrophy in MS, particularly in progressive forms of the disease. The use of high-field MRI and multi-parametric imaging techniques can enhance CSA measurement accuracy and improve disease monitoring.

**Keywords:** Multiple Sclerosis; Spinal Cord; Magnetic Resonance Imaging; Diagnostic Accuracy; Lesion Detection.

## Introduction

Multiple Sclerosis (MS) is a long-term autoimmune disorder targeting the Central Nervous System (CNS), characterized by inflammation, demyelination, and progressive neurodegeneration [1]. According to the World Health Organization (WHO), more than 1.8 million individuals worldwide are affected by MS, underscoring its significant global impact [2]. While brain imaging has been extensively studied for diagnosing and monitoring MS, spinal cord involvement remains underexplored, despite its critical role in motor, sensory, and functional impairments. Magnetic Resonance Imaging (MRI) of the spinal cord, particularly the cervical region, offers valuable insights into MS pathology, including lesions and atrophy, which significantly impact disease progression and patient outcomes [3]. Metrics such as Cross-Sectional Area (CSA) have emerged as promising tools for assessing spinal cord abnormalities; however, challenges in reproducibility,

reliability, and the lack of standardized imaging protocols limit their clinical application [4].

MRI has revolutionized MS research since the 1980s when it demonstrated sensitivity to T2-weighted abnormalities corresponding to MS plaques. However, while brain imaging is extensively used, spinal cord MRI remains underutilized, despite its recognized importance in documenting Dissemination in Space (DIS) as part of McDonald's diagnostic criteria [5]. MRI techniques have advanced to include T1- and T2-weighted imaging, which provide high sensitivity for detecting spinal cord lesions. Magnetic Resonance Imaging (MRI) is a cornerstone in MS diagnosis and disease monitoring due to its ability to detect lesions and atrophy non-invasively. Spinal cord lesions are often associated with clinical disability; therefore, imaging helps clinicians monitor disease progression, therapeutic efficacy, and make treatment decisions. This shows the importance of advanced MRI techniques in providing a comprehensive understanding of MS beyond brain imaging [6].

The introduction of quantitative metrics, such as Cross-Sectional Area (CSA), has enabled researchers to assess spinal cord atrophy, offering insights into disease progression and disability [7]. Cross-sectional area is an essential biomarker for spinal cord atrophy in MS, that provides a non-invasive way to monitor disease progression and disability [8]. CSA measurements provide reliable information on spinal cord changes. However, despite its potential, there are limitations to application of CSA. Variability in reproducibility, across different imaging protocols and rates are significant limitations [9]. Moreover, CSA does not directly correlate with all MS pathology aspects, thus limiting is comprehensive utilization in disease monitoring. Addressing these limitations using automatic deep learning software is essential to establish CSA measurement as a robust diagnostic and monitoring tool in MS [10,4].

Cervical spinal cord atrophy represents a significant factor in evaluating MS progression as well as estimating the degree of axonal loss and lesion load. Various studies have examined the potential of spinal cord MRI. However, there is a notable gap in the literature regarding systematic reviews on spinal cord imaging in MS, regarding the reproducibility of measurements and the quality of images obtained at 3T MRI. Addressing this gaps is important in establishment of standard, and reliable imaging practices in clinical settings. This systematic review aimed to assess the MRI diagnostic performance in identification of spinal cord lesions in patients with MS at 3T.

## Methodology

### Study Registration

The current systematic was carried out based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

### Study Selection (Inclusion and Exclusion Criteria)

Studies were included based on the following criteria; (i) Published in peer-reviewed journals, (ii), studies focused on using MRI at 3T MRI in assessment of spinal cord lesions in patients with MS, (iii) reported diagnostic accuracy metric including sensitivity, specificity, or Diagnostic Odds Ratios (DOR), (iv) published in English, and (v) conducted among adults aged 18years and above. Studies were excluded based on; (i) systematic reviews, or literature reviews, editorials, and opinion papers, and (ii) Studies conducted on brain MRI, without involvement of spinal cord.

### Sources, Search Strategy and Screening

A comprehensive search was carried out in PubMed, Scopus, Cochrane Library, and Google Scholar databases to identify studies published between January 1, 2010, and December 31, 2024, that assessed MRI in assessment of spinal cord lesions. Keywords used included "Multiple Sclerosis," "spinal cord," "Magnetic Resonance Imaging," "MRI," and "assessment.". To refine and combine the key terms, Boolean operators (AND, OR) were used.

### Data Extraction and Collection

Data screening and extraction were conducted by two independent reviewers. This ensured accuracy and reliability of the process. The reviewers screened the abstracts and titles of the identified studies based on eligibility criteria. Disagreements arising were resolved through discussion and consultation of a third reviewer for final decision, where necessary. Both reviewers extracted relevant data independently, using standardized extraction template. This helped in minimizing bias, while ensuring accurate and comprehensive data extraction. Data extraction was completed using a Microsoft excel template. Key factors extracted from the included studies were author and publication date, aim, sample size, study characteristics, outcome measures, statistical information, scanner strength, sequences and key outcomes.

### Outcome Measures

The primary outcome measures included 1), reproducibility, reliability, and repeatability of Cross-

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Sectional Area (CSA) measurements; 2) image quality using Signal-to-Noise Ratio (SNR) and Contrast-to-Noise Ratio (CNR) metrics; 3) a comparative analysis of the differences in CSA parameters between MS patients at different disease stages and healthy controls.

### Risk of Bias

The risk of bias in the included studies were examined using the QUADAS-2 tool. This was used to examine risk of bias across four main domain including; patient selection, reference standards, index test, and flow and timing. The tool helped was essential in determining the reliability and validity of the findings included in the review.

## Results

### Included Studies and Sample Characteristics

The search identified 98 studies. A total of 40 studies remained after removal of duplicate records. Title and abstract screening removed 26 studies, for not meeting the inclusion criteria. The remaining 14 were sought for retrieval and only 10 full text were retrieved. Full text assessment excluded 3 studies with reasons as shown in Figure 1 below. A total of 7 studies met the inclusion criteria and were included in the systematic review.

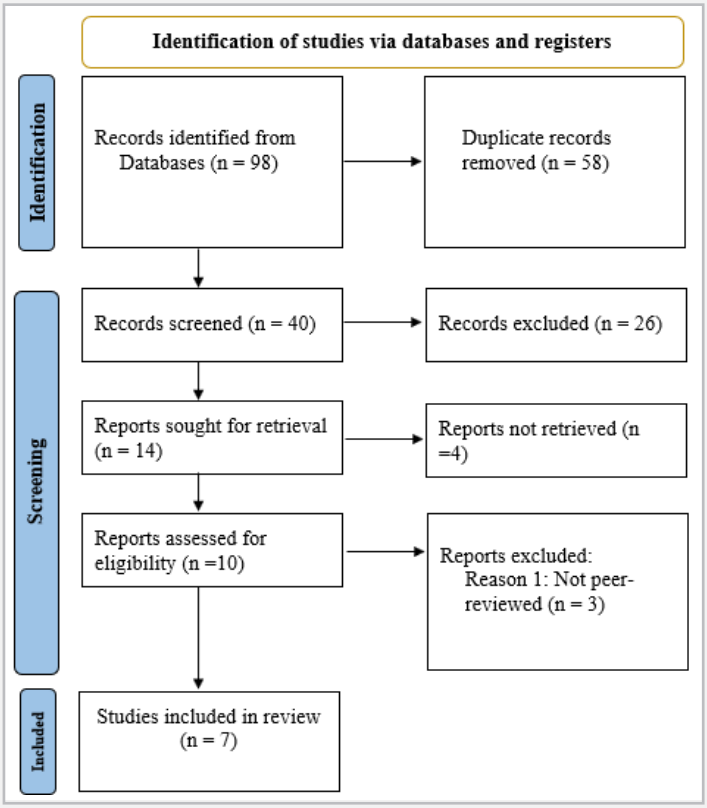


**Figure 1:** Prisma Flow Diagram Showing the Selection of Included Studies.

### Characteristics of Included Studies

## Quality Assessment

The quality assessment of the included studies was carried out using QUADAS-2 tool, which asses the risk of bias [17]. The tool asses the risks of bias across four major domains including patient selection, reference standards, index test, and flow and timing [18]. Overall, the studies were found to have low risk of bias across the domains. Majority of the studies employed consecutive methods of sampling, blinded interpretations and necessary reference standards, thereby enhancing their reliability.

### Reproducibility, Reliability, and Repeatability of CSA Measurements

Reproducibility and reliability of CSA measurements are important in the measurement of spinal cord atrophy in MS. Various studies have made their contribution on the stability of CSA as a biomarker, and the findings support that CSA can be a consistent measure in the disease pathology, however, the variability occurs depending on the imaging standards and state of the patient. Kearney et al. (2014) [13] concluded that a combination of Active Surface Model (ASM) and Phase-Sensitive Inversion Recovery (PSIR) sequences resulted in great reproducibility of CSA measurements. It reported that the reproducibility of both intrarater and interrater had low Coefficients of Variation (COV), indicating that the reliability of the imaging techniques. Al-Tameemi et al. (2023) [4] found that the CSA between MS patients and unhealthy control subjects was significantly reduced, and that the most notable reduction in MS occurred in Secondary Progressive MS (SPMS). The study further determined significant inverse correlations existed between CSA and disease duration, and also with disability scores (EDSS), which proved CSA to be a valid measure of disease severity. However, the study emphasized that differences caused by the evolution of the disease, therapeutic procedures, and rater experience differences may affect reproducibility.

Similar results were reflected by Lukas et al. (2013), who demonstrated that CSA was lower in progressive MS conditions (PPMS and SPMS) than in RRMS, and CSA changes were negatively related to EDSS. The study highlighted the difficulties of making the CSA measurement consistent among raters, and this gives rise to the adoption of standardized protocols that could enhance consistency. Weier et al. (2012) [12] focused on how biplanar use of MRI (both the sagittal and axial planes) enhances the detection of spinal cord lesions as opposed to the conventional MRI techniques. Although the study did not directly estimate the reproducibility of CSA, it has shown that the biplanar

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**Table 1:** Summary and Characteristics of Included Studies.

| Author(s) | Aim | Sample Size | Study Characteristics | Outcome Measures | Scanner strength | Sequences | Statistical Information | Key outcomes |
|---|---|---|---|---|---|---|---|---|
| Dula et al. (2016) [11]. | To study spinal cord in MS patients using 3T MRI. | 28 (13 healthy, 15 MS) | 3T MRI scans of the cervical spinal cord (C2–C5) | MS lesions, signal contrast, lesion count | a Philips Achieva 3T MRI scanner | Axial T2-weighted (FSE)<br>3D T1-weighted FFE | p=0.05 for increased lesion count at 3T | Clinical scans at 3T identified 28 lesions in total across the MS patients, which is an average of 3.1 lesions per patient.<br>WM at 3T, the SNR was 4.7±1.3, while for GM it was 5.4±1.3. |
| Weier et al. (2012) [12]. | To assess the whole spinal cord in MS using biplanar MRI and correlate with clinical scores. | 202 (140 women, 62 men) | Biplanar MRI of whole spinal cord (sagittal and axial T2, T2w) | Lesions, cord abnormalities (atrophy, lesions), correlation with EDSS | Used a 3Siemens MAGNETOM Avanto 1.5T MRI scanner3 for spinal cord imaging. | 3Sagittal PDw3: TR/TE=2000/23 ms, ETL=7, iPAT=2, voxel size=1.0x0.8x3 mm³, TA=2:40 min.<br>3Sagittal T2w3: TR/TE=4440/102 ms, ETL=25, iPAT=2, voxel size=1.0x0.8x3 mm³, TA=2:32 min.<br>3Axial PDw/ T2w3: TR/TE1/ TE2=2120/9.9/89 ms, iPAT=2, voxel size=1.1x0.5x6 mm³, TA=4:51 min. | ρ=0.52 moderate correlation with EDSS | 3Focal Lesions3: 593 lesions, mean 2.9 per patient (range: 0–10), mostly in 3cervical cord3.<br>3Diffuse Abnormalities3: Found in 331 patients3 (15%), affecting 4–17 vertebral segments.<br>3Atrophy3: 336 patients3 (18%) showed 3spinal cord atrophy3 (mean 5.5 segments).<br>3Lesion Count3: Combined sagittal and axial images revealed 39% more lesions3 in 28% of patients.<br>3EDSS Correlation3: Moderate correlation with MRI findings (ρ=0.52). |
| Kearney et al. (2014) [13]. | To identify improved spinal cord CSA measurement methods for MS patients. | 15 controls, 15 MS | 3D phase-sensitive inversion recovery (PSIR) and T1-weighted gradient echo at C2-C3 levels | Spinal cord CSA (cross-sectional area), comparison of methods | 3Philips Achieva 3T MRI3 system with 3RF multitransmit technology3 and a 16-channel neurovascular coil. | 33D-TFE (T1-weighted)3: Voxel size 31×1×1 mm³3, TR=8 msec, TE=3.7 msec, SENSE factor 2, scan time 6:31 min.<br>33D-PSIR (Phase-Sensitive Inversion Recovery)3: Voxel size 30.5×0.5×3 mm³3, TR=8 msec, TE=3.7 msec, flip angle=5°, scan time 14:22 min. | COV: Intrarater 0.002%, interrater 0.03%, scan-rescan 0.1% | Reproducibility: PSIR/ASM3 method showed 3highest reproducibility, with 3COV3 values of 30.002% (intrarater), 30.03% (interrater), and 30.1% (scan-rescan).<br>CSA Changes: No significant CSA changes in controls. Patients showed CSA decrease, but not statistically significant (p>0.05).<br>Correlation with EDSS: Strong negative correlation between 3CSA and EDSS3, especially with 3PSIR/ ASM3 (r=-0.725, p=0.002).<br>Sample Size Calculation: PSIR/ ASM3 required the fewest subjects for clinical trials, especially for 50% treatment effect (n=476 for 6-month trials). |

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| Lukas et al. (2013) [14]. | To determine whether spinal cord atrophy differs among MS subtypes and its clinical relevance. | 440 MS patients | UCCA, brain/spinal cord lesion loads, brain atrophy measured via MRI, including EDSS scores | Spinal cord atrophy, correlation with clinical disability (EDSS), lesion count | MRI was performed using Siemens Vision and Siemens Avanto MRI systems | Sagittal T1-weighted: Magnetization-prepared rapid-acquisition gradient-echo imaging (TR=9.7–20.8 msec, TE=2–4 msec, inversion time=300–400 msec, isotropic resolution 1.0 $mm^3$). Dual-echo Proton-Density T2-weighted: TR=2000–4000 msec, TE=14–20 msec, axial 3.0-mm-thick sections, in-plane resolution 1.0x1.0 $mm^2$. | $p < 0.001$ for differences in UCCA between MS types | UCCA Differences: UCCA was significantly lower in SP MS (79 $mm^2$) and PP MS (77.3 $mm^2$) compared to RR MS (84 $mm^2$) ($p<0.001$). Correlation with EDSS: UCCA showed a significant inverse correlation with EDSS, TWT, and nine-hole peg test scores ($r=-0.39$, $p<0.001$). Spinal Cord Lesions: The number of spinal cord lesions was higher in SP MS compared to RR MS ($p=0.03$). Multivariate Regression: UCCA, number of spinal cord segments, and presence of diffuse abnormalities were significant factors for clinical disability ($R^2=0.564$). |
| Mirafzal et al. (2020) [15]. | To compare 3D PSIR MRI with conventional MRI for spinal cord lesion detection in MS. | 54 MS patients | 3D PSIR vs conventional STIR/T2 images to detect MS lesions in cervical/dorsal regions | Number of spinal cord lesions, LCCR, lesion contrast, inter-observer agreement | Imaging was performed on a 3T Philips Ingenia MRI system, using a 16-channel head coil and a posterior spine coil. | 3D STIR (Short Tau Inversion Recovery) Sagittal T2-weighted Imaging (T2-WI) 3D PSIR: Included two magnitude images and one phase-corrected real image. Optimized for better lesion contrast and lesion delineation in spinal cord imaging. | $p < 0.05$ for PSIR detecting more lesions than conventional MRI | Lesion Detection: 3D PSIR detected significantly more lesions than the conventional dataset (371 vs. 173, $p<0.05$). It also detected more lesions in the cervical (235 vs. 105, $p<0.001$) and dorsal (136 vs. 68, $p<0.001$) regions. Reader Confidence: Confidence in lesion detection was higher with 3D PSIR ($p<0.001$), with 99% of lesions detected with moderate-to-very high confidence. Artifacts: 3D PSIR had fewer artifacts, with 76.2% of exams showing no or minor artifacts compared to 8.1% with the conventional dataset ($p<0.001$). Lesion Contrast: The Lesion-to-Cord Contrast Ratio (LCCR) was significantly higher with 3D PSIR (1.10 vs. 0.41, $p<0.001$). Inter-reader Agreement: Good inter-reader agreement for 3D PSIR (ICC = 0.68) compared to fair agreement for the conventional dataset (ICC = 0.54). Correlation with EDSS: The correlation between the number of lesions and EDSS was poor for both datasets (3D PSIR: $r = 0.36$, $p = 0.02$; Conventional dataset: $r = 0.30$, $p = 0.03$). |

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| Al-Tameemi et al. (2023) [4]. | To assess cervical spinal cord CSA in MS patients and correlate with clinical disability. | 30 MS, 30 controls | MRI of cervical cord (C2 to C3) using T1- and T2-weighted sequences | CSA measurement at C2, C3, C2–C3, correlation with EDSS, disease type, lesion count | A Philips Achieva 1.5T MRI machine for cervical spinal cord imaging. | Sagittal T1-weighted: TR=560 ms, TE=20 ms Sagittal T2-weighted: TR=2175 ms, TE=100 ms Axial T2-weighted: TR=2175 ms, TE=100 ms | $p < 0.001$ for CSA differences between MS and controls | Mean CSA: The mean cervical cord CSA at C2 and C7 was significantly lower in MS patients compared to controls ($p<0.001$). Correlation with EDSS: Strong inverse correlation found between cervical cord CSA and EDSS ($p<0.001$). MS Types: The SPMS group showed significantly lower CSA compared to RRMS and CIS groups ($p<0.001$). Lesion Correlation: No significant correlation between CSA and cervical cord lesions ($p>0.05$). ROC Analysis: CSA at C2, C7, and C2–C7 average were good predictors of RRMS and SPMS, but not CIS ($p<0.05$). |
| Keegan et al. (2024) [16]. | To evaluate spinal cord involvement in MS and provide insights into clinical and radiological correlations. | N/A | Comprehensive review of current spinal cord imaging techniques in MS patients | Spinal cord lesions, atrophy, topographical model, diagnostic imaging challenges | Imaging was conducted using a 3T MRI (Siemens, Philips) with advanced sequences for spinal cord evaluation. | T2-weighted: Used for general lesion detection, particularly in cervical regions. Phase-Sensitive Inversion Recovery (PSIR): Enhanced contrast between spinal cord tissue and lesions. Magnetization Transfer (MT): Assessed changes in tissue microstructure and myelin integrity. | Statistical measures not directly available due to review nature | Lesion Detection: PSIR improved lesion detection in the cervical spinal cord compared to traditional T2-weighted imaging. Atrophy: Spinal cord atrophy, particularly in the cervical cord, was strongly correlated with disease progression and EDSS scores. MTR: Lower MTR values were associated with increased disability and progression in progressive MS. Diffusion MRI: Reduced FA in the cervical spinal cord correlated with clinical disability measures like the EDSS and nine-hole peg test. |

MRI can better assess the spinal cord. This technique would overcome the shortcoming of the single-plane MRI, and the sensitivity of spinal cord imaging is better, indicating that the sensitivity of multiple imaging planes used may be better to determine the reliability of the CSA measurement, particularly in identifying lesions in the spinal cord.

## Image Quality (SNR and CNR) and Its Role in CSA Measurement

SNR and CNR have been measured as important criteria to determine the quality of high-resolution images required in CSA measurements and lesion detection. In several studies, the effect of the field strength of MRI and imaging methods on the clarity of the spinal cord images was determined, whereby an increase in SNR and CNR positively influenced diagnostic precision. Dula et al. (2016) [11] identified that 3T MRI achieved higher SNR and CNR compared to 3T MRI, resulting in optimal tissue contrast and lesion localization. The higher resolution and sensitivity produced by the 3T MRI had positive impacts on detection of small lesions and CSA measurements, suggesting that higher field MRI, are significant in the image quality of spinal cord areas in MS. Keegan et al. (2024) [16] reported the significance of higher field MRI and emphasized their importance to the quality of image in MS. The study established that high quality imaging methods including those that generate susceptibility-weighted imaging provide high contrast difference in white and gray matter contributions to the visualization of lesions and identification of microstructural alteration. This enhanced imaging performance is essential in CSA measurements, particularly in the monitoring of any disease in MS.

Al-Tameemi et al. (2023) [4], conducted a conventional CSA measurement on patients of MS and healthy controls using 3T MRI and noted some significant differences, although, image quality might be less than ideal at smaller lesions detected earlier on in the development of MS. It was postulated in the study that non-standard MRI is adequate in the measurement of CSA, but higher field MRI might provide improved images especially in patients with diffuse lesions.

Weier et al. (2012) [12] emphasized the role of biplanar MRI in the application of which the elements of abnormality

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of the spinal cord are better detected in MS. They showed the benefits of biplanar MRI (sagittal and axial) in addition to overcoming the shortcomings of single-plane imaging. The appearance of this advancement in the image quality enabled to provide a deeper examination of the spinal cord, particularly among the patients whose lesions are complex in nature. Mirafzal et al. (2020) [15] established that 3D PSIR MRI imaging was accurate compared to 3D STIR and T2-weighted MRI imaging in the detection of spinal cord lesions. 3D PSIR detected more lesion and improved lesion contrast, confidence of the reader and inter-reader agreement. This enhancement in image examination, especially for detection of lesion, suggests that utilization of 3D PSIR enhances the sensitivity and specificity of CSA calculations in MS, where lesions are sparse and challenging to identify.

### Comparative Analysis of CSA between MS Patients at Different Disease Stages and Healthy Controls

Making comparisons of CSA in MS at different disease stage, with that of healthy individuals is essential in identification of the extent of spinal cord atrophy and related contributions to the development of the disease. The reviewed studies demonstrates lower CSA in MS patients, particularly among those with progressive types. Al-Tameemi et al. (2023) [4], identified lower levels of CSA in MS patients compared to healthy ones, especially among the SPMS patients. An inverse relationship between EDSS scores and CSA, as well as the duration of the disease was reported in the study, indicating that CSA is essential in predicting the development of the disease.

Lukas et al. (2013) [14] showed that CSA was lower in patients with progressive MS (SPMS and PPMS) than in those with RRMS. Their findings reported that the clinical disability, such as EDSS, was related to CSA reductions, possibly indicating that CSA is an effective instrument for assessing disease progression and, tracking the progression in progressive MS . Kearney et al. (2014) [13] also found that CSA measurements were found to be lower in the patients of SPMS, and that the associated changes were significantly correlated with EDSS scores and functional disability scales (scores). These findings indicated that CSA is an indicator used to determine the level of disease and disease progression among MS patients. Weaver et al. (2012) identified that biplanar MRI provided a detailed examination of the lesions and atrophy in SC.

## Discussion

This systematic review evaluated the effectiveness of cervical spinal cord MRI in individuals with multiple sclerosis at various stages of the disease, with a specific focus on imaging the cervical region. The studies included in this review provide information on the significance of CSA measurements in determining MS development and progression. Reproducibility and reliability of CSA measurements are important in assessing the significance of CSA for atrophic MS spinal cord atrophy. The reviewed studies have documented the utilization of CSA measurement. Kearney et al. (2014), demonstrates the combination of Active Surface Model (ASM) and Phase Sensitive Inversion Recovery (PSIR) sequences yields low Coefficients of Variation (COV) for both intra and inter rate reproducibility. These findings highlight that the proper imaging protocols implementable can allow for CSA metrics to produce uniform outcome across various raters and clinical situations. This is critical because for CSA to become a reliable and routinely used clinical biomarker for patients and clinical trials across multiple centers, consistency across contexts and raters is critical [14,4]. Despite the fact that the findings were greatly optimistic, reproducibility challenges continue to persist. Lukas et al. 2013 highlighted the challenges of achieving consistency across raters, particularly regarding spinal cord lesions that are poorly defined, a frequent occurrence in patients with MS and more diffuse spinal cord involvement. The concerns raised illustrate that CSA can be reproducible but suggest that the fundamental elements of the measurement protocols have to be standardized across different centers and raters. Al-Tameemi et al. 2023 stated that CSA measurements could be affected by multiple factors including disease stage, treatment regimens and patient elements, thus increasing variability. For example, disease modifying therapies can have a significant impact on the lesion burden and inflammatory levels, thus greatly affecting CSA measurement.

Consequently, sustaining the reliability of CSA measurement CSA across multiple stages of MS, protocols of treatment, and diverse patient cohorts still poses the biggest challenge for clinical use. These findings suggest the importance of standard measurement protocols, automated measurement devices, and ongoing attempts to minimize variability due to the rater. Furthermore, rater- dependent automated systems for measurement of cross-sectional areas of spinal structures, such as the ASM method described by Kearney et al. (2014) [13], may assist in enhancing interrater reliability to refine process CSA measurement, thus CA availability would be increased as a more reliable method for monitoring atrophy during multiple sclerosis. In spinal cord imaging for which SNR and CNR are relevant, their metric assesses whether CSA measurements are correct and accurate. Detection and imaging tissue with SNR and CNR bone are required for

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Sclerosis appreciation with its subtle spinal cord changes. Works of literature show how modern imaging, especially high-field Magnetic Resonance Imaging (MRI), enhances picture clarity (Kearney et al., 2014) [13].

Dula et al. (2016) argued how varying SNR and CNR at 3T MRI enables to visualize more lesions and acquire more accurate CSA ascertainments. These findings suggest under the conviction that spinal cord lesions, especially during the onset of Multiple Sclerosis (MS), are more prevalent than MRI scans indicate and that lower field systems impact CSA accuracy. It is, therefore, possible with more 3T systems that high-unstainable MRI (lesions) monitoring systems will be more accurate with MS progression than with others (Dula et al., 2016) [11]. Keegan et al. (2024) [16] pointed out 3T MRI's in resolving spinal cord images with more clarity, especially for microstructural alterations. As part of their study, they noted that the use of advanced imaging techniques, such as susceptibility weighted imaging, allowed for improved lesion detection, which in turn enhances the measurement of CSA. This is consistent with Weier et al. (2012) [12], who reported improved imaging with x-y biplanar MRI that combines sagittal and axial slices of the spinal cord. In multiple sclerosis, biplanar imaging is particularly useful because lesions oriented along the spinal cord may traverse several segments or be in more complicated configurations. This offers more evidence for the hypothesis that lesions have regionally varying permeability [16,13].

On the other hand, Al-Tameemi et al. (2023) have noted that the 3T MRI, whilst providing reasonable quality images for measuring the CSA, fails to identify lesions or more diffuse changes that become progressively more important in the advanced stages of multiple sclerosis. This underscores the typical limitations of MRIs on the spinal cords of people suffering from Multiple Sclerosis, as most of the atrophy or lesions are much less pronounced and thus difficult to detect. Advanced MP MRI could address these issues and thus improve lesion measurement and CSA estimation. Mirafzal et al. (2020) supports these conclusions by demonstrating that, of the 3D STIR and T2-weighted MRI methods, the 3D PSIR MRI, was better at identifying spinal lesions because it has higher contrast and improves the delineation of the lesions. This improve detection, but it also aids in CSA measurement as the spinal and lesion boundaries corresponding to the CSA are better defined [15].

In this review, one of the findings is that CSA is lower in MS patients relative to the healthy controls, and this is more prominent in the forms of progressive MS (SPMS and PPMS). These findings remained stable within studies, which shows that CSA represents a valuable parameter in the characterization of RRMS and progressive MS. According to Al-Tameemi et al. 2023 study, SPMS patients reduced most in CSA and had the strongest inverse correlation between CSA and clinical disability, as measured via EDSS. Lukas et al. (2013) [15], emphasized that CSA was reduced in the progressive MS patients. Kearney et al (2014) [13] showed that progressive MS patients with various degrees of CSA paired with SPMS had greatest change, and also correlated with EDSS and other functional disability assessments. Weier et al. (2012) [12] classifies MRIs into the more useful sagittal and axial planes for spinal imaging. These findings are useful as they show that new methods of imaging may augment the precision of the CSA measurement in patients with complex lesions of the spinal cord. Multi-plane imaging may provide additional spinal cord atrophy and, in turn, provide additional evidence for the CSA as a marker of MS progression.

The findings of this review highlights the potential of cervical spinal cord MRI, especially, CSA measurements in assessment of disease progression in MS. However, various issues were identified across the studies that need further consideration. The findings showed disagreement among studies related to reproducibility of CSA measurements at 3T MRI. While some studies revealed high reliability with some imaging protocols, including ASM and PSIR sequences (Kearney et al.,2014) [13], other studies revealed measurement variabilities (Al-Tameemi et al., 2023) [4]. This inconsistency may be associated with differences in imaging techniques utilized, rater experience, patient population, that affects CSA reliability. This highlights the need for standardized imaging protocols to enhance reproducibility of CSA for MS monitoring.

Moreover, the reviewed studies highlights a critical gap of absence of longitudinal studies examining the reproducibility of CSA measurements over time at 3T MRI. CSA has been identified as essential biomarker for MS progression, however, its utilization in monitoring long-term changes in spinal cord atrophy have not been examined extensively. Furthermore, most of included studies were from western regions. This highlights underrepresentation of certain groups of patients in the current review. Specifically, there is absence of studies from the Middle Eastern cohorts, thus limiting the generalizability of this review findings. This gap reveals the need for inclusive research to comprehend MS variations across different regions and ethnic groups.

## Implication of the Findings

The findings of this systematic review indicates the importance of spinal cord MRI in CSA measurement in MS.

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This helps healthcare providers to use CSA measurement in monitoring the rates of spinal cord atrophy among MS patients. This is particularly progressive forms such as secondary and primary progressive MS. This helps healthcare providers to monitor disease progression, treatment decisions, and examine the efficacy of disease-modifying therapies. The ability of use CSA as a monitoring tool provides essential opportunity for refining patient management measures. Moreover, the results emphasize the significance of high quality imaging protocols to ensure accurate and reproducible CSA measurements. For healthcare professionals, adoption of standardized imaging techniques will be crucial in obtaining consistent results.

## Conclusions

This systematic review reveals that cervical spinal cord MRI, especially the Cross-Sectional Area (CSA) measurements, is an essential tool for assessment of disease progression in Multiple Sclerosis (MS). CSA demonstrated strong correlations with clinical disability and provides a reliable method for monitoring spinal cord atrophy, especially in progressive forms of MS. However, the findings, also revealed challenged associated with quality of imaging, reproducibility, image quality, and the standardization of imaging protocols. This need to be addressed for SCA to be adopted in clinical practices.

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