Relative risk factors of nerve root sedimentation sign (Sedsign) in patients with severe central lumbar spinal stenosis (LSS)

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Research Article

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Abstract

Here we evaluated the incidence of positive nerve root sedimentation sign (Sedsign) and its correlation with MRI parameters in patients with severe lumbar spinal stenosis (LSS) to explore its pathogenesis. Among 209 patients with severe LSS, there were 290 levels with intervertebral narrowing, among which 248 had a positive Sedsign (a prevalence of 85.52%). We then analyzed those levels with a positive Sedsign relative to those with a negative Sedsign (42 levels). There was no significant difference between the two groups for the minimum cross-sectional area (CSA) of the dural sac or the minimum posteroanterior diameter (PAD) of the spinal canal. In contrast, there was a significant difference between the groups for the grade of degenerative facet joint (DFJ) ($p < 0.05$), the maximum thickness of ligamentum flavum (TLF) ($p < 0.01$), and the maximum cross-sectional area difference (CSAD) of the dural sac ($p < 0.01$). In addition, receiver operating characteristic (ROC) curves were used to identify associated factors. The area under the ROC curve for PAD was 0.608 (95%CI: 0.55–0.665, $p < 0.05$), for DFJ was 0.634 (95%CI: 0.576–0.69, $p < 0.05$), for TLF was 0.74 (95%CI: 0.742–0.839, $p < 0.01$), and for CSAD was 0.911 (95%CI: 0.875–0.943, $p < 0.01$). In summary, a positive Sedsign has notable advantages in assisting with the diagnosis of severe LSS. Compression of the dural sac from the rear may be the main cause of a positive Sedsign, and the TLF and DFJ parameters were the main relative risk factors.

Introduction

Lumbar spinal stenosis (LSS) is represented by the reduction of the lumbar spinal canal capacity, compression of the dural sac, and entrapment of nerve roots, which collectively induce a series of clinical dysfunction in patients[1, 2]. Although patient history, clinical examination, electrophysiological analyses, and confirmatory imaging findings such as cross-sectional area (CSA) [3, 4] and posteroanterior diameter (PAD) [5] can be used to diagnose LSS, there are currently no universally accepted diagnostic criteria for LSS [6–8]. Because diagnosis of LSS is difficult when clinical symptoms such as pain and functional limitations often occur only during activity but disappear at rest, imaging findings do not always correlate with clinical symptoms [9, 10].

To improve the ability to diagnose LSS, Barz et al. [11] introduced a new radiological index, the nerve root sedimentation sign (SedSign). The Sedsign is a phenomenon visible in axial MRI scans: when a patient is in the supine position, an MRI scan shows that the lumbar nerve roots sediment, as a result of gravity, to the dorsal part of the dural sac in patients with no suspicion of LSS. In contrast, in patients with severe LSS, such sedimentation is almost always absent, this phenomenon were referred to as a positive sedimentation sign. According to the report from Barz et al., the Sedsign is 94% sensitive and 100% specific for LSS, when used in conjunction with the criteria of walking distance $\leq$ 200 m and CSA of the dural sac $\leq$ 80 mm^2 to define probable LSS cases [11]. Tomkins-Lane et al. [12] also reported that the sensitivity of the Sedsign was 60–96%. Both studies suggest that a positive Sedsign is a sensitive MRI parameter of patients with LSS, especially patients with severe morphological spinal stenosis.

A Sedsign measurement is simple, intuitive, and easy to obtain and is considered a good indicator for the use of diagnosing severe LSS in clinical practice [13, 14]. However, the mechanism responsible for a positive Sedsign is still not clear. What risk factors are related specifically to the phenomenon of a positive Sedsign? We hypothesized that a positive Sedsign is associated with a change in the dural sac at the level of intervertebral stenosis of patients with LSS. To test our hypothesis, we investigated the incidence of a positive Sedsign and correlations with MRI parameters in patients with severe LSS.

Results

According to the inclusion/exclusion criteria, 209 patients were included in the current study (age, 60.52 ± 12.94 year; male = 84; female = 125). Among these patients, 290 intervertebral levels were identified as having severe LSS, which included 248 intervertebral levels with a positive Sedsign and 42 levels with a negative Sedsign. The occurrence of positive and negative Sedsign measurements at different intervertebral levels for the 290 levels with severe LSS is shown in Table 2. The prevalence of a positive SedSign was 85.52% for all levels.

We then compared several parameters, including the minimum posteroanterior diameter (PAD) of the spinal canal and the minimum cross-sectional area (CSA) of the dural sac, the grade of degenerative facet joint (DFJ), the maximum thickness of ligamentum flavum (TLF) and the maximum cross-sectional area difference (CSAD), between the levels with a positive Sedsign (n = 248) and those with a negative Sedsign (n = 42), and the results were showed in Fig. 3. Between the positive and negative Sedsign groups, there was no significant difference with respect to the minimum PAD and CSA($p > 0.05$). However, there was a significant difference in the maximum TLF and the grade of DFJ, and the maximum CSAD($p < 0.05$).

To evaluate any correlations between a positive Sedsign and the above parameters, we further studied the sensitivity between the prevalence of a positive Sedsign and these parameters with the ROC curve method (Fig. 4). Our results suggested that there is no obvious correlation between the prevalence of a positive Sedsign and minimum CSA($p > 0.05$). However, the prevalence was moderate correlated with minimum PAD and DFJ($p < 0.05$). At last, the significant correlation were observed between he prevalence of a positive Sedsign and the maximum TLF and CSAD($p < 0.01$).

Discussion

Here we conducted a retrospective study to evaluate the lumbar MR images of 209 patients with severe LSS. In total, 290 lumbar sections were diagnosed severe LSS based on our inclusion criteria, and the 248 intervertebral discs that were assigned to the positive Sedsign group. There were only 2 section at the L1/2 level and 12 at the L2/3 level were diagnosed severe LSS, which all were assessed as positive Sedsign(100%). Meanwhile, the incidence of a positive Sedsign increased to 76 in 87 L3/4 levels

(87.36%) and 158 in 189 L4/5 levels (83.6%). Therefore, the overall incidence of a positive Sedsign was 85.52% in this study. Our results suggested a positive Sedsign was most common in the lower lumbar spine, which is consistent with the segments that show a high incidence of LSS [15, 16], and further suggested that the positive Sedsign was sensitive to the diagnosis of severe LSS. In addition, our result was also consistent with those reported previously. Tomkins-Lane et al. [12] reported that the sensitivity of Sedsign scoring was 60–96% in severe LSS. In another study, the Sedsign was positive in 100% of patients with severe LSS [13]. All the above findings all demonstrated that a positive Sedsign should be used as an image parameter for the diagnosis of and screening for LSS in clinical practice.

Although the Sedsign has been reported to be high diagnostic sensitivity, specificity, and efficacy and good clinical application value for the diagnosis of LSS [11–14]. However, the pathogenesis and correlated risk factors of positive Sedsign was still unclear. In this study, the PAD of spinal canal, as a linear indicator of the spinal canal, were measured the distance from the midpoint of the anterior wall to the midpoint of the posterior wall, which was used to assess the degree of spinal stenosis in the sagittal plane[17]. There was no significant difference in the PAD between the positive and negative Sedsign groups in present study, although the ROC curve for the PAD showed a mid-correlation between a positive Sedsign and the PAD. The mainly reason may be the physiologically invalid cavity filled with adipose tissue existed between the posterior of the dural sac and the posterior wall of the spinal canal, which may affected the PAD of spinal canal to reflect the degree of spinal canal stenosis effectively. In addition, the CSA of dural sac, as spinal canal area parameter, was superior to vertebral canal diameter line parameters in diagnosing LSS[18], due to the characteristics of the spinal canal morphology, some degenerative changes occur in the non-midline part of the spinal canal often induced lateral recess stenosis and finally lead to reduction in spinal canal volume[18]. However, some researcher considered that the CSA could be insufficient as a diagnostic tool [19, 20]. Lohman et al [21] confirmed that the degree of LSS and the CSA of the dural sac had no significant correlation with the severity of clinical symptoms. Our results also showed that the minimum CSA was not significantly different between the positive Sedsign group and the negative Sedsign group, at the same time, the ROC curve also showed that there was no significant correlation between the prevalence of a positive Sedsign and the minimum CSA. Thus, it is also believed that the CSA of dural sac and PAD of spinal canal can’t fully explain the involvement of nerves in LSS due to the great individual differences.

To further investigate the possible pathogenesis that leads to a positive Sedsign, we conducted a novel radiological parameter, the maximum cross-sectional area difference (CSAD) of the dural sac, to describe the narrowing change of the dural sac. In present study, we observed the sagittal and axial MR images of the patient with severe LSS who was determined to have a positive Sedsign at the L4/5 level(Fig. 5). The dural sac was pushed ventrally or toward the center of the spinal canal by posterior compression in the region where the most severe narrowing occurred (Fig. 5c), and the CSA was at its minimum in this scan image. However, the dural sac at the adjacent sites was less compressed, as shown in Fig. 5b, and the corresponding CSA was more normal. The maximum CSAD of the dural sac was large, which indicated an acute change in the dural sac between the most narrow section and the normal section. As a result, the nerve roots were pulled toward the center of the spinal canal and a positive Sedsign was observed on

the MR image. In contrast, when the maximum CSAD was small, there was only minor variation in the dural sac between the level at which narrowing occurred and normal levels, resulting in minimal displacement of the nerve roots and the absence of a positive Sedsign in the MR image at the levels adjacent to the stenosis. Meanwhile, the significant difference also were observed in the maximum CSAD between the positive group and the negative group, and the ROC curve result also showed that there was the highest correlation between the maximum CSAD and incidence rate of positive Sedsign. All these results suggested that the positive Sedsign is more closely related to a change in the dural sac caused by posterior compression at the level of stenosis, which may be the main reason for the appearance of sedimentation syndrome.

To verify the hypothesis, two posterolateral parameters, thickness of ligamentum flavum(TLF) and degeneration of facet joint(DFJ), were further assessed their correlation with the positive Sedsign. The ligamentum flavum and facet joint are the main structures that make up the posterior and lateral spinal canal walls, and has a protective effect on the spinal cord[22], which had been confirmed to be important roles in the development of LSS [23–25]. TLF and DFJ can induce a decrease in the central tube volume by compression from the behind a dural sac, which is the cause of LSS [26–28]. Therefore, we analyzed the TLF and DFJ between the two groups and found a significant difference for each of these parameters between the positive and negative groups. In addition, The ROC curve result also showed that a positive Sedsign was significantly correlated with the grade of DFJ and the TLF. All these demonstrated that a positive Sedsign was high related to risk factors from the posterior spinal canal. This would also explain why there is a different prevalence of a positive Sedsign between cases of severe LSS and moderate/mild LSS. The change of compressed dural sac was gently in patients with mild-to-moderate LSS, and for whom the MR images rarely show a positive Sedsign. However, when the dural sac(nerve roots or the cauda equina) was obviously squeezed from the posterior side and moved sharply toward the center or ventrally of the spinal canal at the level where stenosis occurred. The adjacent unaffected O nerve roots (or the cauda equina) were also pulled to shift center or ventrally of the spinal canal, a positive Sedsign was observed in MR images. Bartz et al[29] reported that a positive Sedsign was more common when the epidural pressure was increased in LSS patients, which also indirectly supports our results.

Of course, as LSS from complex pathophysiological changes, there are many factors that can decrease the volume of the spinal canal, such as lumbar kyphosis [30, 31], loss of physiological lordosis [32], giant central lumbar disc herniation [33, 34], and lateral recess stenosis [35], and can result in typical clinical symptoms of LSS. Not all LSS cases will show a positive Sedsign, which suggests that there are limitations of Sedsign determination in clinical practice. In addition, in the current study, we focused only on the distribution of Sedsign in patients with severe LSS. The validity of this theory on a wider scale is not currently known. Further study is needed to determine the distribution of a positive Sedsign among patients with mild-to-moderate LSS.

Conclusion

In summary, the incidence of a positive Sedsign was 85.52% among 290 levels with spinal canal narrowing in 209 patients with severe LSS in this study. The results show that a positive Sedsign can be used as a parameter to assist with the diagnosis of severe LSS, along with other criteria. The prevalence of a positive Sedsign showed a higher correlation with changes in the compression of the dural sac relative to other imaging parameters. Compression from the posterior spinal canal, such as thickening of the ligamentum flavum and facet joint degeneration, may be the main cause of a positive Sedsign.

Methods

1.1 Participants

This study was a retrospective review, which was approved by the ethics committee of Qiqihar Medical College in accordance with the Declaration of Helsinki. And all participants signed a informed consent when they were enrolled in the study. The MR images of patients with severe LSS were obtained from our hospital for individuals admitted for inpatient or outpatient treatment between January 2017 and June 2019, all of whom were consistent with LSS diagnostic criteria and were assessed for eligibility based on the following criteria: (1) a cross-sectional area (CSA) of the dural sac of ≤80 mm^2 for at least one level in an axial MRI scan; (2) typical intermittent claudication, with or without lower back pain or leg pain; and (3) walking distance ≤ 500 m. The exclusion criteria were as follows: (1) presence of lower extremity arterial occlusive syndrome, lumbar tumor, multiple nerve injury, spinal trauma, or limited mobility caused by osteoarthritis; (2) presence of coronary thrombosis or a previous stent surgery; (3) LSS at level L5/S1 was excluded because the S1 and S2 nerve roots leave the dural sac in a ventral position, inhibiting sedimentation to the dorsal part of the dural sac according to Barz et al. [11].

1.2 MRI data acquisition

A total of 209 patients who had undergone MRI examination of the lumbar spine were included in this study. MRI scans were made with a magnetic resonance instrument (HITACHI echelon 1.5T, Japan) and consisted of sagittal T1- and T2-weighted images and axial T2-weighted images (thickness, 4 mm; 20% gap size). All patients were imaged while in the standard supine position, with both legs straight. The scanning range covered L1/2 to L5/S1, and the three scans described above were acquired for each level. We used a complete digital image storage area measurement system (Accurad V4.0 software) to process the obtained data. All MRI parameters for each image scan were separately assessed by three radiologists who are experienced independent investigators. The mean value of the three calculations was used as the measurement for further analysis.

For each patient, the posteroanterior diameter (PAD) of the spinal canal was measured in three MRI scans of narrow levels as the distance between the midpoint of the posterior margin of the disc and the midpoint of the posterior wall of the spinal canal (Fig. 1a). The minimum PAD was used for further investigation as it is indicative of the narrowing of the spinal canal in the sagittal plane. The thickness of

the ligamentum flavum (TLF) was measured on axial T2-weighted MR images at the level of the facet joint as shown in Fig. 1b. The maximum TLF was determined as an indicator of dural sac posterior compression. In addition, the lumbar facet joints were graded on both the left and right side at levels L1/2, L2/3, L3/4, and L4/5, and then the average value was used to determine the degenerative facet joint (DFJ) grade. Four grades of DFJ were defined using criteria similar to those published by Kalichman et al. [36] and Weishaupt et al. [37]; these criteria are shown in Table 1.

1.3 Definition of the maximum cross-sectional area difference (CSAD)

The cross-sectional area (CSA) of the dural sac was measured based on the area bounded by the edge of the epidural sac (Fig. 1a) in each of the three MRI scans to determine the minimum CSA, which represents the absolute compression of the dural sac. To describe the change in the dural sac, we introduced the maximum cross-sectional area difference (CSAD) of the dural sac, which was calculated by subtracting the minimum CSA measured across the three scans at each level where stenosis had occurred from the maximum CSA; the difference represents the CSAD value for that particular level. A higher CSAD value indicates a greater change in the dural sac at the level of narrowing. Conversely, a lower CSAD value indicates a more gradual narrowing of the dural sac under pressure.

1.4 Determining the nerve root Sedsign

Patients were rated by the other three investigators as Sedsign positive or negative based on their MR images. In each axial T2-weighted image, a vertical line was drawn along the midpoint of the posteroanterior diameter of the spinal canal, and a horizontal line was drawn that divided the dural sac into an upper and lower part. A negative Sedsign was defined as having all caudae equinae located in the lower part of the dural sac with the exception of the two ventral nerve roots that exit caudal to the level at which the observations were made (Fig. 2a). A positive Sedsign was defined as an absence of cauda equina sedimentation because of the tight canal, a result of the distortion of the dural sac, with the majority of nerve roots located in the upper part of the sac (Fig. 2b). Where there was a disagreement between the raters, a consensus was reached between both investigators, who were assisted by another experienced independent investigator as a third opinion. All imaged levels for each individual] were classified as having a positive or negative Sedsign.

1.5 Statistical Analysis

Data are shown as the mean ± standard deviation. The *t*-test was applied for comparisons between the positive Sedsign group and the negative group. The receiver operating characteristic (ROC) curve was used to assess correlations between morbidity of positive Sedsign and parameters such as the minimum

CSA, minimum PAD, maximum TLF, grade of DFJ, and maximum CSAD. SPSS18.0 software was used for all statistical analyses, and $p < 0.05$ was considered as statistically significant.

Declarations

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Author contributions

Haiming YU: Methodology, Validation, Formal analysis, Investigation, Writing-original draft. Yunfeng HAN: Methodology, Software, Formal analysis, Investigation. Rui ZHANG: Data curation, Investigation. Chu SUN: Investigation, Data curation. Mingda WANG: Visualization, Software. Bo YUE: Resources, Investigation.Kaiping CHOU: Visualization, Software. Bin LI: Visualization, Investigation. Nan ZHANG: Supervision, Project administration, Conceptualization, Funding acquisition, Writing - review & editing.

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Tables

Table 1
Criteria for grading degeneration of the facet joint

Grade	Criteria
0	Normal facet joint space (2–4 mm wide)
1 2 3	Narrowing of the joint space (< 2 mm) and/or small osteophytes and/or mild hypertrophy of the articular process Narrowing of the joint space (< 1 mm) and/or moderate osteophytes and/or moderate hypertrophy of the articular process and/or mild subarticular bone erosions Severe narrowing of the joint space and/or large osteophytes and/or severe hypertrophy of the articular process and/or severe subarticular bone erosions and/or subchondral cysts and/or vacuum phenomenon in the joints

Table 2
Distribution of a positive Sedsign across 290 levels of LSS

Distribution	Sedsign (positive)	Sedsign (negative)	Morbidity
L1/2 level	2	0	100%
L2/3 level	12	0	100%
L3/4 level	76	11	87.36%
L4/5 level	158	31	83.6%
Total	248	42	85.52%

Figures

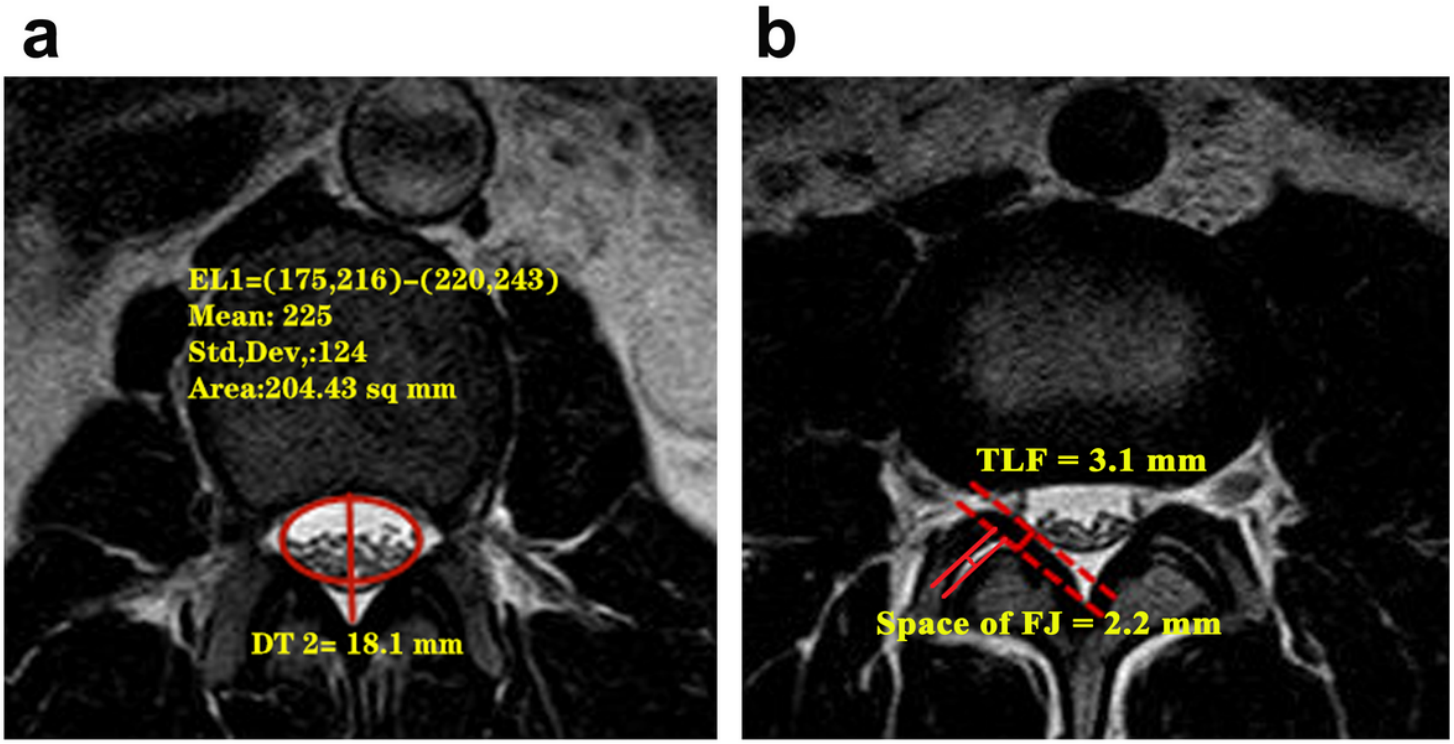

Figure 1

a: Measurement of the cross-sectional area (CSA) of the dural sac and the posteroanterior diameter (PAD) of the spinal canal. b: Measurement of the thickness of the ligamentum flavum (TLF) and the space of the facet joint (FJ) which can used to evaluate DFJ.

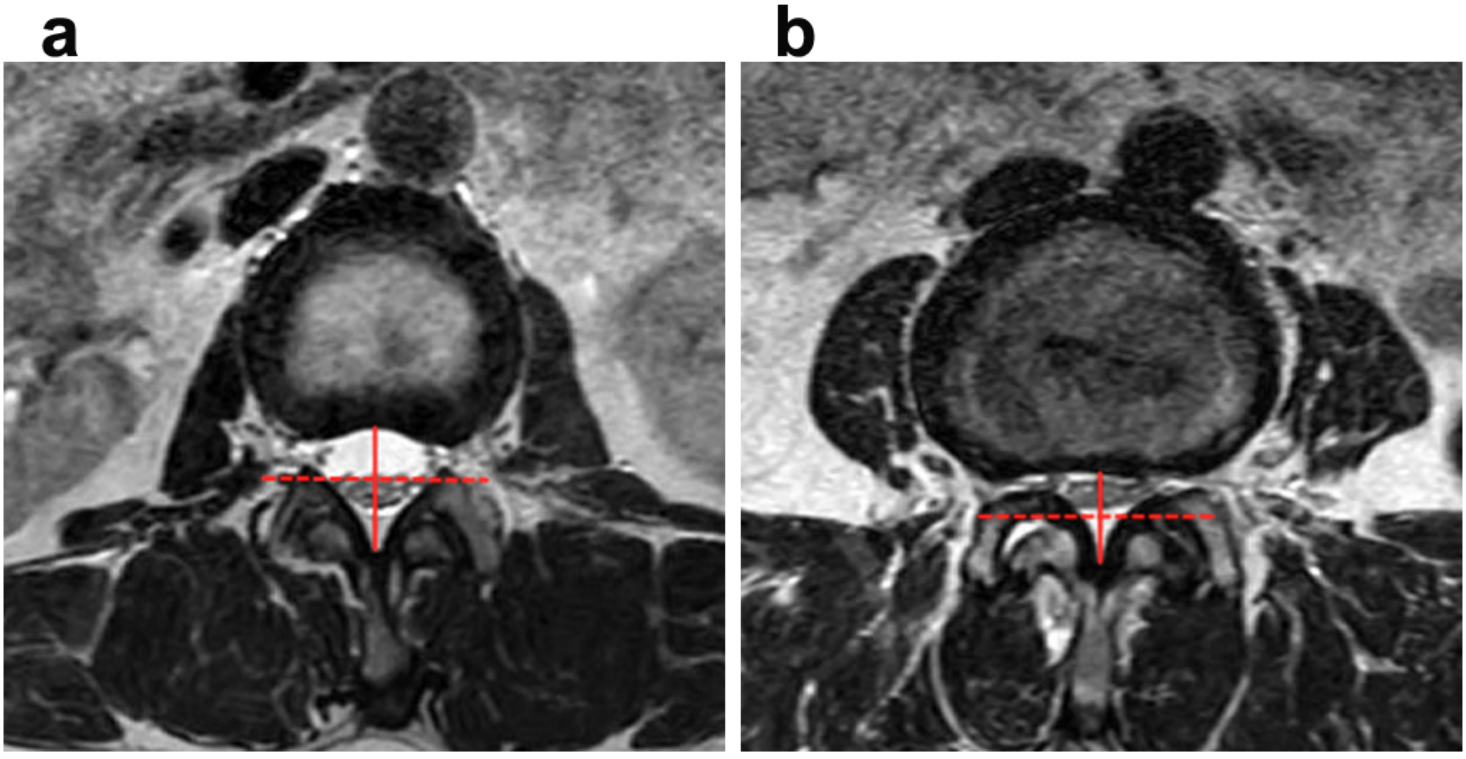

Figure 2

a: A negative SedSign was defined as having all caudae equinae located in the lower part of the horizontal red dashed line with the exception of the two ventral nerve roots that exit caudal to the level at which the image was taken. b: A positive SedSign was defined as an absence of cauda equina sedimentation, and a “squashing” of the dural sac, with the majority of nerve roots located above the horizontal red dashed line. The horizontal dashed line passes through the midpoint of the posteroanterior diameter of the spinal canal(the red solid line).

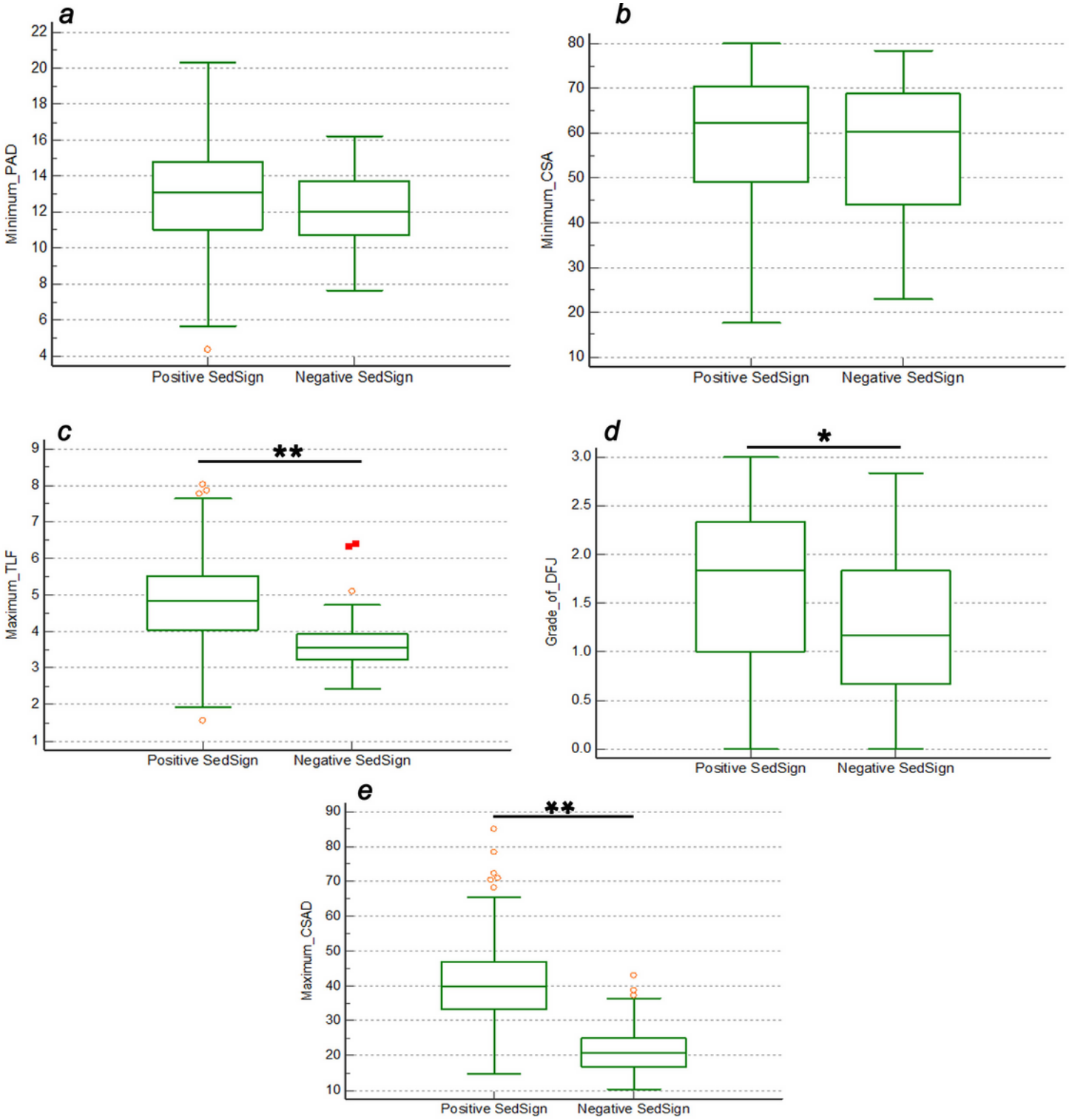

Figure 3

The MRI parameters were evaluated between the positive Sedsign group and the negative Sedsign group. a: The minimum CSA. b: The minimum PAD. c: The maximum TLF. d: The grade of DFJ. e: The maximum CSAD. *p < 0.05 and **p < 0.01.

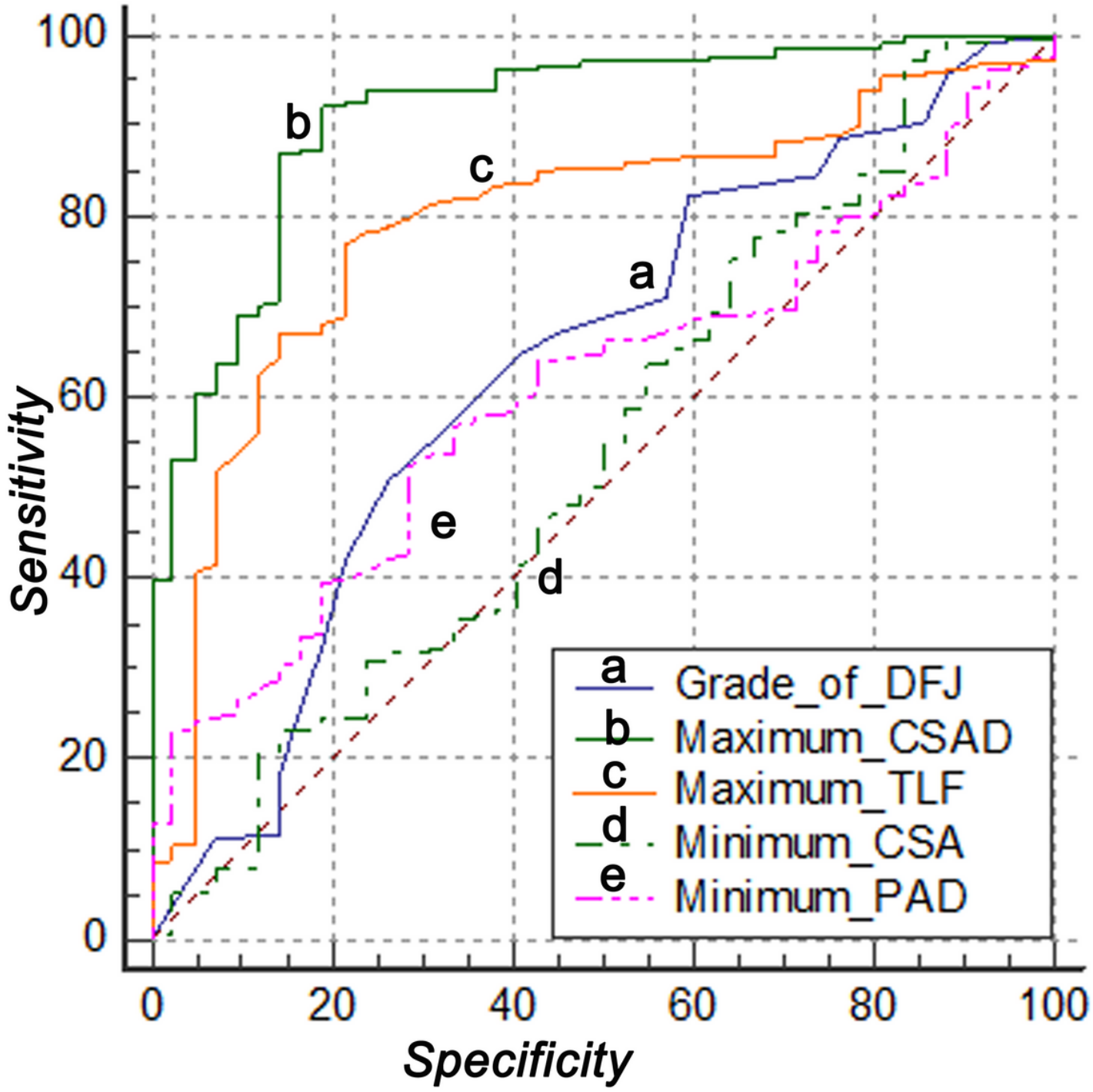

Figure 4

Correlation between the prevalence of a positive Sedsign and a minimum CSA and PAD, grade of DFJ, and maximum TLF and CSAD. The area under the ROC curve (AUC) for minimum CSA was 0.543 (95% CI: 0.4840.601, p > 0.05). The AUC for minimum PAD was 0.608 (95% CI: 0.55[0]0.665, p < 0.05). The AUC for

the grade of DFJ was 0.634 (95% CI: 0.5760.69[0], p < 0.05). The AUC for maximum TLF was 0.793 (95% CI: 0.7420.839, p < 0.01). The AUC for maximum CSAD was 0.913 (95% CI: 0.8750.943, p < 0.01).

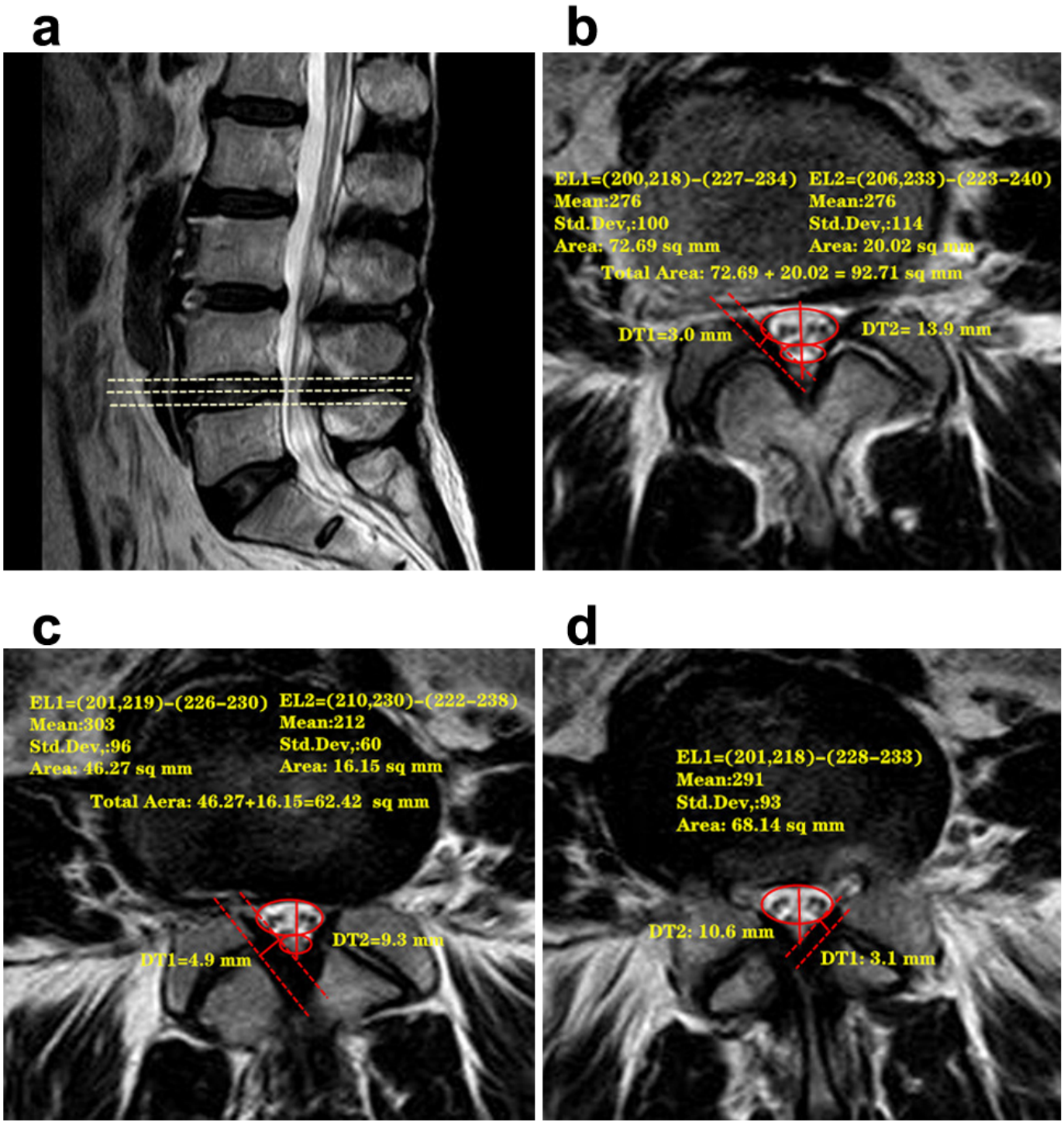

Figure 5

The relationship between a positive Sedsign and a change in the CSA of the dural sac at the level of stenosis. a: A sagittal T2-weighted image of L4/5 shows compression of the dural sac because of substantial narrowing in the third MRI scan. b: The first transverse layer of level L4/5, at which point the

dural sac was lightly compressed, and there was minimal tendency of the never roots or cauda equina to move ventrally or toward the center of the spinal canal. A suggestion of a positive Sedsign was observed, although not definitively. c: The second transverse layer of level L4/5 OR MR image, at which point the narrowing of the dural sac was increased, the nerve roots were shifted substantially, and a positive Sedsign was present. d: The third transverse layer of level L4/5 showed the greatest stenosis. Because of the narrowing of the canal, the nerves were “squashed” and therefore present on both sides of the equator, such that a positive Sedsign was apparent.