

An analysis of clinical risk factors for adolescent scoliosis caused by spinal cord abnormalities in China: Proposal for a selective whole-spine MRI examination scheme

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Abstract

Objective This study examined the risk factors for non-idiopathic scoliosis with intramedullary abnormalities (IA). **Method** The clinical data of adolescent patients between July 1, 2013, and December 31, 2018, were reviewed. According to the whole-spine MRI results, the patients were divided into either the idiopathic group or the intramedullary abnormality group. 12 data were compared between the two groups. Student's t test and the chi-square test were used to evaluate the differences in the continuous variables and categorical variables. Logistic regression was used to evaluate the correlation between the multivariate risk factors and intramedullary abnormalities. **Result** A total of 714 adolescent patients with scoliosis with a mean age of 13.5 (10-18 years) were included in the study, and IA were found in 68 (9.5%) patients. There were statistically significant differences in the incidence rates of intramedullary abnormalities between males and females, left and right thoracic curvatures, angular scoliosis and smooth scoliosis, and abnormal abdominal wall reflex and ankle clonus ($P < 0.01$). Logistic regression showed that the ratios for sex, scoliosis direction, scoliosis type, abdominal wall reflex and ankle clonus were 2.987, 3.493, 4.823, 3.94 and 8.083, respectively. The ROC curve showed a sensitivity of 66.18% and a specificity of 89.01% (0.5519). **Conclusion** The incidence of scoliosis caused by IA was approximately 9.5%. The risk factors associated with AS caused by abnormal IA included the male sex, thoracic scoliosis on the left side, a sharp curvature of the spine, an abnormal abdominal wall reflex and ankle clonus.

Background

Scoliosis is a common three-dimensional spinal deformity that can be clearly diagnosed with a physical examination. Scoliosis can be classified as idiopathic, congenital, or neuromuscular scoliosis; neurofibromatosis scoliosis; spinal scoliosis caused by intramedullary abnormalities; etc. Idiopathic scoliosis is the most common form, accounting for approximately 75-85% of all scoliosis cases^{1,2}. Magnetic resonance imaging (MRI) is the gold standard for identifying idiopathic scoliosis, but the cause of scoliosis often remains unidentified due to the associated high costs and poor medical environments, e.g., long wait times and a lack of MRI equipment³.

Intramedullary abnormalities can lead to scoliosis deformities, including Chiari malformations, syringomyelias, and hydromyelias⁴. Idiopathic scoliosis is difficult to diagnose based on a patient's appearance. The gold standard MRI examination is not a routine scoliosis examination; therefore, patients with scoliosis caused by spinal cord abnormalities are easily misdiagnosed with idiopathic scoliosis, but there are differences in the treatment methods for these two forms of scoliosis⁵. The early treatment of idiopathic scoliosis is primarily supportive, and surgical correction may be required if the scoliosis continues to progress. Spinal scoliosis with intramedullary abnormalities should first be treated with neurosurgery to resolve the cause of scoliosis. Patients who are misdiagnosed and treated for idiopathic scoliosis who undergo direct scoliosis correction may suffer permanent nerve damage, leading to serious complications, such as lower limb weakness, pain and numbness, and even paralysis⁶. On the other hand, the early detection of scoliosis caused by intramedullary abnormalities and timely

neurosurgical treatment can prevent further exacerbation; therefore, some scholars believe that MRI should be a routine examination for patients with scoliosis. However, other scholars believe that because the incidence of scoliosis caused by intramedullary lesions is low, MRI screening is a waste of money, time and medical resources; therefore, the diagnosis of scoliosis does not require an MRI examination, and an MRI examination can cause panic among patients, which is still the focus of debate⁷.

In recent years, several articles have suggested that MRI examination of scoliosis patients is necessary. Studies have found that the incidence of scoliosis with spinal cord abnormalities is 6.3% to 9.9%^{3,4}. However, considering the current medical situation in China, it is particularly difficult for all patients with scoliosis to undergo an MRI examination of the whole spine. Therefore, this study aims to explore the risk factors for scoliosis caused by intramedullary abnormalities, identify the patient population that would benefit from selective MRI examination, explore the feasibility of MRI examination and provide a theoretical basis for the routine diagnosis and treatment of scoliosis.

Method

The ethics committee approved the review of adolescent scoliosis surgery cases in Shanghai Tongren Hospital and Shanghai Changhai Hospital before December 2018 for this retrospective study.

1. Research Objective

- (1) Inclusion criteria: patients with scoliosis aged 10-18 years with complete spinal X-ray and MRI data.
- (2) Exclusion criteria: patients with congenital scoliosis (bone dysplasia), neuromuscular scoliosis, neurofibromatosis scoliosis, metabolic scoliosis, Marfan syndrome and other clearly diagnosed scoliosis types.
- (3) Groupings: the spinal cord abnormality group (Group A) contained patients who exhibited lesions in the spinal cord, such as Chiari malformations, syringomyelia, and hydromyelia, on MRI examination. The idiopathic group (Group B) contained patients with no abnormalities on MRI examination.

2. Data Measurement and Recording

- (1) General information: age and sex.
- (2) Imaging examination: angle of the main bend, scoliosis direction (thoracic scoliosis on the left, thoracic scoliosis on the right), angle of thoracic vertebrae kyphosis, and scoliosis shape (Figure 1, smooth shape is the concave side line is a smooth curve, angular shape is the concave side line is a angular curve).
- (3) Neurologic examination: assessment of motor, sensory, and reflex functions of the upper and lower extremities; pathologic signs; abdominal reflexes; tendon reflexes (radial membrane reflex, knee reflex, Achilles tendon reflex); paraesthesia; and ankle clonus.

3. Clinical and Imaging Evaluation

A whole-spine 1.5 T Philips MRI machine (Philips, the Netherlands) was used to detect potential spinal abnormalities, including Chiari malformations, syringomyelia, vertebral compression, longitudinal spinal fractures, and spinal cord tumours. All diagnoses were made by a spine surgeon and reviewed by an experienced radiologist. According to the MRI findings, patients were assigned the spinal cord abnormality group or the idiopathic group to determine the imaging and clinical indicators of spinal cord abnormalities in the two groups.

Positive and lateral X-ray images of the whole spine were taken to measure the Cobb angle, scoliosis direction, scoliosis shape, thoracic kyphosis angle from T5 to T12 in the sagittal plane (defined as kyphosis deformity if the angle was greater than 10 degrees), the coronal plane balance (according to the central sacral vertical line (CSVL)), and the sagittal plane balance (according to the C7-S1 line) in the main bend. CSVL: A line passing through the midpoint of the upper edge of S1 perpendicular to the horizontal plane. C7-S1: The distance between the plumb line of C7 and the upper edge of S1.

4. Statistical Analysis

Sex, age, main curvature angle, kyphosis angle, scoliosis direction, scoliosis type, coronal plane balance, sagittal plane balance, abdominal wall reflex, sensory abnormalities, ankle clonus and tendon reflexes were compared between the spinal cord abnormality group and the idiopathic group. Statistical analyses were performed using the SPSS 21.0 statistical package (SPSS Inc., Chicago, IL). Continuous variables were compared using t tests, and rates were compared using chi-square tests. Fisher's exact test was used to compare the rates of internal abnormalities between the groups. Logistic regression was used to evaluate the correlation between multiple variables and the incidence of intramedullary abnormalities, with the following values: intramedullary abnormalities =1 and no abnormalities =0. A p value less than 0.05 was defined as statistically significant.

Results

Patient data from July 2013-December 2018 were retrieved from Tongren Hospital in Shanghai and from Shanghai Changhai Hospital. A total of 714 adolescent patients with scoliosis met the inclusion criteria. The patients had an average age of 13.5 (10 to 18) years, and 68 (9.5%) patients presented intramedullary abnormalities. Thirty-one patients underwent neurosurgical procedures, such as cerebellar tonsillar hernia resection, expanded foramen magnum decompression, vertebral reconstruction, and spinal cord cavity catheter drainage. The patients' characteristics are shown in Table 1.

There were significant differences in the incidence rates of intramedullary abnormalities between males and females, patients with left and right thoracic curvatures, patients with angular scoliosis and smooth scoliosis, and patients with abdominal wall reflex abnormalities and ankle clonus. There were no significant differences between the other influencing factors, as shown in Table 2.

Logistic regression showed that patients with intramedullary abnormalities were 2.987 times more likely to be male, were 3.493 times more likely to present scoliosis on the left thoracic side, were 4.823 times more likely to have lateral smooth scoliosis, were 3.94 times more likely to have abnormal abdominal wall reflexes, and were 8.083 times more likely to have ankle clonus than patients with idiopathic scoliosis, as shown in Table 3.

Regression equation:

Logit (P)=-3.522+1.094 sex +1.251 scoliosis direction +1.573 scoliosis shape +1.371 abdominal wall reflex +2.090 ankle clonus

The area under the receiver operating characteristic (Receiver Operating Characteristic,ROC) curve for the incidence of intramedullary abnormalities was 0.842 (95% confidence interval: 0.813-0.868, P<0.001). The sensitivity was 66.18%, the specificity was 89.01%, and the Youden index corresponding to the optimal critical point was 0.5519, as shown in Figure 2. The ROC reflects the relationship between the sensitivity and specificity of the prediction formula. Generally speaking, an AUC(Area Under Curve) between 0.7 and 0.9 indicates high accuracy of the prediction formula. Figure 3 shows a 13-year-old female who weighed 38 kg, was 138 cm tall and had a spinal deformity for 1 year.

Coronal Plane: T1-T6: 35°, T7-L3:100°, CB: 22 mm, Risser: 0~I°

Sagittal Plane: T2-T5: 13°, T5-L12: 21°, L1-L5: 25°, SVA: 19 mm

The patient presented left thoracic curvature, right lumbar curvature, an abnormal abdominal wall reflex, paraesthesia, and ankle clonus.

The whole-spine MRI showed a Chiari malformation and syringomyelia.

First step: In the first step of the patient's treatment, Neurosurgery department performed posterior fossa decompression. Second step: In the second step, Spinal surgery was performed to correct scoliosis from T4 to L4. Spinal surgery was performed 3-6 months after neurosurgery.

Discussion

According to the appointment registration statistics of major hospitals in Shanghai, the wait time for a spinal MRI appointment is approximately 4 weeks, and the cost of an MRI examination for a single spinal section (cervical spine, thoracic spine, and lumbar spine) is 460 RMB(65 USD). A whole-spine MRI examination costs 1380 RMB(196 USD); however, 90% of the cost will be reimbursed by Shanghai Medical Insurance, and only 10% will be paid by the patients themselves. So the MRI is still a cost-effective test and I want to call on the patient to have an MRI. There were a lot of severe scoliosis due to no early diagnosis, and I thought if we could find it early by MRI, we could treat it early.

According to previous studies and this study, the incidence of intramedullary abnormalities in patients initially diagnosed with idiopathic scoliosis is approximately 6.3% to 9.9%⁴. As 90.1% to 93.7% of patients have idiopathic scoliosis, a whole-spine MRI to determine whether there is an intramedullary abnormality could be considered a waste of resources. Therefore, some scholars believe that whole-spine MRI is not necessary for idiopathic scoliosis patients⁸. However, there have been cases of spinal cord injury in patients with idiopathic scoliosis who underwent surgical correction, with very serious consequences⁹. The purpose of this study was to develop accurate intramedullary abnormality screening criteria to reduce medical resource waste. A retrospective study with a large sample size found that intramedullary abnormalities were associated with five risk factors. The results showed that if the incidence of the five factors associated with intramedullary abnormality was 66.18%, an MRI should not be conducted, but if the incidence rate of the five factors was 89.01%, the patient should undergo a whole-spine MRI. Therefore, regarding selective whole-spine MRI, applying the five risk factors as a condition for whole-spine MRI can improve the whole-spine MRI intramedullary abnormality positivity rate and reduce unnecessary medical treatments. This scheme is completely feasible in the current Chinese medical environment. The more consistent the risk factors are, the higher the probability of intramedullary abnormalities will be. Selective examinations can be conducted for high-risk patients to further clarify the aetiology of adolescent scoliosis, which provides a theoretical basis for selective MRI examination and has important clinical practical significance.

There are not many relevant studies searched on pubmed. Choon et al⁹ suggested that males and patients with increased thoracic kyphosis are risk factor. Zhang et al¹⁰ considered that aged less than 10 years, being male or having left thoracic or right lumbar curve are risk factor. Beyond that long curve span, apex at thoracolumbar spine and hyperthoracic kyphosis and so on are also risk factor^{3,6-8,10-25}. This study includes the second largest research sample to date. The risk factors identified in this study can be divided into three categories, namely, general, imaging, and neurologic characteristics; a total of 12 clinical indicators were included in the correlation analysis. The content of this study is more comprehensive than that in previous studies.

This study retrospectively analysed the incidence of intramedullary abnormalities in adolescent scoliosis patients and proposed the idea of selective whole-spine MRI examination, which has a strong guiding role in clinical work. However, this study had the following limitations. 1. Patients from two hospitals were included in the analysis, and this study contains the second largest sample size (714 patients) in the current literature. However, the sample size is still insufficient to study disease incidence, although this did not affect the research conclusion. 2. Although 12 factors were included in this study, the specificity (66.18%) and sensitivity (89.01%) for predicting intramedullary abnormalities still require further improvement; the factors affecting intramedullary abnormalities included in this study are not sufficiently comprehensive. 3. Due to the limitations of retrospective studies, the data must be supplemented with additional prospective studies that include further analyses of influencing factors and larger sample sizes to obtain more-conclusive research results.

In this study, the incidence of adolescent scoliosis caused by an intramedullary abnormality was 9.5%. MRI assessment showed that the spinal cords of patients were not excessively damaged. We recommend that high-risk patients (males and those with a lateral thoracic spine angle on the left side of the curve, an angular curve, abdominal wall reflection and ankle clonus) undergo selective spinal MRI, because neurological complications (paraplegia, nerve damage, etc.) can cause irreparable damage. These complications can be prevented by preoperative management. For example, syringomyelia causes scoliosis, and scoliosis correction before appropriate neurosurgery or surgical interventions can avoid spinal cord damage during scoliosis correction surgery. Therefore, the spine surgeon should pay close attention to the diagnosis of preoperative patients. Currently, we are using this method to conduct a prospective study on high-risk adolescent patients with scoliosis to further verify the feasibility of this method and further identify risk factors while increasing the sample size to further improve the prediction equation.

Conclusion

Adolescent scoliosis caused by intramedullary abnormalities is associated with male sex, thoracic scoliosis on the left side, a sharp curve, abdominal wall reflection and ankle clonus. The incidence of adolescent scoliosis caused by intramedullary abnormalities was approximately 9.5%. Clinical indicators suggest that there is a high-risk population of adolescent patients with scoliosis who should undergo whole-spine MRI preoperatively to rule out intramedullary abnormalities.

Abbreviations

Magnetic Resonance Imaging,MRI

Central Sacral Vertical line,CSVL

Receiver Operating Characteristic,ROC

Area Under Curve,AUC

Declarations

Ethics approval and consent to participate.If the participant is a child (under 16) from a parent or guardian, the informed consent to participate has been obtained.

This retrospective study was approved and consented to participate by the Ethics Committee

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing financial interests to disclose and no financial conflicts of interest exist for any of the authors.

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Authors' contributions

XW, ZXY and ZY conceived and designed the study. CLW,LDC and JJJ measured and recorded the data. LZK and ZXD wrote the paper. WSL, BYS and LM reviewed and edited the manuscript. All authors read and approved the manuscript.

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Availability of data and materials

not applicable

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Tables

Table.1 Overview of spinal anomalies

Anomalies	Number of cases (%)
Isolated Arnold-Chiari malformation	49.5%
Arnold-Chiari malformation combined with syringomyelia	20.1%
Isolated syringomyelia	10%
Tethered cord combined with diastematomyelia	6%
Diastematomyelia	6%
Tethered cord	4%
Intrinsic spinal cord tumor	3%
Syringomyelia combined with tethered cord and tumor	1%
Total number	68

Table.2 Comparison between patients with and without neural abnormality on MRI screening examination

	Intramedullary Abnormalities n=68	Idiopathic n=646	P
Gender			
Male[1]	38	148	<0.01 ^b
Female[0]	30	498	
Age	14.1±1.9	14.3±1.7	NS ^a
Imaging			
Main Cobb	39.6 ± 8.1°	36.1 ± 11.7°	NS ^a
Left Thoracic curve[1]	15	74	0.012 ^b
Right Thoracic curve[0]	53	572	
T-Kyphosis[1]	17	50	<0.01 ^b
No T-Kyphosis[0]	51	596	
Angular curve[1]	16	61	<0.01 ^b
Smooth curve[0]	52	585	
The trunk balance			
Coronal-imbalance[1]	5	42	NS ^b
Coronal-balance[0]	63	604	
Sagittal-imbalance[1]	9	70	NS ^b
Sagittal-balance[0]	59	576	
Nervous System			
Abnormal abdominal wall reflex[1]	19	40	<0.01 ^b
No-Abnormal abdominal wall reflex[0]	49	606	
paresthesia[1]	10	52	0.064 ^b
euesthesia[0]	58	594	
Ankle clonus[1]	15	49	<0.01 ^b
No-Ankle clonus[0]	53	597	
Abnormal tendon reflex[1]	16	65	0.001 ^b
Normal tendon reflex[0]	52	581	

a The student t test

b the chi-square test

NS indicates no statistical significance

Table 3. Logistic regression results

	B	P	OR	95%CI
Gender	1.094	<0.01		1.612-5.534
Female			1	
Male			2.987	
Direction of Scoliosis	1.251	<0.01		1.756-6.948
R-Thoracic curve			1	
L-Thoracic curve			3.493	
T11-L2 Cobb	-0.974	0.054		0.140-1.016
Normal			1	
Kyphosis			0.377	
Shape of Curve	1.573	<0.01		2.278-10.211
Smooth curve			1	
Angular curve			4.823	
Coronal Plane	-0.858	0.112		0.147-1.223
Imbalance			1	
Balance			0.424	
Sagittal Plane	-0.226	0.637		0.312-2.041
Imbalance			1	
Balance			0.798	
Abdominal reflexes	1.371	<0.01		1.810-8.574
Normal			1	
Abnormal			3.940	
Feeling	-0.119	0.817		0.324-2.433
Normal			1	
Abnormal			0.888	
Ankle Clonus	2.090	<0.01		3.945-16.562
Normal			1	
Abnormal			8.083	
Tendon Reflex	-0.828	0.088		0.168-1.132
Normal			1	
Abnormal			0.437	
Constant	-3.522	<0.01	0.030	

Table 4. Recent 10 years of research on abnormal scoliosis in the spinal cord on Pubmed

Reference	Year	Author	Cases	Incidence Rate	Risk Factors
	2018	Li Zhikun	714	68(9.5%)	male, thoracic scoliosis on the left, Sharp curve, abdominal wall reflection anomaly and ankle clonus anomaly
3	2017	Pereira EAC	71	4(5.6%)	-
9	2017	Choon Sung Lee	378	24(6.3%)	Males and patients with increased thoracic kyphosis
10	2016	Wen Zhang	504	94(19%)	aged less than 10 years, being male or having left thoracic or right lumbar curve.
11	2016	Faizah	19	5(26%)	Cobb angle progression is not a reliable indicator for predicting neuroaxial abnormality in patients with asymptomatic AIS.
12	2015	Ameri	271	27(10%)	The incidence of neuroaxial abnormalities was higher in male patients and in those with early onset disease.
13	2014	Karami	143	17(12%)	A total spine MRI is recommended at presentation in patients with younger age, abnormal neurologic findings and severe coronal shift.
6	2014	Martin	43	7(16%)	For younger patients with small curves (<30 degrees) who do not require orthopedic treatment, MRI under sedation can be delayed or avoided.
14	2013	Koç	72	8(11%)	-
15	2013	Qiao	446	35(8%)	right curves, long curve span, apex at thoracolumbar spine and hyperthoracic kyphosis.
16	2013	Singhal	206	20(10%)	There was no statistically significant difference between the group of patients who had intrinsic spinal cord anomalies on preoperative MRI and those did not have a cord abnormality with regard to age at presentation, gender, side of dominant curve and degree of curve
17	2012	Lee	171	15(9%)	Our audit demonstrates that neither coronal nor sagittal misbalance should be used as an indicator of neural axis abnormalities.
18	2011	Nakahara	472	18(4%)	We recommend routine use of MRI in male patients, younger than 11 years old, and abnormal superficial abdominal reflexes. Even if a patient has no specific indications for MRI, we recommend its routine use in preoperative planning.
7	2011	Diab	923	91(10%)	Significant risk factors for neural abnormality were thoracic hyperkyphosis and juvenile onset. Other characteristics, including apex left thoracic curve, Risser less than or equal to 1, large curve magnitude, triple major curve, male sex, and obesity were not associated with neural abnormality. There were no differences in complication rates between normal and abnormal MRI patients. Our data question the routine use of MRI as a screening tool for adolescent idiopathic scoliosis.
19	2010	Wu	70	37(54%)	When a left thoracic curve pattern is present in patients with "idiopathic" scoliosis, especially in male patients or patients with severe curve, strong consideration should be

					given to the possibility of the presence of neural axis abnormalities, and acquisition of an MRI scan considered.
²⁰	2010	Richards	529	36(7%)	with those having increased rotation and/or increased kyphosis at higher risk.
²¹	2010	Rajasekaran	94	15(16%)	The high incidence of intraspinal anomalies in presumed idiopathic scoliosis in our study group emphasizes the need for detailed examination for subtle neurological signs that accompany neuro-axial anomalies. Preoperative MRI screening is recommended in patients with presumed 'idiopathic' scoliosis who present at young age, with neurological findings and in curves with apical thoracic kyphosis.
²²	2009	Pahys	54	7(13%)	This study represents the largest evaluation of intraspinal anomalies in IIS to date. Our patient population exhibited a smaller percentage (13%) of neural axis abnormalities than previously reported. On the basis of these findings, the close observation may be a reasonable alternative to an immediate screening MRI in patients presenting with presumed IIS and a curve >20 degrees.

Figures

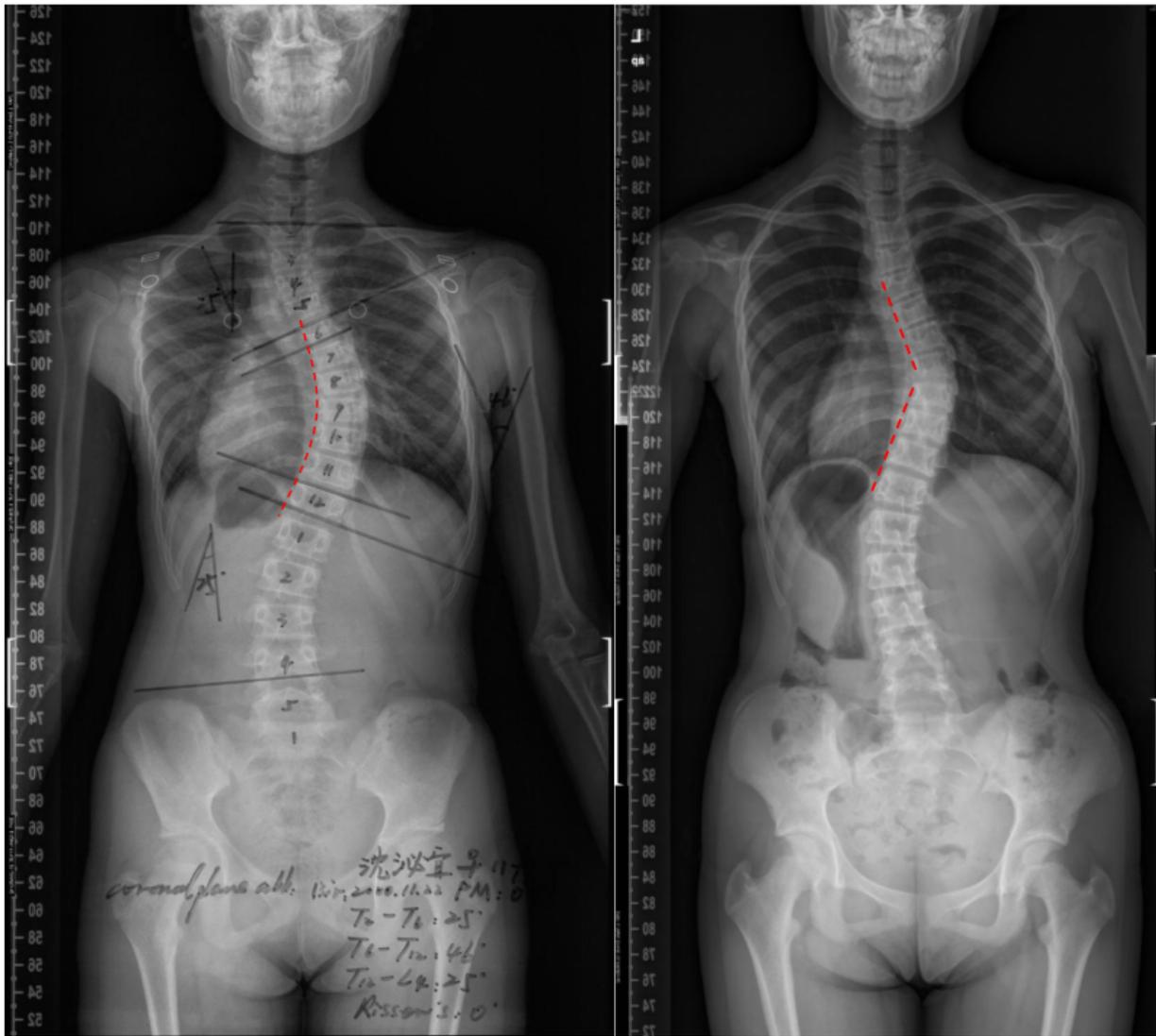


Figure 1

smooth shape is the concave side line is a smooth curve, angular shape is the concave side line is a angular curve

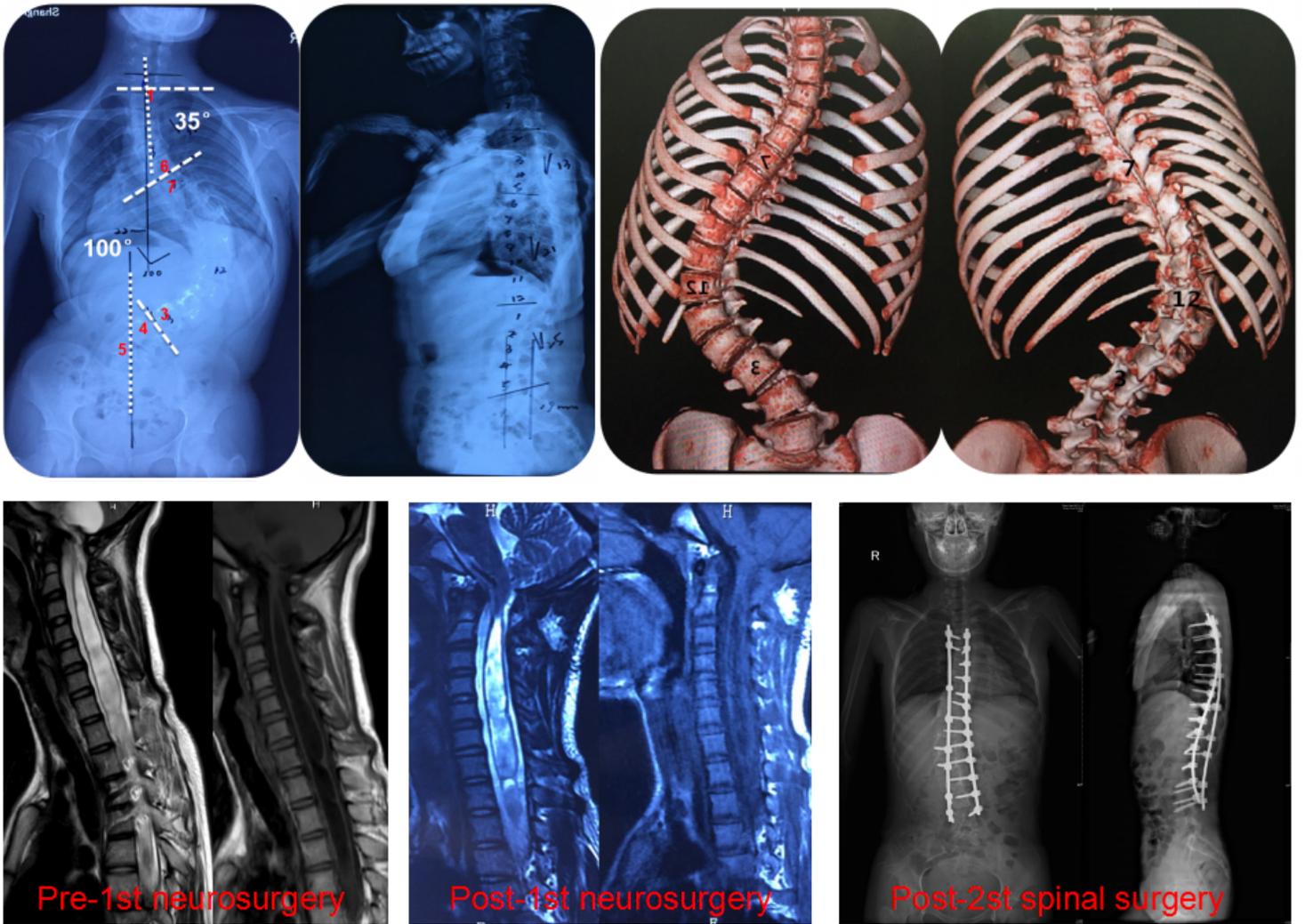


Figure 2

The sensitivity was 66.18%, the specificity was 89.01%, and the Youden index corresponding to the optimal critical point was 0.5519

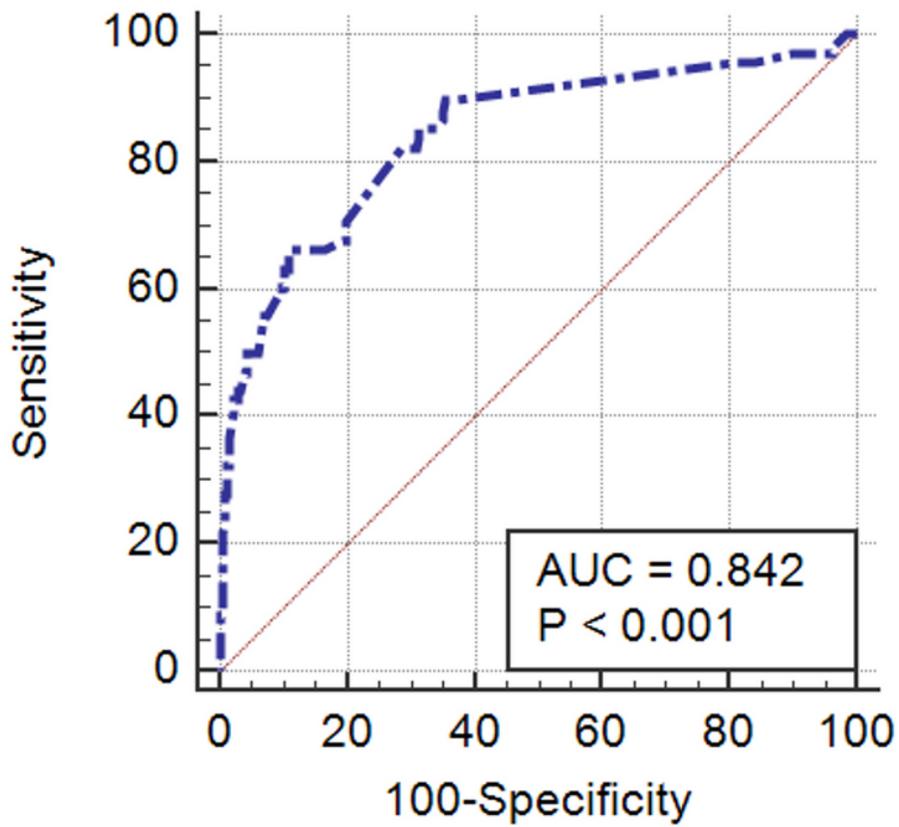


Figure 3

13-year-old female who weighed 38 kg, was 138 cm tall and had a spinal deformity for 1 year.