Cervical spine fracture prediction by simple plain X-ray in ankylosing spondylitis patients after low-energy trauma

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Research article

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Abstract

Background Due to various reasons, the diagnosis of cervical spine fracture (CSF) in patients with ankylosing spondylitis (AS) may be missed or delayed in clinical practice.

Objective To explore the prediction ability of simple plain X-ray for the possibility of CSF in AS patients who suffer from low-energy trauma (LET).

Methods From January 2010 to December 2019, AS patients who experienced LET were retrospectively reviewed. Their clinical data, including gender, age, body mass index, time interval between AS diagnosis and trauma, smoking or not, and a presence of continuous bony bridge between anterior margin of C1 and C2 body or not was collected. Besides, distances and angles were measured by the lateral cervical X-ray.

Results 129 AS patients were divided into Fracture group (41 cases) and Non-fracture group (88 cases) based on whether CSF existed. A total of twelve parameters had significantly statistical differences between two groups ($P < 0.05$). According to the binary logistic regression model, four of the twelve parameters showed a further correlation with the occurrence of CSF after LET in AS patients, namely, mean Pavlov ratio ($P < 0.001$, OR = 0.067), Angle D ($P = 0.031$, OR = 1.057), Borden's index ($P = 0.042$, OR = 1.131), the time interval between the AS diagnosis and the trauma ($P < 0.020$, OR = 0.935). Their 95% CI were (0.023 to 0.194), (1.005 to 1.112), (0.994 to 1.287), and (0.883 to 0.990), respectively. The ROC curve and the AUC further revealed the mean Pavlov ratio had the largest AUC (0.793) (95% CI: 0.873 to 0.986), whose cut-off value was 0.72 based on the highest Youden's index value. The optimal cut-off value, sensitivity, and specificity of the other three parameters were Angle D (45.65°, 61.0%, 78.4%), Borden's index (9.79, 87.8%, 37.5%), and the time interval between AS diagnosis and trauma (15.50 years, 70.7%, 56.8%).

Limitations The number of the included patients in the present study was relatively small.

Conclusions Four parameters measured by simple X-ray show prediction ability for the occurrence of CSF in AS patients who encounter LET.

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease which predominantly affects the axial skeleton, causing ossification of paraspinal ligaments and intervertebral discs, leading to the decrease of spinal flexibility [1]. With inflammation progression, osteoporosis and deformity gradually develop in the involved spine with the typical appearance of bamboo spine [2, 3]. Besides, AS is associated with impaired balance and difficulty in taking protective measures during a fall due to flexibility loss. These adverse factors jointly lead to high incidence of post-traumatic spine facture in AS patients, even after a low-energy trauma (LET) [4, 5]. Generally, the cervical spine is most prone to fracture in AS patients, accounting for up to 78% of all AS spinal fractures [6]. Timely diagnosis is an essential prerequisite for both prompt, effective intervention and favorable prognosis in the therapeutic strategy of cervical spine fracture (CSF) with AS (ASCSF).

Plain X-ray is usually employed in the initial examination of emergency patients suffering from accidental trauma, but revealing the fracture configuration is not sufficient to ASCSF diagnosis and is difficult for interpretation by non-expert doctors. Simple two-dimensional X-ray images cannot clearly display anatomical structures and minor fracture lines. Even when a fracture is clinically suspected, the diagnosis can be difficult on the basis of X-ray alone, given the highly abnormal spinal structure in patients with AS, including ossified ligaments, surrounding osseous proliferation, poor outlining of the disc space, and osteoporosis [7, 8]. Moreover, the diagnosis may be complicated by the presence of long-standing pain and the application of corticosteroid therapy and NSAIDs, which can mask the acute fracture symptoms [9]. In a study by Caron *et al.*, 30% of the AS cases with spine fractures did not initially obtain correct diagnosis [10]. Additionally, Anwar *et al.* [7] found that the diagnosis was missed in up to 59.4% of the cases when conventional radiography was used. Unfortunately, such a delay could result in kyphosis worsening and an increase in the risk of neurological complications. In clinical practice, although computed tomography (CT) and magnetic resonance imaging (MRI) can help to detect obscure fractures that are not visible on plain radiographs [11, 12], these techniques are costly and require longer appointment intervals, and thus these advanced examinations might not be readily available to patients suffering from LET. Therefore, the risk of missed diagnosis would be decreased and the service efficiency would be improved if the risk of ASCSF could be predicted *via* simple X-ray radiography, followed by CT or MRI, reasonably recommended based on the predicted results.

In the present study, we attempted to predict the risk of ASCSF in patients suffering from LET from daily life by measuring certain radiological distances and angles. To our knowledge, no existed reports have mentioned such an exploration. Our hypothesis was that reasonable radiographical predictors could effectively increase potential for early diagnosis of CSF in AS patients suffering from trivial trauma and symptoms and would further contribute to the reduction of the occurrence of disastrous complications due to delayed or missed diagnosis. Our research findings will be crucial to clinical emergency practice, especially considering that ASCSF in most cases was caused by LET according to previous reports [4, 7].

Materials And Methods

Study design

From January 2010 to December 2019, AS patients who experienced LET such as simple falls from standing or sitting height were initially recruited in this retrospective study. The following inclusion criteria were applied: (1) age over 18; (2) good mental health; and (3) complete post-traumatic CT or MRI that confirmed the existence of cervical fracture. The exclusion criteria were as follows: (1) high-energy and severe trauma such as from traffic or high-fall injury; (2) incomplete clinical materials. The clinical and radiological data of the patients were acquired by reviewing their medical history and measuring the values by the Picture Archiving and Communication Systems (PACS). Basic data were collected by reviewing patients' medical records, including gender, age, body mass index (BMI), time interval between AS diagnosis and trauma, smoking or not, and a presence of continuous bony bridge between anterior margin of C1 and C2 body or not. The study was reviewed and approved by the Ethics Committee of Peking University Third Hospital, Beijing, China (No. M2017331).

Radiological measurement

Radiological data were obtained by lateral cervical X-ray which was performed to patients maintaining the neutral position. All data were evaluated using a radiography information system (Centricity RIS-IC CE V3.0; GE Healthcare, Little Chalfont, UK). Firstly, the atlanto-occipital gap (X1), modified sagittal diameter of each vertebral body (mVB) and vertebral canal (mVC) from C2 to C7 were measured (Figure 1). As displayed in Figure 2, the mVB was the sum of the thickness of the anterior longitudinal ligament ossification, vertebral body diameter, and the thickness of the posterior longitudinal ligament ossification, while mVC indicated the distance between the posterior longitudinal ligament ossification and the yellow ligament ossification. mVC/mVB was expressed as a Pavlov ratio [13]. Secondly, as can be seen in Figure 3, certain angles were obtained by measuring the intersection angles of typical lines. Angle A represented the intersection angle between Line 1 and Line 2; Angle B indicated the intersection angle between Line 3 and Line 4; Angle C showed the intersection angle between Line 3 and Line 5; Angle D was used for the intersection angle between Line 3 and Line 6. Thirdly, as illustrated in Figure 4, Borden's index (X8) [14] and Harrison's value (Angle E) [15] were further applied to reflect the cervical curvature.

Statistical analysis

SPSS 22.0 software was used to conduct statistical analysis. The normality of the distribution was determined by Kolmogorov-Smirnov test. Normally distributed continuous variables were analyzed by independent-sample *t*-test, whereas non-normal variables were assessed by Mann-Whitney test. Categorical data were evaluated by the Chi-square test. Then, a binary logistic regression model was applied to discriminate among multivariate predictors. Odds ratio (OR) and 95% confidence interval (95% CI) revealed the strength of each association. The receiver operating characteristic (ROC) curve was employed to describe the discrimination ability of the predictive indicators. Area under the curve (AUC) was applied as a quantitative index. Youden's index (= sensitivity + specificity - 1) was calculated, and the highest score was considered as an optimal predictive cut-off value. $P < 0.05$ was considered to indicate statistically significant differences.

Results

A total number of 129 patients (mean age = 52.4 ± 8.1 years) were enrolled in this study, including 119 males and 10 females. The patients were divided into a Fracture group (41 cases) and a Non-fracture group (88 cases) based on the existence of a cervical fracture. Patients' demographics and measurement data were listed in Table 1. According to the statistical analysis results, twelve parameters had significant differences between the two groups ($P < 0.05$), namely, the time interval between the AS diagnosis and the trauma ($P = 0.013$), the presence of a continuous body bridge between the anterior margin of the C1 and

C2 body ($P < 0.001$), Pavlov ratio of C2 to C7, mean Pavlov ratio ($P < 0.001$), Angle D ($P = 0.001$), Borden's index ($P = 0.013$), and Harrison's value ($P = 0.001$).

Table 1
Demographics and measurement data between two groups

Parameters	Fracture group (n = 41)	Non-fracture group (n = 88)	Statistic (χ^2/z/t)	P-value
Gender (n)			0.694	0.41
Male	39 (95.1%)	80 (90.9%)		
Female	2	8		
Age (years)	54.1 ± 11.7	51.5 ± 10.2	1.288	0.200
BMI (kg/m^2)	23.8 ± 4.4	24.9 ± 3.6	-1.546	0.125
Time interval between AS diagnosis and trauma (years)	21.5 ± 11.1	16.6 ± 7.3	-2.490	0.013
Smoke (n)			2.023	0.155
Yes	12 (29.3%)	16 (18.2%)		
No	29	72		
Presence of continuous bony bridge between C1 and C2			14.355	< 0.001
Yes	18 (43.9%)	12 (13.6%)		
No	23	76		
X1 (mm)	5.9 ± 2.5	5.3 ± 3.3	0.890	0.375
Pavlov ratio				
C2	0.71 ± 0.16	0.79 ± 0.12	-2.842	0.004
C3	0.63 ± 0.13	0.75 ± 0.13	-4.987	< 0.001
C4	0.61 ± 0.14	0.76 ± 0.15	-5.385	< 0.001
C5	0.64 ± 0.13	0.78 ± 0.16	-4.980	< 0.001
C6	0.67 ± 0.14	0.80 ± 0.15	-4.488	< 0.001
C7	0.66 ± 0.11	0.80 ± 0.14	-5.099	< 0.001
Mean Pavlov ratio	0.65 ± 0.10	0.77 ± 0.14	-5.355	< 0.001

Parameters	Fracture group (n = 41)	Non-fracture group (n = 88)	Statistic (χ^2/z/t)	P-value
Angle A (°)	101.84 ± 7.62	101.23 ± 10.09	0.348	0.729
Angle B (°)	37.97 ± 7.38	35.33 ± 8.61	1.692	0.093
Angle C (°)	44.20 ± 8.11	44.01 ± 11.09	0.099	0.921
Angle D (°)	45.13 ± 9.39	52.61 ± 11.98	-3.460	0.001
Borden's index (mm)	5.87 ± 3.00	8.28 ± 4.94	-2.486	0.013
Harrison's value (°)	15.61 ± 8.14	22.68 ± 12.01	-3.222	0.001

Based on the binary logistic regression model (Forward: LR) presented in Table 2, four of the twelve mentioned parameters with significant differences between two groups showed a further correlation with the occurrence of cervical fracture after LET in AS patients. These included the mean Pavlov ratio ($P <$ 0.001, OR = 0.067), Angle D (P = 0.031, OR = 1.057), Borden's index (P = 0.042, OR = 1.131), the time interval between the AS diagnosis and the trauma ($P <$ 0.020, OR = 0.935). Their 95% CI were (0.023 to 0.194), (1.005 to 1.112), (0.994 to 1.287), and (0.883 to 0.990), respectively.

Table 2
The binary logistic regression model (Forward: LR) of the enrolled variables

Parameters	B	Wald	P-value	OR	95% CI
Mean Pavlov ratio	-2.704	24.867	< 0.001	0.067	0.023, 0.194
Angle D	0.056	4.648	0.031	1.057	1.005, 1.112
Borden's index	0.123	3.482	0.042	1.131	0.994, 1.287
Time interval	-0.068	5.370	0.020	0.935	0.883, 0.990
Time interval indicates time interval between AS diagnosis and trauma.					

The ROC curve and the AUC were used to further understand the predictive ability of the four parameters established by the logistic regression model. As presented in Table 3 and Fig. 5, the mean Pavlov ratio had the largest AUC (0.793) (95% CI: 0.873 to 0.986), and the AUCs of Angle D, Borden's index, and the time interval between the AS diagnosis and the trauma were between 0.6 and 0.7. According to the highest Youden's index value, the optimal cut-off value of the mean Pavlov ratio was 0.72 (sensitivity = 82.9%, specificity = 73.9%), and the optimal cut-off value, sensitivity, and specificity of the other included parameters were Angle D (45.65°, 61.0%, 78.4%), Borden's index (9.79, 87.8%, 37.5%), and the time interval between the AS diagnosis and the trauma (15.50 years, 70.7%, 56.8%).

Table 3
The AUC and the optimal cut-off value based on the highest Youden's index

Parameters	AUC	Highest Youden's index	Optimal cut-off value	Sensitivity	Specificity
Mean Pavlov ratio	0.793	0.568	0.72	0.829	0.739
Angle D	0.690	0.394	45.65	0.610	0.784
Borden's index	0.636	0.253	9.79	0.878	0.375
Time interval	0.636	0.275	15.50	0.707	0.568

Time interval indicates time interval between AS diagnosis and trauma.

Discussion

In some situations, cervical fracture in AS patients might escape from recognition due to physicians' lack of clinical experience or the limitations of the basic radiological examination. Therefore, it is imperative to have a high index of suspicion in AS patients who present with a history of trauma or without any neurological symptoms and to treat these patients as if they had a fracture until this had been excluded either by CT or MRI. X-ray is usually deemed as a primary option to discriminate the potential fracture in patients suffering from a trauma under emergency conditions but bidimensional images are easily influenced by abnormal ossification and position, which leads to the misdiagnosis of a minor fracture without an obvious fracture line and dislocation. However, based on our experience, certain X-ray imaging characteristics can offer more information beyond visible fractures; they can also warn for the possibility of a fracture. Hence, in the present study, we explored the predictive ability of radiological measurements used to establish the risk of cervical fracture in AS patients suffering LET.

An important reason why patients with AS are susceptible to LET is that the continuous ligament ossification and degenerative discs collectively reduce cervical elasticity, whose mechanical function behaves as a long force arm like extremities, acting as a rigid lever, incapable of appropriately dissipating the energy of a traumatic event [8]. Besides, a thicker ossification is associated with higher stiffness and fragility; the fused spinal columns have lost their elasticity and movements resulting in altered biomechanics. In this study, to establish the severity of ligament ossification, measurements of the sagittal diameter of both the vertebral body and the canal were accomplished considering the ossification of the anterior longitudinal ligament, posterior longitudinal ligament, and ligamentum flavum. As can be seen in Fig. 2, thicker ossification of the anterior and posterior longitudinal ligament caused longer mVB (Fig. 2B), whereas thicker ossification of the posterior longitudinal ligament and ligamentum flavum caused shorter mVC (Fig. 2C). Additionally, thicker ossification of the three ligaments can cause both shorter mVC and longer mVB (Fig. 2D), and these three factors can decrease the Pavlov ratio (= mVC/mVB). According to the statistical results, the Pavlov ratios of C2 to C7 in Fracture group were all significantly lower than that in Non-fracture group ($P < 0.05$). Furthermore, the results of the binary logistic regression and ROC curve showed that the mean Pavlov ratio was significantly correlated to the occurrence of cervical fracture in AS patients who suffered from LET. The highest AUC of the mean Pavlov ratio manifested its best predictive ability among other parameters. The cut-off value of the mean Pavlov ratio was 0.72 (sensitivity = 0.829, specificity = 0.739), indicating that for patients with AS who encountered LET, those whose mean Pavlov ratio was less than 0.72 had a higher risk of cervical fracture. In this premise, if the X-ray examination appears normal, further CT and MRI are highly recommended.

The maintenance of cervical natural physiological lordosis contributes to buffering the action of a force when the skull and the neck suffer from trauma [16, 17]. The aggravating cervical rigidity caused by chronic inflammation leads to a reduction in the cervical buffer capacity. Besides, stress concentration becomes more pronounced under cervical rigidity, and the mobility trend in the vertical and horizontal directions becomes more obvious, which causes a state of instability of the cervical spine. In the present study, a total number of three parameters related to cervical curvature showed a significant difference between the two groups ($P < 0.05$), namely, Angle D (the intersection angle between the line parallel to the upper border of C1 body and the line passing through the anterior-inferior point and the posterior-inferior point of C7 body), Borden's index, and Harrison's value. In addition, straight cervical curvature for all three parameters (namely lesser cervical lordosis) was all exactly detected in the Fracture group. In the further analysis, Angle D and Borden's index were incorporated into the binary logistic regression and ROC curve, and their AUC were 0.690 and 0.636, respectively. The cut-off value of Angle D and Borden's index were 45.65° and 9.79 mm, indicating a higher possibility of cervical fracture in AS patients suffering from LET when Angle D and Borden's index are lower than 45.65° and 9.79 mm.

Time interval between AS diagnosis and trauma is an objective reflection index for the severity of AS progression. Theoretically speaking, a longer time interval might be related to more seriousligament ossification and cervical rigidity. Besides, as previously reported, the risk of incurring a spine fracture after injury in AS grows gradually with time, and the risk of sustaining a vertebral fracture could reach an added 1.3% per year [18]. A study conducted by Deminger *et al*. [18] explored the spinal radiographic progression in AS based on the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). They found that the mean progression was 1.6 mSASSS units over five years ($P < 0.001$). Other studies revealed the progression of mean 4.2 per four years [20] and 1.3 mSASSS units per year [21]. An investigation including 132 AS patients in the OASIS (Outcome in AS International Study) cohort further revealed that new syndesmophytes occurred in 33% and 48% of the patients after two and four years, respectively [20]. Though the predictive ability of time interval between AS diagnosis and trauma was not high with its AUC of 0.636, the time interval of the Fracture group was significantly longer in the present study (21.5 years vs 16.6 years, $P = 0.013$). The cut-off value of the time interval between the AS diagnosis and the trauma was 15.50 years, indicating that if a patient who encountered LET more than 15.50 years after the diagnosis of AS should be considered with increased vigilance to have a potential cervical fracture to avoid missed diagnosis.

In the present study, the morbidity of the continuous bony bridge between C1 and C2 also had significant difference between the two groups (43.9% vs 13.6%, $P < 0.001$). The atlantoaxial joint plays an important role in the cervical natural motion, especially in the rotation function. A recent *in vivo* study showed that the flexion-extension of C1-2 was 13.7 ± 4.2°, accounting for 14.5% of the overall flexion-extension ROM; the lateral bending neck motion of C1-2 was 7.6 ± 2.7°, accounting for 13.2% of the overall lateral bending ROM; and the axial torsion neck motion of C1-2 was 72.9 ± 7.6°, accounting for 73.2% of the overall rotation ROM [22]. Previous investigations also achieved similar results [23, 24, 25]. Once the motion of C1-2 joint is restricted by the anterior continuous bony bridge, the bearing force capacity from the skull and the neck is in turn reduced, which further increases the risk of cervical fracture.

However, there are some limitations in our study. On the one hand, the present study included a relatively small number of patients, a larger sample size and a multi-center study might make the results more convincing. On the other hand, this was a retrospective study, and a prospective study for predicting the possibility of CSF in AS patients suffering minor trauma might have the potential to provide more references to clinical practice.

Conclusion

Four parameters from simple plain X-ray possess higher prediction ability for CSF in AS patients who encounter LET. They have potential to help us reduce the rate of missed diagnosis and increase the service efficiency of CT and MRI.

Abbreviations

AS: Ankylosing spondylitis; LET:Low-energy trauma; CSF:Cervical spine fracture; ASCSF:Cervical spine fracture with ankylosing spondylitis; CT:Computed tomography; MRI:Magnetic resonance imaging; PACS:Picture Archiving and Communication Systems; BMI:Body mass index; mVB:Modified sagittal diameter of vertebral body; mVC:Modified sagittal diameter of vertebral canal; OR:Odds ratio; ROC:Receiver operating characteristic; AUC:Area under the curve.

Declarations

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Authors’ contributions

BCL and ZWY collected data and wrote the article; GJH made the data analysis. FZ, HQJ and YT designed the study.

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Availability of data and materials

All data and materials used to support the findings of this study are included within the article.

Ethics approval and consent to participate

The Ethics Committee of Peking University Third Hospital approved this subject.

Consent for publication

All authors agree to publish “Cervical spine fracture prediction by simple plain X-ray in ankylosing spondylitis patients after low-energy trauma” in Journal of Orthopaedic Surgery and Research.

Competing interests

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

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Figures

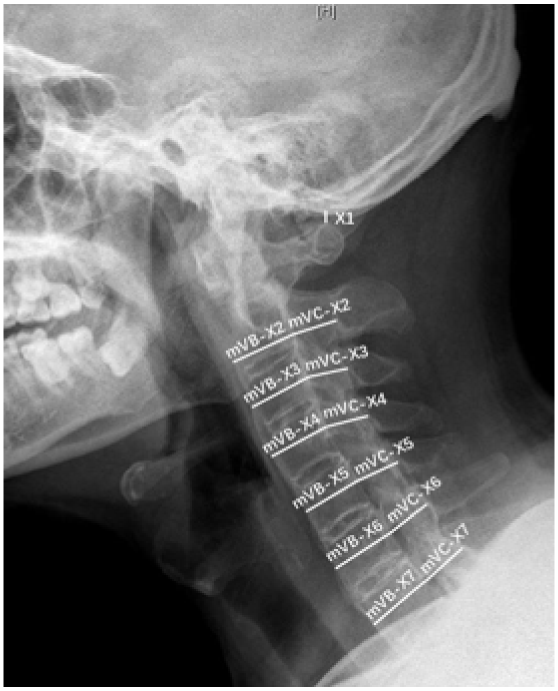

Figure 1

Distance measurement on the lateral cervical X-ray in the neutral position. X1: atlanto-occipital gap; mVB-X(2-7): modified sagittal diameter of C2 to C7 body; mVC-X(2-7): modified sagittal diameter of C2 to C7 canal (VB: vertebral body; VC: vertebral canal).

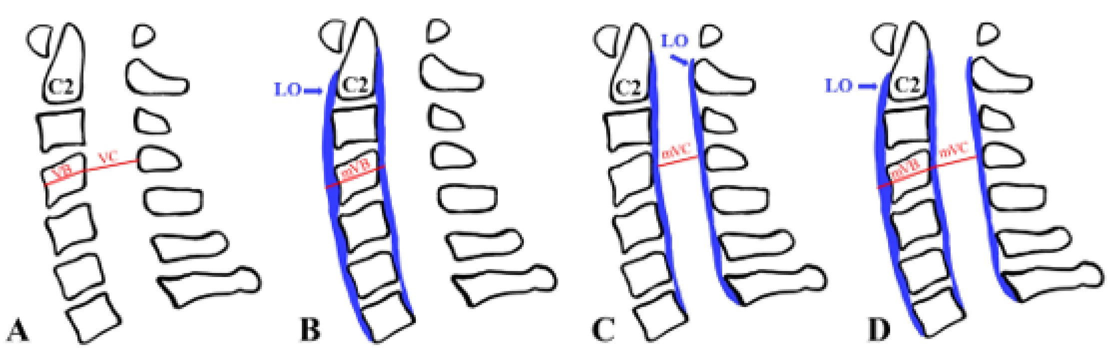

Figure 2

The illustration of the measurement difference between normal and modified VB and VC. A: normal sagittal diameter of VB and VC; B: sagittal diameter of mVB (the blue arrow indicates the ossification of paraspinal ligaments); C: sagittal diameter of mVC; D: sagittal diameter of mVB and mVC (VB: sagittal diameter of vertebral body; VC: sagittal diameter of vertebral canal; LO: ligament ossification; mVB: modified sagittal diameter of vertebral body; mVC: modified sagittal diameter of vertebral canal).

Figure 3

Angle measurement on the lateral cervical X-ray in the neutral position. Line 1: a line parallel to hard palate; Line 2: a line passing through anterior-inferior border of the sixth cervical vertebra and the most anterior aspect of the first cervical vertebra; Line 3: a line parallel to the upper border of C1 body; Line 4: a line passing through the anterior-inferior point and the posterior-inferior point of C2 body; Line 5: a line passing through the anterior-inferior point and the posterior-inferior point of C4 body; Line 6: a line passing through the anterior-inferior point and the posterior-inferior point of C7 body.

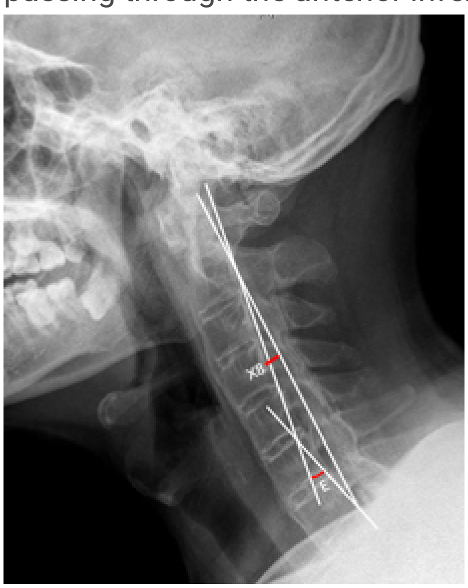

Figure 4

Measurement of cervical curvature by Borden's index and Harrison's value on the lateral cervical X-ray in the neutral position. X8: the vertical distance from the midpoint of C4 posterior marginal to the line passing through the posterior superior marginal of C2 odontoid process and posterior inferior edge of C7 body; Angle E: the intersection angle between tangent lines along the cervical curve of the posterior margins of C2 and C7 body.

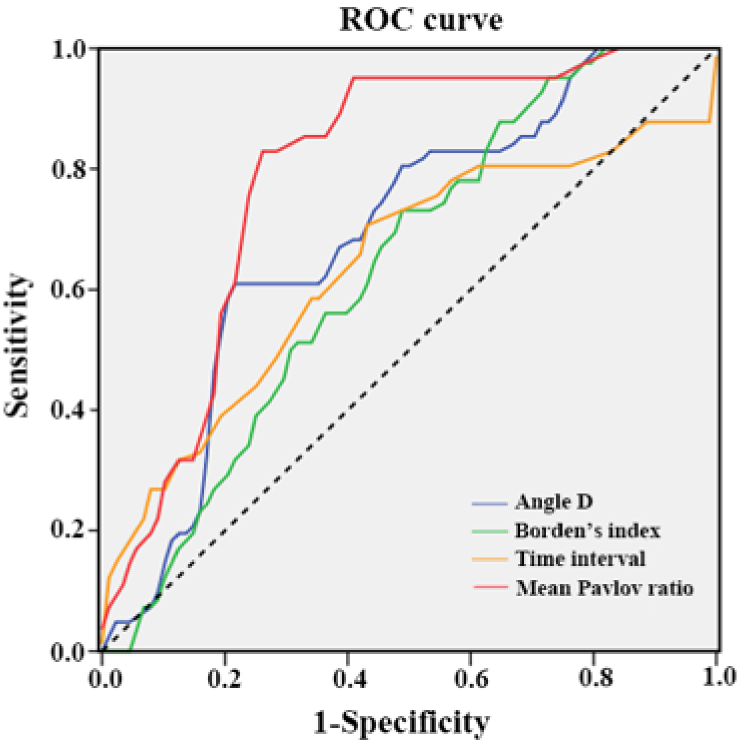

Figure 5

ROC curve of the 4 parameters including Angle D, Borden's index, Time interval (time interval between AS diagnosis and trauma) and mean Pavlov ratio.