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Research article

A diagnostic support tool for lumbar spinal stenosis: a self-administered, self-reported history questionnaire

Shin-ichi Konno*[1], Shin-ichi Kikuchi[1], Yasuhisa Tanaka[2], Ken Yamazaki[3], You-ichi Shimada[4], Hiroshi Takei[5], Toru Yokoyama[6], Masahiro Okada[6] and Shou-ichi Kokubun[2]

Address: [1]Department of Orthopaedic Surgery, Fukushima Medical University School of Medicine, Fukushima City, Fukushima, Japan, [2]Department of Orthopaedic Surgery, Tohoku University, Sendai City, Miyagi, Japan, [3]Department of Orthopaedic Surgery, Iwate Medical College, Morioka City, Iwate, Japan, [4]Department of Orthopaedic Surgery, Akita University, Akita City, Akita, Japan, [5]Department of Orthopaedic Surgery, Yamagata University, Yamagata City, Yamagata, Japan and [6]Department of Orthopaedic Surgery, Hirosaki University, Hirosaki City, Aomori, Japan

Email: Shin-ichi Konno* - skonno@fmu.ac.jp; Shin-ichi Kikuchi - sinichk@fmu.ac.jp; Yasuhisa Tanaka - ytanaka@tohoku-ctr-hsp.com; Ken Yamazaki - yamaken@iwate-med.ac.jp; You-ichi Shimada - yshimada@med.akita-u.ac.jp; Hiroshi Takei - htakei@med.id.yamagata-u.ac.jp; Toru Yokoyama - toru2000@cc.hirosaki-u.ac.jp; Masahiro Okada - akihiro@actv.ne.jp; Shou-ichi Kokubun - kokubun@nishitaga-hp.go.jp

* Corresponding author

Abstract

Background: There is no validated gold-standard diagnostic support tool for LSS, and therefore an accurate diagnosis depends on clinical assessment. Assessment of the diagnostic value of the history of the patient requires an evaluation of the differences and overlap of symptoms of the radicular and cauda equina types; however, no tool is available for evaluation of the LSS category. We attempted to develop a self-administered, self-reported history questionnaire as a diagnostic support tool for LSS using a clinical epidemiological approach. The aim of the present study was to use this tool to assess the diagnostic value of the history of the patient for categorization of LSS.

Methods: The initial derivation study included 137 patients with LSS and 97 with lumbar disc herniation who successfully recovered following surgical treatment. The LSS patients were categorized into radicular and cauda equina types based on history, physical examinations, and MRI. Predictive factors for overlapping symptoms between the two types and for cauda equina symptoms in LSS were derived by univariate analysis. A self-administered, self-reported history questionnaire (SSHQ) was developed based on these findings. A prospective derivation study was then performed in a series of 115 patients with LSS who completed the SSHQ before surgery. All these patients recovered following surgical treatment. The sensitivity of the SSHQ was calculated and clinical prediction rules for LSS were developed. A validation study was subsequently performed on 250 outpatients who complained of lower back pain with or without leg symptoms. The sensitivity and specificity of the SSHQ were calculated, and the test-retest reliability over two weeks was investigated in 217 patients whose symptoms remained unchanged.

Results: The key predictive factors for overlapping symptoms between the two categories of LSS were age > 50, lower-extremity pain or numbness, increased pain when walking, increased pain when standing, and relief of symptoms on bending forward (odds ratio ≥ 2, p < 0.05). The key predictive factors for cauda equina type symptoms were numbness around the buttocks, walking almost causes urination, a burning sensation around the buttocks, numbness in the soles of both

feet, numbness in both legs, and numbness without pain (odds ratio ≥ 2, $p < 0.05$). The sensitivity and specificity of the SSHQ were 84% and 78%, respectively, in the validation data set. The area under the receiver operating characteristic curve was 0.797 in the derivation set and 0.782 in the validation data set. In the test-retest analysis, the intraclass correlation coefficient for the first and second tests was 85%.

Conclusion: A new self-administered, self-reported history questionnaire was developed successfully as a diagnostic support tool for LSS.

Background

Lumbar spinal stenosis (LSS) is a well-recognized spinal disorder and a term used to describe a complex set of symptoms, physical findings, and radiological abnormalities caused by a narrowed spinal canal. The presence of a narrow canal in radiographic imaging does not in itself define the syndrome, and a diagnosis of LSS is defined by symptoms and clinical findings that must be supported by radiographic evidence. Computed tomography and magnetic resonance imaging are often non-specific and there may be discrepancies between clinical symptoms and imaging findings in cases of LSS [1-3].

There is no validated gold-standard diagnostic support tool for LSS, and therefore an accurate diagnosis depends on clinical assessment. However, there are few scientific evaluations of the sensitivity and specificity of diagnoses based on clinical history and physical examinations, or appropriate correlations of these data with imaging and operative findings. Katz et al. used the opinion of two expert orthopedic surgeons to define the presence or absence of LSS [4], and found that the factors in the patient history that were most strongly associated with diagnosis of LSS were a higher age, severe lower-extremity pain, and the absence of pain when seated. The physical findings most strongly associated with the diagnosis were a wide-based gait, an abnormal Romberg test, thigh pain following 30 seconds of lumbar extension, and neuromuscular deficits.

There are two categories of leg symptoms caused by LSS [5]. One type of stenosis presents as unilateral radicular pain (the radicular type), with symptoms of pain, burning, numbness and paresthesia following a specific dermatome or dermatomes. The fifth lumbar nerve root associated with L5 stenosis is most commonly involved. The other type of LSS has symptoms with less dermatomal-specific neurogenic claudication, and nerve roots below L5 are most commonly involved. The typical patient presents with complaints of aching, cramping, or a burning sensation in the bilateral legs. Occasionally, numbness is also apparent and some patients complain of bladder dysfunction and sexual difficulties.

Full-blown cauda equina syndrome only occurs in rare instances, but the above symptoms can occur as a part of cauda equina syndrome [6,7]. Therefore, we hypothesized that leg symptoms in LSS might be divided into two categories: a radicular type and a cauda equina type. There are significant differences between the symptoms of these types, but there is also significant overlap between the symptoms. Since both the central canal and foraminal dimensions increase in flexion and diminish in extension, patients with both types of LSS experience exacerbation of symptoms with extension and improvement with flexion.

Assessment of the diagnostic value of the history of the patient requires an evaluation of the differences and overlap of symptoms of the radicular and cauda equina types; however, no tool is available for evaluation of the LSS category. Therefore, we attempted to develop a self-administered, self-reported history questionnaire as a diagnostic support tool for LSS using a clinical epidemiological approach. The aim of the present study was to use this tool to assess the diagnostic value of the history of the patient for categorization of LSS.

Methods

Derivation study 1

A series of 137 patients with LSS and 97 with lumbar disc herniation who successfully recovered following surgical treatment in our department during 2000 and 2003 were included in this study (Table 1). Patients with cervical

Table 1: Demographic data for patients in derivation study 1

	LSS (n = 137)	LDH (n = 97)
Male (%)	46	58
Female (%)	54	42
Mean age (yr)	68	41
Mean duration of symptoms (mo)	21	5
Cauda equina type intermittent claudication	50	-
Radicular type intermittent claudication	87	-
Findings on MRI		
One level stenosis	102	14
Two level stenosis	23	0
Three level stenosis	12	0

myelopathy, diabetic neuropathy, previous surgery, peripheral vascular disease, inflammatory disorders, and degenerative scoliosis (defined as lateral tilting of more than 10 degrees) were excluded. Each patient was evaluated by the study investigators using a standard protocol. Operative and follow-up visit notes were reviewed to determine if stenosis was confirmed intraoperatively and if symptoms improved following surgery. Nerve root compression resulting exclusively from a herniated nucleus pulposus was not considered as a symptom of LSS.

Assessment of history included questions on location, frequency and severity of pain, and on symptoms including numbness, tingling, and provocative factors. The physical examination included a gait-loading test to confirm neurogenic intermittent claudication; this test involves assessment of walking capacity and symptoms, and a neurological examination of motor, sensory, and reflex activity [8]. We investigated symptoms during gait loading and neurological findings just after gait loading. Reflexes were graded from 0 (no response) to 4 (clonus) at the Achilles tendon and patellar tendon, and strength was graded from 0 (no movement) to 5 (normal) at the knee flexors and extensors, ankle dorsiflexors and plantar flexors, and extensor hallucis longus. A pinprick sensation was graded as absent, decreased, or normal at the dorsomedial foot, dorsolateral foot, medial calf, and lateral calf. MRI radiographical reports were abstracted from patient records.

The LSS patients were categorized into radicular and cauda equina types based on history, physical examination, and MRI findings. The radicular type was characterized by symptoms of pain, burning, numbness, and paresthesias following a specific dermatome with radiological evidence of the responsible nerve root compression, which was confirmed if intermittent claudication was abolished following single nerve root infiltration. Patients of the cauda equina type presented some bilateral symptoms related to cauda equina compression syndrome with less dermatomal-specific neurogenic claudication and radiological evidence of cauda equina compression. The cauda euqina type spinal stenosis is distinct from the cauda equina syndrome. A full blown cauda equina syndrome occurs in rare instances in the cauda equina type spinal stenosis. Therefore, urgent surgery is not required in the cauda equina type spinal stenosis. Predictive factors for overlap symptoms between the two types of LSS were derived from the data and factors for predicting the cauda equina type were also determined. Based on the results of univariate analysis for predictors of LSS, a self-administered, self-reported history questionnaire (SSHQ) was developed as a diagnostic support tool for LSS.

Derivation study 2

This study was performed in six university hospitals, ten medical centers, and thirty one hospitals and clinics affiliated with university hospitals or medical centers during January and March in 2004. A series of 115 patients with LSS gave informed consent to participate in the study and answered the SSHQ before surgery. All these patients recovered following surgery. Patients with cervical myelopathy, diabetic neuropathy, previous surgery, inflammatory disorders, and degenerative scoliosis were excluded. All patients were evaluated by study investigators using the same protocol as that in derivation study 1. Operative and follow-up visit notes were reviewed to determine if stenosis was confirmed intraoperatively and if symptoms improved following surgery. Nerve root compression resulting exclusively from a herniated nucleus pulposus was not considered as a part of LSS syndrome. All LSS patients were categorized into radicular or cauda equina types based on history, physical examination, and MRI findings using the same criteria as those in derivation study 1. There were 55 patients with radicular type LSS and 60 patients with the cauda equina type (Table 2). A responsible nerve root was confirmed if intermittent claudication was abolished following single nerve root infiltration. The sensitivity of each question on the SSHQ was calculated and compared between the radicular and cauda equina types. To assess the cut-off point to distinguish between the types, one point was assigned to each question on the SSHQ, and the clinical prediction rule was defined based on the scores.

Validation study

We prospectively evaluated the association between the diagnosis of LSS and clinical information, including the history and physical examination of patients with leg symptoms. This study was performed in six university hospitals, ten medical centers, and sixty eight hospitals and clinics affiliated with university hospitals or medical centers during July and September in 2004. We enrolled consecutive patients older than 20 years of age with primary symptoms of pain or numbness in the legs. We excluded patients who have been treated by some medical

Table 2: Demographic data for patients in derivation study 2

	Radicular type (n = 55)	Cauda equina type (n = 60)
Male (%)	52	42
Female (%)	48	58
Mean age (yr)	68	71
Mean duration of symptoms (mo)	19	32
Findings on MRI		
One level stenosis	43	47
Two level stenosis	12	10
Three level stenosis	0	3

practices within one year before examination. Patients with cervical myelopathy, previous surgery, degenerative scoliosis (defined as lateral tilting of more than 10 degrees) and inflammatory disorders were also excluded. This study included 250 patients who complained of leg symptoms, including cases of LSS (n = 165), lumbar disc herniation (n = 61), diabetic neuropathy (n = 13), and peripheral vascular disease (n = 11) (Table 3). The study was approved by the institutional review board of each study institution as necessary. Written informed consent was obtained from the all patients. The patients gave informed consent and then answered the SSHQ. The following steps were taken to reach a final diagnosis for each of the enrolled patients (Figure 1). In the first step, at each institution the orthopedic physician who saw a patient made the clinical diagnosis based on the history, physical examination, and radiographic findings. In addition, to verify the diagnosis made by each physician, six board-certified spine surgeons approved by the Japanese Board of Spine Surgery also made a diagnosis for each patient based on the clinical information and findings of the MRI. The opinions of six board-certified spine surgeons approved by the Japanese Board of Spine Surgery were used as the gold standard for diagnosis of LSS. The radicular type was characterized by symptoms of pain, burning, numbness, and paresthesias following a specific dermatome with radiological evidence of the responsible nerve root compression, which was confirmed if intermittent claudication was abolished following single nerve root infiltration. Patients of the cauda equina type presented some bilateral symptoms related to cauda equina compression syndrome with less dermatomal-specific neurogenic claudication and radiological evidence of cauda equina compression.

The sensitivity, specificity, likelihood ratio, and area under the receiver operating characteristic (ROC) curve
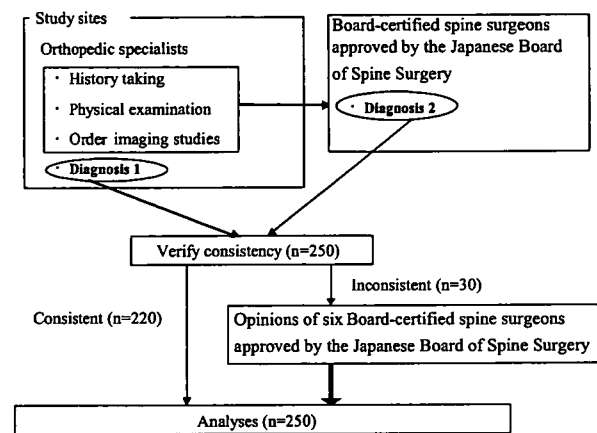

Figure 1
Flow chart of how the diagnosis of LSS was determined.

were estimated. 217 patients classified by investigators as suffering from lower back pain without a significant change in symptoms were given the SSHQ two weeks later during an outpatient visit, and the test-retest reliability over two weeks was investigated in these patients.

Statistical analysis
History and physical examination variables were dichotomized at clinically sensible cut-off values. Pinprick, strength, and Achilles reflexes were each classified as always normal or with at least 1 abnormal finding. Univariate analyses were performed to derive predictors of LSS using logistic regression analysis. Two-by-two contingency tables were prepared to calculate the sensitivity, specificity, and likelihood ratio of the SSHQ. The area under the ROC curve for the derivation data set was estimated to investigate the internal validity of the clinical prediction rule, and the area under the ROC curve for the validation data set was estimated to examine the external validity. Reliability was investigated based on the reproducibility in the test-retest method. Test-retest analysis was performed in 217 patients with a 14-day period between the first and second tests. Test-retest data were examined graphically by plotting the difference between tests against the mean of the 2 tests [9]. The intraclass correlation coefficient of the SSHQ score for the first and second tests was calculated to confirm reproducibility. The κ coefficient was calculated to examine conformity for each item, based on the following criteria: 0 to < 0.2, poor; 0.2 to < 0.4, fair; 0.4 to < 0.6, moderate; 0.6 to < 0.8, substantial; and > 0.8, almost perfect [10]. All the studies were approved by the ethics committee of Fukushima Medical University.

Table 3: Demographic data for patients in the validation study

	LSS (n = 165)	The others (n = 85)
Male (%)	47	51
Female (%)	53	49
Mean age (yr)	71	48
Mean duration of symptoms (mo)	28	24
Clinical impressions of patient condition	Cauda equina type 78	LDH* 61
	Radicular type 87	DN* 13
		PAD* 11
Findings on MRI		
One level stenosis	127	12
Two level stenosis	31	2
Three level stenosis	7	0

* LDH: Lumbar Disc Herniation, DN: Diabetic Neuropathy, PAD: Peripheral Artery Disease

Results

Univariate analysis for predictors of LSS

Key factors for predicting overlapping symptoms between the two types of LSS are shown in Table 4. Five history findings had an odds ratio ≥ 2 or $p < 0.05$: age > 50, lower-extremity pain or numbness, increased pain when walking, increased pain when standing, and improvement of symptoms on bending forward. No physical examination finding had an odds ratio ≥ 2 or $p < 0.05$. There was no significant difference in the odds ratio of all the predictive factors except for age. Key factors for predicting the cauda equina type of LSS are shown in Table 5. Six history findings had an odds ratio ≥ 2 or $p < 0.05$: numbness around the buttocks, walking nearly causes urination, a burning sensation around the buttocks, numbness in the soles of both feet, numbness in both legs, and numbness without pain. Physical examination findings with an odds ratio $\geq$

2 or $p < 0.05$ included the absence of or a weak Achilles reflex response.

A self-administered, self-reported history questionnaire (SSHQ)

Based on the results of univariate analysis for predictors of LSS, we developed the SSHQ as a diagnostic support tool for LSS (see Additional File 1 and 2). The SSHQ included the following questions:

Q1: Numbness and/or pain in the thighs down to the calves and shins.

Q2: Numbness and/or pain increase in intensity after walking for a while, but are relieved by taking a rest.

Q3: Standing for a while brings on numbness and/or pain in the thighs down to the calves and shins.

Table 4: Univariate analyses for factors from the MD and MRI data sheets associated with a diagnosis of LSS

	LSS (-) (n = 97)	LSS (+) (n = 137)	Odds Ratio	95% CI	p-value
Age (years) > 50	20.6%	94.9%	71.50	28.9 – 176.9	< 0.001
Gender (Female)	42.0%	54.0%	1.60	0.95 – 2.71	07
Symptoms					
Leg pain or numbness (+)	87.6%	94.9%	2.62	0.99 – 6.93	0.045
Low back pain (+)	72.2%	65.0%	0.72	0.41 – 1.26	0.245
Worse when walking but relieved by taking a rest	18.6%	94.2%	70.77	29.39 – 170.4	< 0.001
Numbness in both legs (+)	15.5%	24.8%	1.80	0.92 – 3.54	0.083
Numbness in the soles of both feet (+)	13.4%	20.4%	1.66	0.81 – 3.40	0.163
Numbness around the buttocks (+)	9.3%	15.3%	77	77 – 4.05	173
Numbness without pain	8.2%	11.7%	1.53	0.63 – 3.75	0.344
A burning sensation around the buttocks	6.2%	8.2%	0.94	0.32 – 2.80	0.912
Walking nearly causes urination	3.1%	5.1%	1.69	0.43 – 6.70	0.452
Worse when standing for a while	24.7%	84.7%	11.38	6.20 – 20.91	< 0.001
Symptoms improve on bending forward	8.1%	72.3%	25.47	11.66 – 55.64	< 0.001
Physical Examination					
Straight Leg Raising test positive	33.0%	21.9%	0.57	0.32 – 1.02	0.058
Symptoms induced by having patients bend forward (+)	30.9%	20.4%	0.57	0.32 – 1.04	0.067
Symptoms induced by having patients bend backward (+)	53.6%	62.0%	1.38	0.81 – 2.35	0.229
Abnormal manual muscle strength test 1)	8.2%	10.2%	1.27	0.51 – 3.15	0.611
Sensory disturbance					
(-)	57.7%	49.6%	reference		
(+) 2)	37.1%	45.3%	1.40	0.82 – 2.38	0.214
Missing data	5.2%	5.1%	0.99	0.30 – 3.22	0.988
Achilles tendon reflex					
Normal	51.5%	48.2%	reference		
Abnormal 3)	43.3%	46.7%	1.15	0.68 – 1.94	0.605
Missing data	5.2%	5.1%	0.99	0.30 – 3.22	0.988
Patellar tendon reflex					
Normal	70.1%	62.8%	reference		
Abnormal 3)	24.7%	32.1%	1.44	0.80 – 2.58	0.221
Missing data	5.2%	5.1%	0.99	0.30 – 3.22	0.988

1) MMT < = 3, Strength was graded from 0 (no movement) to 5 (normal) at the knee extensors, ankle dorsiflexors, and plantar flexors, and extensor hallucis longus.
2) Hypoesthesia, analgesia, or hyperalgesia at the medial knee, dorsal foot, plantar foot, and perineal lesion
3) Absence or low response of deep reflexes

Table 5: Univariate analyses for factors from the MD and MRI data sheets associated with a diagnosis of the cauda equina type of LSS

	Radicular type (n = 87)	Cauda Equina type (n = 50)	Odds Ratio	95% CI	p-value
Age (years) > 50	94.3%	96.0%	1.46	0.27 – 7.84	0.655
Gender (Female)	51.7%	56.0%	1.20	0.60 – 2.38	0.608
Symptoms					
Leg pain or numbness (+)	97.7%	96.0%	0.56	0.08 – 4.14	0.569
Low back pain (+)	65.5%	62.0%	0.86	0.42 – 1.77	0.679
Worse when walking but relieved by taking a rest	96.6%	96.0%	0.86	0.14 – 5.31	0.868
Numbness in both legs (+)	11.5%	82.0%	35.08	13.20 – 93.19	< 0.001
Numbness in the soles of both feet (+)	6.9%	78.0%	47.86	16.49 – 138.9	< 0.001
Numbness around the buttocks (+)	11.5%	68.0%	6.36	6.74 – 39.73	< 0.001
Numbness without pain	10.3%	37.0%	5.31	2.17 – 13.01	< 0.001
A burning sensation around the buttocks	6.9%	34.0%	6.95	2.52 – 19.19	< 0.001
Walking nearly causes urination	4.6%	26.0%	7.29	2.23 – 23.86	< 0.001
Worse when standing for a while	92.0%	82.0%	0.40	0.14 – 1.15	0.08
Symptoms improve on bending forward	86.2%	74.0%	0.46	0.19 – 1.10	0.07
Physical Examination					
Straight Leg Raising test positive	21.8%	22.0%	1.01	0.44 – 2.34	0.983
Symptoms induced by having patients bend forward (+)	19.5%	22.0%	1.16	0.49 – 2.73	0.731
Symptoms induced by having patients bend backward (+)	63.2%	58.0%	0.80	0.39 – 1.64	0.546
Abnormal manual muscle strength test 1)	9.2%	12.0%	1.35	0.44 – 4.13	0.602
Sensory disturbance					
(-)	49.4%	50.0%	reference		
(+) 2)	43.7%	46.0%	1.40	0.82 – 2.38	0.214
Missing data	6.9%	4.0%	0.56	0.11 – 2.90	0.486
Achilles tendon reflex					
Normal	65.5%	30.0%	reference		
Abnormal 3)	27.6%	66.0%	5.10	2.41 – 10.79	< 0.001
Missing data	6.9%	4.0%	0.56	0.11 – 2.90	0.486
Patellar tendon reflex					
Normal	63.2%	62.0%	reference		
Abnormal 3)	29.9%	34.0%	1.21	0.57 – 2.54	0.617
Missing data	6.9%	4.0%	0.56	0.11 – 2.90	0.486

1) MMT < = 3, Strength was graded from 0 (no movement) to 5 (normal) at the knee extensors, ankle dorsiflexors, and plantar flexors, and extensor hallucis longus.
2) Hypoesthesia, analgesia, or hyperalgesia at the medial knee, dorsal foot, plantar foot, and perineal lesion
3) Absence or low response of deep reflexes

Q4: Numbness and/or pain are reduced by bending forward.

The key questions for diagnosis of cauda equina symptoms were as follows:

Q5: Numbness is present in both legs.

Q6: Numbness is present in the soles of both feet.

Q7: Numbness arises around the buttocks.

Q8: Numbness is present, but pain is absent.

Q9: A burning sensation arises around the buttocks.

Q10: Walking nearly causes urination.

Clinical prediction rule
The sensitivity of each question in the derivation study was calculated for the radicular and cauda equina types of LSS. The sensitivity differed significantly between the categories (Figure 2). To assess the cut-off point to distinguish between the two types, each question was assigned one point. The scores of predictors of cauda equina symptoms (Q5-Q10) were significantly different between the categories, and the cut-off point was two (Figure 3). Based on these results, a clinical prediction rule was defined based on the total scores: a score of 4 points on Q1-Q4 indicates the presence of LSS; a score of 4 on Q1-Q4 and < 1 on Q5-Q10 indicates the radicular type of LSS; and a score of > 1 on Q1-Q4 and > 2 on Q5-Q10 indicates the cauda equina type of LSS.
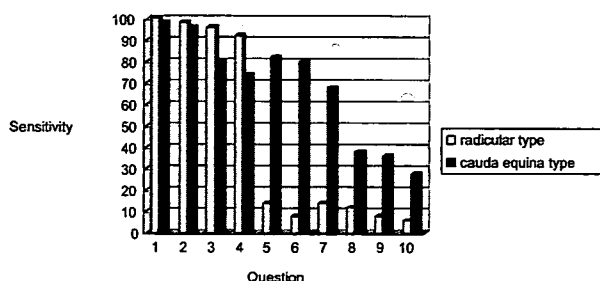
Figure 2
Comparison of the sensitivity of each question for radicular and cauda equina types of LSS.

Validity

It took respondents an average of about 1 minute to answer the 10 questions on the SSHQ. Performance indices for the clinical prediction rule are shown in Table 6. The area under the ROC curve was 0.797 in the derivation set and 0.782 in the validation data set (Figure 4). These findings indicate that the SSHQ has both internal and external validity as a diagnostic tool for LSS. The difference between tests plotted against the mean of the tests indicated no obvious relationship or bias (Figure 5). The intraclass correlation coefficient of the SSHQ score for the first and second tests was 0.85, which indicates sufficient reproducibility. One item of the κ coefficient was found to be "fair" (question 8), and all other items were rated as having a conformity of moderate or above.

Discussion

Spinal stenosis patients frequently present with few objective physical findings. Jonsson and Stromqvist found that about 65% of patients have decreased walking ability [11], but up to 95% of patients treated surgically have only subjective symptoms, principally pain [12,13]. Furthermore, diagnostic imaging cannot be used reliably to diagnose LSS, since CT and MRI are often non-specific and
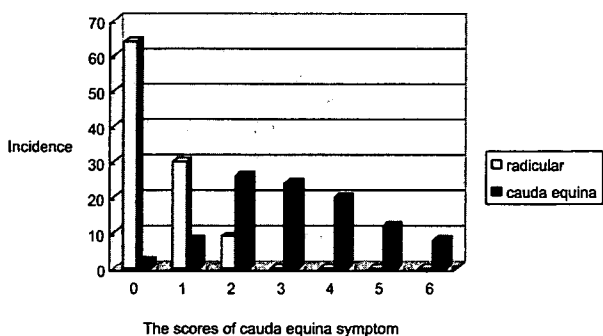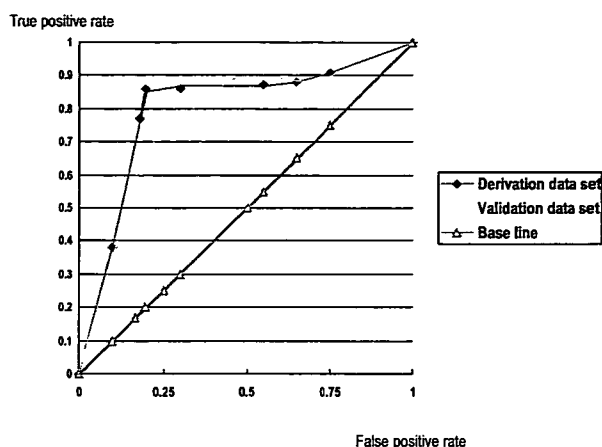

The scores of cauda equina symptom

Figure 3
Cut-off point to distinguish between the categories.

False positive rate

Derivation Data Set : ROC Area=0.797 (95%CI, 0.714-0.862)
Validation Data Set : ROC Area=0.782 (95%CI, 0.685-0.869)

Figure 4
Receiver operating characteristic (ROC) curves for the derivation and validation datasets.

do not prove that symptoms arise from nerve root compression [14,15]. A systematic review of original diagnostic studies on LSS revealed that no firm conclusions about the diagnostic performance of the different tests could be drawn due to heterogeneity and overall poor quality[16].

We developed a simple clinical diagnostic support tool to identify patients with LSS[17]. Although further studies
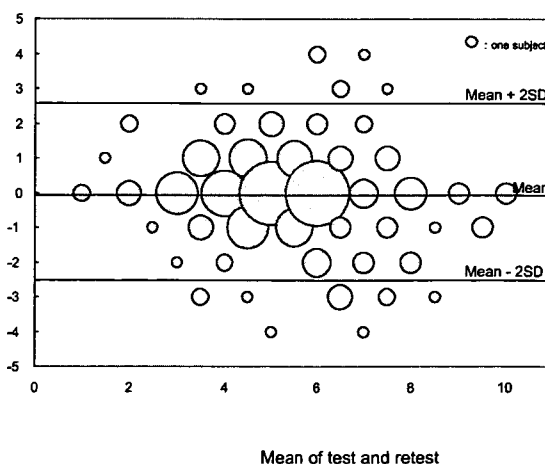
Difference between test and retest

Mean of test and retest

Figure 5
Scatter plot of differences versus the means of the test and the retest.

Table 6: Performance indices for the clinical prediction rule

Index	Estimate	
	Derivation Data Set (n = 234)	Validation Data Set (n = 250)
Sensitivity	0.855	0.843
Specificity	0.791	0.781
Likelihood Ratio		
Positive Test Result	1.951	1.886
Negative Test Result	0.201	0.214
Area under the ROC curve	0.797	0.782

Positive criteria: Total score ≥ 4 (Q1–Q4) or Total score ≥ 1 (Q1–Q4) and ≥ 2 (Q5–Q10)

are needed to validate this tool in primary care settings, it has a sensitivity of 92.8% and a specificity of 72.0%. By asking patients, who presented with back and leg symptoms suggestive of LSS, to fill out a simple questionnaire, consisting of five questions on their medical history (age and history of diabetes) and symptoms (presence or absence of intermittent claudication, aggravation of symptoms by standing and relief of symptoms by forward bending) followed by a short clinical examination checking the postural changes in their leg symptoms, Achilles' tendon reflex, SLR test and the measurement of ABI, the diagnosis of LSS can be established by high sensitivity and spcificity without obtaining MRI. Therefore, misdiagnosis or underdianosis of LSS at the primary care levels can be minimized and patients have a greater chance to get access to appropriate medical service by a referral to a spine specialist. A self-administered, self-reported history questionnaire as a diagnostic support tool for LSS might be more useful for clinician or patients. Therefore, we attempted to develop a self-administered, self-reported history questionnaire as a diagnostic support tool for LSS using a clinical epidemiological approach. To make an accurate diagnosis of LSS from history findings, we categorized the condition into radicular and cauda equina types. A comparison of the sensitivity of each question on the SSHQ showed both overlap and differences between the two categories (Figure 1). These findings suggest that the category of LSS requires consideration to make an accurate diagnosis. The scoring system includes a cut-off point to distinguish the radicular type from the cauda equina type (Figure 2). About 50% of radicular-type cases show relief of symptoms at six months after nerve root block and a further 17% improve with more time after nerve root block. In the cauda equina type, nerve root block is not efficient in relieving the symptoms and therefore surgical intervention is recommended [18]. Therefore, we consider that it is important to define the type of neurogenic intermittent claudication before selecting the therapeutic method, since surgery may be avoidable in certain cases.

The 10 items on the SSHQ for diagnosis of LSS require answers of either "yes" or "no" to minimize any difficulty with responses. As noted above, it took respondents an average of about 1 minute to answer the questions, which indicates that the questionnaire was easy to understand. However, the study has several limitations. First, there is no gold standard for diagnosis of LSS, but in the absence of valid objective criteria we believe that expert opinion is a reasonable strategy for making a diagnosis of a clinical syndrome, and this approach has been used for a variety of disorders. Therefore, we used LSS diagnoses made by six board-certified spine surgeons in our validation study. Second, we did not use logistic regression and multivariate models. Based on the results of this paper, we are planning to use logistic regression and multivariate models in the next project according to STARD checklist for reporting diagnostic accuracy studies [19]. We also note that a larger prospective derivation and validation studies might reveal additional independent factors that correlate with diagnosis of LSS.

Conclusion
The newly developed self-administered, self-reported history questionnaire can be used for diagnosis of LSS with high sensitivity, specificity, and reproducibility.

Competing interests
The author(s) declare that they have no competing interests.

Authors' contributions
SKonno, SKikuchi, SKokuban, YT, YS, KY, MO, TY and HT conceived the study and participated in the study design. SK performed the statistical analysis. SK drafted the initial manuscript for journal submission and participated in revisions. SKonno, SKikuchi, SKokuban, YT, YS, KY, MO, TY and HT coordinated data collection at each site. All authors read and approved the final manuscript.

Additional material

Additional file 1
Japanese version of the SSHQ. A copy of the Japanese version of the SSHQ for Japanese readers
Click here for file
[http://www.biomedcentral.com/content/supplementary/1471-2474-8-102-S1.doc]

Additional file 2
English version of the SSHQ. A copy of the English version of the SSHQ
Click here for file
[http://www.biomedcentral.com/content/supplementary/1471-2474-8-102-S2.doc]

References
1. de Graaf I, Prak A, Bierma-Zeinstra S, Thomas S, Peul W, Koes B: **Diagnosis of lumbar spinal stenosis: a systematic review of the accuracy of diagnostic tests.** *Spine* 2006, **31:**1168-1176.
2. Beattie PF, Meyers SP, Stratford P, Millard RW, Hollenberg GM: **Associations between patient report of symptoms and anatomic impairment visible on lumbar magnetic resonance imaging.** *Spine* 2000, **25:**819-828.
3. Amundsen T, Weber H, Lilleas F, Nordal HJ, Abdelnoor M, Magnaes B: **Lumbar spinal stenosis. Clinical and radiologic features.** *Spine* 1995, **20:**1178-1186.
4. Katz JN, Dalgas M, Stucki G, Katz NP, Bayley J, Fossel AH, Chang LC, Lipson SJ: **Degenerative lumbar spinal stenosis Diagnostic value of the history and physical examination.** *Arthritis & Rheumatism* 1995, **38:**1236-1241.
5. Mirkovic S, Lybulski G, Montgomery DM, Wang AM, Wesolowski DP, Garfin SR: **Spinal stenosis Clinical Evaluation and Different Diagnosis.** *Rothman-Simeone, the spine* 4th edition. 1999:796-806.
6. Rauschning W: **Pathoanatomy of lumbar disc degeneration and stenosis.** *Acta Orthop Scand* 1993, **64:**3-12.
7. Yoshida M, Shima K, Taniguchi Y, Tamaki T, Tanaka T: **Hypertrophied ligamentum flavum in lumbar spinal canal stenosis: Pathogenesis and morphologic and immunohistochemical observation.** *Spine* 1992, **17:**1353-1360.
8. Konno S, Kikuchi S: **Prospective study of surgical treatment of degenerative spondylolisthesis. Comparison between decompression alone and decompression with Graf system stabilization.** *Spine* 2000, **25:**1533-1537.
9. Bland JM, Altman DG: **Statistical methods for assessing agreement between two methods of clinical measurement.** *Lancet* 1986, **1:**307-10.
10. Chalmers I: **Underreporting research is scientific misconduct.** *JAMA* 1990, **263:**1405-1408.
11. Jonnson B, Stromqvist B: **Symptoms and signs in degeneration of the lumbar spine : a prospective, consecutive study of 300 operated patients.** *J Bone Joint Surg Br* 1993, **75:**381-384.
12. Pheasant HC, Dyck P: **Failed lumbar disc surgery: cause, assessment, treatment.** *Clin Orthop Relat Res* 1982, **(164):**93-109.
13. Ray CD: **Extensive lumbar decompression: Patient selection and results.** In *Lumbar spine surgery* Edited by: White AH, Rothman RH, Ray CD. St. Louis CV Mosby Co; 1987.
14. Boden SD, Davis DO, Dina TS, Partronas NJ, Wiesel SW: **Abnormal magnetic resonance scans of the lumbar spine in asymptomatic subjects: a prospective investigation.** *J Bone Joint Surg [Am]* 1990, **72:**403-408.
15. Wiesel SW, Tsourmas N, Feffer HL, Citrin CM, Patronas N: **A study of computer-assisted tomography. The incidence of positive CAT scans in an asymptomatic group of patients.** *Spine* 1984, **9:**549-551.
16. de Graaf I, Prak A, Bierma-Zeinstra S, Thomas S, Peul W, Koes B: **Diagnosis of lumbar spinal stenosis: a systematic review of the accuracy of diagnostic tests.** *Spine* 2006, **31:**1168-1176.
17. Konno S, Hayashino Y, Fukuhara S, Kikuchi S, Kaneda K, Seichi A, Chiba K, Satomi K, Nagata K, Kawai S: **Development of a clinical diagnosis support tool to identify patients with lumbar spinal stenosis.** *Eur Spine J* 2007 in press. [Epub ahead of print]
18. Konno S, Kikuchi S: **Pathomechanism of spinal canal stenosis. The therapeutic effects of nerve root infiltration, selective spinal angiography, and sympathetic nerve block.** *Proceeding of the 30th congress of the international college of surgeons. Bologna* 1996:1309-1313.
19. Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, Lijmer JG, Moher D, Rennie D, de Vet HC: **Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative.** *BMJ* 2003, **326:**41-4.

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ORIGINAL ARTICLE

Development of a clinical diagnosis support tool to identify patients with lumbar spinal stenosis

Shinichi Konno · Yasuaki Hayashino · Shunichi Fukuhara · Shinichi Kikuchi ·
Kiyoshi Kaneda · Atsushi Seichi · Kazuhiro Chiba · Kazuhiko Satomi ·
Kensei Nagata · Shinya Kawai

Abstract No clinical diagnostic support tool can help identify patients with LSS. Simple diagnostic tool may improve the accuracy of the diagnosis of LSS. The aim of this study was to develop a simple clinical diagnostic tool that may help physicians to diagnose LSS in patients with lower leg symptoms. Patients with pain or numbness of the lower legs were prospectively enrolled. The diagnosis of LSS by experienced orthopedic specialists was the outcome measure. Multivariable logistic regression analysis identified factors that predicted LSS; a simple clinical prediction rule was developed by assigning a risk score to each item based on the estimated beta-coefficients. From December 2002 to December 2004, 104 orthopedic physicians from 22 clinics and 50 hospitals evaluated 468 patients. Two items of physical examination, three items of patients' symptom, and five items of physical examination were included in the final scoring system as a result of multiple logistic regression analysis. The sum of the risk scores for each patient ranged from −2 to 16. The Hosmer–Lemeshow statistic was 11.30 ($P = 0.1851$); the area under the ROC curve was 0.918. The clinical diagnostic support tool had a sensitivity of 92.8% and a specificity of 72.0%. The prevalence of LSS was 6.3% in the bottom quartile of the risk score (−2 to 5) and 99.0% in the top quartile (12 to 16). We developed a simple clinical diagnostic support tool to identify patients with LSS. Further studies are needed to validate this tool in primary care settings.

Keywords Lumbar spine · Lumbar spinal stenosis · Diagnosis

S. Konno (✉) · S. Kikuchi
Department of Orthopaedic Surgery, Fukuhsima Medical
University, Hikarigaoka 1, Fukushima 960-1295, Japan
e-mail: skonno@fmu.ac.jp

Y. Hayashino · S. Fukuhara
Epidemiology and Healthcare Research, Kyoto University,
Kyoto, Japan

S. Kawai
Orthopaedic Surgery, Yamaguchi University, Yamaguchi, Japan

K. Kaneda
Orthopaedic Surgery, Bibai Rosai Hospital, Bibai, Japan

A. Seichi
Orthopaedic Surgery, Tokyo University, Tokyo, Japan

K. Chiba
Orthopaedis Surgery, Keio University, Tokyo, Japan

K. Satomi
Orthopaedic Surgery, Kyorin University, Tokyo, Japan

K. Nagata
Orthopaedic Surgery, Kurume University, Kurume, Japan

Background

Lumbar spinal stenosis (LSS) results from compression of the cauda equina or existing nerve roots and leads to substantial functional disability [12, 18, 20]. The diagnosis of symptomatic LSS has implications for treatment, since symptoms that are caused by nerve root compression may respond to either conservative treatments or decompressive surgery. Clinicians cannot rely solely on diagnostic imaging tests to make the diagnosis of LSS. Computed tomography and magnetic resonance imaging are often nonspecific [8], and there are discrepancies between clinical symptoms and imaging findings in lumbar spinal stenosis [1, 3], and these test results cannot determine whether symptoms arise from nerve root compression [4, 17, 22].

Thus, the clinical correlation between imaging test results and symptoms must ultimately be made on the basis of history and physical examination, both of which have not been extensively studied in LSS patients.

Symptoms of LSS are often chronic, frequently missed, and frequently misdiagnosed [11], resulting in severe disability or reduction in patients' quality of life [10]. Possible reasons for this difficulty in making the diagnosis may include a lack of training in the recognition of this disorder or a failure of patients and/or their healthcare providers to discuss health problems during a health care visit. The patients' symptoms, specific questions on history taking, and the findings on physical examination are all used to make the diagnosis of LSS in the primary care setting. A simple clinical support tool may assist primary care physicians to identify patients with LSS more readily; patients would then benefit from an appropriate therapeutic approach.

The objective of this study was to develop and evaluate a user-friendly clinical tool based on a scoring system for the diagnosis of LSS so as to deliver a better quality of care to LSS patients.

Methods

Study design and setting

We prospectively evaluated the association between the diagnosis of LSS and clinical information, including the history and physical examination of patients with low back pain, leg pain, or tingling of the legs. This study was performed in university hospitals, medical centers, and other hospitals and clinics affiliated with university hospitals or medical centers. We enrolled consecutive patients older than 20 years of age with primary symptoms of pain or numbness in the legs. We selected these symptoms, since patients with these symptoms are often misdiagnosed as having peripheral artery disease or are otherwise underdiagnosed even though they have LSS. Such patients would benefit from a diagnostic tool that would improve their quality of care. We excluded patients who have been treated by some medical practices within one year before examination. Patients with cervical myelopathy, previous surgery, and inflammatory disorders were also excluded. The study was approved by the institutional review board of each study institution as necessary. Written informed consent was obtained from the all patients.

We collected the following information for the current alalysis: age (<60, 60–70, ≥70 years), gender, months from onset (quartiles), leg numbness or pain, back pain, intermittent claudication, bilateral plantar numbness, exacerbation of symptoms when standing up, improvement of

symptom when bending forward, symptoms related to cauda equina syndrome, no history of diabetes, history of hypertension, history of hyperlipidemia, peripheral circulation (poor, good), straight leg raising (SLR) test, symptoms induced by having patients bend forward, symptoms induced by having patients bend backward, abnormality on manual muscle testing, any sensory disturbance, abnormal Achilles tendon reflex, abnormal patellar tendon reflexes. Poor peripheral circulation was defined as a dorsalis pedis artery that was not easily palpable or, if the blood pressure of the legs was measured, an ankle brachial index of less than 0.9 [2, 5, 16]. Orthopedic staff physicians in each institution took a history, did a physical examination, and ordered lumbar X-rays and magnetic resonance imaging evaluation (MRI) based on a standardized protocol. The history taken by the physicians included information on the type and distribution of patients' symptoms (such as leg pain and low back pain), the posture that attenuated or worsened these symptoms, and comorbidities, such as diabetes or peripheral artery disease. The physical examination included the ankle brachial index and various tests that are thought to identify dysfunction in the lumbopelvic region [21]. Patients then had lumbar X-rays and MRIs. We allowed all enrolled patients to have diagnostic imaging studies. Each participating physician recorded the clinical and diagnostic test information on a standardized report form, and then sent the form to the study coordinator, an experienced orthopedic surgeon, who verified the information on the form and the diagnosis.

Outcome measure

In the absence of a universally accepted gold standard for LSS, the impression of expert clinicians provides a reasonable method of establishing a clinical diagnosis [9]. Such an approach has been adopted in the development of classification criteria for rheumatic diseases, which, like LSS, cannot be defined by a single laboratory measurement [2, 13].

The following steps were taken to reach a final diagnosis for each of the enrolled patients (Fig. 1). In the first step, at each institution the orthopedic physician who saw a patient made the clinical diagnosis based on the history, physical examination, and radiographic findings. In addition, to verify the diagnosis made by each physician, the study coordinator also made a diagnosis for each patient based on the clinical information and a copy of the diagnostic imaging studies. Interobserver agreement (physicians in each institution and one panel member) was assessed by calculating agreement ratios and the kappa statistic [5].

As there was a substantial discrepancy in the diagnoses [interobserver agreement rate on the diagnosis of LSS was 60.8%, and kappa was 0.261 (95%CI, 0.185–0.336)], we
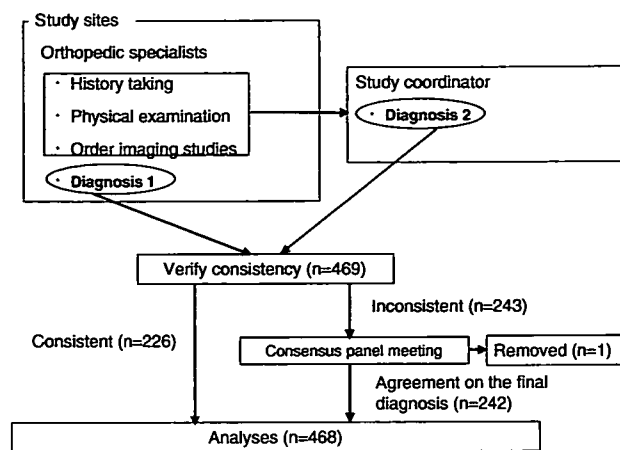
Fig. 1 Flow chart showing how the diagnosis of LSS was determined. Diagnosis 1 denotes the diagnosis made by an orthopedic physician at each study site, and diagnosis 2 denotes the diagnosis made by the study coordinator. Of the 469 patients enrolled in this study, the diagnoses of 226 cases were consistent. Inconsistencies in the remaining 243 cases were resolved by a consensus panel meeting. Only one case was removed from the analysis because no agreement could be reached on the final diagnosis

created a second step for the making the diagnosis. We formed a consensus panel that would meet and resolve any discrepancies. The consensus panel consisted of 10 expert physicians with extensive clinical experience of LSS; all panel members were either professors or associate professors at university hospitals or chiefs of departments of orthopedics at teaching hospitals in Japan. For each case in which there was a discrepancy in the diagnosis in the first step, each panel member scored the probability of LSS on a scale from 1 to 4 (lowest = 1, highest = 4) based on the clinical information and the imaging studies. Then, the mean score for each patient was calculated. If a patient's mean score was equal to or above 3, the diagnosis was confirmed as LSS; if the mean score was equal to or below 2, the case was regarded as non-LSS. When the mean score was between 2 and 3, consensus panel members discussed why there was a discrepancy, and after a thorough discussion a final diagnosis was made. If there was no agreement on the diagnosis, the case was removed from the analysis.

Statistical analysis

The diagnostic support tool was developed in two steps. Step 1 was designed to identify a subgroup of patients who were likely to have LSS and therefore needed additional investigation. In this first step, we tested the all the variables collected for this study. When we derived the model for the scoring system, we did not include variables from the MRI studies, because it is not practical to obtain MRI in

all patients who are complaining low back and leg symptoms. Each questionnaire item was evaluated using simple logistic regression, and the odds ratio was calculated.

In the next step of developing the clinical decision support tool, factors with a P value less than 0.2 on the univariate analyses in step 1, as well as the variables that we thought clinically important from our experience as orthopedic specialists, were included in the stepwise multiple logistic regression model. We identified the significant ($P < 0.05$) predictors of a final diagnosis of LSS, and removed any variable that had a p-value more than 0.05 in the final model. Using a regression coefficient-based scoring system, a score-based prediction rule for a final diagnosis of LSS was developed for each step based on the results of the multivariable logistic regression equations. To generate a simple integer-based point score for each predictor variable, scores were assigned by dividing the β-coefficient by two-fifths of the sum of the two smallest coefficients in the model and rounding up to the nearest integer. The overall risk score for each patient was calculated by summing the scores of each component.

The discrimination ability of the models was assessed by the area under the receiver operating characteristic (ROC) curve, and the calibration was evaluated by using the Hosmer–Lemeshow chi-square statistic ($P > 0.05$ for all models); P equal or greater than 0.05 supports the goodness of fit. Discriminatory power is the ability to identify which patients are likely to have an outcome; An area of 1.00 under the ROC curve indicates perfect discrimination whereas an area of 0.50 indicates complete absence of discrimination. The calibration was also evaluated by comparing the prevalence of LSS in the risk score quartiles. To examine the performance of the support tool, we calculated the sensitivity, the specificity, and the likelihood ratios for positive and negative results. The positivity criterion for the presence of LSS was defined as the point with the highest sum of sensitivity and specificity.

Results

A total of 104 orthopedic surgeons from 22 clinics and 50 hospitals in various sites of Japan evaluated 469 patients from December 2002 to December 2004. The patients' mean age was 64.2 (range 20–96) years, and 45.9% were male. Of the total 469 participants, the diagnoses were consistent between two observers in 226 participants; of these, 126 cases were diagnosed as having LSS. The consensus panel discussed the 243 cases that were given initially discrepant diagnoses. Mean scores of 61 cases were equal or above 3, then the diagnosis of these patients was confirmed as LSS; mean scores of 166 patients were equal or below 2, the case was regarded as non LSS. Mean scores

of 15 cases were between 2 and 3, then consensus panel members discussed why the discrepancy was raised, and after careful discussion final diagnosis was made; of these 15 cases, 11 cases were diagnosed as having LSS. The consensus panel did not reach agreement in one case; this case was removed from the analysis. Thus, 468 cases were included in the current analysis. The overall prevalence of LSS was 47.4%. Other diagnoses included: lumbar disc herniation (17.7%), diabetic neuropathy (2.8%), and peripheral artery disease (8.3%). In 23.7% of patients, no specific diagnosis other than "not LSS" was made.

In step 1, on univariate analysis, the following variables had a P value less than 0.2 (Table 1): age, onset; symptoms including presence of pain or numbness of the legs, presence of low back pain, presence of bilateral plantar numbness, urinary disturbance, presence of numbness in the perineal region, exacerbation of symptoms when standing up, improvement of symptoms when bending forward, presence of symptoms related to the cauda equina syndrome; cormorbidity, including absence of diabetes, hypertension, and hyperlipidemia; physical examination, including good peripheral artery circulation, a positive straight leg raising test, symptoms induced by having patients bend forward, symptoms induced by having patients bend backward, abnormal Achilles tendon reflex, and abnormal patellar tendon reflex (Table 2).

In step 2, on stepwise multivariable logistic regression analysis, we include all variables with a P value less than 0.2. However, since we thought that the history of diabetes was important for the diagnosis of LSS, since diabetic neuropathy is one of the differential diagnoses of LSS, we included the absence of diabetes in the model, even though it had a P value greater than 0.2. Thus, the following variables were included as independent predictors in the multivariable model with a P value less than 0.05: age, absence of diabetes, intermittent claudication, exacerbation of symptoms when standing up, improvement of symptoms

when bending forward, symptoms induced by having patients bend forward, symptoms induced by having patients bend backward, good peripheral artery circulation, abnormal Achilles tendon reflex, and positive SLR test (Table 3). For the final model, the Hosmer–Lemeshow statistic was 11.30 ($P = 0.1851$), which indicates good calibration. To develop a simple clinical diagnostic tool from the results of step 2, an integer score derived from the β-coefficient was assigned to the identified risk factors. For each patient, all applicable risk score values were summed up to attain a total risk score for the patient. The sum of the risk scores for each patient ranged from −2 to 16.

Table 4 presents the model performance indices. The area under the ROC curve was 0.918; thus the model had good discriminatory power (Fig. 1). The positivity cut-off point was defined as 7, since the sum of the sensitivity and the specificity was the highest at that cut-off point. Given that the positivity criterion for risk score was greater than 7, the clinical diagnostic support tool had a sensitivity of 92.8% and a specificity of 72.0%. The prevalence of LSS increased as the risk score increased; LSS prevalences were 6.3% in the first quartile (−2 to 5), 39.3% in the second quartile (6 to 8), 72.4% in the third quartile (9 to 11), 99.0% in the fourth quartile (12 to 16); these results suggest good calibration of the model (Fig. 2).

Discussion

The purpose of a clinical prediction rule is to improve the accuracy of diagnosis [14, 16]. The rule we developed was designed to help non-orthopedic specialists to identify patients with LSS. The prevalence of degenerative spine disease will increase with the continued aging of the population [15]. This will require not only orthopedic specialists to develop greater expertise in diagnosing LSS, but also non-specialists will need to have screening tools for this condition. The diagnostic support tool we developed is simple and easy to use, and thus our results indicate that self-reported symptoms and medical history are useful, and thus this tool may be useful even for non orthopedic specialists to identify patients with LSS.

The presence of a narrowed spinal canal on radiographic imaging does not define LSS [1, 3, 4, 8, 22]. No significant correlation is found between the area of the dural sac in axially loaded CT and the clinical symptoms of spinal stenosis [22]. Confusing clinical findings resembling spinal stenosis are relatively common in patients who have mild or no narrowing of the spinal canal on CT [22]. Symptomatic lumbar spondylosis, peripheral arterial disease (PAD), and peripheral neuropathy must all be considered in the differential diagnosis of LSS. Since both symptomatic lumbar spondylosis and LSS are caused by the aging

Table 1 Participants' demographic characteristics

Variables	($n = 469$)	
Age (mean ± SD years)	65.2 ± 13.7	
Gender (male)	45.9%	
Clinical impressions of patient condition	N	%
LSS	222	47.3
LDH[a]	83	17.7
Diabetic neuropathy	13	2.8
Peripheral artery disease	39	8.3
Other[b]	111	23.7
Undetermined	1	0.1

[a] Lumbar disc herniation

[b] Unknown or unspecified, but regarded as non LSS

Table 2 Univariate analyses for factors from the MD and MRI data sheets associated with a diagnosis of LSS

	LSS (−), n = 246	LSS (+),n = 222	Odds ratio	95% CI	P value
Age (years)					
<60	37.9%	15.3%	Reference		
60–70	23.5%	24.8%	2.61	1.53–4.44	<0.001
>70	31.8%	64.4%	4.66	2.89–7.49	<0.001
Gender (female)	45.5%	46.4%	1.04	0.72–1.49	0.851
Onset					0.003
1st quartile (<1 month)	30.1%	18.5%	Reference		
2nd quartile (1–5 months)	25.6%	23.9%	1.52	0.90–2.58	0.121
3rd quartile (6–12 months)	23.6%	25.2%	1.74	1.03–2.96	0.040
4th quartile (≥13 months)	17.5%	30.6%	2.85	1.66–4.90	<0.001
Missing data	3.3%	1.8%	0.90	0.26–3.18	0.873
Symptoms					
Leg pain or numbness (+)	44.7%	57.7%	1.68	1.17–2.43	0.005
Low back pain (+)	58.5%	66.2%	1.39	0.95–2.02	0.088
Intermittent claudication (+)	22.0%	82.0%	16.18	10.25–25.53	<0.001
Bilateral plantar numbness (+)	12.6%	27.0%	2.57	1.59–4.15	<0.001
Urinary disturbance (+)	2.0%	14.0%	7.82	2.99–20.50	<0.001
Numbness of perineal region (+)	1.2%	4.5%	3.82	1.04–14.07	0.044
Exacerbation of symptoms when standing up	29.7%	68.0%	5.04	3.40–7.47	<0.001
Improvement of symptoms when bending forward	8.1%	51.8%	12.14	7.17–20.58	<0.001
Symptoms related to cauda equina syndrome[a]	0.8%	5.9%	7.59	1.69–34.01	0.008
Comorbidity					
Diabetes (−)	82.9%	83.3%	1.03	0.63–1.67	0.97
Hypertension (+)	23.6%	41.9%	2.34	1.57–3.48	<0.001
Hyperlipidemia (+)	7.3%	13.1%	1.90	1.03–3.53	0.041
Physical examination					
Peripheral artery circulation					
Bad[b]	19.5%	14.9%	Reference		
Good	57.7%	73.9%	1.68	1.02–2.76	0.041
Missing data	22.8%	11.3%	0.65	0.34–1.24	0.191
Straight leg raising test positive	32.9%	16.7%	0.41	0.26–0.63	<0.001
Symptoms induced by having patients bend forward (+)	37.0%	17.6%	0.36	0.24–0.56	<0.001
Symptoms induced by having patients bend backward (+)	45.5%	69.8%	2.77	1.89–4.05	<0.001
Abnormal manual muscle strength test[c]	6.9%	9.5%	1.41	0.72–2.74	0.315
Sensory disturbance					
(−)	56.9%	49.5%	Reference		
(+)[d]	37.8%	44.6%	1.00	0.99–1.01	0.762
Missing data	5.3%	5.9%	1.27	0.57–2.86	0.559
Achilles tendon reflex					
Normal	54.5%	32.4%	Reference		
Abnormal[e]	43.5%	66.2%	2.56	1.75–3.74	<0.001
Missing data	2.0%	1.4%	1.12	0.26–4.81	0.882
Patellar tendon reflex					
Normal	70.3%	63.5%	Reference		
Abnormal[e]	28.5%	36.5%	1.42	0.96–2.10	0.078

Table 2 continued

	LSS (–), $n = 246$	LSS (+),$n = 222$	Odds ratio	95% CI	P value
Missing data	1.2%	0.0%	–	–	–

[a] A burning sensation around the buttocks and/or intermittent priapism associated with walking

[b] Ankle brachial index (API)<0.9, or diminished pulsation of dorsalis pedis artery or posterior tibial artery

[c] MMT ≤ 3, Strength was graded from 0 (no movement) to 5 (normal) at the knee extensors, ankle dorsiflexors, and plantar flexors, and extensor hallucis longus

[d] Hypoesthesia, analgesia, or hyperalgesia at the medial knee, dorsal foot, plantar foot, and perineal lesion

[e] Absence or low response of deep reflexes

Table 3 Multivariable predictors of a diagnosis of LSS and the associated risk scoring system

Characteristic	Regression β-coefficient	95% CI	Risk score assigned*
History			
Age (years)			
60–70	0.91	0.09–1.73	1
>70	1.36	0.60–2.11	2
Absence of diabetes	0.93	0.19–1.68	1
Symptoms			
Intermittent claudication (+)	2.43	1.82–3.04	3
Exacerbation of symptoms when standing up	1.27	0.65–1.89	2
Symptom improvement when bending forward	2.09	1.36–2.82	3
Physical examination			
Symptoms induced by having patients bend forward	–0.91	–1.61 to –0.22	–1
Symptoms induced by having patients bend backward	0.90	0.31–1.49	1
Good peripheral artery circulation	1.96	1.14–2.77	3
Abnormal Achilles tendon reflex	1.03	0.40–1.66	1
SLR test positive	–1.12	–1.87 to –0.37	–2

* Scores were assigned by dividing the β-coefficient by the absolute value of two-fifths of the sum of the two smallest coefficients in the model. Hosmer–Lemeshow statistics, 11.30 ($P = 0.1851$)

Table 4 Performance indices of the clinical prediction rule

Index	Estimates
Sensitivity[a]	0.928
Specificity[a]	0.720
Likelihood ratio[a]	
Positive test result[a]	3.31
Negative test result[a]	0.1
Area under the ROC curve	0.918

[a] Given the positivity criteria for the total risk score ≥7

process, the differential diagnosis may be difficult. The primary distinguishing symptom of LSS seems to be a predominance of leg symptoms. Therefore, in this study, we studied patients whose primary symptoms were pain or numbness of the legs.

Several limitations of this study should be noted. First, there is no good objective reference standard for diagnosing LSS; it is essentially a clinical diagnosis. Imaging studies such as computed tomography (CT) or MRI showing compression of nerve root are insufficient for making the diagnosis of LSS, since false positive and false negative results are well documented [4, 7, 22]. MRI and CT findings of LSS using current qualitative methods result in significant variation of image interpretation [19]. However, in the absence of valid objective criteria, expert opinion is a reasonable strategy for making the diagnosis of a clinical syndrome [9], and has been used in a variety of disorders [2, 13]. In our current study, when there was an inconsistency in diagnosis between the first two observers, the inconsistency was resolved by a consensus panel consisting of 10 orthopedic specialists, and such an expert panel should provided a sufficiently accurate reference standard for the current analysis. Second, this study was
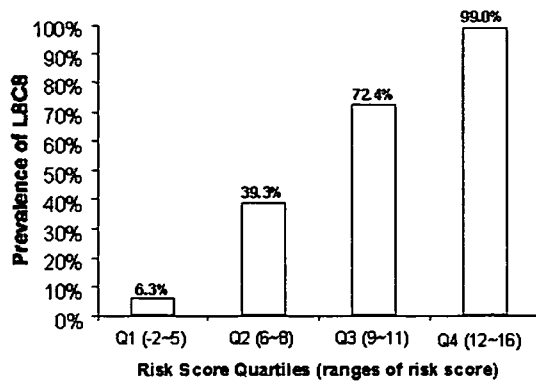
Fig. 2 Incidence of LSS stratified by risk score quartiles. Quartile 1 represents a risk score of –2 to 5, quartile 2 represents a risk score of 6 to 8, quartile 3 represents a risk score of 9 to 11, and quartile 4 represents a risk score of 12 to 17

performed primarily in hospitals, such as university hospitals, medical centers, and other hospitals, while LSS is prevalent in the primary care setting, where it is often underdiagnosed or misdiagnosed. The diagnostic support tool that we developed may play an important role in such settings, though our scoring system has yet to be validated in the further research; in this research, primary care physician use our tool and evaluate the usability of our tool, and the sensitivity, specificity, and discriminatory power should also be evaluated. Pulse palpation is not sensitive for the detection of peripheral artery disease compared to ankle brachial index. It was reported that more than two thirds of the patients with peripheral artery disease of either the left or right leg had a detectable pulse, especially in overweight patients [6]. Although our results suggested that palpation of dorsalis pedis or ankle blood pressure less than 0.9 is useful to predict LSS, caution should be made for our diagnostic tool to be applied to overweight patients.

Despite these limitations, this is the first report of the development of a diagnostic support tool for LSS. Using this tool, it is possible to accurately diagnose patients with LSS. We expect that use of the tool in primary care will improve the accuracy of diagnosis, thus leading to improved quality of patient care.

Conclusions

We developed a simple clinical diagnostic support tool to identify patients with LSS.

References

1. Amundsen T, Weber H, Lilleas F, Nordal HJ, Abdelnoor M, Magnaes B (1995) Lumbar spinal stenosis. Clinical and radiologic features. Spine 20:1178–1186

2. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, Healey LA, Kaplan SR, Liang MH, Luthra HS, et al (1988) The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 31:315–324

3. Beattie PF, Meyers SP, Stratford P, Millard RW, Hollenberg GM (2000) Associations between patient report of symptoms and anatomic impairment visible on lumbar magnetic resonance imaging. Spine 25:819–828

4. Boden SD, Davis DO, Dina TS, Patronas NJ, Wiesel SW (1990) Abnormal magnetic-resonance scans of the lumbar spine in asymptomatic subjects. A prospective investigation. J Bone Joint Surg Am 72:403–408

5. Chalmers I (1990) Underreporting research is scientific misconduct. Jama 263:1405–1408

6. Collins TC, Suarez-Almazor M, Peterson NJ (2006) An absent pulse is not sensitive for the early detection of peripheral arterial disease. Fam Med 38:38–42

7. Coulier B, Devyver B, Ghosez JP (2003) Severe underestimation of lumbar spinal stenosis by supine imaging. Clin Radiol 58:167–169

8. de Graaf I, Prak A, Bierma-Zeinstra S, Thomas S, Peul W, Koes B (2006) Diagnosis of lumbar spinal stenosis: a systematic review of the accuracy of diagnostic tests. Spine 31:1168–1176

9. Feinstein AR (1985) Clinical epidemiology: the architecture of clinical research. WB Saunders, Philadelphia

10. Goldman SM, Funk JD, Christensen VM (1997) Spinal stenosis. A common cause of podiatric symptoms. J Am Podiatr Med Assoc 87:117–124

11. Goldman SM (2004) Diabetic peripheral neuropathy and spinal stenosis: prevalence of overlap and misdiagnosis. An introductory report. Diabet Med 21:394–396

12. Jonsson A, Rydberg T, Sterner G, Melander A (1998) Pharmacokinetics of glibenclamide and its metabolites in diabetic patients with impaired renal function. Eur J Clin Pharmacol 53:429–435

13. Katz JN, Liang MH (1991) Classification criteria revisited. Arthritis Rheum 34:1228–1230

14. Laupacis A, Sekar N, Stiell IG (1997) Clinical prediction rules. A review and suggested modifications of methodological standards. Jama 277:488–494

15. Lawrence JS (1969) Disc degeneration. Its frequency and relationship to symptoms. Ann Rheum Dis 28:121–138

16. McGinn TG, Guyatt GH, Wyer PC, Naylor CD, Stiell IG, Richardson WS (2000) Users' guides to the medical literature: XXII: how to use articles about clinical decision rules. Evidence-Based Medicine Working Group. Jama 284:79–84

17. Powell MC, Wilson M, Szypryt P, Symonds EM, Worthington BS (1986) Prevalence of lumbar disc degeneration observed by magnetic resonance in symptomless women. Lancet 2:1366–1367

18. Spengler DM(1987) Degenerative stenosis of the lumbar spine. J Bone Joint Surg Am 69:305–308

19. Stafira JS, Sonnad JR, Yuh WT, Huard DR, Acker RE, Nguyen DL, Maley JE, Ramji FG, Li WB, Loftus CM (2003) Qualitative assessment of cervical spinal stenosis: observer variability on CT and MR images. AJNR Am J Neuroradiol 24:766–769

20. Stucki G, Liang MH, Lipson SJ, Fossel AH, Katz JN (1994) Contribution of neuromuscular impairment to physical functional status in patients with lumbar spinal stenosis. J Rheumatol 21:1338–1343

21. Waddell G, Somerville D, Henderson I, Newton M (1992) Objective clinical evaluation of physical impairment in chronic low back pain. Spine 17:617–628

22. Wiesel SW, Tsourmas N, Feffer HL, Citrin CM, Patronas N (1984) A study of computer-assisted tomography. I. The incidence of positive CAT scans in an asymptomatic group of patients. Spine 9:549–551

ORIGINAL ARTICLE

Spinal stenosis: assessment of motor function, VEGF expression and angiogenesis in an experimental model in the rat

Kazuyuki Watanabe · Shin-ichi Konno ·
Miho Sekiguchi · Shin-ichi Kikuchi

Abstract Reduction of blood flow in compressed nerve roots is considered as one important mechanism of induction of neurogenic intermittent claudication in lumbar spinal canal stenosis. Vascular endothelial growth factor (VEGF) is a potent stimulator of angiogenesis, and is increased in expression in hypoxic conditions. The objective of this study was to examine if cauda equina compression affects motor function and induces expression of VEGF and angiogenesis. The cauda equina was compressed by placing a piece of silicone rubber into the L5 epidural space. Walking duration was examined by rota-rod testing. The compressed parts of the cauda equina and L5 dorsal root ganglion (DRG) were removed at 3, 7, 14, or 28 days after surgery, and processed for immunohistochemistry for VEGF and Factor VIII (marker for vascular endothelial cells). Numbers of VEGF-immunoreactive (IR) cells and vascular density were examined. Walking duration was decreased after induction of cauda equina compression. The number of VEGF-IR cells in the cauda equina and DRG was significantly increased at 3, 14, and 28 days after cauda equina compression, compared with sham-operated rats ($P < 0.05$). Vascular density in the cauda equina was not increased at any of the time points examined. Cauda equina compression decreased walking duration, and induced VEGF expression in nerve roots and DRG.

K. Watanabe (✉) · S. Konno · M. Sekiguchi ·
S. Kikuchi
Department of Orthopaedic Surgery,
Fukushima Medical University School of Medicine,
1 Hikarigaoka, Fukushima City 960-1295, Japan
e-mail: kazu-w@fmu.ac.jp

Introduction

Compression of the cauda equina by lumbar spinal canal stenosis is a major clinical problem associated with intermittent claudication. Some experimental studies have shown that compression of the cauda equina reduces blood flow in compressed nerve roots, and this is considered one important mechanism of induction of neurogenic intermittent claudication in lumbar spinal canal stenosis [1, 6, 9, 13, 14, 16, 23, 25].

It has also been reported that the chronically compressed cauda equina acquires resistance to additional compression [8]. Another study demonstrated reduction of nerve conduction velocity in chronically compressed cauda equina that recovered over time [15]. These findings suggest that vascular adaptation such as angiogenesis might occur in chronically compressed nerve roots, followed by recovery of nerve function and acquisition of tolerance.

Vascular endothelial growth factor (VEGF) is a potent stimulator of angiogenesis. Increase in hypoxia [3, 19], as in conditions of myocardial ischemia [2, 11], stimulates VEGF expression. Brain ischemia [4, 10], spinal cord ischemia [5], mechanical injury [20], and sciatic nerve ischemia [17] induce VEGF expression in vascular endothelial cells, glial cells, and neurons. We therefore hypothesized that cauda equina compression induces expression of VEGF in the compressed cauda equina and related dorsal root ganglion (DRG). The aim of this study was to examine if cauda equina compression induces expression of VEGF. In addition, we examined

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whether angiogenesis occurred in the compressed cauda equina.

Materials and methods

A total of 72 adult male Sprague-Dawley rats (200–250 g) were used in this study. All animal experiments conformed to the regulations of the Animal Research Committee of Fukushima Medical University and accorded with the Guidelines on Animal Experiments at Fukushima Medical University and the Japanese Government Animal Protection and Management Law (No. 105).

Surgical procedures

Rats were anesthetized with sodium pentobarbital (50 mg/kg i.p.) and placed in prone position. A skin incision was made over the spinal midline, and the lamina of L5 and L6 were exposed with the aid of a microscope. The ligamentum flavum was removed between L5 and L6. A piece of silicon block (length: 4.0 mm, width: 1 mm, thickness: 0.9 mm) [18] was placed into the epidural space under the L5 vertebra ($n = 35$) (Fig. 1). The silicon block occupied about a half AP-diameter of the spinal canal (Fig. 1c).

After surgery, the incision was closed. In sham-operated rats, silicone was not placed in the L5 epidural space ($n = 35$).

Behavioral testing

A total of 18 rats were included in this part of the study. In the compression and sham-operated groups, 9 rats of each group were used to measure the duration of walking on a treadmill (Rota-rod test), which had a circular column with a diameter of 125 mm [24, 27]. The rats were trained on the treadmill for 3 days before surgery. Rotation speed was initially ten rotations per minute, and was increased five rotations per minute every 1 min. Walking time until the rat fell off the rotating rod was measured five times for each animal at 1 day before surgery, and 1, 3, 7, 14, 21, and 28 days after surgery. The interval between each test was 15 min. The mean of five trials were calculated for each rat. Walking times are expressed as mean standard deviation (SD).

Immunohistochemistry

A total of 54 rats (Compression group: $n = 27$, sham group: $n = 27$) were included in this part of the study. At 3, 7, 14

Fig. 1 a The surgical procedure for induction of cauda equina compression. A silicon block (length: 4.0 mm, width: 1 mm, thickness: 0.9 mm) was placed into the epidural space under the L5 vertebra through the interlaminar space between L5 and L6. b This is an anatomic photo coinciding with a. Laminectomy was performed for showing a place of silicon block. c This photo shows a cross sectional image of the spinal canal with the silicon block
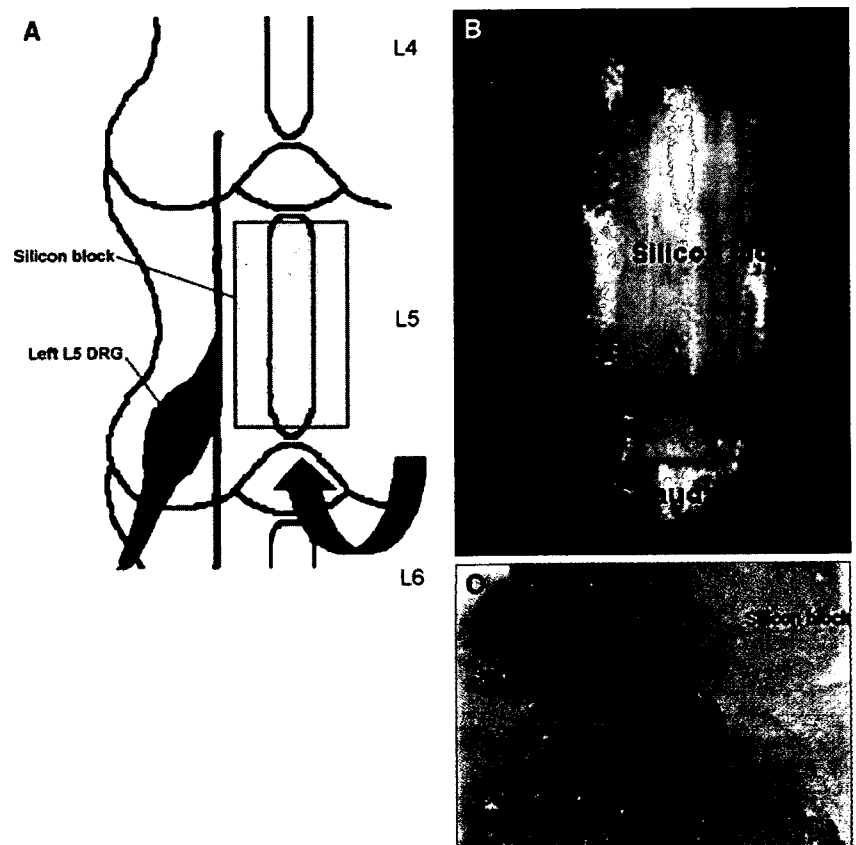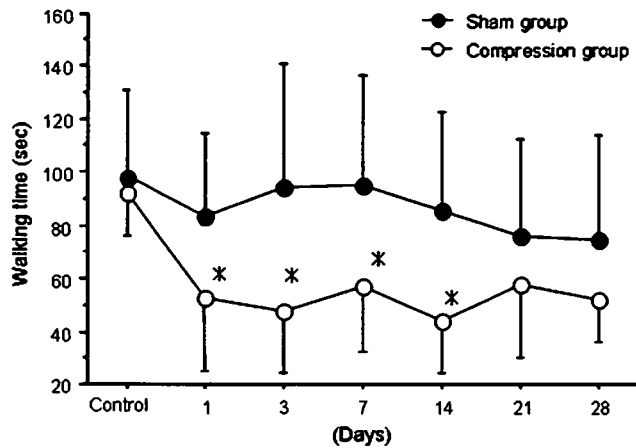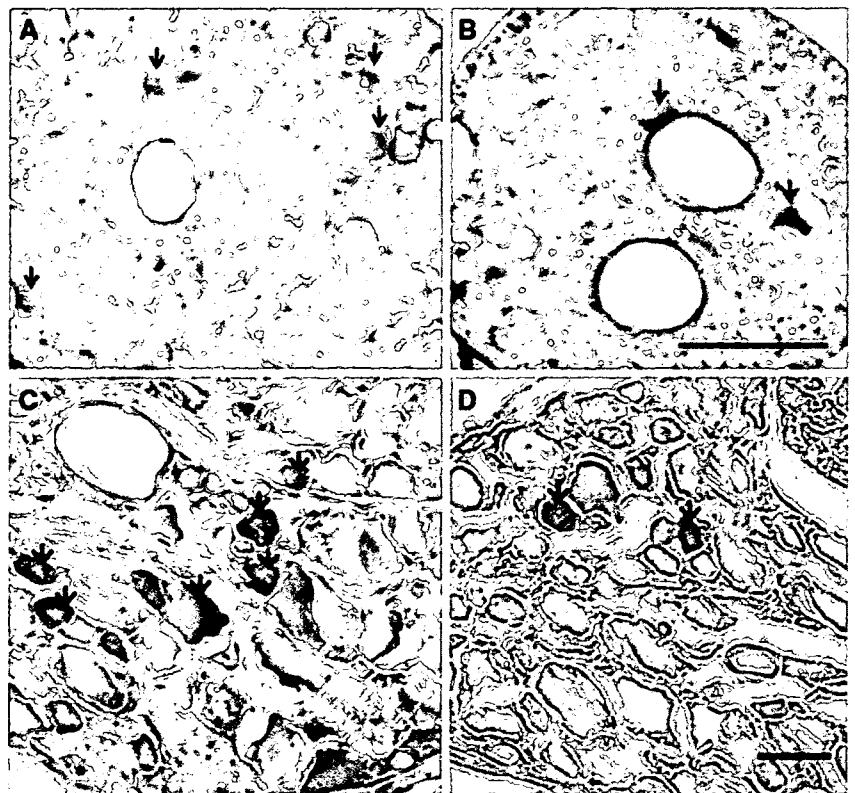
Fig. 2 Time course of changes in walking time. Results are the mean ± standard deviation of walking duration. There were significant differences between the compression and sham-operated groups at days 1, 3, 7, and 14 after surgery (*$P < 0.05$)

and 28 days after surgery, 6–9 rats of each group were deeply anaesthetized by inhalation of ether and underwent intracardiac perfusion with 200 ml saline followed by 300 ml of paraformaldehyde in 0.1 M phosphate buffer saline (PBS). The compressed part (L5) of the cauda equina, and left L5 dorsal root ganglion were removed, postfixed overnight in the same fixative, and dehydrated overnight in 20% sucrose. Transverse frozen sections of

cauda equina and DRG were cut on a cryostat and thaw-mounted on slides. Sections were immunostained with a rabbit polyclonal antibody for VEGF (1:100; NeoMarkers, Fremont, CA) and a rabbit polyclonal antibody for Factor VIII, marker for endothelial cells (1:100; Chemicon, Temecula, CA) as a primary antibody, a biotinylated antibody for rabbit IgG as a secondary antibody (1:200; Vector Laboratories, Burlingame, CA), the avidin-biotin peroxidase complex (Vector Laboratories), and 0.02% 3,3' diaminobenzidine dihydrochrolide as chromogen. Then, tissue sections were dehydrated, xylene-treated, and cover-slipped.

Numbers of VEGF-immunoreactive cells

VEGF-immunoreactive (IR) cells were counted in cauda equina and DRG. VEGF-IR cells in cauda equina were counted in five fields with the highest number of positive cells per section at 400× magnification, with three sections per rat. The mean of fifteen fields was calculated for each rat. Numbers of VEGF-IR cells are expressed as mean ± SD. VEGF-IR neurons and all neurons in DRG were counted in three sections per rat. Percentages of VEGF-IR neurons in DRG were calculated, and are shown as the mean ± SD. The investigator counting the number of VEGF-IR cells in cauda equina and DRG was blind to the experimental procedure.

Fig. 3 Photomicrographs demonstrating VEGF-immunoreactive cells in the cauda equine (**a, b**) and DRG (**c, d**) in compression group (**a, c**) and sham-operated group (**b, d**) at day 28 after surgery. Schwann-like cells in the cauda equina and DRG neurons exhibited immunoreactivity for VEGF (*arrows*). *Scale bar* 50 μm
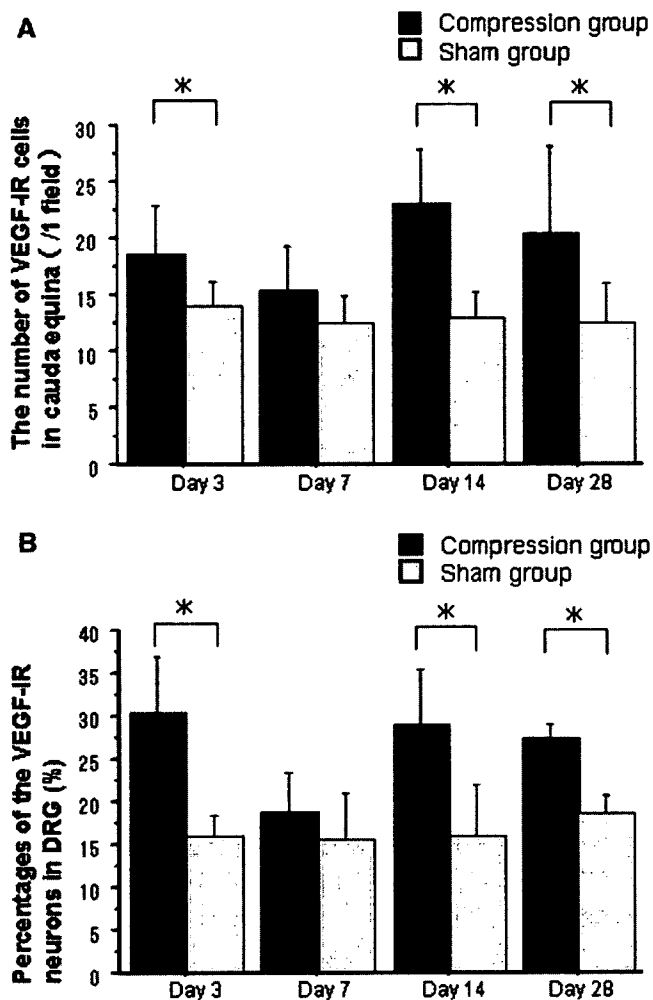
A

B

Fig. 4 Histogram presenting numbers of VEGF-IR cells in the cauda equine (a) and percentages of VEGF-IR neurons in the DRG (b). In the compression group, numbers of VEGF-IR cells in the cauda equina and percentages of VEGF-IR neurons in DRG were significantly increased at days 3, 14, and 28 after surgery compared with the sham-operated group (*$P < 0.05$). Results are the mean ± standard deviation

Vascular density

Factor VIII-positive blood vessels in cauda equina were counted in five sections per rat. The cross-sectional area of cauda equina was calculated by imaging analysis software (KS100, Carl Zeiss, German), and vascular density was expressed as number of blood vessel cells per square millimeter. The mean of five sections was calculated for each rat. Results are expressed as mean ± SD vascular density of the cauda equina. The investigator counting the number of blood vessel cells was blind to the experimental procedure.

Statistical analysis

Statistical analysis of walking duration was performed by repeated-measures ANOVA followed by the unpaired

t-test. For VEGF-positive cells and vascular density, the unpaired t-test was performed. P values less than 0.05 were considered significant.

Results

No wound infection or obvious limb paralysis was observed after cauda equina compression or in sham-operated rats.

Walking time

Walking time was decreased after cauda equina compression, with significant differences observed from day 1 to day 14 compared with sham-operated rats ($P < 0.05$), (Fig. 2).

VEGF-IR cells

In the cauda equina, Schwann-like cells around axons exhibited immunoreactivity for VEGF, (Fig. 3a, b). The VEGF-IR cell number was significantly increased in the cauda equina at 3, 14, and 28 days after cauda equina compression compared with the sham-operated group ($P < 0.05$). However, there were no significant differences in number of VEGF-IR cells between the two groups at 7 days after surgery, (Fig. 4a). In the DRG, DRG neurons exhibited immunoreactivity for VEGF (Fig. 3c, d). The number of VEGF-IR neurons in the compression group was increased at 3, 14, and 28 days after surgery compared with the sham-operated group ($P < 0.01$). However, there were no significant differences in number of VEGF-IR neurons between the two groups at 7 days after surgery (Fig. 4b)

Vascular density

Vascular endothelial cells in the cauda equina exhibited immunoreactivity for Factor VIII, (Fig. 5a). There were no significant differences in vascular density between the compression and sham-operated groups at 3, 7, or 28 days after surgery (Fig. 5b).

Discussion

In the present investigation the walking time decreased after cauda equina compression from day 1 to day 14. Expression of VEGF in the cauda equina and DRG was found after cauda equina compression. VEGF-IR cells in the cauda equina and DRG were increased at 3, 14, and 28 days after cauda equina compression, compared with