

Conservative and Surgical Treatment Improves Pain and Ankle-Brachial Index in Patients with Lumbar Spinal Stenosis

Seiji Ohtori, Masaomi Yamashita, Yasuaki Murata, Yawara Eguchi, Yasuchika Aoki, Hiromi Ataka, Jiro Hirayama, Tomoyuki Ozawa, Tatsuo Morinaga, Hajime Arai, Masaya Mimura, Hiroto Kamoda, Sumihisa Orita, Masayuki Miyagi, Tomohiro Miyashita, Yuzuru Okamoto, Tetsuhiro Ishikawa, Hiroaki Sameda, Tomoaki Kinoshita, Eiji Hanaoka, Miyako Suzuki, Munetaka Suzuki, Takato Aihara, Toshinori Ito, Gen Inoue, Masatsune Yamagata, Tomoaki Toyone, Gou Kubota, Yoshihiro Sakuma, Yasuhiro Oikawa, Kazuhide Inage, Takeshi Sainoh, Kazuyo Yamauchi, Kazuhisa Takahashi, and Chiba Low Back Pain Research Group

Department of Orthopaedic Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan.

Received: July 20, 2012

Revised: September 13, 2012

Accepted: September 17, 2012

Corresponding author: Dr. Seiji Ohtori,
Department of Orthopaedic Surgery,
Graduate School of Medicine,
Chiba University,
1-8-1 Inohana, Chuo-ku,
Chiba 260-8670, Japan.
Tel: 81-43-226-2117, Fax: 81-43-226-2116
E-mail: sohtori@faculty.chiba-u.jp

The authors have no financial conflicts of interest.

Purpose: The pathological mechanism of lumbar spinal stenosis is reduced blood flow in nerve roots and degeneration of nerve roots. Exercise and prostaglandin E1 is used for patients with peripheral arterial disease to increase capillary flow around the main artery and improve symptoms; however, the ankle-brachial index (ABI), an estimation of blood flow in the main artery in the leg, does not change after treatment. Lumbar spinal nerve roots contain somatosensory, somatomotor, and unmyelinated autonomic nerves. Improved blood flow by medication with prostaglandin E1 and decompression surgery in these spinal nerve roots may improve the function of nerve fibers innervating muscle, capillary, and main vessels in the lower leg, resulting in an increased ABI. The purpose of the study was to examine whether these treatments can improve ABI. **Materials and Methods:** One hundred and seven patients who received conservative treatment such as exercise and medication (n=56) or surgical treatment (n=51) were included. Low back pain and leg pain scores, walking distance, and ABI were measured before treatment and after 3 months of conservative treatment alone or surgical treatment followed by conservative treatment. **Results:** Low back pain, leg pain, and walking distance significantly improved after both treatments ($p<0.05$). ABI significantly increased in each group ($p<0.05$). **Conclusion:** This is the first investigation of changes in ABI after treatment in patients with lumbar spinal stenosis. Improvement of the spinal nerve roots by medication and decompression surgery may improve the supply of blood flow to the lower leg in patients with lumbar spinal stenosis.

Key Words: Ankle-brachial index, pain, lumbar, spinal stenosis

© Copyright:

Yonsei University College of Medicine 2013

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Compression of spinal nerve roots by lumbar spinal stenosis (LSS) is a major clin-

ical problem associated with intermittent claudication, pain, numbness, and lack of normal sensitivity. Such compression has been shown to induce neurophysiologic dysfunction, degeneration, and reduced blood flow in nerve roots in animal models and humans.^{1,2}

Reduced blood flow in nerve roots induces neurogenic intermittent claudication, and drugs for the improvement of blood flow in nerve roots have been developed. Prostaglandin E1 (PGE1) causes vasodilation in both arterioles and venules.^{3,4} In a clinical study, intravenous lipo-PGE1 administered for 10 consecutive days to 40 patients produced symptomatic improvement for a limited period in the treatment of neurogenic intermittent claudication associated with lumbar spinal stenosis.⁵ An investigation of 25 cases of lumbar spinal stenosis by myelography revealed that the diameters of blood vessels in the cauda equina differed significantly from those in a control group.⁶

In addition to medication, several therapies may increase blood flow into spinal nerves. In animal studies and clinical trials, lumbar spinal canal stenosis has been treated by electrical acupuncture on the pudendal nerve and at the nerve root.⁷ After stimulation, immediate and sustained pain relief was observed in patients and an increase in sciatic nerve blood flow was observed.⁷ Changes in the microcirculation in the L5 and S1 nerve roots have also been examined in patients with lumbar spinal stenosis during lumbar interbody fusion surgery by endoscopy.⁸ Blood flow significantly decreased after nerve compression and stretching. These findings indicate that damage of spinal nerve roots induces decreased blood flow into the nerve roots, and results in pain.⁸

Patients with peripheral arterial disease (PAD) may be asymptomatic or may present with a spectrum of symptoms including atypical leg pain, classic claudication, rest pain, and critical limb ischemia with gangrene.⁹ PAD is diagnosed based on the ankle-brachial blood pressure index (ABI), a rapid and simple non-invasive diagnostic technique.⁹ ABI reflects blood flow in the main artery in the leg. Exercise and drugs such as PGE1 improve the symptoms of PAD,⁹ generally by increasing flow in capillary vessels without having an effect on the main arterial tract. Thus, most reports have shown that these therapies improve symptoms, but do not influence ABI.^{10,11}

The lumbar spinal ventral nerve roots include somatic and autonomic nerves such as the unmyelinated sympathetic and parasympathetic nerves that innervate the lower leg.¹²⁻¹⁴ Therefore, we hypothesized that treatment with therapies such as exercise, medication, and surgery would increase

blood flow on the surface of compressed and damaged spinal nerves or that functional recovery of spinal nerves could be achieved by decompression surgery. Subsequently, these therapies should improve the function of somatosensory, motor and autonomic nerves innervating the main artery in the lower leg and lead to an increase in ABI. However, after therapy for lumbar spinal stenosis, improvement of blood flow in the main artery in the lower leg has not been previously examined. Therefore, the purpose of this study was to investigate the effects of these therapies on symptoms of lumbar spinal stenosis and on ABI.

MATERIALS AND METHODS

The ethics committee at our institution approved the protocol for the human procedures used in this study. Informed written consent was obtained from each subject.

Patients

One hundred and seven patients with low back and leg pain that had continued for at least 1 month were included. Patients who had previously undergone spinal surgery were excluded from the study. We also excluded patients with spinal tumor, infection, or trauma. Lumbar spinal stenosis was diagnosed using X-rays, magnetic resonance imaging (MRI) and by physical examination by spine surgeons. In the MRI, the degree of spinal stenosis varied from slight to severe. In addition, central stenosis, stenosis of the lateral recess, and foraminal stenosis were apparent. Patients with monoradiculopathy, polyradiculopathies, or cauda equine syndrome were included in the study.

Study design

Patients were divided into groups that received conservative and surgical treatment, respectively. Conservative therapy group was applied in patients who did not undergo any therapy before visiting hospital. Surgery was used for patients in whom previous conservative treatment was ineffective. Therefore, seriously impaired patients underwent surgery and the less impaired patients underwent conservative care.

In the conservative therapy group, treatment included exercise (walking, walking in a pool, muscle training, and muscle stretching), medication, and an epidural block. Without the help of a therapist, patients walked above ground and in a pool. Muscle training and stretching were performed for the

abdominal and lower extremities with the assistance of physical therapists. Medication included NSAIDs, vitamins, muscle relaxants, and PGE1, as determined by the personal physician for each patient. A transforaminal or caudal epidural block was administered in some patients, and exercise, drugs, and blocks were used in some cases. ABI was measured before and 3 months after conservative treatment. Before measuring ABI, patients had not received therapy.

For the surgery group, ABI was measured before and 3 months after surgery. Before surgery, patients had undergone exercise therapy, medication, and epidural block. After surgery, these patients also received exercise therapy and medication, but were not given an epidural block.

Evaluation of pain scores and walking distance before and after treatment

The JOA Back Pain Evaluation Questionnaire (JOABPEQ; including low back pain, lumbar function, walking ability, social life function and mental health) and a visual analogue scale (VAS; from 0 to 100, 100=worst pain) were evaluated for each patient. The range of the JOABPEQ score for each domain is 0 to 100, with higher scores indicating a better condition. The five functional scores were used independently. Maximum walking distance without rest, total walking distance in a day, low back pain, and leg pain were evaluated before and 3 months after treatment.

Determination of ABI

Systolic blood pressures in the brachial, anterior and posterior tibial arteries were measured using inflatable cuffs and

a Doppler probe. The maximum ankle arterial pressure was divided by the maximum brachial arterial pressure to calculate the ABI. ABI was measured according to the Transatlantic Inter Society Consensus (TASC II) guidelines for management of PAD.¹⁵

Evaluation of outcome

This study was performed to investigate the effects of different therapies on symptoms of lumbar spinal stenosis and on ABI, but not to investigate differences in the effects among therapies. Therefore, comparisons before and after treatment were performed in each group, but a comparison between the conservative and surgical groups was not performed.

Statistical analysis

A paired t-test, Wilcoxon test, and McNemar test were used to compare pain scales and ABI before and after treatment. $p < 0.05$ was considered statistically significant.

RESULTS

Patient characteristics

Patient characteristics are shown in Table 1. Age ranged from 39 to 80 years old, with average ages of 68.04 ± 9.11 and 67.00 ± 9.03 years old in the conservative and surgical groups, respectively (mean \pm SD). Among all patients, 19.6% in the conservative group and 17.6% in the surgical group were smokers. Complications included diabetes, hyperlipidemia, hypertension, and vascular occlusion (cerebral, coronary,

Table 1. Demographic Characteristics in Patients Who Received Conservative and Surgical Treatment

Item	Conservative	Surgical
Number of patients	56	51
Sex (male/female)	30/26	27/24
Height (cm)	159.63	160.35
Weight (kg)	61.43	62.44
BMI	24.07	24.16
Age: mean \pm SD (range) (yrs)	68.04 \pm 9.11 (40-80)	67.00 \pm 9.03 (39-80)
Symptom duration, mean (range) (months)	3.2 (1-24)	3.1 (1-24)
Smoking (%)	19.6	17.6
Other complications (n)	30	30
Diabetes (%)	17.5	17.6
Hyperlipidemia (%)	12.5	9.8
Hypertension (%)	39.3	51.0
Vascular occlusion		
Cerebral (%)	3.6	7.8
Coronary (%)	5.4	11.8
Peripheral (%)	7.1	2.0

and peripheral) in both groups.

Treatment

Treatment given over 3 months in the two groups is shown in Table 2. In the conservative group, the patients received exercise therapy (35%), medications (100%), and epidural block (22%). PGE1 was the most common drug (96.5%) and NSAIDs, vitamins, and muscle relaxants were also used. A transforaminal (17.9%) or caudal (3.6%) epidural block was administered for low back pain or leg pain. In the surgical group, patients received exercise therapy (50%) and medication (100%) during the 3 months after surgery. Epidural block (20%) was given only before surgery. Forty patients underwent decompression surgery and 11 underwent decompression and posterior fusion surgery. There

were no perioperative complications. In the conservative group, no patients underwent surgery for severity of symptoms during the 3-month study period.

Changes in pain scores and walking distance

In the conservative group, VAS scores for low back pain, buttock pain, and leg pain showed significant improvements after treatment ($p<0.01$) (Table 3). JOABPEQ scores in all five categories (low back pain, lumbar function, walking ability, social life function, and mental health) (Table 3) also significantly improved after 3 months of conservative treatment (low back pain: $p<0.001$, lumbar function: $p=0.004$, walking ability: $p=0.001$, social life function: $p<0.001$, and mental health: $p<0.001$). There was also a significant improvement in maximum walking distance without rest after

Table 2. Treatment Options in Patients Who Received Conservative and Surgical Treatment

Item	Conservative	Surgical
Surgery (n)	0	51
Exercise (%)	35	50
Walking	14.3	51.0
Walking in a pool	1.8	2.0
Muscle training	16.1	41.2
Muscle stretching	8.9	21.6
Medication (%)	100	100
NSAIDs	55.4	56.9
Vitamins	30.4	33.3
Muscle relaxants	5.4	3.9
Prostaglandin E1	96.5	23.5
Epidural block (%)	22	20
Transforaminal epidural block	17.9	17.6
Caudal epidural block	3.6	2.0

In the surgical group, exercise therapy and medications were given before and after surgery. Epidural block was given only before surgery.

Table 3. Pain Scores, Walking Distance and ABI Before and After 3 Months of Conservative Treatment

	Before	After 3 months	<i>p</i> value
VAS			
Low back pain	35.59±34.47	23.07±28.37	0.026
Buttock pain	44.61±32.97	20.83±23.88	<0.001
Leg pain	67.08±21.57	39.38±30.15	<0.001
JOABPEQ			
Low back pain	58.99±35.65	73.02±34.40	<0.001
Lumbar function	63.78±31.87	71.79±27.52	0.004
Walking ability	41.04±31.55	55.18±32.92	0.001
Social life	43.56±20.11	55.22±24.15	<0.001
Mental health	42.92±16.59	52.43±15.52	<0.001
Walking distance (m)			
Maximum walking distance without rest	492.02±672.78	977.89±974.10	0.009
Walking distance in one day	1251.30±1533.58	1494.35±1366.85	0.058
ABI	1.08±0.12	1.11±0.14	0.003

ABI, ankle-brachial index; VAS, visual analogue scale.

treatment ($p=0.009$) (Table 3). In the surgical group, the VAS scores for low back pain, buttock pain, and leg pain showed significant improvements after surgery ($p<0.001$) (Table 4). JOABPEQ scores in all categories were also significantly improved at 3 months after surgery ($p<0.001$), and there was a significant improvement in walking distance in one day ($p=0.003$) (Table 4).

Change in ABI

The average ABI was improved significantly by both the conservative and surgical treatment groups (1.08 ± 0.12 vs. 1.11 ± 0.14 , $p=0.003$ in the conservative group; 1.08 ± 0.12 vs. 1.12 ± 0.14 , $p=0.018$ in the surgical group) (Table 3 and 4).

DISCUSSION

In the current study, both conservative and surgical treatment improved low back pain, leg pain, walking difficulty that originated from lumbar spinal stenosis, and increased ABI. These findings suggest that conservative and surgical treatment increase blood flow in the anterior and posterior tibial arteries.

Most patients treated conservatively received PGE1, a vasodilator that increases blood flow and inhibits platelet aggregation.³ Intravenous PGE1 is primarily used for chronic peripheral arterial occlusive diseases in the United States and Europe.³ PGE1 also increases blood flow at the surface of spinal nerve roots. Thus, PGE1 analogs have been developed to treat symptoms of lumbar spinal stenosis.^{3,16} Matsudaira, et al.¹⁷ compared limaprost with etodolac, an NSAID,

in 66 patients in a randomized control trial. After eight weeks, subjects receiving limaprost had better scores on the Standard Form-36 subscales for physical function, physical role, bodily pain, vitality, and mental health, and greater improvements for walking distance, leg numbness, and patient satisfaction.¹⁷ In the current study, surgical treatment also improved symptoms. Kovacs, et al.¹⁸ reviewed RCTs comparing any form of conservative and surgical treatment based on a search of the CENTRAL, Medline, EMBASE and TripDatabase databases. In patients with symptomatic LSS, implantation of a specific device or decompressive surgery, with or without fusion, were found to be more effective than continued conservative treatment when the latter had failed for 3-6 months. In the current study, we did not compare conservative treatment with surgical treatment; however, both improved symptoms after a 3-month period.

PAD is diagnosed by assessment of ABI, and ABI reflects blood flow in the main artery in the leg.⁸ Exercise and drugs such as PGE1 and cilostazol improve the symptoms of PAD⁸ and also improve the maximal walking distance by 40% to 60%.^{19,20} These therapies generally increase flow in capillary vessels and do not affect the main arterial tract. For this reason, most reports have shown that these drugs do not improve ABI.^{10,11} However, Mohler, et al.²¹ found that treatment of PAD with cilostazol significantly improved ABI, although with the conclusion that the mechanism was unclear. In the current study, ABI increased after conservative and surgical treatment for lumbar spinal stenosis. We propose the following explanation of these results. Symptoms in lumbar spinal stenosis are caused by compression of

Table 4. Pain Scores, Walking Distance and ABI Before and at 3 Months After Surgical Treatment

	Before	After 3 months	<i>p</i> value
VAS			
Low back pain	55.23±34.71	14.20±20.86	<0.001
Buttock pain	54.11±31.11	10.61±19.16	<0.001
Leg pain	70.97±22.85	19.83±27.05	<0.001
JOABPEQ			
Low back pain	41.56±34.56	79.55±30.09	<0.001
Lumbar function	49.63±29.25	69.81±26.90	<0.001
Walking ability	26.83±26.47	64.92±32.94	<0.001
Social life	32.01±21.07	54.47±25.75	<0.001
Mental health	39.91±18.56	55.20±21.00	<0.001
Walking distance (m)			
Maximum walking distance without rest	107.75±251.90	666.83±1502.65	0.085
Walking distance in one day	659.41±1277.35	1868.07±3053.83	0.025
ABI	1.08±0.12	1.12±0.14	0.018

ABI, ankle-brachial index; VAS, visual analogue scale.

the spinal nerve roots in animal models and humans.^{1,2} Spinal ventral nerve roots contain unmyelinated nerve fibers associated with sensory and autonomic nerves, and myelinated nerve fibers associated with motor fibers.¹²⁻¹⁴ In addition, somatosensory, somatomotor, and autonomic nerve fibers run on the surface of spinal nerves and the dura mater.¹⁴ Animal and human cadaver studies have shown that lumbar and sacral spinal ventral nerve roots contain many unmyelinated nerve fibers and sympathetic and parasympathetic nerves that innervate blood vessels in the lower leg,^{12,13} with no significant difference in the proportions of unmyelinated nerve fibers among sympathetic (T11-L2), parasympathetic (S2) and other (C4-T10 and L3-S1) segments.¹³ These sympathetic and parasympathetic nerve fibers innervate the main artery in the lower leg. Sympathetic and parasympathetic nerve fibers may be damaged and compressed in patients with lumbar canal stenosis. This dysfunction is improved after conservative therapy or surgery, and this results in functional recovery of the autonomic nervous system. Thus, this may explain the increase in ABI after treatment in the current study.

There were several limitations in the study. First, we did not compare conservative and surgical treatment. Second, a normal ABI falls in the range of 0.91-1.30, while a low ABI at rest (<0.90) indicates a high risk of PAD.²² In the current study, most patients had ABI in the normal range and the clinical significance of an increase of ABI in this population is questionable. Third, in the surgical group, patients used PGE1 and other drugs after surgery, so there was possibility that PGE1 and other drugs influenced the outcome in the surgical group. Therefore, further studies are needed to test our hypothesis more rigorously.

In conclusion, ABI was measured before and 3 months after treatment in 107 patients with LSS. ABI was significantly increased after both conservative and surgical treatment. We concluded that improved function of sympathetic and parasympathetic nerves in spinal nerve roots innervating the lower leg may increase blood flow in the main artery of the leg.

REFERENCES

- Konno S, Yabuki S, Sato K, Olmarker K, Kikuchi S. A model for acute, chronic, and delayed graded compression of the dog cauda equina. Presentation of the gross, microscopic, and vascular anatomy of the dog cauda equina and accuracy in pressure transmission of the compression model. *Spine (Phila Pa 1976)* 1995;20:2758-64.
- Sekiguchi M, Kikuchi S, Myers RR. Experimental spinal stenosis: relationship between degree of cauda equina compression, neuropathology, and pain. *Spine (Phila Pa 1976)* 2004;29:1105-11.
- Müller B, Schmidtke M, Witt W. Action of the stable prostacyclin analogue iloprost on microvascular tone and -permeability in the hamster cheek pouch. *Prostaglandins Leukot Med* 1987;29:187-98.
- Takahashi K, Olmarker K, Holm S, Porter RW, Rydevik B. Double-level cauda equina compression: an experimental study with continuous monitoring of intraneural blood flow in the porcine cauda equina. *J Orthop Res* 1993;11:104-9.
- Murakami M, Takahashi K, Sekikawa T, Yasuhara K, Yamagata M, Moriya H. Effects of intravenous lipoprostaglandin E1 on neurogenic intermittent claudication. *J Spinal Disord* 1997;10:499-504.
- Ooi Y, Mita F, Satoh Y. Myeloscopic study on lumbar spinal canal stenosis with special reference to intermittent claudication. *Spine (Phila Pa 1976)* 1990;15:544-9.
- Inoue M, Kitakoji H, Yano T, Ishizaki N, Itoi M, Katsumi Y. Acupuncture Treatment for Low Back Pain and Lower Limb Symptoms-The Relation between Acupuncture or Electroacupuncture Stimulation and Sciatic Nerve Blood Flow. *Evid Based Complement Alternat Med* 2008;5:133-43.
- Dezawa A, Unno K, Yamane T, Miki H. Changes in the microhemodynamics of nerve root retraction in patients with lumbar spinal canal stenosis. *Spine (Phila Pa 1976)* 2002;27:2844-9.
- Ferreira AC, Macedo FY. A review of simple, non-invasive means of assessing peripheral arterial disease and implications for medical management. *Ann Med* 2010;42:139-50.
- Ichihara A, Kaneshiro Y, Takemitsu T, Sakoda M, Itoh H. Benefits of candesartan on arterial and renal damage of non-diabetic hypertensive patients treated with calcium channel blockers. *Am J Nephrol* 2006;26:462-8.
- Sasamura H, Kitamura Y, Nakamura M, Ryuzaki M, Saruta T. Effects of the angiotensin receptor blocker candesartan on arterial stiffness and markers of extracellular matrix metabolism in patients with essential hypertension. *Clin Exp Hypertens* 2006;28:511-20.
- Karlsson M, Hildebrand C, Warnborg K. Fibre composition of the ventral roots L7 and S1 in the owl monkey (*Aotus trivirgatus*). *Anat Embryol (Berl)* 1991;184:125-32.
- Ko HY, Shin YB, Sohn HJ, Chang JH, Ahn YH, Ha YH. Unmyelinated fibers in human spinal ventral roots: C4 to S2. *Spinal Cord* 2009;47:286-9.
- Konnai Y, Honda T, Sekiguchi Y, Kikuchi S, Sugiura Y. Sensory innervation of the lumbar dura mater passing through the sympathetic trunk in rats. *Spine (Phila Pa 1976)* 2000;25:776-82.
- Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG; TASC II Working Group. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg* 2007;45 Suppl S:S5-67.
- Swainston Harrison T, Plosker GL. Limaprost. *Drugs* 2007;67:109-18.
- Matsudaira K, Seichi A, Kunogi J, Yamazaki T, Kobayashi A, Anamizu Y, et al. The efficacy of prostaglandin E1 derivative in patients with lumbar spinal stenosis. *Spine (Phila Pa 1976)* 2009;34:115-20.
- Kovacs FM, Urrútia G, Alarcón JD. Surgery versus conservative treatment for symptomatic lumbar spinal stenosis: a systematic re-

- view of randomized controlled trials. *Spine (Phila Pa 1976)* 2011; 36:E1335-51.
19. Beebe HG, Dawson DL, Cutler BS, Herd JA, Strandness DE Jr, Bortey EB, et al. A new pharmacological treatment for intermittent claudication: results of a randomized, multicenter trial. *Arch Intern Med* 1999;159:2041-50.
 20. Strandness DE Jr, Dalman RL, Panian S, Rendell MS, Comp PC, Zhang P, et al. Effect of cilostazol in patients with intermittent claudication: a randomized, double-blind, placebo-controlled study. *Vasc Endovascular Surg* 2002;36:83-91.
 21. Mohler ER 3rd, Beebe HG, Salles-Cuhna S, Zimet R, Zhang P, Heckman J, et al. Effects of cilostazol on resting ankle pressures and exercise-induced ischemia in patients with intermittent claudication. *Vasc Med* 2001;6:151-6.
 22. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *Eur J Vasc Endovasc Surg* 2007;33 Suppl 1:S1-75.