

## Risk Factors and Incidence for Peripheral Arterial Disease in Patients with Typical Lumbar Spinal Stenosis

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**Objective:** Intermittent claudication (IC) is a typical symptom of peripheral arterial disease (PAD) and lumbar spinal stenosis (LSS). In order to prevent misdiagnosis of vascular disease, it is important to know the incidence of and risk factors for PAD in patients with LSS. Therefore, the aim of our study was to evaluate the incidence of and risk factors for PAD in patients with typical and severe LSS who underwent spinal surgical treatment.

**Methods:** The occurrence of PAD was examined retrospectively in 171 consecutive patients with LSS and severe IC who underwent surgical treatment at our hospital from June 2012 to June 2013. Data were collected on background characteristics (sex, age) and known risk factors for PAD, such as hypertension, diabetes mellitus, smoking, hyperlipidemia, stroke, and ischemic heart disease.

**Results:** Of the 171 patients enrolled, 7 had an abnormal ankle-brachial index (ABI). Computed tomography angiography (CTA) was performed in these patients, and a final diagnosis of PAD was established for all 7 patients. The incidence of PAD in all patients with LSS was 4.1% (7 of 171). Stroke and ischemic heart disease were significantly more common in the LSSPAD group compared with the LSS group. Multiple logistic regression analyses with a forced-entry method revealed that age and stroke ( $p < 0.05$ ) were independent risk factors for PAD.

**Conclusion:** To prevent misdiagnosis of fatal PAD, we recommend ABI be assessed in patients with LSS and history of stroke.

**Key Words:** Peripheral arterial disease • Ankle brachial pressure index • Lumbar spinal stenosis

### INTRODUCTION

Lumbar spinal stenosis (LSS) presents with intermittent claudication (IC) in the lower extremities as a typical symptom<sup>26,28</sup>. Peripheral arterial disease (PAD) also presents with similar symptoms as vascular IC<sup>17,21</sup>. Vascular IC is aggravated by ambulation and relieved by resting. Neurogenic IC, on the other hand, caused by narrowing of the neural foramen and spinal

canal, is aggravated by standing and relieved by sitting. However, it can be difficult to differentiate vascular and neurogenic IC due to atypical signs and variable symptoms. Therefore, when patients report claudication, it is important to correctly identify the accompanying pathology.

PAD includes many pathologies, such as arteriosclerosis obliterans, Buerger's disease, and acute arterial obstruction. Untreated PAD is progressive and increases the risk of severe vascular events and even death<sup>8,13,24</sup>. Therefore, early diagnosis and treatment of PAD is important to reduce fatal or nonfatal vascular events<sup>17,21</sup>. In order to diagnose LSS accompanied by PAD, spine surgeons tend to examine arterial pulse in the lower extremities. However, the argument arises as to whether PAD can be ruled out only by arterial pulse examination. To establish a screening test for PAD, ankle-brachial index (ABI) is commonly used. In previous reports, ABI has been found to be highly sensitive and specific for PAD screening<sup>10,18,20,23,24</sup>.

Several authors have reported PAD in patients with LSS<sup>9,18</sup>,

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<sup>19,27</sup>. Those reports presented the incidence of and risk factors for PAD in patients with LSS with atypical symptoms. However, there has been no study of patients with typical and severe LSS. If a patient has atypical symptoms, and diagnostic imaging shows no significant spinal canal stenosis, spine surgeons are always concerned about accompanying PAD. However, spine surgeons tend to overlook the possibility of accompanying PAD in patients with LSS diagnosed by typical symptoms and diagnostic imaging, such as magnetic resonance imaging (MRI).

In order to prevent misdiagnosis of vascular disease, it is important to know the incidence of and risk factors for PAD in patients with LSS. Therefore, the aim of our study was to evaluate the incidence of and risk factors for PAD in patients with typical and severe LSS who underwent spinal surgical treatment.

## MATERIALS AND METHODS

The occurrence of PAD was examined retrospectively in 171 consecutive patients with LSS and severe IC who underwent surgical treatment at our hospital from June 2012 to June 2013. Patients were diagnosed with LSS by 3 neurosurgeons using neurologic examination and MRI. Three diseases were included in this study: spinal stenosis (ST), degenerative spondylolisthesis (DS) and isthmic spondylolisthesis (IS).

ABI was measured in all patients using previously reported methods<sup>7,8</sup>. ABI is the ratio of arm systolic blood pressure

at the brachial artery to ankle systolic blood pressure at the posterior tibial or dorsalis pedis artery<sup>6,11,16,31</sup>. ABI <0.9 was considered abnormal according to TransAtlantic Inter-Society Consensus (TASC) guidelines<sup>21</sup> (Fig. 1). All patients with abnormal ABI underwent computed tomography angiography (CTA) and consultation with a vascular surgeon (Fig. 2). Data were collected on background characteristics (sex, age) and known risk factors for PAD, such as hypertension, diabetes mellitus, smoking, hyperlipidemia, stroke, and ischemic heart disease. Quality of life (QOL) was evaluated using a visual analog scale (VAS) and the Oswestry Disability Index (ODI)<sup>2,3,7,22</sup>.

Patients with coexisting PAD and LSS were designated the LSSPAD group, while those with LSS but no PAD were denoted the LSS group. Using the LSS group as a control, analyses were conducted to identify the characteristics of the LSSPAD group.

To evaluate clinical characteristics at the time of enrollment, univariate analysis was performed using the Student's *t* test (*v2* test). The Mann-Whitney U-test was used to compare group means of continuous data. Multivariate logistic regression analysis was used to evaluate independent risk factors for coexisting PAD. Any variable with a *p* value of <0.05 on univariate analysis was included in multiple logistic regression models. Statistical significance was defined as *p*<0.05. SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. Data were presented as proportions and means±SDs.

## RESULTS

The study population comprised 79 men and 92 women with a mean age of 64.6±8.6 years. Of the 171 patients enrolled, 7 had an abnormal ABI. CTA was performed in these

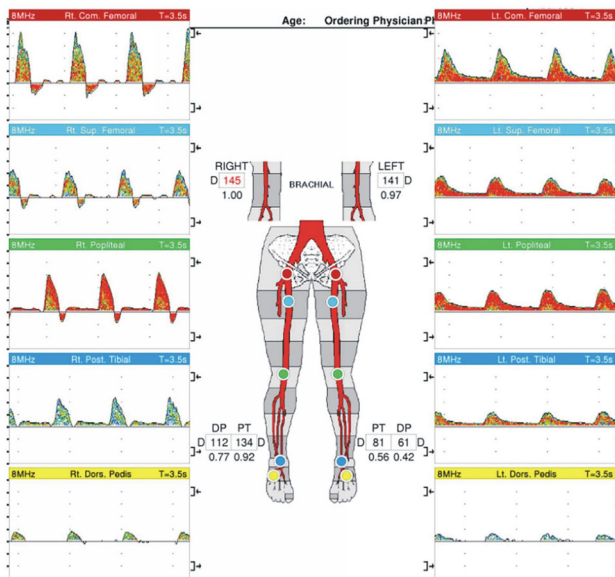


Fig. 1. An illustration of ABI test at left proximal leg arterial stenocclusive pattern.



Fig. 2. An illustration of severe PAD at left iliac location. Compared with the unaffected side (right side arrow), occlusion of arterial lumen (left side arrow) was observed at the left iliac artery.

**Table 1.** Comparative analysis between LSS and LSSPAD

		LSS (n=164)		LSSPAD (n=7)		p-value
Sex	Males	45.1%	(74)	71.4%	(5)	0.25
	Females	54.9%	(90)	28.6%	(2)	
Age*		64.2	±8.6	72.3	±5.5	<0.01
BMI		24.0	±2.4	23.0	±2.8	0.39
Risk factors	DM*	23.8%	(39)	57.1%	(4)	0.07
	HTN	43.3%	(71)	71.4%	(5)	0.24
	Smoker	15.2%	(25)	28.6%	(2)	0.65
	Hyperlipdemia	21.3%	(35)	28.6%	(2)	0.31
Medical history	Stroke*	3.7%	(6)	42.9%	(3)	<0.01
	IHD*	3.7%	(6)	28.6%	(2)	0.04
Disease	ST	61.0%	(100)	85.7%	(6)	
	DS	32.3%	(53)	14.3%	(1)	0.40
	IS	6.7%	(11)	0.0%	(0)	
VAS*		7.1	±1.9	8.1	±0.7	0.16
ODI		25.0	±8.7	26.3	±4.7	0.69

DM, Diabetes mellitus; HTN, Hypertension; IHD, Ischemic heart disease

\*Risk factors for multiple logistic regression analysis

patients, and a final diagnosis of PAD was established for all 7 patients. The incidence of PAD in all patients with LSS was 4.1% (7 of 171). Six of the 7 patients diagnosed with PAD were treated with an endovascular stent, while the remaining 1 patient was recommended observation and regular follow-up. The results of univariate analysis of risk factors for PAD, type of disease, and other clinical parameters are shown in Table 1. The LSSPAD group was significantly older than the LSS group (72.3±5.5 years vs 64.2±8.6 years,  $p<0.01$ ). Stroke and ischemic heart disease were significantly more common in the LSSPAD group compared with the LSS group. The other known risk factors for PAD (diabetes mellitus, hypertension, smoking history, hyperlipidemia) showed no significant differences between groups. Furthermore, there were no significant differences between groups regarding VAS and ODI scores.

Of the 171 patients with LSS, 37 (21.6%) smoked. Among the 164 patients in the LSS group, 100 (61%) had ST, 53 (32.3%) had DS, and 11 (6.7%) had IS. Among the 7 patients in the LSSPAD group, 6 (85.7%) had ST and 1 (14.3%) had DS. There were no significant differences between groups. In multivariate analysis, the entered variables were age, diabetes mellitus, preoperative VAS score, stroke and ischemic heart disease ( $p<0.2$ ) (Table 2). Multiple logistic regression analyses with a forced-entry method revealed that the stroke ( $p<0.05$ ) was independent risk factor for PAD. No differences in age and history of ischemic heart disease were observed between groups.

**Table 2.** Risk factors for PAD in patients with LSS using multiple logistic regression analysis

	Odds ratio	95% CI	p-value
Age	1.20	0.99-1.44	0.06
DM	3.53	0.50-25.09	0.20
Stroke	36.21	3.80-345.40	0.00
IHD	5.39	0.66-44.20	0.11
VAS	1.19	0.54-2.66	0.65

## DISCUSSION

PAD is an atherosclerotic syndrome with a high prevalence of approximately 5.8% to 12% in older adults<sup>1,15</sup>. High incidence of fatal or nonfatal cardiovascular events associated with PAD increases mortality. According to TASC guidelines for PAD, the mortality rate of patients with IC associated with PAD is 2 times that of patients with IC only<sup>2,7,22</sup>. Besides the risk of death, the 10-year incidence of myocardial infarction and cerebral stroke in patients with PAD are increased by about 4 and 3 times, respectively, compared with that in patients without PAD<sup>5,29</sup>. However, PAD is often misdiagnosed in older patients with LSS because it is difficult to distinguish vascular IC from neurogenic IC. Therefore, spine surgeons often overlook the possibility of PAD in patients with severe LSS<sup>18</sup>. In a previous study, the coincidence of PAD with LSS was similar to the prevalence of PAD in older individuals (6.7%)<sup>27</sup>. Therefore, it is very important to understand the

risk factors and to evaluate PAD in patients with LSS.

Arteriography is considered the gold standard for diagnosis of PAD. However, the use of arteriography has some limitations, including complications arising from ionizing radiation, its invasive nature, and nephrotoxic contrast media. Among substitutable tests, ABI is the simplest and most inexpensive<sup>25</sup>. ABI also has high sensitivity (79-95%) and specificity (96-100%) for screening PAD<sup>17</sup>. Thus, we evaluated the coincidence of PAD with LSS and risk factors for PAD using ABI.

There have been several studies to evaluate the incidence of PAD in patients with LSS using ABI. Jeon et al. studied 42 patients with atypical claudication<sup>19</sup>. Their study showed that ABI had high sensitivity and specificity for screening PAD in cases with atypical claudication. Twenty-two of 42 patients in their study were diagnosed with LSS and PAD, showing a high coincidence (54.8%) between diseases. However, their study did not analyze the risk factors for PAD and was limited in that only mild cases of LSS, determined by MRI, were included. Most spine surgeons easily can doubt a hidden disease, such as PAD, in these cases. Therefore, in our study, we enrolled patients with typical symptoms, severe LSS, confirmed by MRI, who underwent decompressive surgery.

Kazuhide et al. studied 570 patients with LSS diagnosed by MRI<sup>27</sup>. They reported that 6.7% of patients had PAD confirmed by ABI. They also showed that comorbidity of diabetes mellitus, history of stroke, and history of ischemic heart disease were characteristics of patients with LSS and PAD. This was the first nationwide multicenter survey of the prevalence of PAD in patients with LSS in Japan. However, the mean VAS score of patients with LSS and PAD was  $53.6 \pm 27.0$ , while that of patients with LSS was  $60.1 \pm 28.4$  (VAS 0-100 mm), indicating that patients with mild IC were included in this study as well as patients with severe IC who required surgical treatment. Spine surgeons occasionally make a mistake in performing surgery in patients who have radiographically asymptomatic stenosis and vascular IC arising from PAD, since it is difficult to distinguish between neurogenic and vascular IC. Therefore, diagnosis of PAD is not important for patients with mild IC, but is important for patients with typical neurogenic IC and definite LSS who require surgical treatment.

We analyzed the incidence of and risk factors for PAD in patients with severe LSS and intractable IC who underwent surgical treatment. The mean preoperative VAS score of all patients was  $7.2 \pm 1.9$ , and there was no response to conservative treatment, such as medication, physical therapy, and epidural nerve block. Although the coincidence of PAD with LSS was not high (7 of 171 patients [4.1%]), 6 of 7 patients had severe vascular insufficiency requiring endovascular stent surgery. Thus, it can be very dangerous if PAD is misdiagnosed in patients with LSS. Previous studies have presented several

risk factors for PAD, such as old age, sex, diabetes mellitus, dyslipidemia, hypertension, smoking history, and body mass index<sup>15,27,30</sup>. In this study, old age and history of stroke was the only significant predisposing factor for PAD. According to this result, we propose ABI examination in old patients with LSS and history of stroke to rule out PAD. If PAD is diagnosed, spine surgeons may be able to decide whether to perform decompressive surgery for LSS. In this decision making process, electrodiagnostic testing can be helpful to differentiate radiographically asymptomatic LSS. Although imaging studies are often not specific for LSS, electrodiagnostic testing is highly specific for diagnosis of LSS<sup>4,12</sup>.

The strength of this study is the severe IC of the patient population, which was analyzed by multivariate logistic regression to identify the incidence of and risk factors for PAD. Diagnosis of PAD by ABI enables spine surgeons to avoid fatal vascular events and unnecessary surgery in patients with radiographically asymptomatic LSS. However, this study is limited by its retrospective nature, relatively small patient population, and short-term duration of follow-up. To further verify the incidence of and risk factors for PAD, we are currently analyzing more patients and collecting longer-term results. In addition, this study did not reveal the sensitivity and specificity of ABI because CTA was not performed in all patients. Therefore, further study is required to confirm the efficacy of ABI.

## CONCLUSION

Misdiagnosis of PAD may increase the risk of severe vascular events and even death. To prevent misdiagnosis of fatal PAD and to avoid unnecessary surgery, we propose further evaluation should be assessed in old patients with history of stroke for diagnosis of PAD.

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