의학석사 학위논문

파행이 있는 요추부 척추관 협착증 환자에 있어서 말초동맥 혈관질환의 유병률 및 위험인자 – 전산화 단층 촬영 혈관조영술 연구

2017년 2월

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Abstract

Purpose:

It can be difficult to differentiate vascular and neurogenic intermittent claudication due to atypical signs and subjective symptoms. The exact diagnosis often cannot be made on clinical evidence alone, and ultimately requires imaging. Perioperative screening of peripheral arterial disease (PAD) in lumbar spinal stenosis (LSS) patients is important because untreated peripheral arterial disease is progressive and increases the risk of severe vascular events. The aims of this study are to study the prevalence of PAD in LSS patients with symptoms of intermittent claudication, and to study the independent risk factors for PAD. We aim to specify the cases where it is necessary to perform CT angiography as a preoperative screening tool in surgery for spinal stenosis.

Patients and Methods:

This study involved a retrospective analysis of 186 consecutive patients with radiographic evidence of lumbar spinal stenosis and symptoms of intermittent claudication, who underwent 3D CT-angiography of the lower extremities at the orthopedics department in our institution during a three-year period from August 2013 to August 2016. Patients' information on gender, age, weight, height, diabetes mellitus (DM), hypertension, ischemic heart disease (IHD), cerebrovascular disease (CVD), hyperlipidemia and smoking history were obtained from hospital medical notes. Statistical analysis was carried out using SPSS version 22.0 software (SPSS

Inc.,Chicago, IL). A p value of < 0.05 was considered to indicate statistical significance.

Results:

Segmental evaluation was done on CT angiogram results and more than 50% luminal narrowing was determined to be clinically significant and placed in the PAD group. 32 patients were diagnosed with PAD and referred to the general vascular team in our hospital, where they received appropriate treatment for PAD. In the non-PAD group (154 patients), 117 underwent definitive surgery for spinal stenosis such as posterior lumbar interbody fusion and a further 37 underwent conservative treatment. Only hypertension, DM, and male gender were found to statistically significant predictors of PAD. The results demonstrated that hypertension (OR, 2.793; 95% CI, 1.054-7.400) was the most significant risk factor, followed by DM (OR, 2.699; 95% CI, 1.084-6.722) and male gender (OR, 2.314; 95% CI, 1.063-6.635).

Conclusion:

The current study showed that male gender, DM and hypertension were the greatest risk factors for PAD. We conclude that male patients with diabetes and/or hypertension should be put under serious consideration for routine CT angiography examination when under evaluation for LSS and intermittent claudication. 3D CT angiography has the added advantage of guiding therapeutic strategies as high-image resolution techniques allow for better evaluation of the entire vascular tree in the lower extremities. Reports on treatment results and follow-up examinations should be studied

in future reports to determine how accurate CT angiography is in guiding decisions for management of intermittent claudication.

Keywords: peripheral arterial disease, stenosis, claudication, computed tomography angiography

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Introduction

Patients with lumbar spinal stenosis (LSS) present with symptoms of the lower extremities, including neurogenic intermittent claudication as a typical symptom. [1, 2] On the other hand, patients suffering from peripheral arterial disease (PAD) present with vascular claudication. [3] It is important for orthopedic surgeons to differentiate between the claudication caused by these two different pathologies. Vascular claudication of PAD typically occurs after walking for a distance with resultant vascular insufficiency caused by an imbalance between muscular oxygen demand and supply. [4] Resting from activity may help to relieve the symptoms. Neurogenic claudication of LSS is caused by narrowing of the spinal canal and neural foramen, which is aggravated by standing and relieved by sitting down and leaning over. [5] It can be difficult to differentiate vascular and neurogenic intermittent claudication due to atypical signs and subjective symptoms. The exact diagnosis often cannot be made on clinical evidence alone, and ultimately requires imaging. [6]

Spine surgeons occasionally make the mistake of performing spinal surgery in patients who have vascular intermittent claudication arising from PAD and radiographically asymptomatic stenosis. However, untreated PAD is progressive and increases the risk of severe vascular events. Therefore, one of the most important aspects in the evaluation of patients with PAD is the earliest possible identification of cases at greater risk of developing critical ischemia and, therefore, of losing the limb. Deep vein

thrombosis (DVT) and pulmonary embolism is a potentially life-threatening complication in patients undergoing elective spine surgery for LSS, and mechanical prophylaxis such as the wearing of elastic stockings is an effective preventive measure. [7] However, elastic stockings may cause acute limb ischemia in patients with PAD, so perioperative screening of PAD in LSS patients becomes all the more important. [8]

The ankle-brachial index (ABI) is currently the most common clinical diagnostic test for PAD because it is simple, noninvasive, inexpensive, and specific. There have been several studies to evaluate the incidence of PAD in patients with LSS using ABI. [9, 10] However, its sensitivity is unreliable, especially in populations with severe calcified arteries. [11]

Run-off computed tomography angiography (CTA) of the lower extremities has become the method of choice for imaging of the vessels in patients with suspected PAD because it is fast, well tolerated, and allows for exact treatment planning even with low-dose protocols. [12, 13]

The aims of this study are to study the prevalence of PAD in LSS patients with symptoms of intermittent claudication, and to study the independent risk factors for PAD. We aim to specify the cases where it is necessary to perform CT angiography as a preoperative screening tool in surgery for spinal stenosis.

Patients and Methods

Patients

This study involved a retrospective analysis of patients with radiographic evidence of lumbar spinal stenosis and symptoms of intermittent claudication, who underwent 3D CT-angiography of the lower extremities at the orthopedics department in our institution during a three-year period from August 2013 to August 2016. Patients with CT or magnetic resonance imaging (MRI) of the lumbar spine suggesting spinal stenosis and with Fontaine stage IIb claudication (intermittent claudication after less than 200 meters of walking), and who were therefore considered to be candidates for spinal surgery or intervention procedures, were selected for CTA examination to rule out peripheral arterial disease. CTA findings were graded according to five categories; normal (0% reduction in diameter), mild (1-49% reduction in diameter), moderate (50-74% reduction in diameter), severe (75-99% reduction in diameter), and complete occlusion. These categories corresponded to those used in other imaging studies on peripheral arterial disease. [14, 15] Patients were diagnosed with LSS when neurological findings were consistent with spinal stenosis found via MRI at that particular lumbar spinal level. Subjects were identified from the picture archiving and communicating system and follow-up data were obtained. Patients′ information on gender, age, weight, height, diabetes mellitus (DM), hypertension, ischemic heart disease (IHD), cerebrovascular disease (CVD), hyperlipidemia and smoking history

were obtained from hospital medical notes.

Inclusion and exclusion criteria

All patients with 3D CT angiograms undertaken after a visit for evaluation of claudication symptoms at our orthopedics outpatient clinic were included in the study. Intermittent claudication was defined as lower-limb cramping or pain brought on by exertion, and relieved by rest. The common symptom for inclusion was intermittent claudication after less than 200 meters walking, over a period of more than three months. Patients with psychiatric diseases, any suspicion of spinal infection or who had already received lumbar spinal surgery were excluded from the study. Patients at high risk for contrast media- induced nephropathy (CIN), such as those already on renal dialysis, could not be included in the study. 204 consecutive patients were recruited. Among those excluded, nine had already received spinal surgery, six had evidence of infection, and three were taking medication for psychiatric diseases. 186 patients were included in the final study.

Statistical analysis

A paired t-test and chi-square test were used to compare each demographic parameter between the two groups. Clinical risk factors were examined using multivariate logistic regression analysis, and odds ratios with 95% confidence intervals (CIs) were

calculated. Statistical analysis was carried out using SPSS version 22.0 software (SPSS Inc.,Chicago, IL). A p value of < 0.05 was considered to indicate statistical significance.

Results

Patient demographics are presented in Table 1. The five categories on CTA findings were divided into two groups; categories 1 and 2 as Group 1(or non-PAD group) and categories 3, 4, and 5 as Group 2(or PAD group) (Table 2). More than 50% luminal narrowing was determined to be clinically significant and considered to be the threshold for treatment for PAD. Thirty-two patients were classified into the second group and referred to the general vascular team in our hospital, where they received appropriate treatment for PAD. Seven patients received antiplatelet or anticoagulant therapy, while 25 patients either received endovascular angioplasty or underwent surgical bypass. The remaining 154 patients were classified into the first group, of which 117 underwent definitive surgery such as posterior lumbar interbody fusion for spinal stenosis and a further 37 underwent conservative treatment.

The non-PAD group had 53 males and 101 females with a mean age of 67.4 years, while the PAD group had 29 males and 3 females with a mean age of 69.5 years. The mean age was not significantly different between the two groups. (Paired T-test, p value = 0.252) (Table 2)

The percentage of males (90.6%) in the PAD group was significantly higher than the non-PAD group (34.4%). The prevalence of diabetes mellitus (DM) was 53.1 % in the PAD group, which was significantly higher than 27.9 % in the non-PAD group (p=0.002 in chi-square test). The prevalence of hypertension in the PAD group was 75.0%, which was significantly higher than 52.6% in the non-PAD group (p=0.032 in chi-square test). The rate of patients with a smoking history, past or present, in the PAD

group was 37.5%, which was also significantly higher than 12.3% in the non-PAD group ($p<0.00$ in chi-square test). The mean body mass index (BMI) in the PAD cohort was significantly lower than the non-PAD cohort. (Paired t-test, $p=0.035$). The percentages of ischemic heart disease, cerebrovascular disease, and hyperlipidemia were not significantly different between the two groups. The percentage of population over 65 years old was 68.8 % in the PAD group versus 68.4 % in the non-PAD group; the difference was not statistically significant ($p=0.963$ in chi-square test).

From the above results, male gender, mean BMI, DM, hypertension, and smoking history were extracted as characteristics of patients with clinically significant PAD. A multivariate regression analysis was conducted for these factors to investigate independent predictors of PAD. (Table 3) Only hypertension, DM, and male gender were found to statistically significant predictors of PAD. The results demonstrated that hypertension (OR, 2.793; 95% CI, 1.054-7.400) was the most significant risk factor, followed by DM (OR, 2.699; 95% CI, 1.084-6.722) and male gender (OR, 2.314; 95% CI, 1.063-6.635). Of the 20 patients that were male with both DM and hypertension, 13 (65%) were diagnosed with PAD. Of the 32 patients in the PAD group, only three (9.3%) were free of both DM and hypertension.

Discussion

Peripheral arterial disease is a growing problem in industrial nations because of its progressive character and the positive correlation with advanced age. [16] The reported prevalence of PAD is 4.5% among men older than 55 years. [17] Both lumbar spinal stenosis and PAD are usually associated with degenerative conditions and share some clinical features; therefore achieving a differential diagnosis in a clinical setting is often difficult.

Screening for PAD commonly includes foot pulses and the ankle-brachial index, but concerns persist regarding their accuracy. Williams reported that diabetic neuropathy was associated with a reduced sensitivity of ABI (38%). [18] The inability of ABI to detect arterial disease in the presence of detectable peripheral neuropathy resulted in false-negative results in one-third of limbs, and was even less sensitive than palpation of foot pulses. In some cases, the ankle artery is incompressible and the systolic pressure at that location cannot be measured in spite of cuff inflation at more than 250mmHg. This situation is related to calcification of the arterial wall and may occur in patients with medical calcinosis, diabetes, and end-stage renal disease. When vascular calcification is present, stenotic disease cannot be detected by the ABI. [19]

When diagnosing LSS, it is important to bear in mind that concurrent PAD is possible. In a nationwide multicenter study in Japan, it was found that 6.7% of LSS patients had PAD and comorbidity of diabetes, history of cerebrovascular disorder, and history of ischemic heart disease are characteristics of LSS patients with PAD. [10]

The purpose of this retrospective cohort study was to use CT angiography in patients with stage IIb claudication and radiographic evidence of LSS to sort out patients with concomitant PAD, and to study any relationship between the prevalence of comorbidities such as diabetes and hypertension with PAD in LSS patients. We demonstrated that the incidence of clinically relevant PAD in LSS patients was 17.2%. In other countries, the prevalence of PAD in the general population is reported to be 3-19% [20, 21], and several studies also demonstrated that the risk of PAD is significantly higher in older people and in men. [22, 23] Although the diagnostic standard for the evaluation of PAD is still digital subtraction angiography (DSA), this technique has several disadvantages such as invasiveness and high cost, and is slowly being replaced by other noninvasive exams such as CT and MR angiography. The clinical utility of CT angiography in the evaluation of PAD has been found in a few studies. [24, 25] Schernthaner et al. showed that CT angiography can be a viable and reliable noninvasive imaging method for the evaluation and triage of patients with stage II PAOD, and that its findings are a highly accurate basis for treatment decisions and planning. [12] In the clinical setting, it is important for surgeons to keep in mind that claudication in a patient with radiographic evidence of lumbar spinal stenosis is not always of neurogenic origin. An arterial pulse examination was deemed to be insufficient for PAD screening in lumbar stenosis patients in a prospective multicenter study [26], while the validity of ABI for the differential diagnosis of PAD and LSS was checked in one retrospective study. [9] To the best of our knowledge, no previous reports have checked CT angiograms as a preoperative study in patients with lumbar

spinal stenosis to rule out PAD. We have shown that routine CTA exams in certain LSS patients can be useful for preventing missed diagnosis of PAD and in guiding further treatment.

Our study has certain limitations. First, based on its retrospective design, uncertainty over missing and erroneous medical records exists. Second, patients at high risk for CIN could not undergo CT angiography and were therefore excluded from the study. CIN, defined as a relative increase of serum creatinine levels of at least 25% over the baseline value, occurs at a rate of 1%-6% in unselected patient populations and up to 40%-50% in high-risk patient populations such as those with preexisting renal insufficiency. [27] This selection bias could have affected the results of our study. Second, ABI was not measured in all patients. Further studies should try to elucidate whether ABI scores are correlated with PAD severity in CT angiography. Other variables such as osteoarthritic pain, neuropathic pain and psychosocial factors should also have been taken into consideration as they may have affected patients' symptoms.

Conclusion

The current study also showed that male gender, DM and hypertension were the greatest risk factors for PAD. We conclude that male patients with diabetes and/or hypertension should be put under serious consideration for routine CT angiography examination when under evaluation for LSS and intermittent claudication. 3D CT angiography has the added advantage of guiding therapeutic strategies as high-image resolution techniques allow for better evaluation of the entire vascular tree in the lower extremities. The disadvantages are the need for radiation exposure to the patient and the usage of potentially nephrotoxic contrast material. Patients under risk for contrast-induced nephropathy should carefully be screened out before the examination takes place. Reports on treatment results and follow-up examinations should be studied in future reports to determine how accurate CT angiography is in guiding decisions for management of intermittent claudication.

Table 1 Demographics of entire cohort

	Entire cohort (n=186)
Mean age	67.8 (range 33-86)
Gender	82 males, 104 females
Mean BMI	24.92 (range 16.51-33.86)
Diabetes mellitus	32.2% (60/186)
Hypertension	56.4% (105/186)
Smoking history	16.7% (31/186)
IHD	13.4% (25/186)
CVD	2.2% (4/186)
Hyperlipidemia	16.7% (31/186)

BMI: body mass index; IHD: ischemic heart disease; CVD: cerebrovascular disease

Table 2 Demographics of PAD cohort and non-PAD cohort

	Non-PAD group (n=154)	PAD group (n=32)	P value
Mean age	67.4 years (SD 9.96)	69.5 years (SD 6.62)	0.252
Gender	53 males, 101 females	29 males, 3 females	**<0.00**
Mean BMI	25.20 (SD 3.64)	23.72 (SD 2.90)	**0.035**
Diabetes mellitus	27.9% (43/154)	53.1% (17/32)	**0.002**
Hypertension	52.6% (81/154)	75.0% (24/32)	**0.032**
Smoking history	12.3% (19/154)	37.5% (12/32)	**<0.00**
IHD	11.7% (18/154)	21.9% (7/32)	0.237
CVD	1.3% (2/154)	6.3% (2/32)	0.117
Hyperlipidemia	15.6% (24/154)	21.9% (7/32)	0.619

BMI: body mass index; IHD: ischemic heart disease; CVD: cerebrovascular disease

Table 3 Multivariate logistic regression analysis

Predictor	Odds ratio (95% CI)	P value
Male gender	2.314 (1.063-6.635)	**0.000**
Diabetes mellitus	2.699 (1.084-6.722)	**0.033**
Hypertension	2.793 (1.054-7.400)	**0.039**
Mean BMI	0.932 (0.810-1.073)	0.327
Smoking history	1.888 (0.648-1.888)	0.244

CI : confidence interval

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국문초록

목적: 요추부 척추관 협착증의 신경성 파행과 말초동맥질환의 혈관성 파행은 주관적인 증상의 차이와 비특이적인 징후들로 인해 임상소견만으로 정확한 감별진단을 내리기 힘들며 결국 영상검사 등의 객관적 검사를 필요로 하게 된다. 하지만 협착증 환자에게 동반된 말초동맥질환은 발견되지 않을 경우 진행하여 심각한 합병증을 일으킬 수 있다. 이번 연구의 목표는 간헐적 파행이 있는 요추부 협착증 환자에 있어서 말초동맥질환의 유병률을 구하고 또한 독립적인 위험인자를 알아보는 것이다. 요추부 협착증 환자중 어떤 환자에서 수술전 검사의 일환으로 전산화단층촬영(CT) 혈관조영술을 실시하는 것이 유용할지도 알아보고자 한다.

방법: 2013년 8월부터 2016년 8월까지 본원 외래로 내원한 환자 중 요추부 협착증의 영상학적 증거가 있고 간헐적 파행을 호소한 환자 중 CT 혈관조영술을 실시한 186명에 대한 후향적 조사를 시행하였다. 환자의 성별, 나이, 키, 몸무게와 당뇨, 고혈압, 허혈성 심장 질환, 뇌혈관 질환, 고지혈증, 흡연력 여부를 조사하였다. SPSS 22.0 프로그램을 이용하여 통계 분석을 실시하였으며 p값은 0.05 미만일 때 통계적으로 유의하다고 보았다.

결과: CT 혈관조영술에서 50% 이상의 혈관협착이 있을 때 말초동맥질환으로 진단하였다. 186명에 대한 CT 검사에서 32명이 말초동맥질환으로

진단(17.2%)되어 혈관외과 팀에서 적절한 치료를 받게 되었다. 나머지 154명의 협착증 환자 중 117명은 후방 요추체간 유합술 등의 수술을 받았고 37명은 보존적 치료를 받았다. 고혈압, 당뇨, 그리고 남성 성별이 말초동맥질환의 유의한 위험인자로 조사되었다. 고혈압이 가장 유의한 위험인자 (OR, 2.793; 95% CI, 1.054-7.400)였고, 당뇨(OR, 2.699; 95% CI, 1.084-6.722), 그리고 남성(OR, 2.314; 95% CI, 1.063-6.635) 순이었다.

결론: 파행이 있는 요추부 척추관 협착증 환자에서 말초동맥질환의 감별을 위한 수술전 평가를 실시할 때 CT 혈관조영술이 유용하며, 특히 당뇨 또는 고혈압이 있는 남성 환자들에게 의미가 있다. CT 혈관조영술은 하지 전체의 혈관을 고해상도로 볼 수 있기 때문에 동맥질환의 치료 방침을 정하는데도 이용할 수 있다. 추후 연구에서는 혈관조영술로 정한 말초동맥질환의 치료 결과를 종합하여 치료방침을 정하는 데 있어서의 정확성을 보고자 한다.

주요어: 말초동맥 혈관 질환, 협착증, 파행, 전산화 단층촬영

학 번: 2015-21993