Acta Derm Venereol 2013; 93: 747–748

SHORT COMMUNICATION

Onychomycosis as a Warning Sign for Peripheral Arterial Disease

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Accepted Dec 3, 2012; Epub ahead of print Mar 25, 2013

Peripheral arterial disease (PAD) is associated with increased risk of cardiovascular and cerebrovascular diseases. Increasing age, smoking, hyperlipidaemia, diabetes, hypertension, and male gender have been identified as risk factors for PAD (1). The possible role of dermatological diseases in the early detection of PAD remains unknown.

Onychomycosis (OM) is a common disease, accounting for up to half of all reported nail diseases, with an estimated prevalence of 10% in the general population (2–4). Previous studies found that OM was associated with increasing age, gender, diabetes, psoriasis, smoking and immune dysfunction (5–7). Meanwhile, a study of patients attending a vascular clinic reported that PAD might be an independent predictor of OM (7).

Based on these results, we hypothesized that OM might represent an independent clinical sign for the early detection of PAD. A university-based cross-sectional study of elderly dermatological patients with or without microscopically confirmed OM was performed to clarify the role of OM as an independent predictor of PAD.

MATERIALS AND METHODS

Patients aged ≥ 50 years old who visited the outpatient or inpatient dermatology clinic of Kobe University Hospitalwere randomly enrolled in this study. This study was approved by the institutional review board. Oral and written informed consents for the study were obtained from all subjects. Both feet were examined clinically in all patients. Nail specimens from patients with clinical dystrophy of any toenails were examined by potassium hydroxide microscopy to detect the presence of fungal filaments. The nail specimens were also cultured in Sabouraud dextrose agar slants with chloramphenicol (Nikken bio medical laboratory, Kyoto, Japan).

Participants completed questionnaires about age, gender, hypertension, hyperlipidaemia, smoking, diabetes, and cardiovascular and cerebrovascular diseases.

The ankle brachial pressure index (ABI) was measured in both legs. Patients with an ABI < 0.9 (8) in at least one side of the leg were considered to have PAD. The mean ABI value for both legs was calculated in the OM and control groups.

All analyses were performed using SPSS 16.0 (SPSS Inc, Chicago, IL, USA). Adjusted odds ratios (ORs) and 95% confidence intervals (CI) were estimated by logistic regression models to investigate independent associations between risk factors (age, gender, hypertension, hyperlipidaemia, smoking, diabetes, cardiovascular disease, cerebrovascular disease, and PAD) and OM. Student's *t*-test and Pearson's χ^2 test were used to compare differences in continuous and categorical variables between the OM and control groups. Two-sided probability values < 0.05 were considered significant. Continuous variables are presented as means ± standard deviation (SD).

RESULTS

A total of 86 subjects participated in the study, 40 men and 46 women, with a mean age of 71.2 years. There were 44 patients in the OM group (found to be positive by microscopy) and 42 patients in the control group (without OM). *Trichophyton rubrum* accounted for 68% ($n = 11$) and *T. mentagrophytes* for 32% ($n = 5$) of OM positive cases , suggesting that microscopy had a higher percentage of positivity than culture like the past reports. There were no significant differences between the groups in terms of most covariates, but the prevalence of diabetes ($p < 0.0001$) and PAD ($p = 0.001$) were significantly higher in the OM.

Multiple logistic analysis identified age (OR 1.11, 95% CI 1.03–1.19), diabetes (OR 175.11, 95% CI 12.57–2,440.32) and PAD (OR 9.85, 95% CI 1.37–70.72) as significant risk factors for OM (Table I). Gender, hypertension, hyperlipidaemia, smoking, cardiovascular disease and cerebrovascular disease were not significantly associated with OM.

Mean ABI values for both legs were significantly lower in the OM group (0.998) compared with the control group (1.133; $p = 0.001$) (Fig. 1).

DISCUSSION

PAD has been shown to be associated with increased risks for premature mortality and cardiovascular and cerebrovascular events (9). Recent studies suggest that the early detection and screening of PAD patients could lead to health benefits in 2 ways: through avoiding the progression of PAD, and by helping prevent cardiovascular and cerebrovascular events and their associated mortalities (10). A recent study showed that the risks of mortality were similar in symptomatic and asymptomatic PAD patients. That study found that approximately 20% of elderly patients visiting primary care physicians had PAD (12.2% asymptomatic, 8.7% symptomatic), indicating that asymptomatic PAD is more common than symptomatic PAD (1). However, the early detection of asymptomatic PAD is difficult for

 doi: 10.2340/00015555-1576
 ISSN 0001-5555

Table I. *Baseline characteristics of patients with and without onychomycosis: multiple logistic analysis*

Baseline characteristic	Onychomycosis ($n=44$)	Control ($n=42$)	Odds ratio[a] (95% CI)	p-value
Age, years, mean	73.6	70.6	1.11 (1.03–1.19)	0.008
Gender, male, *n* (%)	21 (48.9)	19 (45.3)	1.17 (0.29–4.79)	0.83
Hypertension, *n* (%)	19 (43.2)	17 (40.5)	0.65 (0.17–2.49)	0.53
Hyperlipidaemia, *n* (%)	15 (34.1)	8 (19.0)	2.19 (0.50–9.62)	0.3
Smoking, *n* (%)	7 (15.9)	8 (19.0)	0.33 (0.56–1.93)	0.22
Diabetes, *n* (%)	23 (51.1)	1 (2.4)	175.11 (12.57–2440.32)	<0.001
Cardiovascular disease, *n* (%)	15 (34.1)	8 (19.0)	1.55 (0.31–7.68)	0.59
Cerebrovascular disease, *n* (%)	5 (11.4)	6 (14.3)	0.59 (0.08–4.45)	0.61
Peripheral arterial disease, *n* (%)	14 (31.8)	2 (4.8)	9.85 (1.37–70.72)	0.02

[a]Adjusted for age, gender, hypertension, hyperlipidaemia, smoking, diabetes, cardiovascular disease, cerebrovascular disease, and peripheral arterial disease (ABI < 0.9, ABI > 1.4).

non-expert physicians. Guidelines that advocate PAD screening generally recommend measurement of ABI (10). In addition, an ABI < 0.9 has been used as a diagnostic criterion in most studies on PAD, because of its reproducibility and non-invasive nature. We therefore used ABI to diagnose PAD in this study. However, it is not practical to measure ABI in all patients, and we therefore focused on the use of dermatological diseases to detect asymptomatic PAD. Compared with internal diseases, dermatological diseases are easier to identify by routine examination. We hypothesized that OM, which is common in elderly patients, might act as an independent predictor of PAD risk. This study demonstrated that the prevalence of PAD, as well as diabetes, was significantly higher in patients with OM than in those without OM. Furthermore, the higher incidence of PAD in the OM group remained significant even after factoring out the effects of age, gender, hypertension, hyperlipidaemia, smoking, diabetes, cardiovascular disease, and cerebrovascular disease using multiple logistic analysis. Although this was a relatively small, university-based study, the results suggest that patients with OM have a higher risk of PAD than those without OM, and that OM could provide an easily assessed and simple predictor of PAD, at least in general hospitals, such as university hospitals. In addition, the mean ABI was significantly lower in subjects with OM (0.998) compared with those without OM (1.133). A meta-analysis showed that for levels of ABI below 1.00, the hazard ratios for total and cardiovascular mortality increased consistently with decreasing ABI (ABI 0.91–1.00; men: 1.61, 1.68; women: 1.52, 1.84, respectively) (11). The results of this study suggest that attention should be paid to possible substantial cardiovascular events in patients with OM.

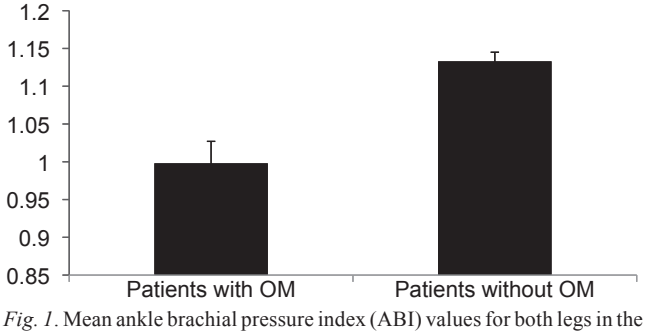

Fig. 1. Mean ankle brachial pressure index (ABI) values for both legs in the onychomycosis (OM) and control groups. The mean ABI was significantly lower in the OM group (0.998) compared with the control group (1.133; $p=0.001$).

The authors declare no conflicts of interest.

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