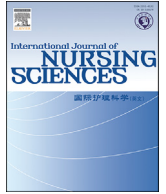


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Investigation and analysis of lower extremity arterial disease in hospitalized elderly type 2 diabetic patients

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ABSTRACT

Background: The risk of lower extremity arterial disease (LEAD) is increased in diabetic patients. LEAD in diabetic patients occurs earlier and is often more severe and diffuse; however, it is largely under-diagnosed and untreated. The purposes of this study were to investigate and analyze LEAD situation of hospitalized elderly type 2 diabetic patients.

Methods: The ankle-brachial index (ABI) was used to screen LEAD in hospitalized elderly type 2 diabetic patients. The patients were divided into 5 groups based on the screening results: non-LEAD group and LEAD group; the LEAD group was divided into mild stenosis group, moderate stenosis group, and severe stenosis group.

Results: The percentage of patients who had LEAD was 43%. Significant difference in age, diabetes duration, peak velocity, microalbuminuria, and vibratory sensory neuropathy was observed between patients with and without LEAD; regression analysis showed that urinary albumin and vibratory sensory neuropathy were independent risk factors for LEAD. Significant difference in age, body mass index (BMI), peak velocity, urinary albumin, and high-density lipoprotein cholesterol (HDL-C) was observed between mild stenosis group, moderate stenosis group, and severe stenosis group; regression analysis showed that urinary albumin, BMI, and HDL-C were independent risk factors for accelerating vascular stenosis.

Conclusions: The incidence of LEAD in hospitalized elderly type 2 diabetic patients is high; age, diabetes duration, peak velocity, BMI, urinary microalbumin, vibratory sensory neuropathy, and HDL-C are the major risk factors for LEAD. Active control of risk factors is helpful to reduce or delay LEAD.

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1. Introduction

Lower extremity arterial disease (LEAD) is a chronic atherosclerotic occlusive disease that occurs in the lower extremities. It occurs earlier in diabetic than in nondiabetic individuals and is often more severe, diffuse, and popular [1,2]. In comparison with nondiabetic subjects, patients with diabetes have a twofold increased risk of developing LEAD [3,4]. In the United Kingdom Prospective Diabetes Study, 1.2% of nearly 5000 individuals with newly diagnosed type 2 diabetes had LEAD at the time of diagnosis [5]. Although LEAD is common, most of the cases are asymptomatic and underdiagnosed [6], especially in elderly diabetic populations

[7]. The presence of LEAD increases the risk of claudication, ischemic ulcers, gangrene, and possible amputation. Apart from this, LEAD patients, whether they are symptomatic or asymptomatic, have an increased risk of death and cardiovascular events because of the coexisting clinical or subclinical atherosclerosis in the coronary and the cerebral arteries [8]. Studies revealed that mortality is cardiovascular related in approximately 75% [2], and the 5-year survival rate of LEAD patients with diabetes is just about 50% [9]. Therefore, screening for LEAD is strongly encouraged in every patient with diabetes to optimize medical treatment in this specific population [2].

Ankle-brachial index (ABI), defined as the ratio of systolic pressure in the ankle arteries (the highest one among the dorsalis pedis arterial systolic pressure and the posterior tibial arterial systolic pressure) and systolic pressure in the brachial artery, is an important, noninvasive, and practical measurement for the detection of arterial obstructive disease, especially for LEAD [10]. ABI has a validated sensitivity and specificity in detecting LEAD which is

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alternative to conventional digital subtraction angiography [11]. Decrinis [12] et al. strongly proved the validity of ABI in detecting arterial stenoses in lower extremity, and revealed that the sensitivity and specificity of ABI were respectively 94% and 100%.

However, despite the recognition that LEAD is associated with a three- to sixfold increased risk of death from cardiovascular causes [13], particularly in diabetic patients, this specific manifestation of systemic atherosclerosis is largely underdiagnosed and undertreated [2]. Hence, this study aims to investigate LEAD in hospitalized elderly type 2 diabetic patients and analyze the risk factors to provide possible evidence for intervention.

2. Methods

2.1. Subjects

From May 2013 to June 2014, hospitalized elderly patients with type 2 diabetes mellitus were investigated at Huadong Hospital in Shanghai, China. The inclusion criteria were (1) diagnosed with elderly type 2 diabetes based on the criteria of Chinese Medical Association Diabetes Branch and (2) conscious and voluntarily participated in the research. The exclusive criteria were (1) with past lower limb amputation history, (2) presented serious lower limb edema, and (3) presented lower limb skin damage. Informed consent was obtained from each patient included in the study. A total of 237 patients were enrolled (120 males, 117 females), mean age was 71.4 ± 7.9 years old, and mean duration of diabetes was 12.8 ± 9.3 years.

2.2. Demographic information and biochemical parameters

As part of the standard clinical evaluation of each patient, the following demographic data were compiled for this study: age, gender, duration of diabetes, height and weight (for the calculation of body mass index [BMI]), presence of hypertension, and so on. A finding of $18.5 \leq \text{BMI} < 24 \text{ kg/m}^2$ was considered normal. Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg or if the patient was receiving antihypertensive treatment [14]. All subjects underwent assessments of a range of clinical and biochemical variables. Venous blood samples for serum total cholesterol (TCH), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), glycated hemoglobin (HbA1c), and glycated albumin (GA) were collected. Microalbuminuria was measured by random daytime urine sample. Microalbuminuria was defined entirely by calculation of albumin-to-creatinine ratio in urine specimen. The normal range of each parameter are as follows: TCH < 5.72 mmol/L, TG < 1.70 mmol/L, LDL-C < 3.64 mmol/L, HDL-C < 1.29 mmol/L in females and < 1.03 mmol/L in males, HbA1c 4.0%–6.0%, GA 11.0%–17.0%, microalbuminuria < 2.26 mg/mmol·Cr [14,15].

2.3. LEAD screen

The ABI values were measured by using Doppler blood stream probe (Bidop ES-100V3, Hadeco, Japan). All the ABI measurements were performed with the subjects in the supine position after the participants rested in a supine position for 10 min in a temperature-controlled ($23\text{--}25$ °C) and quiet room. A blood pressure cuff was placed on subjects' upper arms, and it was inflated until no brachial pulse was detected by the Doppler device. Then, the cuff was slowly deflated until the Doppler detected that the pulse returned (the systolic pressure). This methodology was repeated on the legs to measure the dorsalis pedis and the posterior tibial arterial systolic pressure [16]. The higher systolic pressure in the dorsalis pedis and

the posterior tibial arteries serves as ankle systolic pressure. The ABI was calculated by dividing the ankle systolic pressure by the higher brachial systolic pressure [16]. $\text{ABI} > 1.3$ increased, thereby suggesting arteriosteo-genesis; $0.9 < \text{ABI} \leq 1.3$ was normal; $\text{ABI} \leq 0.9$ was reduced, suggesting LEAD; $0.7 < \text{ABI} \leq 0.9$ suggested mild vascular stenosis; $0.4 < \text{ABI} \leq 0.7$ suggested moderate vascular stenosis; $\text{ABI} \leq 0.4$ suggested severe vascular stenosis [17]. Patients with $\text{ABI} > 1.3$ were excluded because such results usually reflect arterial rigidity, preventing arterial compression; diagnosis of LEAD was based on $\text{ABI} < 0.9$ on either leg. Patients were divided into 4 groups based on the screening results: non-LEAD group and LEAD group; the LEAD group was divided into mild stenosis group, moderate stenosis group, and severe stenosis group. Peak velocity, which was measured by Doppler blood stream probe, is the maximum velocity in the cross-sectional area of the blood vessel when the heart is contracted, thereby reflecting the extent of arterial stenosis.

2.4. Peripheral neuropathy examination

Diabetic peripheral neuropathy was diagnosed on the basis of typical symptoms and peripheral sensory nerve function examination in the feet, including the nylon filament test for diminished or no pressure sensation, temperature sense examination tool for abnormal temperature sensation, and 128 Hz tuning fork for abnormal vibrations. The 128 Hz tuning fork was applied twice at the back of the first metatarsal. Vibration sensation was abnormal if patients did not perceive the vibration sensation either time. In the pressure sensation examination, five positions of the foot were screened, including the first toe, the first and fifth metatarsal, the arch of the foot, and heel (avoid the corpus callosum). A 10 g nylon monofilament was vertically pressed at those five positions, lasting 1–2 s, and the patients were then asked whether they feel pressure. Patients had abnormal pressure sensation if pressure on 2 or more positions cannot be felt. The temperature sense examination tool, whose one end is metal and another one is polyester, was used to test abnormal temperature sensation. The examination positions and the judging of temperature sensation is the same with pressure sensation. Besides, populations were considered having peripheral neuropathy if they have obvious neuropathy symptoms.

2.5. Statistical analysis

All statistical analyses were performed using SPSS (the statistical package for social science program, Windows, version 17.0). Continuous variables were presented as mean \pm standard deviation. Categorical variables were expressed as a percentage. The independent-samples *t*-test and one-way analysis of variance were used to examine continuous variables, the chi-square test and rank test were used to examine categorical differences. All parameters were first analyzed by univariate analysis, and those significantly differing were enrolled in multiple logistic regression with forward stepwise procedure to identify independent risk factors. Difference between values were considered statistically significant when $P < 0.05$.

3. Results

3.1. Clinical characteristics

This study included 237 hospitalized elderly type 2 diabetic patients. The male/female ratio was 120/117, the mean age was 71.4 ± 7.9 years old, the mean BMI was $24.7 \pm 3.7 \text{ kg/m}^2$, the mean diabetes duration was 12.8 ± 9.3 years, the mean hypertension duration was 10.8 ± 11.8 years, the mean HbA1c level was

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