Risk Factors in Patients with Venous Stasis-Related Skin Lesions without Major Abnormalities on Duplex Ultrasonography

Kotaro Suehiro, MD, Noriyasu Morikage, MD, Osamu Yamashita, MD, Takesuke Harada, MD, Makoto Samura, MD, Yuriko Takeuchi, MD, Takahiro Mizoguchi, MD, and Kimikazu Hamano, MD

Division of Vascular Surgery, Department of Surgery and Clinical Science, Yamaguchi University Graduate School of Medicine, Ube, Yamaguchi, Japan

Received: June 16, 2016; Accepted: July 22, 2016

Corresponding author: Kotaro Suehiro, MD. Division of Vascular Surgery, Department of Surgery and Clinical Science, Yamaguchi University Graduate School of Medicine, 1-1-1, Minamikogushi, Ube, Yamaguchi 755-8505, Japan
Tel: +81-836-22-2260, Fax: +81-836-22-2423
E-mail: ksuehiro-circ@umin.ac.jp

Purpose: To clarify the risk factors for venous stasis-related skin lesions in the legs in patients without major abnormalities on duplex ultrasonography (DUS).

Methods: Fifty patients (nine males and 41 females, age 27–93 years) with symptoms of C4 or greater according to the Clinical, Etiological, Anatomical, Pathological (CEAP) classification, but having no abnormalities on DUS were reviewed for known risk factors for chronic venous insufficiency (CVI) such as older age (>70 years), obesity (body mass index [BMI] >30 kg/m²), short walking distance (<200 m/day), reduced ankle range of motion (<20°), and occupation requiring prolonged standing (>8h per day).

Results: The risk factor was different between male and female patients; although all patients had at least one of the above risk factors, the most commonly found risk factor in male patients was occupation requiring prolonged standing (63%), while advanced age (78%) and limited walking distance (83%) were risk factors in female patients.

Conclusions: Although male and female patients had different risk factors, insufficient walking seemed to be closely related to the development of venous stasis-related skin lesions.

Keywords: chronic venous insufficiency, duplex scan

Introduction

Approximately 50% to 88% of superficial veins and 48% to 72% of deep veins in patients with chronic venous insufficiency (CVI), defined as C4 or greater in the Clinical, Etiological, Anatomical, Pathological (CEAP) classification, have been reported to exhibit anatomical venous disorders which can be confirmed using duplex ultrasonography (DUS). However, a certain number of patients with CVI do not have any abnormality that can be confirmed on DUS. Older age and obesity are well-known risk factors for CVI. In addition, any condition that impacts the calf muscle pump, such as immobility, ankle dysfunction, or loss of muscle bulk, as well as prolonged standing, can potentially result in CVI. In the current study, we reviewed patients who presented with symptoms typically seen in CVI without major abnormalities on DUS, and investigated whether these patients had any of above-described risk factors.

Methods

This retrospective study was approved (H28-019) by the Institutional Review Board of Yamaguchi University Hospital (Ube, Yamaguchi, Japan) and conducted according to the principles of the Declaration of Helsinki; the need for individual patient consent was waived.

Between April 2009 and November 2015, 660 patients who presented with leg symptoms regarded as C4 or greater in the CEAP classification visited our clinic. Patients with different symptoms in each leg were regarded as suffering from the more severe symptom. DUS was performed by a qualified cardiovascular technician during their initial visits, which confirmed the absence of reflux and/or occlusion in the deep veins (from the common femoral vein to crural muscular veins), saphenous veins, or accessory saphenous veins, and perforators in 50 patients (7.6%). The characteristics of these patients are summarized in Table 1. The systemic conditions that could cause similar leg symptoms, e.g. right heart failure, were excluded by patient histories, physical examinations, blood tests, chest radiograms, electrocardiograms, echocardiography, etc. Whenever the skin manifestation was confusing, we referred to dermatologists and pathologists and the diagnoses were made by our agreement.
Among these patients, the presence of any of the following five factors, each of which is a known risk factor for CVI, was investigated: older age (>70 years), obesity (body mass index [BMI] >30),\(^6\) short walking distance (<200 m/day), reduced ankle range of motion (AROM; <20°),\(^12\) or occupation requiring long periods of standing (>8h per day). A reduced calf-ankle circumference ratio can indicate reduced calf muscle bulk,\(^12\) which may be a risk factor for CVI. However, this was not investigated because the ratio could not be accurately assessed due to leg edema of varying degrees. Gender, family history, and ethnicity were also not included in this study because their ability to predict the risk of CVI is controversial.\(^6\)

### Statistical analysis

Results are expressed as means ± standard deviation or count, unless otherwise indicated. The differences in the ratio of having symptoms and risk factors between male and female patients were studied using the \(\chi^2\) test. The differences in age and BMI between male and female patients were tested using the Mann-Whitney U-test. Statistical analyses were performed using JMP 11.0 (SAS Institute, Cary, NC, USA). P-values <0.05 were considered statistically significant.

### Results

As demonstrated in Table 1, clear differences were observed in the characteristics of male and female patients. Male patients tended to present with C5 or C6, were relatively younger, and had occupations requiring prolonged standing, while more female patients presented with C4, were older, and walked for limited distance per day. Additionally, another difference was found in the number of risk factors between male and female patients (Fig. 1). Even though all patients had at least one of the above-described risk factors, female patients had more risk factors (male 1.1 vs. female 2.1, P < .01). Four male patients (4/9, 44%) had only one risk factor, while 38 of 41 female patients (93%) had multiple risk factors. Of those, the most frequent combination of risk factors was older age and limited walking distance (28/41, 68%), which was not noticed in male patients. Among these 28 female patients, 10 patients exhibited reduced AROM as a complication. BMI >30 kg/m\(^2\) was found in four patients. In terms of symptom laterality, 74% had similar symptoms in both legs and only 8% had more severe symptoms in the left leg. There was no sexual difference in this regard.

**An occupation requiring prolonged standing, which was the most significant risk factor among male patients (6/9, 67%), was also found in four female patients. Details of these patients’ occupations are provided in Table 2. Patients with occupations requiring prolonged standing but possibly included walking (teaching and cleaning) presented with C4 symptoms, while patients**

### Table 1  Patient characteristics

|                  | Total (N = 50) | Male (N = 9) (% in male) | Female (N = 41) (% in female) | P-value (male vs. female) |
|------------------|---------------|--------------------------|-------------------------------|--------------------------|
| **Symptoms**     |               |                          |                               |                          |
| C4               | 33 (66%)      | 3 (33%)                  | 30 (73%)                      | <.05                     |
| C5,6             | 17 (34%)      | 6 (67%)                  | 11 (27%)                      | N.S.                     |
| **Symptom laterality** |       |                          |                               |                          |
| Right dominant   | 9 (18%)       | 1 (11%)                  | 8 (20%)                       | N.S.                     |
| Left dominant    | 4 (8%)        | 1 (11%)                  | 3 (7%)                        |                          |
| Right = Left     | 37 (74%)      | 7 (78%)                  | 30 (73%)                      |                          |
| **Age**          |               |                          |                               |                          |
| Mean (range)     |               |                          |                               |                          |
| >70 years        | 72 (27–93)    | 58 (27–82)               | 75 (39–93)                    | <.05                     |
| **BMI**          |               |                          |                               |                          |
| Mean (range); kg/m\(^2\) |       |                          |                               |                          |
| >30 kg/m\(^2\)  | 28 (15–42)    | 28 (18–42)               | 28 (15–41)                    | N.S.                     |
| **AROM**         |               |                          |                               |                          |
| <20°             | 14 (28%)      | 2 (22%)                  | 13 (32%)                      | N.S.                     |
| **Walking distance** |         |                          |                               |                          |
| <200 m/day       | 35 (70%)      | 2 (22%)                  | 34 (83%)                      | <.001                    |
| **Occupation**   |               |                          |                               |                          |
| Standing >8 h/day | 9 (18%)       | 6 (67%)                  | 4 (10%)                       | <.0001                   |

---

C: clinical class in the CEAP classification\(^{2,3}\); BMI: body mass index; AROM: ankle range of motion; N.S.: not significant between male and female patients; CEAP: clinical, etiological, anatomical, pathological

**Fig. 1** Number of risk factors.
with occupations requiring prolonged standing in a narrow space with little walking (chef, baker) presented with venous ulcers. Patients who exhibited reduced AROM presented with C6 despite being engaged in a standing occupation with walking.

**Discussion**

In the current study, the study population was represented by two distinct groups: elderly female patients with insufficient walking duration and male patients with occupations requiring prolonged standing.

Advanced age has been persistently reported as a risk factor for CVI. This may be the result of increased superficial venous pressure due to the weakening of calf muscles as well as the deterioration of vessel walls. Walking for limited distances, which is also a well-known risk factor for CVI, may not only be due to the weakening of calf muscles, but also due to lumbago or arthritis that are commonly seen in aged women. Although the additional complication of obesity was only a minor factor in the current study, studies report that obese patients present with severe CVI symptoms without anatomical evidence of venous disease. The causes of venous hypertension in obese patients are considered to be venous outflow obstruction and failure of the calf muscle pump owing to leg immobility. It may also be true that patients with CVI are less physically active due to their leg symptoms such as heaviness and aching, and are more prone to overweight. Hence, these factors were considered to be confounding factors in this patient group.

Although controversial, having an occupation requiring prolonged standing has been considered a risk factor for CVI. In the current study, patients with occupations that require prolonged standing and no regular walking presented with more severe symptoms compared with those with occupations that required walking. This may partly be explained by the fact that the increase in venous pressure and production of reactive oxygen species in the legs of standing workers who cannot walk are more prominent than those found in standing workers who can walk. Additionally, this factor may be related to the development of venous ulcer. Standing still may be regarded as a forced reason for irregular walking in contrast to not walking due to physical weakness.

It is well known that the venous return is achieved by the combination of competent venous valves and calf muscle pump. Therefore, even without major abnormalities on DUS, the dysfunction of the calf muscle pumps which leads to ineffective emptying of venous blood from the distal lower extremities could be a significant mechanism for venous hypertension and the development of CVI. Although often overlooked, it should be regarded as functional venous insufficiency rather than as an anatomical problem.

**Limitations**

Since this study was a single-center (at a university hospital in a rural area) and retrospective study that included a very limited number of subjects, reaching a definite conclusion was difficult. Patient characteristics may be largely different in different clinics, e.g. in a large city or outside Japan. Therefore, a multi-center study with larger numbers of patients would be needed to establish the impact of reduced leg mobility on the development of CVI. Although minor, there were 8% patients who had more severe symptom in the left leg, which might be caused by the left iliac vein compression. The inferior vena cava occlusion was excluded by the physical examination, e.g. absence of collateral veins on the abdominal wall, only, but this might not be sufficient. These should have been elucidated using other methods such as CT scan and air plethysmography.
Conclusions

We reviewed patients who presented with venous stasis-related skin lesions in the legs but showed no abnormalities on DUS. The study revealed two typical scenarios: aged female patients with insufficient walking duration and male workers with occupations requiring prolonged standing. Although patient backgrounds were quite different, the common problem seemed insufficient walking.

Disclosure Statement

The authors declare that there is no conflict of interest.

References

1) Bergan JJ, Schmid-Schönbein GW, Smith PD, et al. Chronic venous disease. N Engl J Med 2006; 355: 488-98.
2) Porter JM, Moneta GL. Reporting standards in venous disease: an update. International Consensus Committee on Chronic Venous Disease. J Vasc Surg 1995; 21: 635-45.
3) Eklöf B, Rutherford RB, Bergan JJ, et al. Revision of the CEAP classification for chronic venous disorders: consensus statement. J Vasc Surg 2004; 40: 1248-52.
4) Padberg F, Cerveira JJ, Lal BK, et al. Does severe venous insufficiency have a different etiology in the morbidly obese? Is it venous? J Vasc Surg 2003; 37: 79-85.
5) Comerota A, Lurie F. Pathogenesis of venous ulcer. Semin Vasc Surg 2015; 28: 6-14.
6) Wittens C, Davies AH, Bækgaard N, et al. Editor’s choice - management of chronic venous disease: clinical practice guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg 2015; 49: 678-737.
7) Araki CT, Back TL, Padberg FT, et al. The significance of calf muscle pump function in venous ulceration. J Vasc Surg 1994; 20: 872-7; discussion 878-9.
8) Suehiro K, Morikage N, Murakami M, et al. A study of leg edema in immobile patients. Circ J 2014; 78: 1733-9.
9) Bradbury AW. Epidemiology and aetiology of C4-6 disease. Phlebology 2010; 25: 2-8.
10) Carpentier PH, Mariq HR, Biro C, et al. Prevalence, risk factors, and clinical patterns of chronic venous disorders of lower limbs: a population-based study in France. J Vasc Surg 2004; 40: 650-9.
11) Beebe-Dimmer JL, Pfeifer JR, Engle JS, et al. The epidemiology of chronic venous insufficiency and varicose veins. Ann Epidemiol 2005; 15: 175-84.
12) Milic Dj, Zivic SS, Bogdanovic DC, et al. Risk factors related to the failure of venous leg ulcers to heal with compression treatment. J Vasc Surg 2009; 49: 1242-7.
13) Fowkes FG, Evans CJ, Lee AJ. Prevalence and risk factors of chronic venous insufficiency. Angiology 2001; 52: S5-15.
14) Krijnen RM, de Boer EM, Ader HJ, et al. Venous insufficiency in male workers with a standing profession. Part 1: epidemiology. Dermatology (Basel) 1997; 194: 111-20.
15) Flore R, Gerardino L, Santoliquido A, et al. Enhanced oxidative stress in workers with a standing profession. Occup Environ Med 2004; 61: 548-50.
16) Christopoulos D, Nicolaides AN, Cook A, et al. Pathogenesis of venous ulceration in relation to the calf muscle pump function. Surgery 1989; 106: 829-35.