

How specific are venous symptoms for diagnosis of chronic venous disease?

SK Van der Velden¹, NH Shadid², PJ Nelemans³ and A Sommer⁴

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Abstract

Objective: The objective of this study is to evaluate whether and which ‘venous’ symptoms are characteristic for patients affected with chronic venous disease compared to patients with other diseases of the lower limbs (e.g. arthrosis, peripheral arterial disease, spinal disc herniation).

Methods: A cross-sectional study was performed to compare the frequency of venous symptoms among 76 patients with chronic venous disease and reflux and 74 patients with other diseases of the legs without reflux. The VEINES-Sym of the VEINES-QOL/Sym questionnaire was used to evaluate the frequency of symptoms. Demographic, clinical classification and ultrasound findings were also noted.

Results: A total of 122 patients were included for analysis (response rate of 87%). Presence of venous symptoms was slightly more often reported in the chronic venous disease group than in the non-chronic venous disease group, but differences were small and statistically non-significant. Severity of chronic venous disease as classified by the CEAP classification was not associated with higher proportions of patients reporting symptoms than in non-chronic venous disease patients, except for swelling ($p = .016$) and itching ($p = .007$) in C3-C6 patients. The largest difference between the chronic venous disease and non-chronic venous disease group was observed for the time of the day at which symptoms were most intense; patients with chronic venous disease were more likely to experience symptoms at the end of the day ($p < .001$).

Conclusions: The small differences in prevalence of reported ‘venous’ symptoms between chronic venous disease patients and patients with other diseases of the legs suggest that these symptoms may be less specific for patients with chronic venous disease and refluxing veins than is usually assumed.

Keywords

Symptoms, chronic venous disease, specificity, prevalence, leg diseases

Introduction

Chronic venous disease (CVD) is a common health problem in Western countries affecting about one-quarter of the adult population.¹ It is commonly assumed that this condition is associated with symptoms such as tingling, aching, burning, pain, muscle cramps, swelling, sensation of throbbing or heaviness, itching skin, restless legs, leg-tiredness and/or fatigue.

In daily practice, the presence of one or more venous symptoms, together with clinical and duplex ultrasound findings of venous disease is an indication for the treatment of varicose veins.

However, equivocal results from previous studies suggest that the association between CVD and venous symptoms may not always be that strong as is assumed and that these symptoms may also have a non-venous cause.^{2,3} Furthermore, it has been observed that despite

successful treatment of the refluxing saphenous trunk, reduction of symptoms such as restless legs, oedema, cramps, pain and heavy or tired feeling was reached

¹Department of Dermatology, Erasmus Universal Centre, Rotterdam, The Netherlands

²Department of Dermatology, Medical Centre Haaglanden, Den Haag, The Netherlands

³Department of Epidemiology, Maastricht University Medical Centre, Maastricht, The Netherlands

⁴Department of Dermatology, Reinaert Clinics, Maastricht, The Netherlands

Third and fourth authors share authorship.

Corresponding author:

SK van der Velden, Department of Dermatology, Erasmus Medical Centre, Burgemeester s' Jacobplein 51, 3015 CA Rotterdam, The Netherlands.

Email: s.vandervelden@erasmusmc.nl

in only part (40–83%) of the treated patients.^{4–6} Alternatively, local recurrences of varicose veins or recanalized refluxing veins on duplex ultrasound are not always correlated with the presence of symptoms.^{7,8} These observations raise the question, to what extent venous symptoms are specific for patients with CVD and reflux.

The prevalence of CVD is increasing with age and in particular the older population is affected with CVD.¹ In this population, the relationship between symptoms and presence of reflux may be further obscured by the presence of other diseases of the lower limbs, such as knee or hip arthrosis (AR), peripheral arterial disease (PAD) or spinal disc herniation (SDH) which may cause comparable symptoms in the leg. The present study explores this issue by comparing the distribution of symptoms between a patient group with CVD and a patient group with other diseases of the legs. The underlying hypothesis was that the so-called venous symptoms (tingling, aching, burning, pain, muscle cramps, swelling, sensation of throbbing or heaviness, itching skin, restless legs, leg-tiredness and/or fatigue) are non-specific for patients with CVD. The secondary objective was to compare the mean number of symptoms, the mean symptom score and the time of the day at which symptoms were experienced as most intense.

Methods

Patients

This study was performed in the outpatient clinics of Dermatology, Neurology, Vascular surgery and Orthopaedics at the Maastricht University Medical Centre between November 2010 and June 2011. Eligible were patients older than 18 years visiting the outpatient department of Dermatology with one or more venous symptoms. Patients of the outpatient departments of Vascular Surgery, Orthopaedics or Neurology visiting because of complaints of the leg(s) due to PAD, knee or hip AR or SDH, respectively, were also eligible. Diagnosis was confirmed by ankle brachial index (ABI) and arterial pulse-wave Doppler recordings, X-ray or magnetic resonance imaging (MRI), respectively.

A trained physician examined patient's affected legs and classified them according to the clinical component ('C') of the CEAP classification.⁹ Venous signs, such as telangiectasia, reticular veins, varicose veins, edema, skin changes (hyperpigmentation, lipodermatosclerosis) or ulceration were recorded. Subsequently, ultrasound examination of both superficial and deep venous systems was performed in standing position.¹⁰ All patients in the CVD group had to have symptoms of venous disease and confirmed saphenous trunk reflux

(>0.5 seconds) on duplex ultrasound. Patients with other diseases of the legs (PAD, knee or hip AR or SDH) were excluded if saphenous trunk reflux of more than 0.5 seconds on duplex ultrasound was observed. CVD patients did not undergo ABIs, X-ray or MRI. We hypothesized that patients affected with clinical classes C5 or C6 would report more symptoms than patients affected with C1–C4 disease.¹¹ However, in clinical practice, C5 or C6 disease is relatively rare in patients affected with varicose veins compared to the other clinical classes. Therefore, we aimed to include 20 patients with healed or active ulceration of the lower leg.

Patients gave written informed consent to participate in the study.

Questionnaire

Patients were asked to complete the VEINES-Sym of the VEINES-QOL/Sym questionnaire.¹² Patients were requested to complete the questionnaires at home and return it by prepaid mail. In case of missing questionnaire items, patients were contacted by phone in order to retrieve the missing data.

The VEINES-Sym is part of the VEINES-QOL/Sym questionnaire and measures symptom frequency and severity. The VEINES-Sym consists of ten items including nine venous symptoms (heavy legs, aching legs, swelling, night cramps, heat or burning sensation, restless legs, throbbing, itching, tingling sensation) rated on a five-point scale of frequency (1 = every day, 2 = several times a week, 3 = about once a week, 4 = less than once a week, 5 = never) and leg pain rated on a six-point scale of intensity (1 = very severe, 2 = severe, 3 = moderate, 4 = mild, 5 = very mild, 6 = none). In this study, we focused on these nine venous symptoms.

In addition, descriptive information concerning the time of the day at which the symptoms are experienced most intensely was recorded (e.g. on walking, at mid-day, at the end of the day, during the night, at any time of the day, never). Summary symptom scores (VEINES-Sym) were computed from these ten items. The presence of lower VEINES-Sym scores indicates more severe symptoms (range 0–100).

Statistical analysis

Patients were categorized into two groups according to the reported frequency of symptoms: 'every day/several times a week/about once a week/less than once a week' versus 'never'. Proportions and absolute numbers of patients who reported presence of a specific symptom were compared between patients with and without CVD using the Chi square test. In an additional analysis, subgroups of patients reporting a specific symptom 'every day' was compared to the subgroup of

patients who experienced that specific symptom several times a week or less.

Patients with missing scores on three or more items were excluded from the analysis. For patients with missing scores on one or two items, missing values were imputed by median values on the completed items reported by an individual. To calculate VEINES-Sym scores, raw scores were first transformed to *z* score equivalents (mean 0; standard deviation 1), which then are transformed to T scores (mean 50, standard deviation 10).¹²

All analyses were performed using SPSS (SPSS Inc., Chicago, IL, USA). Two-sided *p* values of 0.05 or less were considered to indicate statistical significance.

Results

Study population

Eligible were 76 CVD patients with confirmed reflux and 74 patients with PAD, AR or SDH without reflux (26 PAD, 25 AR, 23 SDH) (Figure 1).

A total of 132 patients completed the questionnaire. The response rate was 88% (69/77) in the CVD group and 86% (64/74) in the group with other diseases of the legs. Questionnaires were incomplete in 10 patients, resulting in a total sample of 122 patients remaining for analysis.

Table 1 summarizes the distribution of baseline characteristics in the various subgroups. It can be observed that 62% of the patients with CVD were female and the mean age was 61 years (SD 13, range 30–94; Table 1). In the non-venous disease group, half of the patients were female and the mean age was 59 years (SD 12, range 32–83). Six patients (10%) of the CVD group showed a combination of

superficial and deep venous insufficiency. C3-C6 venous disease was present in 57% of the CVD group and in 7% of the patients in the group with other leg diseases.

Presence of venous symptoms according to diagnosis

Seven out of nine symptoms (heavy legs, aching legs, swelling, night cramps, restless legs, itching and tingling) were reported by more than 50% of the patients in the CVD group. This finding is in contrast to the patients in the non-CVD group where only four out of nine symptoms (heavy legs, aching legs, night cramps and tingling) were reported by more than half of the patients (Figure 2). Higher proportions in the CVD group were observed for six symptoms: heavy legs (67% vs 61%), swelling (52% vs 31%), night cramps (71% vs 53%), restless legs (51% vs 47%), throbbing (40% vs 29%) and itching (52% vs 31%); Table 2. However, no statistical significance was reached. Presence of aching legs, heat or burning sensation and tingling was reported by a higher proportion of patients in the non-CVD group (Table 2).

When patients were categorized according to frequencies of symptoms 'every day' versus 'less than every day,' the differences in proportions of patients between both groups increased only for aching legs (32% vs 49%, *p* = 0.05).

Clinical severity and presence of symptoms

Patients in the CVD group were categorized according to clinical classes (C1-C2 vs C3-C6) and these categories were compared with the non-CVD group (Table 2). The difference in proportion of patients with presence of symptoms between the CVD and

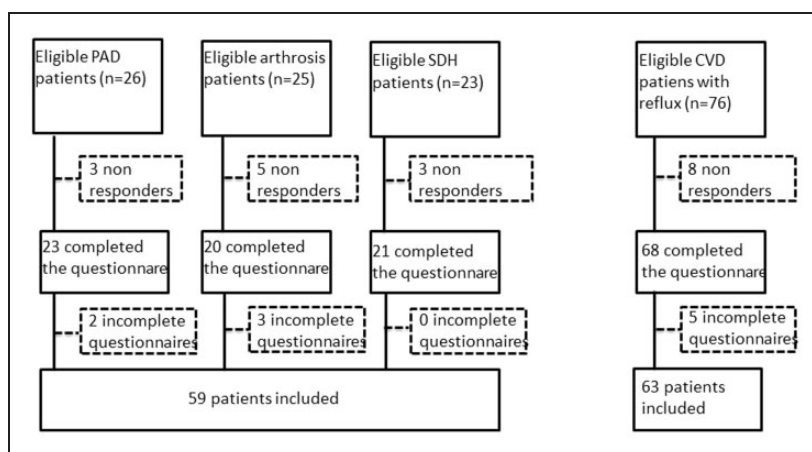


Figure 1. Flowchart.

PAD: peripheral arterial disease; SDH: spinal disc herniation; CVD: chronic venous disease.

Table 1. Distribution of patient characteristics.

	CVD, n (%)	SDH, n (%)	PAD, n (%)	AR, n (%)
Sex				
Male	24 (38%)	13 (62%)	13 (62%)	4 (24%)
Female	39 (62%)	8 (38%)	8 (38%)	13 (76%)
Age				
Mean	61	52	64	62
(SD, min–max)	(13, 30–94)	(12, 33–83)	(9, 45–80)	(12, 36–83)
Clinical classes				
C0	0	5 (24%)	11 (52%)	3 (18%)
C1	7 (11%)	13 (62%)	5 (24%)	12 (72%)
C2	20 (32%)	2 (10%)	3 (14%)	1 (5%)
C3	16 (25%)	1 (4%)	2 (10%)	1 (5%)
C4	2 (3%)	0 (0%)	0 (0%)	0 (0%)
C5	1 (2%)	0 (0%)	0 (0%)	0 (0%)
C6	17 (27%)	0 (0%)	0 (0%)	0 (0%)
Reflux				
Superficial system	63 (100%)	0 (0%)	0 (0%)	0 (0%)
Perforating veins	1 (2%)	0 (0%)	0 (0%)	0 (0%)
Deep system	6 (10%)	0 (0%)	0 (0%)	0 (0%)

CVD: chronic venous disease; SDH: spinal disc herniation; PAD: peripheral arterial disease; AR: arthrosis.

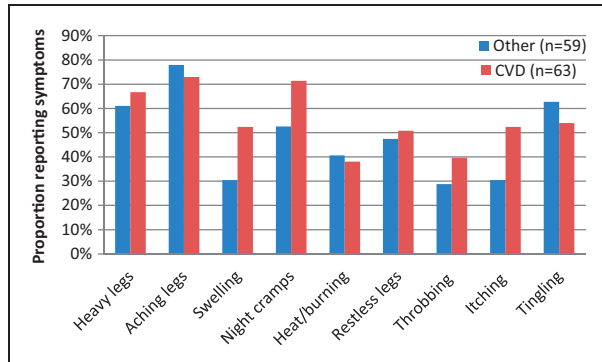


Figure 2. Proportions of patients with presence of symptoms among patients with chronic venous disease (CVD) and ‘other’ non-CVD patients (including arthrosis, peripheral arterial disease, spinal disc herniation).

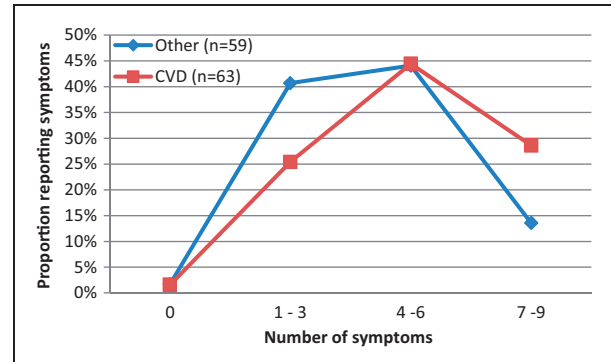


Figure 3. Proportions of patients with a total number of 0, 1–3, 4–6 and 7–9 symptoms according to diagnosis.

non-CVD group increased for the symptoms swelling, night cramps, throbbing and itching if only the CVD patients with clinical class C3-C6 were taken into consideration. In the latter comparison, statistically significant difference was reached for the symptoms swelling ($p = .016$) and itching ($p = .007$). When we categorized patients according to frequencies of symptoms ‘every day’ versus ‘less than every day,’ the differences between the CVD with clinical class C3-C6 and non-CVD group did not increase.

Number of venous symptoms according to diagnosis

Patients were allocated according to the number of reported symptoms (out of a total of nine) into four groups: 0 symptoms, 1–3 symptoms, 4–6 symptoms and 7–9 symptoms. In both the CVD and non-venous group 44% of the patients presented with 4–6 symptoms (Figure 3). In addition, the proportion of patients with 7–9 symptoms in the CVD group was not much higher than in patients affected by other diseases of the leg (29% vs 14%).

When we calculated the summary Sym-scores of the non-CVD and CVD group, both groups showed similar

Table 2. Proportions of patients with presence of symptoms among patients with chronic venous disease (CVD), categorized according to clinical class and 'other' non-CVD patients (including: arthrosis, spinal disc herniation and peripheral arterial disease).

	Non-CVD N = 59	CVD N = 63	CVD (C1-C2) N = 27	CVD (C3-C6) N = 36
Heavy legs	61%	67%	70%	64%
Aching legs	78%	73%	74%	72%
Swelling	31%	52%	48%	56%
Night cramps	53%	71%	70%	72%
Heat/burning	41%	38%	37%	39%
Restless legs	47%	51%	59%	44%
Throbbing	29%	40%	30%	47%
Itching	31%	52%	44%	58%
Tingling	63%	54%	63%	47%

mean scores (51 versus 50, $p = .513$). Mean Sym-scores decreased when we compared clinical classes C3-C6 to clinical classes C1-C2 (50 vs 51, $p = .324$), indicating a deterioration of symptoms.

Time of the day at which symptoms are experienced most intensely

For half of the patients with CVD, symptoms were most intense at the end of the day versus 21% of patients affected by other disease of the legs ($p < .001$) (Figure 4). The latter group of patients was more likely to experience their symptoms at any time of the day (40%).

Discussion

This study showed that the majority of symptoms that are commonly attributed to CVD (heavy legs, swelling, night cramps, restless legs, throbbing and itching) are slightly more often reported in patients affected by CVD compared to patients affected with other diseases of the lower legs. Furthermore, there was no strong correlation between type of symptoms and extent and severity of CVD. When CVD patients with clinical class C3-C6 were compared with patients with other leg diseases, differences were small and statistical significance was only reached for the symptoms swelling and itching. The largest difference between the CVD and non-CVD group was observed with respect to the timing of symptoms. Patients with CVD are more likely to experience symptoms at the end of the day than patients who have symptoms due to other diseases of the legs.

In the present study, the mean VEINES-Sym summary score was comparable to that found in other studies.^{11,13} Kahn et al.¹¹ reported mean Sym scores of 50.5 in males and 49.8 in females. As Kurz et al.¹³ already demonstrated, mean Sym scores decrease

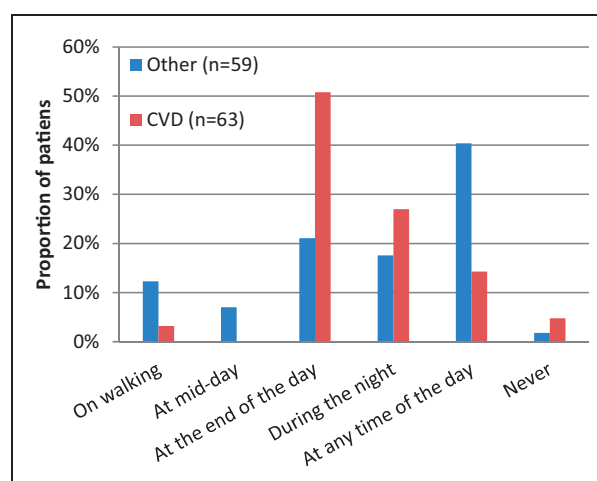


Figure 4. Time of the day at which symptoms are experienced most intensely.

with higher clinical classes, ranging from 52.3 for clinical class 1 to 43.1 for clinical classes C5-C6.¹¹ However, although mean scores were slightly lower in clinical classes C3-C6 versus clinical classes C1-C2, a significant decrease in mean Sym scores with increasing severity could not be confirmed in this study.

The considerable overlap between venous symptoms reported by patients with CVD and by patients with other diseases of the lower leg confirms lack of specificity of venous symptoms. Marston¹⁴ postulated that none of the venous symptoms are specific to venous disease and multiple etiologies may be confused with CVD. The population-based Bonn Vein Study revealed that 62.1% of women and 49.1% of men reported leg symptoms, but only 27.8% of men and 34.1% of women had CVD with clinical class above C2 and only 21.0% had reflux in the superficial venous system.^{15,16} The Edinburgh Vein Study also showed that lower limb symptoms are not only caused by venous problems.

Venous symptoms such as aching and cramps were reported by 54% and 34%, respectively, in the general population.³ The San Diego Population study related symptoms to CVD and found that swelling, heaviness and itching were reported by participants with visible or functional venous disease about twice as often than by participants with normal legs, but for other symptoms the contrasts were less strong.²

Interestingly, we observed a statistically significant difference between both groups in proportion of patients that experienced their symptoms most intensely at the end of the day. This finding is in line with another study that showed that circumstances that elicit or exacerbate symptoms were more characteristic for CVD rather than the number of symptoms or symptom type.¹⁷ Several studies already emphasized the importance of a thorough medical history to evaluate the circumstances that elicit and exacerbate symptoms (the time of the day, relief of symptoms by elevation of the legs) and physical examination in combination with venous ultrasound examination.^{14,17,18} However, available questionnaires do not incorporate questions, which explicitly address such symptom-provoking factors. The reason why we used the VEINES-Sym for this study is that it is the most thorough and comprehensive questionnaire on symptom type and symptom frequency that is currently available. Other questionnaires such as the Chronic Lower Limb Venous Insufficiency (CIVIQ) and Aberdeen Varicose Vein Questionnaire (AVVQ) rather focus on impairment of health-related quality of life and clinical class-related items and to a lesser extent on symptoms.^{19,20} The VEINES-Sym questionnaire includes one question concerning at what time of the day the symptoms are most intense. However, precisely this question is not included for calculation of the mean summary Sym-scores and is only used to provide descriptive information.¹²

The present study has a few limitations. First, the groups of patients with and without CVD are small and therefore the power to detect significant differences is limited. The sample size in this study allowed for detection of absolute differences of 25% or more in proportions of reported symptoms with a power of 90% and two-sided alpha of 5%. We assumed that between-group differences smaller than 25% are not clinically relevant, because in case of high specificity of symptoms we expect much larger differences in proportions with reported symptoms between the groups with and without CVD.

Second, we did not include a control group of healthy subjects and therefore we were not able to compare the results of the patients with CVD to the proportion of healthy patients reporting symptoms. Third, presence of venous disease in a small fraction of the groups with other disease may have contributed to lack of contrast in symptom frequency between

groups but does not fully explain the finding of small differences in reported prevalence of symptoms between groups with CVD and other diseases.

In conclusion, the lack of difference in prevalence of reported 'venous' symptoms between CVD patients with confirmed reflux and patients with other diseases of the legs suggest that these symptoms may be less specific for patients with refluxing veins than is usually assumed. This finding implies that venous symptom questionnaires can only be used to quantify the degree of symptoms perceived by patients affected with CVD. The VEINES-QOL/Sym questionnaire is not suitable as a diagnostic or screening tool. The results of this study confirm the importance of a thorough history and physical examination, including specific questions about circumstances that elicit, exacerbate or alleviate symptoms, for the differentiation between patients with and without CVD.

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Conflict of Interest

None declared.

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