Chronic venous disorders: Correlation between visible signs, symptoms, and presence of functional disease

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Background: **The aim of this study was to investigate the frequency of chronic venous disorders (CVD) in different demographic groups in Italy and to provide correlations between patterns of valve incompetence and clinical feature of disease severity.**

Methods: **Advertisements in television and newspapers in 53 Italian cities were used to solicit 16,251 subjects (13,826 women, mean age 50.4 years; 2,425 men, mean age 59.1 years). They underwent a clinical examination of the lower limbs, including presence and severity of visible signs (CEAP classification), and assessment of functional disease by color-coded duplex ultrasound imaging.**

Results: **Varicose veins and telangiectases were the most common objective signs in both men and women. Older people were more severely affected. Telangiectases were more frequent in women, and men had a higher incidence of trunk varices, trophic changes, and venous reflux. Frequency of both visible and functional venous disease increased with family history and body mass index. Presence of reflux correlated positively with increasing CEAP grade of visible disease (*P* for trend < .0001 for all superficial venous segments). A large number of subjects, especially women, complained of subjective symptoms in the legs, and the presence of symptoms correlated almost always positively with both worsening of visible findings (*P* for trend < .001) and presence of hemodynamic change in both genders.**

Conclusions: **The frequency of reflux increased with the severity of visible signs of disease as described by the CEAP classification. In men, the occurrence of subjective symptoms was mostly correlated with functional disorders. (J Vasc Surg 2007;46:322-30.)**

Chronic venous disorders (CVD) is a common condition that changes dynamically in the adult population.[1-5] Pharmaceutic or surgical intervention may delay disease progression, but unfortunately, many individuals with CVD are referred to medical treatment too late, only after tissue changes have already started. In such cases, intervention is difficult and frequently unsuccessful.[6] The prognostic value of early, clinically detectable, pathologic changes associated with patterns of valve insufficiency is still unclear. Several studies have shown a correlation between clinical severity of venous disease and the extent of superficial and deep venous incompetence.[7,8] These investigations, however, have focused on patients with CVD who had been referred to specialist clinics and not on a more general population.

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Recently, we reported the results of a large epidemiologic nationwide survey done in 2003 in Italy as a part of a CVD prevention program in which >5000 individuals in three arbitrarily defined geographical regions of Italy voluntarily enrolled.[9-11] The results of the survey allowed us to predict a geographic distribution of CVD-related abnormalities in the general population as detected by color-coded duplex ultrasound imaging.

Although our previous study was based on an already large sample size, some questions remained unanswered because we did not consider a number of factors that were subsequently found to be relevant to establish correlations between visible signs of the disease and its functional expression.[10,11] Thus, we designed this new survey to collect data on the presence or absence of correlations between patterns of valve incompetence and CVD severity in a very large population of Italian subjects.

METHODS

Participants. The survey was conducted in Italy between May and July 2004 as a part of a CVD prevention program organized by the Scientific Institute Hospital San Raffaele in Milan. A large cross-sectional, nonrandom sample of women and men was to be recruited throughout Italy, selected by means of advertising in television, newspapers, and leaflets distributed by a press agency. The advertising addressed explicitly people who claimed to have CVD. All subjects were recruited on a spontaneous and voluntary basis, and could schedule, through a call center or

Table I. Percentage of occurrence of objective signs of chronic venous disorders in the population studied according to sex, age, family history, and body mass index using the CEAP clinical classification

	Study group (n = 1651)	*C_0 No signs (n = 3392)*	*C_1 Telangiectasia (n = 10,679)*	*C_2 Varicoses*		*C_3 Edema (n = 2251)*	*$C_{4a,4b}$ Eczema/skin changes (n = 1444)*	*$C_{5\text{-}6}$ Ulcers (n = 63)*
				Not saphenous vein (n = 5863)	*Saphenous vein (n = 3204)*			
	%	%	%	%	%	%	%	%
Total of population*	100.0	20.9	65.7	36.1	19.7	13.9	8.9	0.4
Sex†								
Male	14.9	34.9	36.5	39.8	26.4	14.1	12.4	0.7
Female‡	85.1	18.4	70.8	35.4	18.5	13.8	8.3	0.3
No pregnancies	28.9	29.0	60.5	22.8	9.8	10.3	4.1	0.2
≥1 pregnancy	71.1	14.2	74.7	40.6	22.2	15.2	10.0	0.4
Age§								
<30	8.3	39.3	50.4	16.2	4.8	8.7	1.4	0.0
30-49	34.2	22.4	66.2	29.8	13.9	10.3	4.4	0.1
≥50	57.5	17.3	67.6	42.6	25.3	16.7	12.7	0.6
Family history‖								
Yes	66.7	18.5	68.2	38.1	21.0	14.0	8.7	0.4
No	33.3	24.4	62.0	32.3	17.4	13.5	9.3	0.4
Body mass index¶								
≤20	11.2	28.0	64.6	23.0	10.5	5.7	3.3	0.1
21-26	55.6	20.8	66.6	34.3	17.8	11.0	7.0	0.2
27-32	28.4	18.9	64.9	42.8	25.4	19.3	12.7	0.6
≥33	4.8	15.2	64.8	47.3	28.5	33.4	22.1	1.1

*Percentages do not always add to 100, as some patients are assigned to more than one CEAP category.
†Differences between male and female all statistically significant, $P < .001$, with the exception of C_3, edema ($P = .745$, NS) and $C_{5\text{-}6}$, ulcers ($P = .024$).
‡Differences between no pregnancies and ≥1 pregnancies all statistically significant, $P < .001$, with the exception of $C_{5\text{-}6}$, ulcers ($P = .034$).
§Age groups all statistically significantly different, $P > .001$.
‖Family history of chronic venous disease: two subgroups statistically significantly different ($P > .001$), with the exception of C_3, edema ($P = .36$, NS), C4, eczema/skin changes ($P = .21$, NS), and C5-6, ulcers ($P = .71$, NS).
¶All body mass index groups statistically significantly different ($P > .001$), with the exception of C_1, telangiectasia ($P = .12$, NS).

a dedicated Internet Web site, a free medical visit that included a color-coded duplex ultrasound imaging.

Men and women aged 18 to 89 years who responded were contacted. Those who agreed to participate were invited for a medical ambulatory examination at the participating hospitals or in a specially equipped mobile unit, in which they underwent all diagnostic procedures. A total sample size of 20,000 participants was foreseen, based on the time needed for an accurate clinical examination of each subject and in accordance with the number of visits planned for each unit in operation.

Fifty-three vascular surgery units distributed throughout the nation participated in the study. The physicians were all vascular surgeons experienced with Doppler ultrasound imaging. Methods and questionnaires were standardized across centers and followed a protocol from the recommendations issued by the Italian Society of Vascular and Endovascular Surgery. Data quality was assured by regular checks of the data collected by the study coordinators.

Procedures. At the study visit, the examining physician gathered detailed information on demographics (age, sex, pregnancies, height, and weight), lifestyle (physical activity and smoking habit), and contraceptive use. Family history of varicose veins was restricted to first-degree relatives and was obtained directly from the subjects (family members were not examined). Specific medical questions included history of deep thrombotic events, leg arteriopathy, hemorrhoids, and varicocele. A detailed physical examination was performed by a trained vascular surgeon to assess visible signs of venous disease, including telangiectases, varicose veins, edema, trophic changes, and ulcers. Signs were classified according to the CEAP clinical classification:

- C_0, no visible or palpable signs of venous disease;
- C_1, telangiectases or reticular veins;
- C_2, varicose veins;
- C_3, edema;
- C_{4a}, pigmentation or eczema;
- C_{4b}, lipodermatosclerosis or atrophie blanche;
- C_5, healed venous ulcer; and
- C_6, active venous ulcer.[12]

Classification of visible signs of the disease was made before and thus independently of duplex ultrasound imaging. Patients with varices in the extrasaphenous veins were allocated to group C_2 (Table I), whereas patients who had reflux in nonsaphenous veins, such as the vulvar and gluteal veins, or those in the lateral thigh and absence of reflux in saphenous veins were considered functionally normal for the purpose of this survey.

Subjects were asked to report their subjective perception of CVD-related lower limb symptoms commonly present just in the early stages of the pathology such as heavy/tired legs, pain, and swollen leg.[12]

Color-coded duplex ultrasound imaging was used to collect information on the presence or absence of functional hemodynamic disturbances in the superficial venous system. We therefore only collected hemodynamic data for the saphenofemoral junction (SFJ), the great saphenous vein (GSV) over the length of the whole leg, and the saphenopopliteal junction (SPJ). Appropriate probes were selected according to the depth of the vessels examined (convex 2-MHz to 5-MHz probes or linear 5-MHz to 12-MHz probes).

Subjects underwent duplex examination standing in full erect posture. For the examination of the thigh, subjects flexed the leg slightly at the knee and transferred the body weight on the other leg. The examinations were performed using calf manual compression-release to provoke superficial venous reflux. The beginning and the end of the period of reflux was identified. Normal reflux was defined as <500 milliseconds of reverse flow.[13] A reflux time of >500 milliseconds in the GSV, SFJ, or SPJ was considered superficial functional disease. There were no therapeutic interventions in this study.

Statistical analysis. Information from case report forms and questionnaires was made anonymous, tracked, and collected in an Excel database (Microsoft Inc, Redmond, Wash), checked for accuracy of input and reliability, and then transferred into SAS 8.02 software (SAS Institute, Inc, Cary, NC) for subsequent statistical analysis.

Differences between continuous variables were tested using the Student *t* test for independent groups, and categoric differences were tested with the χ^2 statistics and the Cochran-Armitage trend test. No adjustments were made for multiple comparisons because this survey had no confirmatory character.

In the case of patients reporting symptoms and having signs on both legs, the presence of reflux was not analyzed separately for each leg, but data derived from the more affected leg were analyzed. The correlation between the presence of visible signs of disease (CEAP classification) or self-assessed subjective leg symptoms with an abnormal reflux was assessed separately for each of the three vein segments of the superficial venous network. Because gender appeared to be a significant covariate for almost all objective signs of CVD, the degree of correlation between visible signs of the disease and functional disease was evaluated separately by sex.

RESULTS

The survey included 18,560 subjects living in the urban area of 53 large towns in Italy. A total of 16,251 subjects were evaluable, consisting of 13,826 women (mean age, 50.4 years) and 2425 men (mean age, 59.1 years). Excluded were 2075 subjects for whom data for objective symptoms were incomplete and 234 for whom age, weight, or height was not available. More women (85.1%) than men (14.9%) were enrolled in the survey. Complete duplex scans were available for 12,496 subjects (10,377 women, 2119 men).

Frequency of visible and functional signs of chronic venous disease. Table I summarizes the frequency of visible signs of CVD (CEAP classification) in each demographic group of the study population. Overall, physical examination of the legs showed that about one fifth of the subjects examined were free of visible signs of CVD (Table I). Men were twice as likely as women to have symptomless legs (34.9% vs 18.4%, $P < .001$). A small number of respondents had a history of arteriopathy (women, 0.96%; men, 5.53%), and an even smaller proportion had a history of thrombosis (women, 1.33%; men, 1.77%). We did not examine separately the patients who underwent any kind of previous surgery, including endovenous ablation or sclerotherapy.

Telangiectases were very widespread in most subjects, but mainly in women. Men, however, appeared to have a consistently, and statistically significantly, higher incidence of varicose veins than women ($P < .0001$ for both trunk and extrasaphenous varicose veins).

No differences were found in the frequency of edema between the two genders, but trophic changes, including ulcers, were nearly three times as common in men than in childless women. Pregnancies were clearly related to an increase of the major visible signs of the disease, increasing monotonically with increasing number of pregnancies (Fig 1).

An age-dependent, linear increase in edema, varicose veins, and trophic changes could be observed, with subjects aged >50 being almost five times as likely to show trunk varicoses than the younger respondents in the survey. The frequency of venous ulcers increased rapidly from 0.1% before age 50, to 0.6% at age ≥50. A similar picture could be seen for telangiectases. The frequency of telangiectases and varicose veins was higher when a family history of the disease was reported. In both sexes, body mass index (BMI) was positively and statistically significantly correlated with visible signs of CVD, telangiectases being the only exception.

More than 40% of the study population showed some degree of superficial venous incompetence at the duplex examination (Table II). Men were more severely affected than women (48.3% vs 33.0% of women with no previous pregnancy, $P = .001$). Less than 25% of the men and women in the age class <30 showed some degree of superficial functional disease. The percentage of hemodynamic disturbances then increased quite rapidly with age, and reflux could be seen in approximately 50% of the population aged >50 years old. In the patients with CEAP 4 to 6, only 20.9% of the men and 29.1% of the women had no reflux (Table III). The frequency of reflux increased monotonically with body weight from 33.3% for BMI ≤20 to 55.3% for BMI ≥33 ($P = .001$) and was also positively related to a family history of venous disease ($P = .001$).

Most of the respondents in the survey complained of some symptoms, women having more complaints than men ($P < .0001$). The most relevant symptoms were tired,

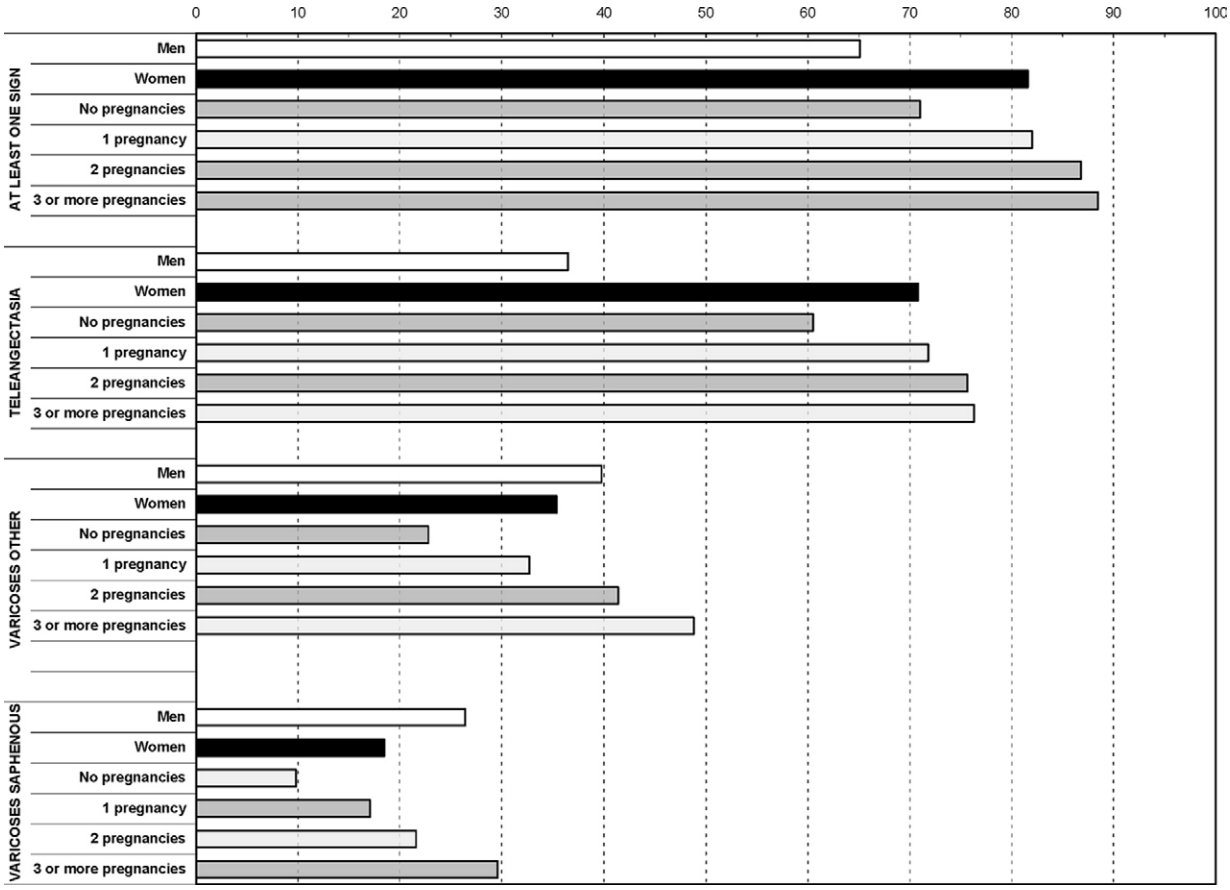

Fig 1. Percentage of occurrence of signs of chronic venous disorders in the study population according to sex and number of pregnancies.

heavy legs, reported by approximately 67% of the men and 80% of the women (Table IV). All symptoms tended to increase with increasing BMI ($P < .001$).

Correlation of clinical signs with color-coded duplex ultrasound imaging. The relation between CEAP grade and functional disease or subjective leg symptoms was assessed using the Cochran-Armitage test for linear trend. Table III summarizes the overall results of the duplex scan performed on 12,496 subjects. Overall, approximately 80% of functionally healthy legs had no visible CVD signs. Conversely, among subjects with functional disease, no visible signs of CVD were detected in 10% of cases, and nearly half of the legs with spider veins were functionally normal (Table III). In the subgroup with overt CVD signs and abnormal venous function, worsening of CVD was associated with an increasing frequency of reflux (P value for trend $< .001$ for all superficial venous segments). This relationship was seen in both sexes but was more evident in men than in women, with the exception of CEAP C_0 (Fig 2).

The men in the study had significantly less telangiectases than the women, but the superficial venous incompetence in presence of this visible sign was twice as frequent in men as in women. The difference between the genders, as for the correlation between visible signs and functional disorder, became less evident as the disease worsened. For legs with superficial functional disease of the GSV level, the sex-adjusted frequency of edema was 59% in men and 44% in women compared with 28% and 39%, respectively, for functionally normal legs.

A correlation between reflux and presence of subjective symptoms in the legs could also be seen (Table V). Symptoms were less frequent in the men but were more frequently related to hemodynamic disturbances than in the women.

The frequency of subjective symptoms is presented in Table VI. Lower limb symptoms such as heaviness, pain, and feeling of swelling were very common in the general population independently of the presence or absence of visible signs of the disease. Symptoms were more frequent in women, but their frequency correlated positively in both genders with the CEAP grade (P value for trend $< .001$ for all symptoms with the exception of pain, for which no significant correlation could be seen in the men).

DISCUSSION

This survey confirms that CVD is very common in Italy, with approximately one fifth of the study population showing trunk varicose veins.[8] Venous incompetence increases

Table II. Percentage of occurrence of venous reflux in the population studied according to sex, age, family history, and body mass index (12,496 subjects with complete scans)

		Reflux					
	No reflux (n = 7111)	*Right SFJ (n = 2526)*	*Right GSV (n = 2639)*	*Right SPJ (n = 1413)*	*Left SFJ (n = 2533)*	*Left GSV (n = 2612)*	*Left SPJ (n = 1453)*
	%	%	%	%	%	%	%
Total population*	56.9	20.2	21.1	11.3	20.3	20.9	11.6
Sex							
Men	51.7	24.2	26.3	14.9	24.5	26.3	15.9
Women	58.0	19.4	20.1	10.6	19.4	19.8	10.8
No pregnancies	67.1	13.5	12.8	8.2	13.3	13.0	8.1
≥1 pregnancy	54.2	21.9	23.1	11.7	22.0	22.6	12.1
Age*							
<30	77.4	9.9	8.3	6.5	8.3	8.1	6.8
30-49	63.6	15.8	16.2	8.9	16.3	16.7	9.2
≥50	50.5	24.0	25.5	13.3	24.1	25.0	13.6
Family history*							
Yes	55.2	21.1	21.7	11.9	21.6	22.0	12.0
No	60.4	18.7	19.9	10.4	18.4	19.4	11.2
Body mass index*							
≤20	68.7	14.0	14.2	7.1	11.5	11.8	7.1
21-26	59.0	17.7	19.2	10.6	18.4	19.1	11.1
27-32	50.2	25.5	25.8	12.9	25.1	25.6	13.4
≥33	44.7	31.1	29.5	18.8	32.6	34.4	17.7

SFJ, Saphenofemoral junction; *GSV,* great saphenous vein; *SPJ,* saphenopopliteal junction.
*Values of $P\ \chi^2$ square test for independence were all <.001.

Table III. Prevalence of venous reflux in the population studied in relation to the CEAP clinical classification (12,496 subjects with complete scans)

	*Visible signs of disease**					
	C_0	C_1	C_2	C_3	$C_{4\text{-}6}$	
	No. (%)	*No. (%)*	*No. (%)*	*No. (%)*	*No.(%)*	P
Functional disease†						
No reflux (n = 7111)						
Male	611 (81.9)	324 (42.0)	222 (22.0)	83 (28.0)	53 (20.9)	<.001
Female	1562 (76.9)	4102 (56.9)	1288 (30.8)	546 (38.7)	233 (29.1)	<.001
Presence of reflux (n = 5385)						
Male	135 (18.1)	447 (58.0)	789 (78.0)	213 (72.0)	201 (79.1)	<.001
Female	469 (23.1)	3107 (43.1)	2892 (69.2)	866 (61.3)	567 (70.9)	<.001
Segments‡						
SFJ						
Male	67 (9.2)	306 (42.1)	533 (56.9)	149 (55.4)	140 (61.1)	<.001
Female	212 (10.7)	1849 (27.0)	1930 (50.6)	563 (43.5)	397 (54.7)	<.001
GSV						
Male	65 (9.0)	325 (45.2)	586 (63.5)	156 (59.1)	153 (67.7)	<.001
Female	208 (11.0)	1936 (29.1)	2015 (54.4)	550 (43.9)	393 (55.6)	<.001
SPJ						
Male	44 (6.0)	179 (23.7)	325 (33.2)	95 (34.3)	95 (39.4)	<.001
Female	114 (6.0)	1028 (14.9)	1009 (25.5)	373 (28.3)	258 (34.1)	<.001

C_0, No signs; C_1, telangiectasis; C_2, varicose veins; C_3, edema; $C_{4\text{-}6}$, eczema, skin changes, ulcers; *SFJ,* saphenofemoral junction; *GSV,* great saphenous vein; *SPJ,* saphenopopliteal junction.
*Percentages do not add to 100% because when several visible signs were present at the same time in a given subject, every single sign was analyzed separately. Single cases of visible disease expressed as percentage of total sample (N = 12,461, 100%) were as follows: C_1, 4698 (37.7%); C_2, 333 (10.7%); C_3, 274 (22.0%); $C_{4\text{-}6}$, 50 (0.4%); $C_1 + C_2$, 439 (27.6%); $C_1 + C_3$, 449 (3.6%); $C_1 + C_{4\text{-}6}$, 187 (1.5%); $C_1 + C_2 + C_3$, 660 (5.3%); $C_1 + C_2 + C_{4\text{-}6}$, 474 (3.8%); $C_1 + C_3 + C_{4\text{-}6}$, 75 (0.6%); $C_2 + C_3$, 199 (1.6%); $C_2 + C_{4\text{-}6}$, 112 (0.9%); $C_2 + C_3 + C_{4\text{-}6}$, 100 (0.8%); $C_3 + C_{4\text{-}6}$, 37 (0.3%); $C_1 + C_2 + C_3 + C_{4\text{-}6}$, 374 (3.0%).
†Data from both legs were pooled.
‡Percentages do not add to 100% because if more than one vein segment of the superficial venous network was affected in a given subject, the presence of each single visible sign of the disease was analyzed separately for each of the three vein segments.

Table IV. Percentage of occurrence of subjective leg symptoms in the population studied according to sex, age, family history and body mass index

	Study group (n = 16,251)	*No symptoms (n = 1711)*		*Tired/heavy legs (12,548)*		*Pain (n = 8968)*		*Swollen legs (n = 8801)*	
	%	%	P*	%	P	%	P	%	P
Sex									
Men	14.9	17.1	<.001	66.8	<.001	49.6	<.001	39.1	<.001
Women	85.1	9.4		79.0		56.2		56.8	
No pregnancies	28.9	11.2	<.001	78.2	.22	50.4	<.001	57.5	<.001
≥1 pregnancy	71.1	8.7		79.2	NS	58.5		56.3	
Age									
<30	8.3	11.1	.038	78.7	<.001	50.7	<.001	57.0	<.001
30-49	34.2	9.7		79.9		53.1		56.0	
≥50	57.5	11.0		75.4		57.1		52.7	
Family history									
Yes	33.3	8.7	<.001	79.2	<.001	58.5	<.001	56.3	<.001
No	66.7	11.2		78.2		50.4		57.5	
Body mass index									
≤20	11.2	12.0	<.001	77.2	<.001	49.8	<.001	46.7	<.001
21-26	55.6	11.4		76.3		52.5		51.0	
27-32	28.4	9.3		78.2		60.0		58.9	
33+	4.8	3.4		83.0		68.1		79.0	

**P* values: χ^2 test for independence.

with age, and age-related factors such as obesity and the number of pregnancies in women help to induce or aggravate CVD. In previous studies, obesity has been reported to be a risk factor for varicose veins.[14,15] Correspondingly, we detected a statistically significant positive association between BMI or family history of CVD and frequency of venous disease. Large BMI values, and therefore overweight, are risk factors for CVD. The correlation with family history must be interpreted with caution, however, because family history from self-reporting is likely to be biased, and the study was not planned to specifically study this aspect of the disease.

Approximately 80% of subjects with no visible signs of venous disease but complaining of subjective symptoms had functionally healthy legs. When visible signs of disease were seen, the frequency of valve incompetence correlated positively with worsening of symptoms. Spider and reticular veins, therefore, could be early and easily detectable alarm symptoms that may help to timely refer patients to medical care, with subsequent monitoring of the progress of the disease that could allow the physicians to start therapy before more serious stages of CVD set in.

Because varicose veins were associated with incompetence in the superficial venous system in approximately 80% of the subjects, a good therapeutic outcome could be expected from surgery on the superficial veins in these patients. The other 20%, represented by subjects with varicoses other than of the saphenous vein, could also benefit by the treatment of varicoses without any intervention on the saphenous vein.

Subjects with edema but otherwise functionally normal legs were also frequent in this survey. These patients probably had deep venous or nonvenous problems that could have accounted for their CVD symptoms. This study did not undertake duplex scanning of deep vein segments, and therefore, we cannot exclude deep venous incompetence.

In addition, we did not study the osteoarticular system and therefore cannot exclude that some of the symptoms referred were actually derived from joint problems. The gender-related patterns in the frequency of edema in both functionally diseased and normal legs observed in the present study suggest that the higher proportion of edematous legs in women is probably of nonvenous etiology. Conversely, only few cases of functionally diseased legs did not show any visible signs of the disease.

The correlation between visible and functional disease appears to be higher in men than in women, especially for milder forms. Mild signs of venous disease, such as telangiectases, are much more frequent in women than in men, but telangiectases are associated with a functional disorder twice as frequently in men than in women. The difference between the two sexes becomes less evident with the worsening of the disease. The larger degree of overlapping between visible findings and venous incompetence in men was not a surprising finding in this study, because we had already observed it[11] and is in good agreement with findings from other randomized epidemiologic studies conducted in Western European countries.[16,17]

According to this survey, symptoms such as heaviness, pain, and the feeling of swelling in the legs cannot be considered necessarily an alarm bell for objective venous disease. Even if we could observe an apparently strong positive correlation between symptoms in the legs and the worsening of clinically diagnosed CVD, many subjects, especially young people with no diagnose of reflux or CVD abnormality, self-reported a whole range of venous symptoms in the lower limbs. The correlation between symptoms (especially pain in the legs) and visible signs of the

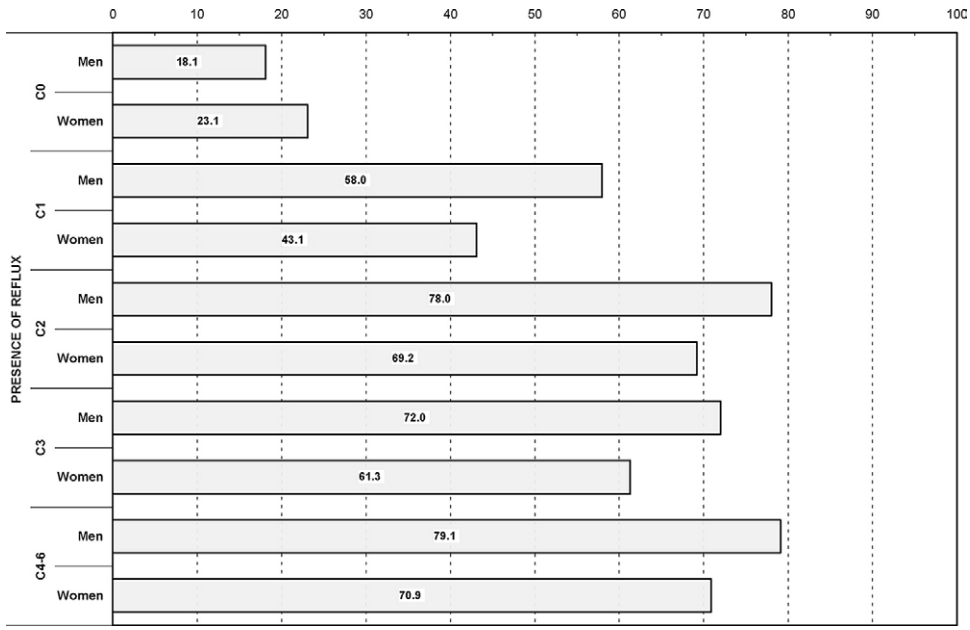

Fig 2. Percentage of the respondents with reflux according to their sex.

Table V. Prevalence of venous reflux in the population studied in relation to the subjective leg symptoms (12,496 subjects with complete scans)

	*Subjective symptoms in the legs**							
	No symptoms		*Tired/heavy legs*		*Pain*		*Swollen legs*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Functional disease†								
No reflux (n = 7111)								
Male	207	58.3	709	49.6	544	51.3	349	42.7
Female	579	64.1	4720	56.8	3238	54.5	3249	55.4
Presence of reflux (n = 5385)								
Male	148	41.7	720	50.4	516	48.7	469	57.3
Female	324	35.9	3592	43.2	2702	45.5	2618	44.6
Segments‡								
SFJ								
Male	97	28.1	466	34.5	340	33.8	311	41.0
Female	184	21.3	2134	27.0	1625	29.0	1577	28.4
GSV								
Male	100	29.4	494	36.9	370	37.0	322	43.0
Female	190	22.8	2194	28.8	1702	31.3	1630	30.3
SPJ								
Male	54	15.7	290	20.8	206	19.9	187	23.7
Female	92	10.8	1152	14.7	878	15.6	880	15.8

SFJ, Saphenofemoral Junction; *GSV,* great saphenous vein; *SPJ,* Saphenopopliteal junction.

*Percentages do not add to 100% because when several leg symptoms were present at the same time in a given subject, each single symptom was analyzed separately.

†Data from both legs were pooled.

‡Percentages do not add to 100% because if more than one vein segment of the superficial venous network was affected in a given subject, the presence of each single leg symptom was analyzed separately for each of the three vein segments.

disease appears to be more marked in women than in men. The 10% difference in aching complaints between subjects with normal legs and those with skin changes seems to be of limited clinical value. In men, aching legs were rather correlated with the presence of a superficial functional disorder, although we observed no significant relationship between pain and severity of visible symptoms in this subsample.

The major strengths of this survey are the large sample studied and the use of an objective measurement tool such

Table VI. Prevalence of leg symptoms in the population studied in relation to the CEAP clinical classification (N = 16,251)

	*Visible signs of disease**					
	C_0	C_1	C_2	C_3	$C_{4\text{-}6}$	
Leg symptoms	*No. (%)*	*No. (%)*	*No. (%)*	*No. (%)*	*No. (%)*	P
No symptoms						
Male	169 (20.0)	130 (14.7)	175 (15.1)	30 (8.8)	37 (12.2)	<.001
Female	294 (11.5)	868 (8.9)	458 (8.0)	87 (4.6)	70 (6.1)	<.001
Symptoms†						
Male	677 (80.0)	756 (85.3)	984 (84.9)	311 (91.2)	267 (87.8)	<.001
Female	2252 (88.5)	8925 (91.1)	5294 (92.0)	1823 (95.4)	1085 (93.9)	<.001
Tired/heavy legs						
Male	540 (63.9)	620 (70.1)	799 (68.9)	249 (73.0)	215 (70.7)	.023
Female	1917 (75.3)	7849 (80.2)	4660 (81.0)	1609 (84.3)	926 (80.2)	<.001
Pain						
Male	413 (48.9)	454 (51.3)	584 (50.4)	177 (51.9)	158 (52.0)	.16
Female	1375 (54.0)	5535 (56.5)	3512 (61.1)	1217 (63.8)	745 (64.5)	<.001
Swollen legs						
Male	240 (28.4)	396 (44.7)	522 (45.0)	224 (65.7)	178 (58.6)	<.001
Female	1362 (53.5)	5593 (57.1)	3448 (60.0)	1474 (77.2)	772 (66.8)	<.001

C0, No signs; C_1, telangiectasia; C_2, varicose veins; C_3, edema; $C_{4\text{-}6}$, eczema, skin changes, ulcers.
*Percentages do not add to 100% because when several visible signs of disease were present at the same time in a given subject, each single sign was analyzed separately.
†Percentages do not add to 100% because if more than one symptom was present in a given subject, the presence of each single sign was analyzed separately for each leg symptom.

as the Doppler ultrasound imaging, as well as the coordinated and standardized data collection. Our study, however, suffers from some limitations. The results of our survey must be put in perspective, because mass advertising has most likely biased the inclusion of subjects toward those people who had some sort of subjective leg symptoms or who were interested in a free medical visit. For example, we cannot exclude that gender differences may be due in part to a difference in awareness of lower limb symptoms between the sexes, as suggested by the higher voluntary participation by women compared with men. In addition, the symptoms questionnaire used had to be as short and compact as possible. The use of a validated quality-of-life questionnaire might have yielded more accurate results.

Because of the large number of subjects included in the survey in a very short time, no stringent quality assurance of the data collection could be implemented, and this is reflected in the large number subjects whose data were not evaluable. The data collection included medical history of venous diseases but was not designed to collect detailed information on patients who underwent any kind of previous surgery (including endovenous ablation or sclerotherapy) and these patients could not be analyzed separately.

Finally, Doppler ultrasound imaging was limited in extent to superficial venous systems, and this may have led to some underestimation of the frequency of CVD in the population studied. This notwithstanding, the data reported here confirm on a large scale those already collected in previous research.[4,5,9,14-16]

CONCLUSIONS

This survey has analyzed a very large sample of respondents. Even if patients voluntarily responded to the screening and the study cannot be thus considered a classic epidemiologic analysis, we have observed a number of correlations that are either new or at least partly confirm already published data. We have seen a clear association between BMI or family history of CVD and other venous disorders. The frequency of valve incompetence increases with worsening of visible findings of the disease, becoming large at age ≥50 years and increasing monotonically with the number of pregnancies in women. Although the correlation between subjective symptoms and visible findings was more evident in women, the occurrence of legs symptoms in men frequently reflected a functional venous disorder. Also striking in this study is the high percentage of those subjects with symptoms and signs, such as edema, who had no venous abnormality and vice versa. This is important information showing that these so-called markers of chronic venous disorders may be present without venous disease and that they can also commonly be absent when the disease is present.

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REFERENCES

1. De Backer G. Epidemiology of chronic venous insufficiency. Angiology 1997;48:569-76.
2. Marshall M, Loew D. Diagnostic measures do demonstrate the therapeutic effect of preparation for varicose veins. Phlebologie 1994;23:85-91.
3. Bradbury A, Evans C, Allan P, Lee A, Ruckley CV, Fowles FGR. What are the symptoms of varicose veins? Edinburgh vein study cross sectional survey. BMJ 1999;318:353-6.
4. Criqui MH, Jamosmos M, Fronek A, Denenberg JO, Langer RD, Bergan J, et al. Chronic venous disease in an ethnically diverse population. The San Diego population study. Am J Epidemiol 2003;158:448-56.
5. Rabe E, Pannier-Fischer F, Bromen K, Schuldt K, Stang A, Poncar Ch, et al. Bonn Vein Study by the German Society of Phlebology: Epidemiological study to investigate the prevalence and severity of chronic venous disorders in the urban and rural residential populations. Phlebologie 2003;32:1-14.
6. Ruckley CV. Socioeconomic impact of chronic venous insufficiency and leg ulcers. Angiology 1997;48:67-9.
7. van Bemmelen PS, Bedford G, Beach, Strandness DE Jr. Status of the valves in the superficial and deep venous system in chronic venous disease. Surgery 1991;109:730-4.
8. Labropoulos N, Delis K, Nicolaides AN, Leon M, Ramaswami G. The role of the distribution and anatomic extent of reflux in the development of signs and symptoms in chronic venous insufficiency. J Vasc Surg 1996;23:504-10.
9. Chiesa R, Marone EM, Limoni C, Volonté M, Schaefer E, Petrini O. Chronic Venous Insufficiency in Italy: the 24-Cities Cohort Study. Eur J Vasc Endovasc Surg 2005;30:422-9.
10. Chiesa R, Marone EM, Limoni C, Volonté M, Schaefer E, Petrini O. Demographic factors and their relationship with the presence of CVI signs in Italy: the 24-Cities Cohort Study. Eur J Vasc Endovasc Surg 2005;30:674-80.
11. Chiesa R, Marone EM, Limoni C, Volonté M, Schaefer E, Petrini O. Impact of chronic venous insufficiency on daily activities and quality of life, and correlation of demographic factors with the outcome of duplex-ultrasound measurements. Angiology 2007;58 [in press].
12. Eklöf B, Rutherford RB, Bergan JJ, Carpentier PH, Gloviczki P, Kistner RL, et al. Revision of the CEAP classification for chronic venous disorders: consensus statement. J Vasc Surg 2004;40:1248-52.
13. MacKenzie RK, Allan PL, Ruckley CV, Bradbury AW. The Effect of Long Saphenous Vein Stripping on Deep Venous Reflux. Eur J Vasc Endovasc Surg 2004;28:104-7.
14. Lee AJ, Evans CJ, Allan PL, Ruckley CV, Fowkes FGR. Lifestyle factors and the risk of varicose veins. Edinburgh Vein Study. J Clin Epidemiol 2003;56:171-9.
15. Brand FN, Dannenberg AL, Abbott AD, Kannel WB. The epidemiology of varicose veins: the Framingham Study. Am J Prev Med 1988;4:96-101.
16. Evans CJ, Fowkes FGR, Ruckley CV, Lee AJ. Prevalence of varicose veins and chronic venous insufficiency in men and women in the general population: Edinburgh Vein Study. J Epidemiol Community Health 1999;53:149-53.
17. Schultz-Ehrenburg U, Weindorf N, Matthes U, Hirche H. An epidemiologic study of the pathogenesis of varices. The Bochum study I-III. Phlebologie 1992;45:497-500.

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