Chronic Venous Disease in an Ethnically Diverse Population

The San Diego Population Study

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In a 1994–1998 cross-sectional study of a multiethnic sample of 2,211 men and women in San Diego, California, the authors estimated prevalence of the major manifestations of chronic venous disease: spider veins, varicose veins, trophic changes, and edema by visual inspection; superficial and deep functional disease (reflux or obstruction) by duplex ultrasonography; and venous thrombotic events based on history. Venous disease increased with age, and, compared with Hispanics, African Americans, and Asians, non-Hispanic Whites had more disease. Spider veins, varicose veins, superficial functional disease, and superficial thrombotic events were more common in women than men (odds ratio (OR) = 5.4, OR = 2.2, OR = 1.9, and OR = 1.9, respectively; $p < 0.05$), but trophic changes and deep functional disease were less common in women (OR = 0.7 for both; $p < 0.05$). Visible (varicose veins or trophic changes) and functional (superficial or deep) disease were closely linked; 92.0% of legs were concordant and 8.0% discordant. For legs evidencing both trophic changes and deep functional disease, the age-adjusted prevalences of edema, superficial events, and deep events were 48.2%, 11.3%, and 24.6%, respectively, compared with 1.7%, 0.6%, and 1.3% for legs visibly and functionally normal. However, visible disease did not invariably predict functional disease, or vice versa, and venous thrombotic events occurred in the absence of either.

cross-sectional studies; diagnostic imaging; ethnic groups; population; thrombosis; ultrasonics; veins

Abbreviations: CEAP, Clinical-Etiologic-Anatomic-Pathophysiologic; OR, odds ratio.

Chronic venous disease causes significant morbidity in diverse populations around the world (1–4). It has been estimated that 1–3 percent of total health care expenditures are linked to venous disorders (4, 5). However, disease definitions have not been uniform (1, 5–10), and little information is available concerning ethnic differences.

Most previous studies have defined chronic venous disease by visual inspection of the lower limbs for varicose veins, or, in some studies, for telangectasias (spider veins), or by visual evidence of trophic changes of chronic venous insufficiency such as hyperpigmentation, edema, and ulcers (1–6). The previous "gold standard" for diagnosing functional disease (i.e., obstruction or reflux) was venography. However, in recent years, a noninvasive assessment, duplex ultrasound, which allows both real-time B-mode visualization and measurement of flow velocity, has been shown to be the equal of venography in terms of diagnostic accuracy (11–13).

An ethnically diverse population was studied for venous disease by using the diagnostic methods of physical examination, duplex ultrasonography, and clinical history. This paper reports on that study.

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MATERIALS AND METHODS

The population for this 1994–1998 study was selected from current and retired employees of the University of California, San Diego. Selection was made within strata defined by age (40–49, 50–59, 60–69, and 70–79 years), sex, and ethnicity (African American, Asian, Hispanic, and non-Hispanic White and other). We overselected for women to increase power for certain female-specific hypotheses. We attempted to randomly recruit 15 percent of subjects from each of the three minority groups to provide statistical power for contrasts by ethnicity. The spouse or significant other of each randomly selected participant, regardless of age, was also invited to participate in the study.

The study design was cross-sectional. At the study visit, trained interviewers followed a standardized protocol and collected information on demographics, lifestyle, and personal and family medical history. Specific questions included "a blood clot in a leg vein" and "phlebitis or inflamed vein in your leg" in a superficial or deep vein, "pulmonary embolism or blood clot in lung," and "heparin or coumadin/warfarin therapy for a problem with your veins." Clots or phlebitis in superficial veins was classified as "superficial thrombotic events," whereas clots or phlebitis in a deep vein, a history of pulmonary embolus, and heparin or coumadin therapy for a vein problem were classified as "deep thrombotic events."

Certified vascular technologists, trained in the protocol and unaware of the subject's interview responses, performed the venous examination. With the subject standing, the technologist recorded simple telangiectasias >3 cm in length, reticular telangiectasias (web >8 cm across), simple varicosities, and reticular varicosities (four or more interconnected varicosities) on five anatomic regions of each leg—thigh, knee, calf, ankle, and foot—as well as evidence of trophic changes: hyperpigmentation, lipodermatosclerosis, or healed or active ulcer (at the level of the calf or below) and the presence of edema (calf or below).

For functional disease, reflux and obstruction were determined by using an Acuson model 128 duplex ultrasonograph (Siemens Corporation, Mountain View, California) with a 5-MHz transducer. Measurements were recorded at prespecified anatomic levels with the subject on a tilt table in a 15° reverse Trendelenburg position, the legs slightly flexed in minimal external rotation. With the patient at rest, a probe was used to determine vein wall compressibility. Standardized pressure determined by using an automatic cuff inflator (Hokanson, Bellevue, Washington) with rapid inflation and deflation of cuffs placed sequentially at midthigh, midcalf, and foot level was used to identify reflux. For Valsalva reflux testing, a pressure monitoring system was used to maintain a reading of 40 mmHg for 3 seconds of subject effort.

Reflux duration of ≥0.5 seconds or Valsalva reflux of ≥0.5 seconds was taken as evidence of valvular insufficiency (14). Partial and complete venous obstruction was assessed by the degree of compressibility of venous walls; complete compressibility was normal (15, 16). Information on the reproducibility of these measurements in our study has been published previously (17).

For all study procedures, participants provided signed informed consent following a detailed explanation of the study. The Committee on Investigations involving Human Subjects of the University of California, San Diego, approved the study.

Disease classification

Venous disease was classified by using the four visible and three functional categories defined below. We simplified the Clinical-Etiologic-Anatomic-Pathophysiologic (CEAP) classification (10) for this epidemiologic study because of the large number of CEAP categories (seven clinical, five etiologic, 18 anatomic, and three pathophysiologic) and because of the implicit CEAP assumptions that we wanted to test, such as whether, for example, edema and pigmentation always indicate underlying venous disease. For comparison, the CEAP equivalents for each of our categorical definitions are detailed below.

Visible disease categories

Visible classification of each leg was made prior to and thus independent of duplex interrogation. Four hierarchic categories were established: normal, spider veins, varicose veins, and trophic changes. Thus, normal legs were free of spider veins, varicose veins, or trophic changes; legs in the spider veins category were free of varicose veins and trophic changes; those in the varicose veins category may or may not have also had spider veins present and were free of trophic changes; and legs in the trophic changes category may or may not have had spider veins or varicose veins present. Legs that were visibly normal but for which there was a history of sclerotherapy were arbitrarily classified as having spider veins (n = 7), and legs visibly normal or with spider veins for which there was a history of vein stripping were classified as having varicose veins (n = 29). For comparison with the CEAP classification, normal corresponds to class 0, spider veins to class 1, varicose veins to class 2, and trophic changes to classes 4, 5, and 6 combined.

Functional disease categories

When the duplex criteria were used, the hierarchic classification was normal, superficial functional disease, and deep functional disease. Superficial functional disease was defined as reflux or abnormal compression (i.e., partial or complete obstruction) in the long or short saphenous veins, or at the sapheno-femoral junction (including Valsalva challenge), or at the sapheno-popliteal junction, or in another superficial vein noted by a technologist. Deep functional disease was defined as reflux or abnormal compression in the common femoral vein (including Valsalva challenge) or in the superficial femoral, popliteal, or posterior tibial veins; or as abnormal compression at the peroneal vein. Legs functionally normal for which there was a history of vein stripping were arbitrarily classified as evidencing superficial functional disease (n = 26). These functional categories correspond to a combination of the CEAP anatomic classification (superficial, deep, perforating veins) and pathophysi-

TABLE 1. Visible and functional chronic venous disease by strata of sex, age, and ethnicity, San Diego, California, 1994–1998*

	Study group		Visible disease (%)				Functional disease (%)		
	No.	%	Normal	Spider veins	Varicose veins	Trophic changes	Normal	Superficial functional disease	Deep functional disease
All subjects	2,211	100	19.0	51.6	23.3	6.2	72.1	19.0	9.0
Men	780	35.3	33.6	43.6	15.0	7.8	75.6	13.1	11.3
Women	1,431	64.7	11.0	55.9	27.7	5.3	70.1	22.2	7.8
Age (years)									
<50	534	24.2	33.0	47.9	16.9	2.3	81.8	11.2	6.9
50–59	608	27.5	22.5	52.8	20.7	4.0	78.0	14.5	7.6
60–69	557	25.2	12.4	52.8	26.0	8.8	66.1	23.5	10.4
≥70	512	23.2	7.4	52.5	29.9	10.2	61.3	27.3	11.3
Ethnicity									
Non-Hispanic White	1,282	58.0	14.3	54.8	24.0	6.9	69.7	20.0	10.3
Hispanic	338	15.3	18.9	50.0	26.3	4.7	71.0	22.8	6.2
African American	318	14.4	27.7	45.3	20.8	6.3	76.7	16.4	6.9
Asian	273	12.4	31.1	45.4	18.7	4.8	78.8	12.5	8.8

* Some percentages do not total 100 because of rounding.

ologic classification (reflux, obstruction, both) categories (10).

Statistical methods

For statistical analyses, DBMS Copy software (Conceptual Software, Inc., Houston, Texas) was used to extract the data required for these analyses into a file usable by SAS version 6.12 for Windows (Statistical Analysis System; SAS Institute, Inc., Cary, North Carolina). Differences in means were tested by using one-way analysis of variance, and categorical differences were tested with chi-square statistics. Differences in adjusted prevalences were assessed by using the general linear models procedure. The contributions of different factors to the various disease categories (spider veins, varicose veins, trophic changes, superficial functional disease, and deep functional disease), and potential interactions, were tested by using multiple logistic regression. All p values reflect two-tailed tests. No adjustments were made for multiple comparisons.

RESULTS

Of 6,115 persons randomly selected for the study, along with their spouses or significant others, 2,215 participated. Four participants did not complete the duplex examination, leaving 2,211 subjects whose data were analyzed for this report. Older persons, women, and non-Hispanic Whites were somewhat more likely to participate than were younger persons, men, and members of the three minority ethnic groups. However, since recruitment by random selection was attempted within strata by age, sex, and ethnicity, the age, sex, and ethnic distribution of the study population was quite close to the intended target (table 1).

Table 1 shows the age, sex, and ethnic distribution of the study population and the prevalences of visible and functional disease in each of the demographic groups. The average age was 59.9 years for the men and 59.2 years for the women (data not shown).

The data in table 1 are based on the subject's "worst" leg. Overall, visible examination of the legs showed that 19.0 percent were normal, 51.6 percent had spider veins, 23.3 percent had varicose veins, and 6.2 percent had trophic changes. According to the functional evaluation, 72.1 percent were normal, 19.0 percent had superficial functional disease, and 9.0 percent had deep functional disease.

Men's legs were more than three times as likely as those of women to be visibly normal (33.6 percent vs. 11.0 percent), whereas women had substantially more spider veins and varicose veins. However, the prevalence of trophic changes was higher in men. With age, there was little change in spider veins but a linear increase in varicose veins and a marked increase in trophic changes. For varicose veins, the prevalence increased from 16.9 percent at age <50 years to 29.9 percent at age ≥70 years. For trophic changes from ages <50 to ≥70 years, the prevalence more than quadrupled, from 2.3 percent to 10.2 percent. For functional disease, superficial functional disease was more common in women than men (22.2 percent vs. 13.1 percent), but deep functional disease was more common in men (11.3 percent vs. 7.8 percent). The prevalence of both superficial and deep functional disease increased monotonically with age: from 11.2 percent at age <50 years to 27.3 percent at age ≥70 years for superficial functional disease and from 6.9 percent at age <50 years to 11.3 percent at age ≥70 years for deep functional disease. Compared with non-Hispanic Whites, minority groups in general had lower prevalences of both visible and functional disease. An exception was for varicose veins and superficial functional disease in Hispanics, who

TABLE 2. Edema, and superficial and deep thrombotic events, by strata of sex, age, and ethnicity,* San Diego, California, 1994–1998

	Edema	Superficial events	Deep events
All subjects	5.8	2.4	3.2
Men	7.4	1.5	4.0
Women	4.9	2.8	2.7
Age (years)			
<50	2.6	2.1	2.4
50–59	4.1	2.5	2.5
60–69	6.1	2.2	3.8
≥70	10.7	2.7	4.1
Ethnicity			
Non-Hispanic White	7.8	2.6	4.4
Hispanic	1.8	3.6	1.5
African American	4.1	0.9	1.9
Asian	3.3	1.5	1.1

* All values are expressed as percentages.

had slightly higher prevalences of these conditions than non-Hispanic Whites did.

Table 2 shows similar data for edema and for a history of superficial and deep thrombotic events. The prevalence of edema was higher among men and increased sharply with age, from 2.6 percent at age <50 years to 10.7 percent at age ≥70 years, and was highest by far among non-Hispanic Whites. Superficial events were nearly twice as common in women as men, 2.8 percent versus 1.5 percent, and this sex difference and the ethnic differences paralleled the findings for superficial functional disease. The findings for deep thrombotic events paralleled the findings for deep functional disease, with more events in men, in non-Hispanic Whites, and at older ages.

In the logistic models shown in table 3, the data in tables 1 and 2 were adjusted for any confounding by age, sex, or ethnicity; this table also shows the odds ratio for each venous condition compared with the reference group. For visible and functional disease separately, the reference group is the combination of groups whose disease was less severe than that in the group being evaluated.

Compared with the normal visible category, spider veins were more common in women, increased with age, and occurred less frequently in all three minority groups compared with non-Hispanic Whites (all $p < 0.05$). Female sex and age were strongly related to varicose veins. For trophic changes, women were at a significantly lower risk than men were (odds ratio (OR) = 0.65). The increase with age was more pronounced for trophic changes than for varicose veins.

Superficial functional disease was significantly more common in women (OR = 1.85) and increased with age, and prevalence was significantly lower among Asians compared with non-Hispanic Whites (OR = 0.65). Conversely, the

prevalence of deep functional disease was significantly lower among women than men (OR = 0.69).

The higher prevalence of edema at ages 60–69 and ≥70 years and the lower prevalence of edema among Hispanics (OR = 0.29) were highly significant. Superficial thrombotic events were somewhat more common in women (OR = 1.89) and less common in African Americans (OR = 0.34), but neither odds ratio attained significance. Compared with non-Hispanic Whites, Hispanics and Asians reported significantly fewer deep thrombotic events (OR = 0.35 and OR = 0.25, respectively).

To evaluate the degree of overlap between visible and functional venous disease, the analyses shown in table 4 were performed for individual legs rather than by person. Table 4 shows the overall results for the 4,422 legs of the 2,211 participants. Visible inspection showed that 23.0 percent of the legs were normal, 54.6 percent had spider veins, 17.7 percent had varicose veins, and 4.6 percent evidenced trophic changes. Functionally, 79.5 percent of the legs were normal, 14.9 percent evidenced superficial functional disease, and 5.6 percent showed deep functional disease. Thus, the majority of legs had spider veins but were also functionally normal. When spider veins were considered a "normal" visible finding, visible (varicose veins or trophic changes) and functional (superficial or deep) disease were closely linked; 92.0 percent of the legs were concordant (17.4 percent concordant for disease presence and 74.6 percent concordant for disease absence), and 8.0 percent of the legs were discordant (4.9 percent evidencing visible but not functional disease and 3.1 percent functional but not visible disease).

Surprisingly, 21.0 percent of all legs with varicose veins and 25.9 percent of all legs with trophic changes were functionally normal. More legs with trophic changes evidenced superficial functional disease alone (52.2 percent) than deep functional disease (22.0 percent). Of the legs with varicose veins, 89.1 percent also had spider veins; in legs showing trophic changes, 91.7 percent also had spider veins and 68.8 percent also had varicose veins. Of the legs with deep functional disease, 48.0 percent also evidenced superficial functional disease.

Table 5 shows, for each cell in table 4, the age-adjusted proportion of legs with 1) edema on clinical examination, 2) a history of superficial thrombotic events, and 3) a history of deep thrombotic events. Percentages statistically significantly different from the normal/normal reference group are noted.

Edema was closely associated with trophic changes. For legs with spider veins and varicose veins, the presence of superficial or deep functional disease increased the probability of edema, as did deep functional disease in limbs visibly normal. In the 45 legs evidencing trophic changes and deep functional disease, edema occurred in 48.2 percent.

Of the 208 edematous legs, 55 (26.4 percent) were either normal or had spider veins and showed normal venous function. These findings provide an estimate of the minimum proportion of legs, on a population basis, with edema of nonvenous etiology.

Superficial thrombotic events were unrelated to visible disease in legs that functioned normally but were increased

TABLE 3. Multivariate odds ratios for age, sex, and ethnicity† in categories of chronic venous disease, edema, and thrombotic events, San Diego, California, 1994–1998

	Data adjusted from table 1					Data adjusted from table 2		
	Spider veins‡	Varicose veins§	Trophic changes¶	Superficial functional disease#	Deep functional disease††	Edema‡‡	Superficial events§§	Deep events¶¶
Sex								
Men	1.00##	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Women	5.36*	2.18*	0.65*	1.85*	0.69*	0.70	1.89	0.77
Age (years)								
<50	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
50–59	1.71*	1.37*	1.75	1.39	1.02	1.36	1.23	0.84
60–69	3.42*	1.96*	4.16*	2.59*	1.52	2.19*	1.07	1.39
≥70	4.91*	2.42*	4.85*	3.23*	1.54	3.42*	1.28	1.22
Ethnicity								
Non-Hispanic White	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Hispanic	0.66*	1.15	0.93	1.24	0.66	0.29*	1.31	0.35*
African American	0.33*	0.81	1.16	0.77	0.72	0.64	0.34	0.43
Asian	0.36*	0.79	0.93	0.65*	0.94	0.53	0.55	0.25*

 * $p < 0.05$.
 † Odds ratios for sex, age, and ethnicity are each adjusted for the other two demographic variables.
 ‡ Compared with the normal visible group.
 § Compared with the normal + spider veins visible groups.
 ¶ Compared with the normal + spider veins + varicose veins visible groups.
 # Compared with the normal functional group.
 †† Compared with the normal + superficial functional disease functional groups.
 ‡‡ Compared with no edema.
 §§ Compared with no thrombotic events.
 ¶¶ Compared with no deep events.
 ## All values of 1.00 correspond to the reference group.

similarly by both superficial and deep functional disease, and these results were significant for three of four superficial functional disease subcells. This finding is concordant with the large proportion of legs evidencing deep functional disease in which superficial functional disease also occurred (48.0 percent).

A history of deep thrombotic events was independently related to both trophic changes and deep functional disease but not to varicose veins or superficial functional disease. The highest prevalence of deep thrombotic events by far, 24.6 percent, occurred in the group of limbs showing both trophic changes and deep functional disease.

TABLE 4. Visible and functional chronic venous disease in 4,422 legs of 2,211 study participants, San Diego, California, 1994–1998

Visible disease	Functional disease							
	Normal		Superficial functional disease		Deep functional disease		Total	
	No.	%*	No.	%	No.	%	No.	%*
Normal	978	22.1	5	0.1	36	0.8	1,019	23.0
Spider veins	2,321	52.5	20	0.5	75	1.7	2,416	54.6
Varicose veins	164	3.7	526	11.9	92	2.1	782	17.7†
Trophic changes	53	1.2	107	2.4	45	1.0	205	4.6‡
Total*	3,516	79.5	658	14.9	248	5.6§	4,422	100.0

 * Percentages do not total 100 because of rounding.
 † Of the 782 legs with varicose veins, 697 (89.1%) also had spider veins.
 ‡ Of the 205 legs showing trophic changes, 188 (91.7%) also had spider veins and 141 (68.8%) also had varicose veins.
 § Of the 248 legs showing deep functional disease, 119 (48.0%) also had superficial functional disease.

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TABLE 5.   Age-adjusted prevalence (%) of edema, history of superficial thrombotic events, and history of deep thrombotic events, by visible and functional disease, San Diego, California, 1994–1998

	Normal	Superficial functional disease	Deep functional disease
Edema			
Normal	1.7†	0.6	6.6
Spider veins	1.8	14.9*	10.5*
Varicose veins	3.9	7.4*	15.6*
Trophic changes	40.8*	30.0*	48.2*
Superficial events			
Normal	0.6†	0.0	5.3*
Spider veins	0.4	10.0*	0.0
Varicose veins	1.2	4.1*	1.2
Trophic changes	0.2	4.9*	11.3*
Deep events			
Normal	1.3†	0.0	5.4
Spider veins	1.7	0.0	5.4*
Varicose veins	3.0	2.4	6.6*
Trophic changes	7.7*	7.6*	24.6*

* $p < 0.005$.

† Reference group.

DISCUSSION

Visible disease

A recent review noted that nearly all previous epidemiologic studies have defined venous disease by visible findings (1). To our knowledge, only one other study, from Edinburgh, Scotland, has separately assessed visible and functional disease in a defined population (18–20).

Most previous studies found a higher prevalence of both spider veins and varicose veins in women and a linear increase in prevalence with age, consistent with findings from the present study. Our data provide a carefully standardized assessment of ethnic differences and show significantly lower prevalences of spider veins in three minority ethnic groups compared with non-Hispanic Whites. It is possible that the lower prevalence of spider veins in ethnic groups with, on average, darker skin might reflect to some degree a detection bias, but our technologists were trained to avoid such a bias.

Earlier literature typically used ulcers as a specific marker of chronic venous insufficiency. Data from Australia (21) and Sweden (22) showed an exponential increase in the prevalence of venous ulcers with age for both men and women, in the 1 percent range before age 50 years and increasing to 3–8 percent by age 75 years. In our study, trophic changes showed a similar trend, but at higher prevalences, because we included hyperpigmentation and lipodermatosclerosis as well as ulcers. Previous studies have suggested a small excess of chronic venous insufficiency in women, as reflected by ulcers, particularly at the oldest ages.

Our study showed significantly fewer trophic changes in women (OR = 0.65). However, we included very few subjects older than 79 years of age.

Despite population and ethnic differences, the data from the Edinburgh study (20) can be roughly compared with ours. Visibly normal participants were less common in Edinburgh, fewer than 15 percent of men and 7 percent of women versus 34 percent of men and 11 percent of women in our study. Within a comparable age stratum (55–64 years), 61 percent of Scottish men and 51 percent of Scottish women had varicose veins versus 15 percent of men and 28 percent of women in our study. Finally, the prevalences of chronic venous insufficiency in this same age group in the Edinburgh study were 25 percent in men and 12 percent in women versus prevalences of trophic changes in our study of 8 percent in men and 5 percent in women. In summary, even after ethnic differences were considered, the prevalences of all visible conditions were substantially higher in Scotland than in southern California. In addition, although both studies showed higher prevalences of spider veins in women and of chronic venous insufficiency/trophic changes in men, the Edinburgh study showed higher prevalences of varicose veins in men, whereas our study and most other population studies of varicose veins have found higher prevalences in women (1, 23–28).

Functional disease

Previous population studies have not used duplex technology to delineate visible from functional abnormalities, with the exception of the Edinburgh study. Thus, these studies inferred the presence of superficial and/or deep functional disease from visible findings of varicose veins and trophic changes. However, our data clearly show the limitations of such assumptions. Although a strong overall association was found between visible disease and functional disease, there were numerous exceptions.

Regarding functional disease, the Edinburgh investigators evaluated reflux but not obstruction (19). Nonetheless, considerably more functional disease was found in Scotland than in southern California, albeit with a similar sex ratio. The duplex examination in Edinburgh was conducted with the subject in a 45° reverse Trendelenburg position versus 15° in our study, so gravity may have resulted in somewhat more reflux in Edinburgh. However, this possibility would account for only a small part of the difference. In addition, in both studies, the visible examination was performed while the subject was standing, and the prevalence of visible (as well as functional) disease was much higher in Edinburgh.

Comparing visible and functional disease in the same leg

To our knowledge, our study is the first to report the concordance of visible and functional disease on an individual limb basis, and it indicates the expected strong, but far from perfect, association between visible and functional venous disease. The finding of deep functional disease in limbs visibly normal is well known clinically (29). The Edinburgh investigators compared visible and functional disease

on a person rather than a limb basis and, similar to our data, found a substantial number of subjects with deep vein reflux and no varicose veins or trophic changes (19). In addition, similar to our data, discordance for reflux and visible disease was considerably more common in deep versus superficial veins.

Our data are consistent with previous literature showing that, with trophic changes, superficial functional disease alone is present at least as often as deep functional disease (30–34). However, the finding that 25.9 percent of legs evidenced trophic changes but functioned normally was a surprise. Thus, we were careful not to use the term "chronic venous insufficiency" for trophic changes, because chronic venous insufficiency by definition implies venous insufficiency. Some limbs showing trophic changes but normal venous function probably represent chronically increased venous pressure from restricted return in the absence of a specific finding of superficial or deep functional disease, or such limbs may have had distal pigmentation or lipodermatosclerosis from chronic dermatitis or other nonvenous conditions. However, in our study, more severe trophic changes nearly always implied chronic venous insufficiency, a finding consistent with previous research (35).

With regard to our discordant visible/functional findings, also surprising was the finding of a significant minority of legs with varicose veins but normal function. We looked intensively at all legs with varicose veins to attempt to demonstrate reflux, but we were unable to do so for 21.0 percent of them. The Edinburgh group also found varicose veins without reflux (19). A recent report indicated some discordance between varicose veins, chronic venous insufficiency, and reflux (36), but the prevalences of varicose veins and chronic venous insufficiency, and the proportion with reflux, were not consistent in the data presented.

Edema

The strong age gradient for edema in our population was expected. The marked ethnic differences were concordant with the generally lower prevalence of visible and functional venous disease in the three minority groups compared with non-Hispanic Whites in our study.

Population studies typically have not used edema alone to define chronic venous insufficiency and have relied on the conservative finding of active or healed leg ulcer. On the basis of the CEAP classification, edema is considered clinical class 3 of chronic venous disease (10). However, edema can result from a number of conditions, such as congestive heart failure, in which venous disease is not the primary underlying pathology. Our data suggest that in at least a fourth of all limbs with clinically recognizable edema, there is no functional venous pathology.

The Edinburgh group reported a higher prevalence of edema than in our population (20). They surprisingly reported more than twice as much edema in women but more than twice as much chronic venous insufficiency in men. In contrast, men in our study had a somewhat higher prevalence of both edema and trophic changes, an expected concordance.

Superficial thrombotic events

Superficial venous thrombosis was nearly twice as prevalent in women in our study. A period of high risk of superficial thrombosis following childbirth may contribute to this female preponderance (37). Other hormonal factors may also account for some of the discrepancy. An increased risk (relative risk = 2.7) of superficial and deep thrombotic events with use of ethinyl estradiol was found in one study (38).

Deep thrombotic events

Our study showed a monotonic age gradient in past experience with deep thrombotic events, and some studies have suggested an exponential increase (39, 40). Our study showed a nonsignificant excess in males. Similarly, in a short-stay hospital study, there were equal overall incidences for males and females (across all age groups) of 48/100,000 (39). The deep-event prevalences in the four age groups in our study (2.4 percent, 2.5 percent, 3.8 percent, and 4.1 percent) appear quite similar to the "lifetime prevalence" of deep venous thrombosis of 3.1 percent in a population-based, 5-year follow-up of 5,568 persons (41). Any study evaluating clinical deep events may substantially underestimate the incidence and prevalence of venous thrombosis due to asymptomatic events, which have been documented in air travelers (42). No studies were identified that provide data enabling the fraction of asymptomatic deep thrombotic events to be calculated.

The data in table 5 show, as expected, a strong association of deep thrombotic events with both visible and functional venous disease. To our knowledge, no previous population study has reported data comparable to those presented in table 5.

In terms of disease prevalence, our study must be considered exploratory given the selected population and modest response rate. Either our selection algorithm or the response rate could have biased our results compared with a random sample of the population. Nonetheless, our prevalence results were concordant from earlier studies using sundry recruitment designs. In addition, estimates of risk of venous disease by various predictors, and the overlap between visible and functional disease, are less likely to be biased than prevalence estimates, since such bias would require an interaction between a selection or participation factor and a predictor (43–46).

Conclusion

The prevalence of both visible (81.0 percent) and functional (27.9 percent) venous disease makes this condition the most prevalent vascular disease. In general, we found that women had more superficial functional disease whereas men had more deep functional disease. Venous disease increased with age, and non-Hispanic Whites had more disease than did Hispanics, African Americans, or Asians. Visible and functional disease were closely linked, and both were strongly associated with edema and thrombotic events. Nonetheless, discordance within a leg for visible, functional, and clinical disease was not uncommon. Thus, visible did

not necessarily imply functional disease, or vice versa, and, although edema and thrombotic events were much more common in the presence of visible and/or functional disease, they also occurred in normal limbs.

REFERENCES

1. Adhikari A, Criqui MH, Wooll V, et al. The epidemiology of chronic venous disease. Phlebology 2000;15:2–18.
2. da Silva A, Widmer LK, Martin H, et al. Varicose veins and chronic venous insufficiency. Vasa 1974;3:118–25.
3. Daver J. Socio-economic data on venous disease. Int Angiol 1984;3:84–6.
4. Lafuma A, Fagnani F, Peltier-Pujol F, et al. Venous disease in France: an unrecognized public health problem. (In French). J Mal Vasc 1994;19:185–9.
5. Task Force on Chronic Venous Disorders of the Leg. The management of chronic venous disorders of the leg: an evidence-based report of an international task force. Chapter 6: economic outcomes. Phlebology 1999;14(suppl 1):35–42.
6. Callam MJ. Epidemiology of varicose veins. Br J Surg 1994; 81:167–73.
7. Widmer LK, Kamber V, Leu HJ. Documentation and classification of venous disorders. In: Widmer LK, ed. Peripheral venous disorders: prevalence and socio-medical importance. Bern, Switzerland: Hans Huber, 1978:17–32.
8. Porter J, Rutherford R, Clagett RP, et al. Reporting standards in venous disease. J Vasc Surg 1988;8:172–81.
9. 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.
10. Ad Hoc Committee, American Venous Forum. Classification and grading of chronic venous disease in the lower limbs. A consensus statement. J Cardiovasc Surg 1997;38:437–41.
11. van Bemmelen PS, Bedford G, Beach K, et al. Functional status of the deep venous system after an episode of deep venous thrombosis. Ann Vasc Surg 1990;4:455–9.
12. Neglen P, Raju S. A comparison between descending phlebography and duplex Doppler investigation in the evaluation of reflux in chronic venous insufficiency: a challenge to phlebography as the "gold standard." J Vasc Surg 1992;16:687–93.
13. Weingarten MS, Branas CC, Czeredarczuk M, et al. Distribution and quantification of venous reflux in lower extremity chronic venous stasis disease with duplex scanning. J Vasc Surg 1993;18:753–9.
14. van Bemmelen PS, Bedford G, Beach K, et al. Quantitative segmental evaluation of venous valvular reflux with duplex ultrasound scanning. J Vasc Surg 1989;10:425–31.
15. Talbot SR. Use of real-time imaging in identifying deep venous obstruction: a preliminary report. Bruit 1982;6:41–6.
16. Nypaver TJ, Shepard AD, Kiell CS, et al. Outpatient duplex scanning for deep vein thrombosis: parameters predictive of a negative study result. J Vasc Surg 1993;18:821–6.
17. Fronek A, Criqui MH, Denenberg JO, et al. Common femoral vein dimensions and hemodynamics including Valsalva response as a function of gender, age, and ethnicity in a population study. J Vasc Surg 2001;33:1050–6.
18. Evans CJ, Fowkes FGR, Ruckley CV, et al. Edinburgh Vein Study: methods and response in a survey of venous disease in the general population. Phlebology 1997;12:127–35.
19. Evans CJ, Allan PL, Lee AJ, et al. Prevalence of venous reflux in the general population on duplex scanning: the Edinburgh Vein Study. J Vasc Surg 1998;28:767–76.
20. Evans CJ, Fowkes FG, Ruckley CV, et al. 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.
21. Baker SR, Stacey MC, Jopp-McKay AG, et al. Epidemiology of chronic venous ulcers. Br J Surg 1991;78:864–7.
22. Nelzén O, Bergqvist D, Lindhagen A. Venous and non-venous leg ulcers: clinical history and appearance in a population study. Br J Surg 1994;8:182–7.
23. Bobek K, Cajzl L, Cepelak V, et al. Study on the incidence of phlebologic diseases and the influence of some etiologic factors. Phlebologie 1966;19:217–30.
24. Coon WW, Willis PW, Keller JB. Venous thromboembolism and other venous disease in the Tecumseh Community Health Study. Circulation 1973;48:839–46.
25. Abramson JH, Hopp C, Epstein LM. The epidemiology of varicose veins. A survey in western Jerusalem. J Epidemiol Community Health 1981;35:213–17.
26. Franks PJ, Wright DDI, Moffatt CJ, et al. Prevalence of venous disease: a community study in West London. Eur J Surg 1992; 158:143–7.
27. Sisto T, Reunanen A, Laurikka J, et al. Prevalence and risk factors of varicose veins in lower extremities: Mini-Finland Health Survey. Eur J Surg 1995;161:405–14.
28. Capitão LM, Menezes JD, Gouveia-Oliveira A. Epidemiological characterization of chronic venous insufficiency in Portugal. (In Portuguese). Acta Med Port 1996;9:69–77.
29. Raju S. Venous insufficiency of the lower limb and stasis ulceration. Changing concepts and management. Ann Surg 1983; 197:688–97.
30. Nelzén O, Bergqvist D, Lindhagen A. Leg ulcer etiology—a cross-sectional population study. J Vasc Surg 1991;14:557–64.
31. Cornwall JV, Dore CJ, Lewis JD. Leg ulcers: epidemiology and etiology. Br J Surg 1986;73:693–6.
32. McEnroe CS, O'Donnell TF Jr, Mackey WC. Correlation of clinical findings with venous hemodynamics in 386 patients with chronic venous insufficiency. Am J Surg 1988;156:148–52.
33. Nelzén O, Bergquvist D, Lindhagen A. The prevalence of chronic lower-limb ulceration has been underestimated: results of a validated population questionnaire. Br J Surg 1996;83:255–8.
34. Shami SK, Sarin S, Cheatle TR, et al. Venous ulcers and the superficial venous system. J Vasc Surg 1993;17:487–90.
35. Welch HJ, Young CM, Semegran AB, et al. Duplex assessment of venous reflux and chronic venous insufficiency: the significance of deep venous reflux. J Vasc Surg 1996;24:755–62.
36. Cesarone MR, Belcaro G, Nicolaides AN, et al. 'Real' epidemiology of varicose veins and chronic venous diseases: the San Valentino Vascular Screening Project. Angiology 2002;53:119–30.
37. McColl MD, Ramsay JE, Tait RC, et al. Superficial vein thrombosis: incidence in association with pregnancy and prevalence of thrombophilic defects. Thromb Haemost 1998;79:741–2.
38. Helmerhorst FM, Bloemenkamp KW, Rosendaal FR, et al. Oral

contraceptives and thrombotic disease: risk of venous thromboembolism. Thromb Haemost 1997;78:327–33.

39. Anderson FA Jr, Wheeler HB, Goldberg RJ, et al. A population-based perspective of the hospital incidence and case-fatality prevalences of deep vein thrombosis and pulmonary embolism. The Worcester DVT Study. Arch Intern Med 1991; 151:933–8.

40. Nordstrom M, Lindblad B, Bergqvist D, et al. A prospective study of the incidence of deep-vein thrombosis within a defined urban population. J Intern Med 1992;232:155–60.

41. Saarinen J, Laurikka J, Sisto T, et al. The incidence and cardiovascular risk indicators of deep venous thrombosis. Vasa 1999; 28:195–8.

42. Scurr JH, Machin SJ, Bailey-King S, et al. Frequency and prevention of symptomless deep-vein thrombosis in long-haul flights: a randomised trial. Lancet 2001;357:1485–9.

43. Criqui MH. Response bias and risk ratios in epidemiologic studies. Am J Epidemiol 1979;109:394–9.

44. Criqui MH, Austin M, Barrett-Connor E. The effect of nonresponse on risk ratios in a cardiovascular disease study. J Chronic Dis 1979;32:633–8.

45. Austin MA, Criqui MH, Barrett-Connor E, et al. The effect of response bias on the odds ratio. Am J Epidemiol 1981;114:137–43.

46. Greenland S, Criqui MH. Are case-control studies more vulnerable to response bias? Am J Epidemiol 1981;114:175–7.