GASTROENTEROLOGY

Hemorrhoidal disease and chronic venous insufficiency: Concomitance or coincidence; results of the CHORUS study (Chronic venous and HemORrhoidal diseases evalUation and Scientific research)

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Abstract

Background and Aim: The CHORUS study (Chronic venous and HemORrhoidal diseases evalUation and Scientific research) was conducted to provide data on patients presenting with hemorrhoidal disease (HD) in clinical practice and to explore the frequency with which it coexists with chronic venous disease (CVD) and shared risk factors.

Methods: This international, noninterventional study enrolled adult patients attending a consultation for hemorrhoidal complaints. The questionnaire completed by physicians established the subjects' demographic and lifestyle characteristics and collected information on HD grade and symptoms and signs of CVD.

Results: A total of 5617 patients were analyzed. Symptoms commonly reported were bleeding (71.8%), pain (67.4%), swelling (55.0%), itching (44.1%), and prolapse (36.2%). Multivariate analysis revealed the variables with the strongest association with HD severity were older age, higher CVD CEAP (Clinical manifestations, Etiologic factors, Anatomic distribution of disease, and underlying Pathophysiology) class, constipation, and male gender (all $P < 0.0001$). Elevated BMI was a risk factor for HD recurrence. Among women, number of births had a significant association with both HD grade and recurrence. The presence of CVD, reported in approximately half the patients (51.2%), was strongly associated with advanced grade of HD ($P < 0.0001$). Treatments most commonly prescribed were venoactive drugs (94.3%), dietary fiber (71.4%), topical treatment (70.3%), analgesics (26.3%), and surgery (23.5%).

Conclusions: CHORUS provides a snap shot of current profiles, risk factors, and treatments of patients with HD across the globe. The coexistence of HD and CVD in more than half the study population highlights the importance of examining for CVD among patients with a hemorrhoid diagnosis, particularly when shared risk factors are present.

Introduction

Hemorrhoidal disease (HD) is a common cause of anal pathology, but its exact prevalence is difficult to determine as patients are often reluctant to seek medical attention.[1,2] Levels of spontaneous consultation for anal symptoms are only around 2%, increasing to around 14% when patients presenting for an unrelated condition are subject to targeted questioning.[1,2]

Most population-based information on anal symptoms is collected via patient surveys alone.[3] However, many HD symptoms

are nonspecific, and without any confirmatory anal examination prevalence results can vary widely.[1,3–5]

Data on the coexistence of hemorrhoids with other conditions are also sparse. Some data are consistent with a common pathophysiological link between straining at stool, constipation, and obstetrical events such as pregnancy and delivery.[6] These factors are also involved in the development of chronic venous disease (CVD). Interference with venous return in the internal hemorrhoidal plexuses and saphenous veins may be a common anatomical mechanism.[7]

Given the paucity of information on the profiles of patients with HD, the aim of the CHORUS study (Chronic venous and HemORRhoidal diseases evalUation and Scientific research) was to provide current, global data on patients presenting with HD in clinical practice and to explore the frequency of its coexistence with CVD and their shared risk factors.

Methods

This was an international, cross-sectional, observational study, consisting of a one-time survey conducted between January 2015 and December 2016. Physicians (general practitioners, proctologists, gastroenterologists, and other types of physician) from seven countries enrolled subjects aged 18 and over attending a consultation for hemorrhoidal complaints. The only patients excluded were those attending for emergency visits. Informed consent was obtained.

The CHORUS study assessed two pathologies managed by different specialties with a diagnosis based on patient interview with or without a physical examination. As not all physicians may have been familiar with the requirements for a CVD or hemorrhoid diagnosis, they were provided with simple classifications based on clinical criteria in the form of the Goligher's classification[8] (hemorrhoidal disease) and CEAP classification[9] (CVD), both of which are designed to allow easy use and reproducibility, regardless of the practitioner. Demographic data were collected and subjects asked to describe their anal complaints including symptoms over the last 15 days, presence and duration of constipation, use of laxatives, time required for stool evacuation, stool consistency based on the seven-category Bristol stool scale,[10] and any previous consultations for hemorrhoids. The patient examination, if performed, was described (digital and/or anoscopy), and the type (internal, external, or mixed) and grade of hemorrhoids were noted. Internal hemorrhoids were graded from I to IV according to the classification of Goligher et al's.[8] CVD of the lower extremities was graded according to the revised CEAP (Clinical manifestations, Etiologic factors, Anatomic distribution of disease, and underlying Pathophysiology) classification (Table S1).[9] Physicians recorded details of any hemorrhoidal treatment prescribed including dietary fiber, topical treatment, venoactive drugs, pain killers, and surgery (including minimally invasive procedures).

For the statistical analysis, continuous variables were expressed as mean ± SD and categorical variables as number and frequency. Between-group differences were evaluated by the chi-squared analysis, Fisher's exact test, independent Student *t*-test, or the Wilcoxon rank-sum test as appropriate depending on whether variables were categorical or continuous.

Between-group differences according to CVD CEAP class were evaluated by the Cochran–Mantel–Haenszel statistic. Univariate and multivariate logistic regression analyses were used to identify potential risk factors for HD and its recurrence. All variables testing significant in univariate analysis were included in the multivariate models (stepwise algorithm with a cumulative logit model). All *P* values were based on two-tailed tests and $P < 0.05$ was considered significant. Data were analyzed using SAS® (SAS Institute, Cary, North Carolina, USA) software 9.4 TS1M4 for Windows Professional 64 bits.

Results

Patient characteristics. CHORUS enrolled 9381 subjects. The analysis set comprised 5617 (59.9%) subjects with available data for the main variables and no major deviations from protocol. Subjects were recruited from the following countries: Russia (*n* = 2362), India (*n* = 1510), Pakistan (*n* = 628), Mexico (*n* = 465), Belgium (*n* = 424), Slovenia (*n* = 129), and Thailand (*n* = 99). Comparison of the analysis set with the total population showed both were similar for demographic variables and baseline characteristics (Table 1).

Hemorrhoidal symptoms and diagnosis. Most subjects with HD had suffered anal symptoms in the last 15 days (97.4%). The mean number reported was 2.9 ± 1.3 most commonly bleeding (71.8%), pain (67.4%), swelling (55.0%), itching (44.1%), prolapse (36.2%), soiling (9.2%), and fecal incontinence (2.9%). The frequency of symptoms increased with disease severity but occurred in a high proportion of subjects from as early as Grade I disease (Fig. 1).

A physical examination was performed in 5572 (99.2%) subjects: digital (90.0%) and/or anoscopic (71.8%). General practitioners were more likely to perform a digital examination (78.7%) than anoscopic (25.9%). Hemorrhoids were diagnosed in 98.5% of respondents and a previous history of hemorrhoids in 56.5% of respondents.

Influence of subject characteristics on severity of hemorrhoidal disease. Variables shown by univariate analysis to be significantly associated with grade of HD were male gender, older age, elevated BMI, previous pregnancies and number of births, constipation, and CVD (Table 2). In the multivariate analysis, the variables with the strongest association with hemorrhoid grade were in descending order: age group, CVD CEAP class, constipation, and male gender (all *P* values < 0.0001). In women, constipation and number of births were stronger risk factors than CEAP class, while in men, CEAP class was a stronger risk factor than constipation.

Bowel habits. Constipation was reported by 2685 (49.3%) subjects, and its presence influenced hemorrhoid grade (Table 2). Duration of constipation was <18 months in 1334 (49.7%) subjects and chronic (>18 months) in 1351 (50.3%) subjects.

Duration of evacuation was described as <5 min in 41.5%, between 6 and 30 min in 54.7%, and ≥31 min in 3.9%. In those with a duration of evacuation ≥31 min the proportion of Grade III and IV hemorrhoids was 28.6% and 10.7%, respectively, compared with 14.0% and 2.0%, respectively, in patients with a duration <5 min.

Table 1 Patient demographics and baseline characteristics for total enrolled population and analysis population

	Number (%)	
	Analysis population (N = 5617)	Enrolled population (N = 9381)
Gender		
Male/female	3020 (53.7) /2597 (46.2)	4768 (51.2) /4548 (48.8)
Missing data	0 (0.0)	65 (0.7)
Age (years) (mean ± SD)	45.3 ± 13.8	45.6 ± 14.1
Age groups (years):		
18–34	1416 (25.2)	2199 (24.6)
35–50	2199 (39.2)	3495 (39.1)
51–64	1465 (26.1)	2310 (25.9)
≥65	537 (9.6)	924 (10.3)
Missing data	0 (0.0)	453 (4.8)
BMI (kg/m^2) (mean ± SD)	26.7 ± 4.8	27.2 ± 5.3
BMI groups (kg/m^2):		
≤18	112 (2.0)	157 (1.8)
19–24	1825 (32.5)	2582 (29.6)
25–30	2696 (48.0)	4219 (48.4)
≥31	984 (17.5)	1761 (20.2)
Missing data	0 (0.0)	662 (7.1)
Hemorrhoid grade (Goligher et al[9]):		
I	1631 (29.0)	2166 (29.5)
II	2398 (42.7)	3092 (42.1)
III	1301 (23.2)	1693 (23.0)
IV	287 (5.1)	398 (5.4)
Missing data	0 (0.0)	2032 (21.7)
Constipation		
Yes	2685 (47.8)	4474 (51.1)
No	2759 (49.1)	4273 (48.9)
Missing data	173 (3.1)	634 (6.8)
Current venous leg problems		
Yes	2878 (51.2)	4493 (51.9)
No	2739 (48.8)	4162 (48.1)
Missing data	0 (0.0)	726 (7.7)
Time spent standing		
≤2 h	1727 (30.8)	2801 (30.3)
3–6 h	2780 (49.5)	4438 (48.0)
≥7 h	1110 (19.8)	2005 (21.7)
Missing data	0 (0.0)	137 (1.5)
Smoking status:		
Never smoked	3222 (57.4)	5496 (59.6)
Current smoker	1468 (26.1)	2212 (24.0)
Previous smoker	927 (16.5)	1511 (16.4)
Missing data	0 (0.0)	162 (1.7)
Previous consultation for hemorrhoids	3176 (56.5)	4759 (50.7)
Number of previous consultations:		
One	1210 (38.1)	1737 (37.3)
Two	1151 (36.2)	1640 (35.2)
3–5 times	667 (21.0)	1022 (22.0)
≥6 times	148 (4.7)	257 (5.5)
Missing data	0 (0.0)	103 (2.2)
Among women participants:	N = 2597	N = 4548
Use of hormonal contraception:		
Yes	464 (17.9)	765 (18.4)
No	1998 (76.9)	3387 (92.4)
Missing data	135 (5.2)	396 (8.7)
Use of hormone replacement therapy:		
Yes	157 (6.1)	294 (7.6)
No	2177 (83.8)	3593 (92.4)

(Continues)

Missing data	263 (10.1)	661 (14.5)
Given birth:		
Yes	2101 (80.9)	3569 (83.1)
No	496 (19.1)	724 (16.9)
Missing data	0 (0.0)	255 (5.6)
Number of births (among women with history of pregnancy)[†] (mean ± SD)	2.18 ± 1.34	2.51 ± 1.62

[†]Among the 2597 women in the study, 2101 had given birth of whom 2080 had the number of births recorded and 21 did not.
BMI, body mass index.

Bowel habits were also assessed using the Bristol stool scale, which allows a classification of the form of human feces, albeit not an accurate grading of the severity of constipation or diarrhea. Nearly two thirds of subjects with hemorrhoidal complaints (64.4%) had normal stools (stool Type 3, 4, and 5). The proportions of Type 1 and 2 stools (suggesting constipation) were 9.2% and 21.4%, respectively, and the proportions of Type 6 and 7 (suggesting diarrhea) were 3.9% and 1.1%, respectively. The proportion of patients with more severe constipation (Type 1 stool) increased with age group, from 7.0% in those aged 18–34 years to 11.9% in those aged ≥65 years. BMI had no impact on stool type.

According to the Bristol stool scale, a greater proportion of people with constipation had more severe hemorrhoid grades compared with patients with normal stools (Table S2; $P = 0.0236$, Fisher's exact test). The numbers of patients with diarrhea were too low for conclusions to be drawn.

CVD. Coexistence with CVD was more frequent as HD severity increased: concomitant CVD was present in 43.1%, 54.0%, 54.8%, and 58.2% of those with hemorrhoid grades of I, II, III, and IV, respectively. The severity of CVD was strongly associated with hemorrhoid severity ($P < 0.0001$) (Table 3).

Influence of subject characteristics on HD recurrence. Univariate analyses indicated a significant association between previous consultations for HD (hemorrhoid recurrence) and older age (56.6% in 35–50 year-olds, 65.7% in 51–64 year-olds, and 67.8% in ≥65 year-olds, $P < 0.0001$); elevated BMI (49.1% normal BMI, 58.2% overweight category, and 68.3% obese category, $P < 0.0001$); and constipation (46.0% no constipation, 67.6% with constipation, $P < 0.0001$). In women, risk was higher in those who had given birth (58.8% *vs* 41.7% in those who had not given birth, $P < 0.0001$), and increased with number of births ($P < 0.0001$). Risk of hemorrhoid recurrence was also more likely in those with concomitant CVD (63.6% *vs* 49.1% in those without CVD, $P < 0.0001$) and increased with CVD CEAP class ($P < 0.0001$). Gender had no influence on likelihood of hemorrhoid recurrence in univariate analysis ($P = 0.1539$).

A higher proportion of patients enrolled in Thailand, Pakistan, India, and Mexico (1693 out of 2702, 62.8%) had previously consulted for HD compared with those enrolled in Russia, Belgium, and Slovenia (1445 out of 2915, 49.6%).

Multivariate analyses confirmed univariate findings. Variables with the strongest association with hemorrhoid recurrence were in descending order: constipation (OR 2.20, 95%CI 1.96, 2.46), age group (OR 2.11, 95%CI 1.68, 2.65 for the comparison 18–34 years *vs* >65 years), CVD CEAP class (OR 3.75, 95%CI 1.30, 10.90 CEAP C0a *vs* C6) (Fig. 2), BMI category (OR 2.34, 95%CI 1.51, 3.64 for the comparison 12–18 years *vs* ≥31 kg/m^2), and male gender (OR 1.25, 95%CI 1.11, 1.41). Among women, having given birth and number of births were the most important risk factors ($P < 0.0001$), followed by constipation ($P < 0.001$), age group ($P < 0.0001$), presence of CVD ($P = 0.0089$), and BMI category ($P = 0.0123$). Among men, constipation was the most important risk factor ($P < 0.0001$) followed
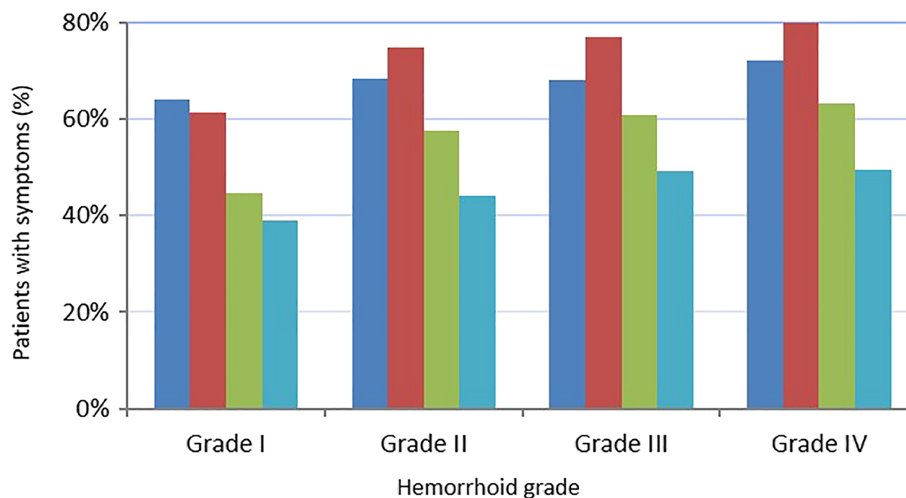
Figure 1 Frequencies of declared hemorrhoidal symptoms according to hemorrhoid grade. ■, Pain; ■, Bleeding; ■, Swelling; ■, Itching. [Color figure can be viewed at wileyonlinelibrary.com]

Table 2 Patients' characteristics at baseline according to hemorrhoid grade

Grade of hemorrhoid:	Patients' characteristics (%)												
	Gender*		Age group**				BMI**				Given birth**	Presence of constipation**	Presence of CVD**
	Male (N = 3020)	Female (N = 2597)	18–34 (N = 1416)	35–50 (N = 2199)	51–64 (N = 1465)	≥65 (N = 537)	12–18 (N = 112)	19–24 (N = 1825)	25–30 (N = 2696)	≥31 (N = 984)	(N = 2101)	(N = 2685)	(N = 2878)
I (N = 1631)	51.93	48.07	38.20	35.25	18.88	7.66	2.94	38.07	45.25	13.73	70.92	40.53	43.10
II (N = 2398)	52.63	47.37	23.31	41.49	28.86	8.34	1.79	32.65	47.71	17.85	83.18	48.50	54.00
III (N = 1301)	58.11	41.89	15.30	40.58	32.13	11.99	1.31	26.21	51.58	20.91	89.72	54.50	54.80
IV (N = 287)	54.01	45.99	12.20	35.19	33.10	19.51	1.39	27.87	49.83	20.91	84.09	52.96	58.19

Univariate analysis: *$P < 0.004$. **$P < 0.0001$.

Among the 2597 women in the study, 2101 had given birth of whom 2080 had the number of births recorded and 21 did not.

BMI, body mass index. CVD, chronic venous disease.

Table 3 Proportion of patients with concomitant CVD defined by CEAP classification according to hemorrhoid grade

	Subjects with CVD by CEAP class (%)						
	C0$_A$ (N = 2739)	C0$_S$ (N = 552)	C1 (N = 847)	C2 (N = 708)	C3 (N = 472)	C4 (N = 263)	C5–C6 (N = 36)
Grade of hemorrhoid							
I (N = 1631)	56.9	11.0	14.3	8.9	5.8	2.6	0.6
II (N = 2398)	46.0	11.5	16.6	12.9	8.4	4.2	0.5
III (N = 1301)	45.2	6.0	14.1	15.7	11.1	7.1	0.8
IV (N = 287)	41.8	6.6	11.1	17.8	11.1	9.8	1.7

CEAP, Clinical manifestations, Etiologic factors, Anatomic distribution of disease, and underlying Pathophysiology; CVD, chronic venous disease.

by age group ($P < 0.0001$), BMI category ($P = 0.0011$), and presence of CVD ($P < 0.0001$).

Characteristics of subjects with concomitant CVD. In the CHORUS survey, 51.2% of participants with hemorrhoidal complaints also presented with signs and/or symptoms of CVD: C0s–C2 (73.2%), C3 (16.4%), C4 (9.1%), and C5–C6 (1.3%).

Patients with CVD were on average 7 years older and were more frequently women (59.3% *vs* 32.5%, respectively), overweight (21.8% *vs* 12.9%), constipated (53.1% *vs* 42.2%), and had more severe and recurrent hemorrhoids than subjects without CVD (Table 4).

According to multivariate analysis, variables with the strongest association with the presence of CVD in individuals with HD were in descending order: female gender, older age, elevated BMI, constipation, and severe hemorrhoid grade (all $P < 0.0001$). Among women, number of births ranked second after age group, followed by constipation and BMI class, while among men hemorrhoid grade ranked second after age group, followed by BMI class and constipation.

Treatment patterns. Nearly all patients (99.8%) were prescribed at least one treatment for their HD: venoactive drug (94.3%), dietary fiber (71.4%), topical treatment (70.3%), analgesics (26.3%), surgical procedures (23.5%), or other (14.7%). Most patients (97.9%) were prescribed at least one of the following: venoactive drug, dietary fiber, topical treatment, or analgesic; 1037 (18.8%) received all four treatments, 2248 (40.9%) received

three, 1627 (29.6%) received two, and 590 (10.7%) received one. Among the venoactive drugs the most commonly prescribed was micronized purified flavonoid fraction (93.5%), followed by diosmin (3.5%). For these agents, the mean prescription duration was ≥4 weeks in 61.0% of participants, 2–3 weeks in 27.6%, and ≤1 week in 10.0%. Other venoactive drug classes such as calcium dobesilate, horse chestnut seed extract (escin), rutosides, ruscus extracts, proanthocyanidines, and ginkgo biloba accounted for <3.0% of prescriptions.

Venoactive drugs were prescribed in over 94.0% of subjects with Grade I to III hemorrhoids and in 86.8% of subjects with Grade IV hemorrhoids (Fig. 3). Dietary fiber and topical treatments were prescribed in around two thirds of patient across hemorrhoid grades of I to III, and slightly less in Grade IV (65.5% and 63.4%, respectively). Prescription of analgesic drugs increased with hemorrhoid grade.

Surgical procedures (including minimally invasive procedures) were prescribed in 48.1% of Grade III individuals and 68.3% of Grade IV. Among the 1319 patients who underwent surgical procedures, 1159 (87.8%) were also prescribed a venoactive drug, 847 (64.2%) dietary fiber, 838 (63.5%) topical treatment, and 363 (27.5%) an analgesic.

Discussion

Almost all CHORUS participants (99.2%) underwent a clinical examination, either digital and/or anoscopic. Although a digital examination cannot always confirm a diagnosis of lower grade HD, it is important to eliminate any local malignancies. Anoscopy is
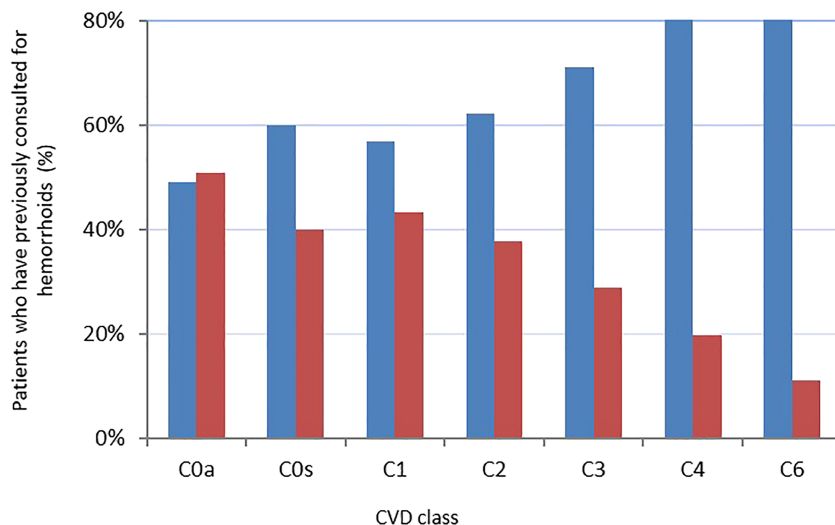
Figure 2 Distribution of patients with and without previous consultation for hemorrhoids according to stage of chronic venous disease (CVD) based on the Clinical manifestations, Etiologic factors, Anatomic distribution of disease, and underlying Pathophysiology (CEAP) classification. ■, Yes; ■, No. [Color figure can be viewed at wileyonlinelibrary.com]

Table 4 Characteristics of patients with hemorrhoids according to concomitant CVD

	Patients without CVD (n = 2739)	Patients with CVD (n = 2878)
Male/female (%)	67.5/32.5	40.7/59.3
Age years (mean ± SD)	41.9 ± 13.1	48.6 ± 13.6
Age class (%)		
18–34 (N = 1416)	33.8	17.1
35–50 (N = 2199)	40.6	37.7
51–64 (N = 1465)	19.6	32.3
≥ 65 (N = 537)	6.0	12.9
BMI (kg/m^2) (mean ± SD)	26.1 ± 4.5	27.3 ± 5.0
BMI class (%)		
≤18 (N = 112)	2.6	1.4
19–24 (N = 1825)	35.9	29.3
25–30 (N = 2696)	48.5	47.5
≥31 (N = 984)	13.0	21.8
Constipation (%)	42.2	53.1
0–18 months	25.5	22.1
19 months to 5 years	8.7	14.4
>5 years	8.0	16.7
Use of laxatives (%)	20.4	29.4
Duration of evacuation (%)		
<5 min	46.1	37.0
≥6 min	53.9	63.0
Standing position (%)		
≤2 h (N = 1727)	31.3	30.2
3–6 h (N = 2780)	49.5	49.4
≥7 h (N = 1110)	19.1	20.4
Smoking status (%)		
Never smoked (N = 3222)	56.7	58.0
Current smoker (N = 1468)	27.5	24.9
Previous smoker (N = 927)	15.9	17.1
Hemorrhoid grade (%)		
I	33.9	24.4
II	40.3	45.0
III	21.5	24.5
IV	4.4	5.8
Previous consultation for hemorrhoids (%)	42.1	57.9
Among women	N = 890	N = 1707
Use of hormonal contraception (%)	21.9	15.8
Use of HRT (%)	5.6	6.3
Previous pregnancy (%)	71.9	85.6

BMI, body mass index; CVD, chronic venous disease; HRT, hormone replacement therapy.

necessary for the diagnosis of Grade I hemorrhoids and was performed in the majority of patients with low-grade hemorrhoids, thus confirming the high level of diagnostic evidence in this study.

CHORUS confirmed that HD affects both sexes with peak presentation in those aged 35–50 years. An unexpected finding was the male predominance (53.8% *vs* 46.2% women predominance), but this may reflect the large proportion of male subjects enrolled in India and, cultural habits making women participants with HD less likely to come forward.

Most female participants presenting with hemorrhoids (80.7%) had had at least one full-term pregnancy, and pregnancy was a risk factor for all hemorrhoid grades. Hemorrhoids are common during pregnancy, particularly the last trimester,[11,12] and although they generally resolve after delivery these women are at greater risk of hemorrhoids later in life. Hemorrhoids were also more common in those with a BMI in the overweight or obese category. Previous studies have hypothesized that this may be because of increased intraabdominal pressure and increased stress on rectal muscles.[13]

Multiple logistic regression analysis identified male gender, older age, pregnancy and number of births, constipation, and CVD presence and severity as being significantly associated with HD grade. Several studies, including those that have used colonoscopy to confirm hemorrhoids, have shown an increased risk in patients with chronic constipation.[14–16] Whether causal or a contributory factor in the presence of a primary cause prolonged straining increases intraabdominal pressure and raises venous pressure in the hemorrhoidal tissue. In the current study, half the respondents (50.9%) were suffering from constipation according to the Bristol stool scale, and 54.7% reported a straining duration of 6–30 min. Severe constipation was also observed more frequently in individuals with Grade IV HD than less severe forms of the disease.

Hemorrhoid recurrence rates have been reported to range from 4% to 30% after treatment.[17] In CHORUS, 56.5% of patients had previously consulted for hemorrhoids. Constipation, older age, higher CVD CEAP class, elevated BMI, and male gender had a statistically significant association with hemorrhoid recurrence. Among women, pregnancy and number of births had the strongest association. Constipation was an important risk factor for recurrence in both men and women. BMI was associated with HD recurrence even though it was not linked to HD severity. Recurrence rates were higher in countries that typically have a greater consumption of spices. This may indicate a possible influence of diet on likelihood of hemorrhoid recurrence, but could also be related to the stage of HD at which patients were enrolled in the study.

HD and CVD may have a common cause in the form of loss of vascular integrity,[7] but there are few published papers on the coexistence of the two disorders and recent data are lacking.[18] An early review of epidemiologic evidence for a link between HD and CVD hypothesized that chronic constipation associated with a low fiber diet was involved by increasing intraabdominal pressure.[18] It was suggested that this pressure would easily be transmitted to the hemorrhoidal plexus, which have no valves. The valves of the lower limb veins would offer initial protection but would eventually become incompetent and expose the veins to elevated pressure.[18] This hypothesis is supported by data from a Hungarian epidemiologic study of pregnant women, which found that around half with a diagnosis of HD also had constipation. Varicose veins were also more common in pregnant women with hemorrhoids compared with those without.[19]

Just over half the CHORUS subjects also presented with signs and/or symptoms of CVD, the majority having a CEAP classification of C0s to C2. In multivariate analyses, independent risk factors for CVD among patients with HD were female gender, older age, elevated BMI, constipation, and more severe hemorrhoid grade. Among women, number of births was also an importan risk factor. The finding that HD coexists with CVD in over half the study population should prompt physicians treating patients with a hemorrhoid diagnosis to also ask about CVD and vice versa, particularly in the presence of the risk factors above.
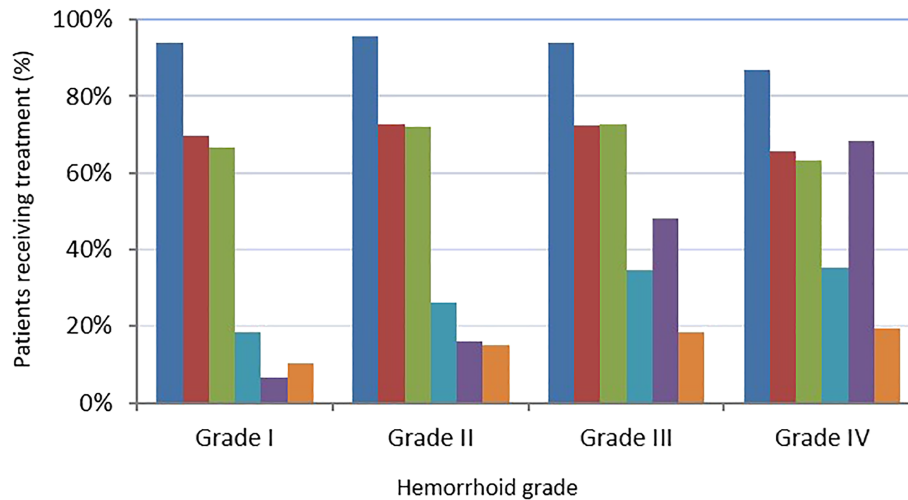
Figure 3 Distribution of prescribed treatments for hemorrhoidal disease according to the hemorrhoid severity stage. VAD, venoactive drug. ■, VAD; ■, Dietary fiber; ■, Tropical treatment; ■, Analgesic; ■, Surgery; ■, Other. [Color figure can be viewed at wileyonlinelibrary.com]

Nonsurgical approaches are preferred for lower grade hemorrhoids because of the physiologic importance of the hemorrhoid cushions and potential self-limiting nature of many hemorrhoid symptoms.[12,17,20,21] When conservative therapy fails, clinical practice guidelines recommend office-based procedures such as banding, sclerotherapy, and infrared coagulation for Grade I to III hemorrhoids.[20,22] Surgical options such as hemorrhoidectomy, stapled hemorrhoidopexy, or hemorrhoidal artery ligation may be the initial step in patients with Grade III or IV hemorrhoids or in those who are refractory to or cannot tolerate office procedures.[20,22] However, conservative therapy can still play a role, creating favorable conditions for a smooth postoperative recovery.[23] Adherence to these guideline recommendations is important to avoid repetitive and prolonged treatment and severe complications in Grade IV disease.

Among pharmacological approaches, venoactive drugs can address the underlying causes of both symptomatic hemorrhoids and CVD via their beneficial effects on venous tone, inflammatory processes, and microcirculatory permeability.[24] Early use of such agents may play a role in preventing or slowing the development and recurrence of both hemorrhoidal and CVD signs and symptoms.[25,26] Hemorrhoid recurrence was more likely in those with concurrent CVD. This association is an indirect argument for the use of a targeted medical treatment on the vein in both pathologies.

This study was subject to the inherent limitations of observational surveys, which include sample bias, incomplete survey response data, as well as the potential inaccuracy of self-reported behavior. A comparison of the demographic data for per protocol and total enrolled population illustrates their similarity and indicates that a selection bias was unlikely to have been introduced by restricting the study to patients with no relevant protocol deviations. However, the authors acknowledge that representativeness is also linked to whether participating sites reflect the management of disease in that country in terms of specialty and place of practice. During this investigation, symptoms of pain were defined by the patients themselves. Pain intensity was not evaluated as the use of a visual analogue scale in such a population was not considered feasible. The use of a broad definition of pain inevitably led to

a relatively high percentage of pain symptoms in this survey. The link with HD nevertheless remains plausible as the incidence of pain increased with the grade of disease (Fig. 1).

While neither HD nor CVD is likely to have a single causative agent, some risk factors may contribute or exacerbate disease in predisposed patients. Further studies are now warranted to determine the proportion of patients with hemorrhoids who subsequently develop CVD and whether this is more likely in patients with certain risk factors. Any changes in lifestyle or pharmacologic treatment that target these conditions in their early stages would be advantageous to prevent progression to more severe forms.

Conclusion

CHORUS provides large-scale data on the profiles of patients presenting with HD in clinical practice. Factors identified as having a statistically significant association with both hemorrhoid grade and recurrence were older age, CVD CEAP class, constipation, and male gender. Among women, additional factors were pregnancy and number of births. Physicians should be aware of these risk factors and be proactive in questioning patients about potential hemorrhoid symptoms and conduct the appropriate examinations. As symptoms affect patients from Grade I disease, a conservative treatment should be the cornerstone of care. Further studies are needed to confirm the correlation between HD and CVD so that a common targeted therapy can be developed for both these diseases.

Acknowledgment

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. CVD of the lower extremities graded according to the clinical classification of the CEAP (Clinical manifestations, Etiologic factors, Anatomic distribution of disease, and underlying Pathophysiology).[10]

Table S2. Distribution of Bristol stool types according to hemorrhoid grade.