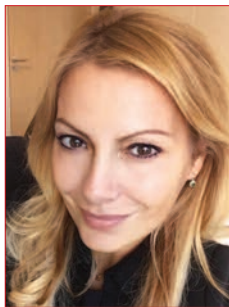


“The use of early pharmacological treatment with a venoactive agent, particularly with MPFF, may play a significant role in preventing or slowing the development and recurrence of the signs and symptoms of both hemorrhoidal disease and chronic venous disease.

Up-to-date data from the CHORUS survey: association of hemorrhoidal disease with chronic venous disease

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Hemorrhoidal disease is known to affect large numbers of individuals worldwide, thus there are limited recent data on the profile of affected patients in different continents and on the associated conditions. The CHORUS study (Chronic venous and HemORrhoidal diseases evalUation and Scientific research), a multicenter, observational study, has addressed this shortfall by providing up-to-date information on the characteristics of patients with hemorrhoidal disease in clinical practice in different regions of the world, and, for the first time, the frequency with which it coexists with chronic venous disease and associated risk factors. This report focuses on new data showing the coexistence of hemorrhoidal disease and chronic venous disease. Just over half the subjects (51.2%) with hemorrhoidal complaints also presented with signs and/or symptoms of chronic venous disease, the majority (73.2%) with a clinical, etiological, anatomical, and pathophysiological (CEAP) classification of C_{0s} to C₂, and a greater proportion of patients with current venous leg problems had more severe grades of hemorrhoids. These outcomes should be considered in daily practice for optimizing the diagnosis and treatment.

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Background and objective

Hemorrhoidal disease is recognized as one of the most common causes of anal pathology, but the exact incidence of the condition is difficult to determine as patients are often reluctant to seek medical attention.^{1,2} In a survey of French physicians questioned about their patient consultations over 2.5 days, there was a high incidence of anal symptoms (14%) in patients who visited their family physician for an unrelated condition, but this was only found after targeted questioning.¹ The level of spontaneous consultation for anal symptoms was only 2%. These findings have recently been confirmed in a similar study, also from France, which reported that only 2.3% of individuals consulted spontaneously for an anal problem, whereas 15.6% were found to have a problem after targeted questioning.²

Most epidemiological data are obtained via population-based surveys that collect information on anal symptoms via patient questioning alone. Nevertheless, many symptoms of hemorrhoidal disease are nonspecific, and the prevalence results can vary without any confirmatory anal examination.^{1,3} The largest epidemiologic study conducted to date was published in 1990 and included health interview data and hospital discharge data collected over a number of years for several hundred thousand

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individuals.⁴ Based on these data, it was estimated that around 10 million people in the US were suffering from hemorrhoidal disease, corresponding to a prevalence rate of 4.4%.⁴ In both sexes, peak prevalence occurred between the ages of 45 and 65 years. It has been reported that 50% of the US population over 50 years of age will experience symptomatic hemorrhoids at some point in their life.⁵ More recent data from an Austrian nationwide health care program for colorectal cancer screening, in which all individuals underwent a colonoscopy and detailed examination, found that 380/976 (38.9%) suffered from hemorrhoids.⁶

The exact pathophysiology of hemorrhoidal disease has not been completely elucidated and several hypotheses have been put forward, without a universal consensus. It is likely that several mechanisms are involved, resulting in an alteration of the connecting tissue and a dilatation of the altered vascular network. The anal cushions of patients with hemorrhoidal disease show significant pathologic changes resulting in a loss of vascular integrity, including abnormal venous dilatation, vascular thrombosis, disrupted collagen fibers and fibroelastic tissues, and distortion and rupture of the anal sub-epithelial muscle.⁷ In addition to the above findings, a severe inflammatory reaction involving the vascular wall and surrounding connective tissue has been demonstrated in the hemorrhoidal plexus.⁸ In practice, the dilated venous plexuses can slip down through the anal canal and protrude at the anal verge, leading to stretching of the suspensory muscles and prolapse of hemorrhoidal tissue through the anal canal. The engorged tissue is easily traumatized, causing rectal bleeding.

Factors that increase intra-abdominal pressure, such as constipation, straining during defecation, pregnancy, and obesity, may exacerbate the above-described pathologic changes. A causal role of constipation and inadequate fiber intake was challenged because marked differences are observed in the epidemiologic patterns of hemorrhoidal disease and constipation in some observational studies.⁴ A case-control study of 325 patients who underwent a proctologic examination and who were questioned about hemorrhoidal disease and bowel habits also found no evidence that constipation was a risk factor, whereas diarrhea was significantly associated with the development of hemorrhoids.⁹ On the other hand, analysis of data from a US health coverage organization found that, among the 105 130 patients who saw a physician at least once for constipation, the most common comorbid condition was hemorrhoids, which occurred in 5657 (5.4%) patients within 1 year of the first visit

for constipation.¹⁰ In the absence of robust data on the link between bowel habits and hemorrhoids, current guidelines include regularization of bowel habits as a first stage in the medical treatment in all cases.

Data on the coexistence of hemorrhoids with other conditions are infrequent. Some data are consistent with a common pathophysiological link between straining at stool, constipation, and obstetrical events, such as pregnancy and delivery.¹¹ These factors are also accepted to be related to the development of chronic venous disease. In light of these data, the CHORUS study (Chronic venous and HemORrhoidal diseases evaluation and Scientific research) was designed to provide up-to-date information on the characteristics of patients presenting with hemorrhoidal disease in clinical practice across the world and to explore, for the first time, the frequency with which it coexists with chronic venous disease and associated risk factors.

Methods

The CHORUS study was an international, cross-sectional, observational study consisting of a one-time survey conducted between 2015 and 2016. The program was performed in seven countries from different geographical zones (Belgium, Slovenia, Russia, India, Pakistan, Thailand, and Mexico) (Figure 1) by a group of general practitioners and specialists in-



Figure 1. Countries that participated in the CHORUS study.

involved in hemorrhoidal disease management. Subjects were eligible if aged 18 and over and if they were attending the practice for a consultation for hemorrhoidal complaints. Patients attending for emergency visits were excluded.

The questionnaire was completed by physicians and established the subjects' demographic and lifestyle characteristics, including: sex, age, body mass index, smoking habits, time per day spent standing, and, among women, the number of previous pregnancies and use of hormonal therapy. Subjects

Patients characteristics	Patients (n=5617)
Sex	
Male, n (%)	3020 (53.8%)
Female, n (%)	2597 (46.2%)
Age (years), mean±SD	45.3±13.8
Body mass index (kg/m ²), mean±SD	26.7±4.8
Hemorrhoid grade, n (%)	
I	1631 (29.0%)
II	2398 (42.7%)
III	1301 (23.2%)
IV	287 (5.1%)
Previous consultation for hemorrhoids, n (%)	3176 (56.5%)

Table I. Patient demographics and baseline characteristics for analysis population.

were asked to describe their anal complaints, including symptoms over the last 15 days, presence and duration of constipation, time required for stool evacuation, stool consistency based on the seven-category Bristol stool scale,¹² and any previous consultations for hemorrhoids. The patient examination, if performed, was described and the type (internal, external, or mixed) and grade of hemorrhoid was noted. Internal hemorrhoids were graded from I to IV according to the classification of Goligher et al.¹³ Patients were also questioned about symptoms and signs of CVD and the severity of CVD of the lower extremities was graded according to the revised clinical, etiological, anatomical, and pathophysiological (CEAP) classification.¹⁴

The details of any hemorrhoidal treatment prescribed were recorded by the physicians. The statistical analysis was conducted for all patients with complete information for the main variables and no relevant deviations from the protocol. Continuous variables were expressed as mean±SD and categorical variables as number and frequency. Between-group differences were evaluated with a chi-squared analysis, a Fischer's exact test, and an independent Student *t* test or the Wilcoxon rank sum test as appropriate depending on whether the variables were categorical or continuous. Univariate and multivariate logistic regression analyses were used to evaluate potential risk factors for hemorrhoidal disease and recurrent disease. All *P* values were based on two-tailed tests and a *P*-value <0.05 was considered significant.

	Patients (n=5617)	
	n	%
Belgium	424	7.55%
India	1510	26.88%
Mexico	465	8.28%
Pakistan	628	11.18%
Russia	2362	42.05%
Slovenia	129	2.30%
Thailand	99	1.76%

Table II. Repartition of the patients per country.

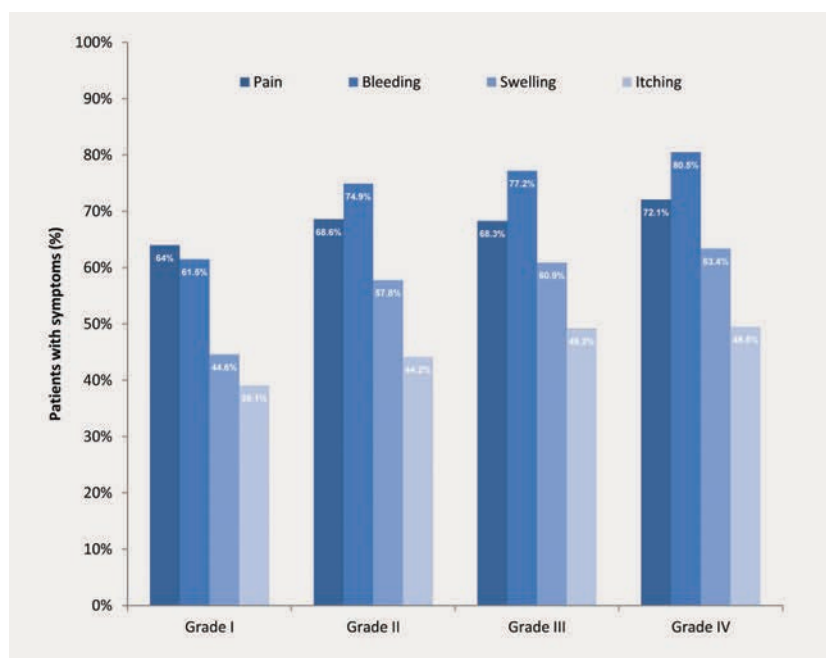


Figure 2. Frequency of hemorrhoidal complaints according to hemorrhoid grades.

	Hemorrhoid grade			
	Grade I n (%)	Grade II n (%)	Grade III n (%)	Grade IV n (%)
Belgium	102 (24.06%)	166 (39.15%)	137 (32.31%)	19 (4.48%)
India	417 (27.62%)	723 (47.88%)	320 (21.19%)	50 (3.31%)
Mexico	245 (52.69%)	163 (35.05%)	51 (10.97%)	6 (1.29%)
Pakistan	185 (29.46%)	234 (37.26%)	170 (27.07%)	39 (6.21%)
Russia	613 (25.95%)	1047 (44.33%)	563 (23.84%)	139 (5.88%)
Slovenia	36 (27.91%)	39 (30.23%)	35 (27.13%)	19 (14.73%)
Thailand	33 (33.33%)	26 (26.26%)	25 (25.25%)	15 (15.15%)
Total	1631 (29.04%)	2398 (42.69%)	1301 (23.16%)	287 (5.11%)

Table III. Repartition of the grades of hemorrhoidal disease by country.

Results

The first results of the CHORUS study were presented at the 19th Annual Meeting of the European Venous Forum in Athens, Greece on June 28-30, 2018 by Dr Sheikh.¹⁵ The program enrolled 9381 patients, of whom 5617 (men, 54%; women, 46%) had complete data for the main variables and were the focus of the results that were reported. The mean age was 45±14 years and the mean body mass index was 26.7±5 kg/m² (Table I; Figure 1). Russia and India had the highest number of patients in the study with 42% and 27%, respectively (Table II). There were no sex differences in the repartition of the patient groups except in Pakistan and India, where 78% and 64%, respectively, were men, which may be a result of cultural habits. The most frequently encountered complaints were pain (67%), bleeding (72%), swelling (55%), itching (44%), and prolapse (36%) (Figure 2).

In almost all patients (98.5%) consulting spontaneously for hemorrhoids, the presence of hemorrhoids was confirmed by the physician as grades I, II, III, and IV in 29%, 43%, 23%, and 5% of the patients, respectively (Table III). Exceptionally for Mexico, the patients with grade I hemorrhoids represented 53% of the population. According to the pooled analysis, 56% of the patients had recurrent hemorrhoids (Table IV). The highest rate of recurrent hemorrhoids occurred in Pakistan (74%), Mexico (71%), and Belgium (65%). Among the patients consulting for hemorrhoids, 51% presented with chronic venous disease at the same time (19% were C_{0s}, 29% C₁, 25% C₂, 16% C₃, and 10% C₄-C₆ according to the CEAP classification) (Figure 3). The concomitance of chronic venous disease in patients with hemorrhoids in different geographical areas were 77% in Mexico, 61% in Russia, 44% in Belgium, 43% in Slovenia, 40% in Pakistan, 38% in India, and 24% in Thailand (Table V).

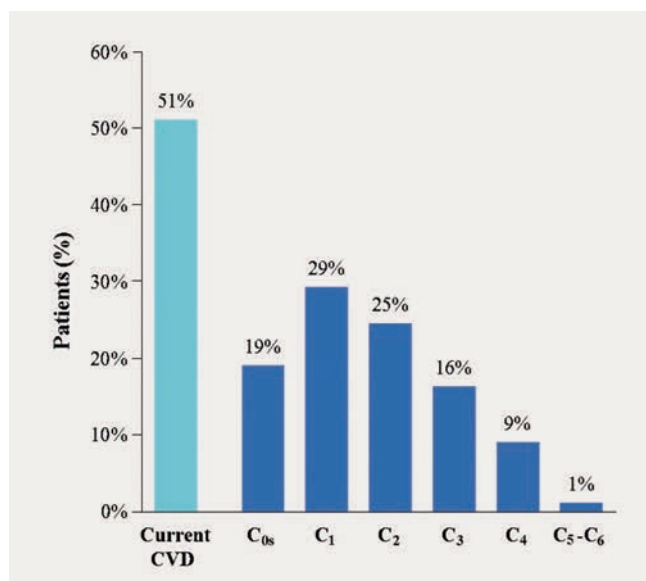


Figure 3. Hemorrhoidal disease and chronic venous disease concomitance.

	Hemorrhoid disease recurrence	
	No n (%)	Yes n (%)
Belgium	149 (35.14%)	275 (64.86%)
India	625 (41.39%)	885 (58.61%)
Mexico	134 (28.82%)	331 (71.18%)
Pakistan	162 (25.80%)	46 (74.20%)
Russia	1256 (53.18%)	1106 (46.82%)
Slovenia	58 (44.96%)	71 (55.04%)
Thailand	57 (57.58%)	42 (42.42%)
Total	2441 (43.46%)	3176 (56.54%)

Table IV. Repartition of hemorrhoidal disease recurrence by country.

	Concomitant chronic venous disease	
	No n (%)	Yes n (%)
Belgium	236 (55.66%)	188 (44.34%)
India	939 (62.19%)	571 (37.81%)
Mexico	107 (23.01%)	358 (76.99%)
Pakistan	379 (60.35%)	249 (39.65%)
Russia	930 (39.37%)	1432 (60.63%)
Slovenia	73 (56.59%)	56 (43.41%)
Thailand	75 (75.76%)	24 (24.24%)
Total	2739 (48.76%)	2878 (51.24%)

Table V. Repartition of the concomitant chronic venous disease in patients with hemorrhoidal disease by country.

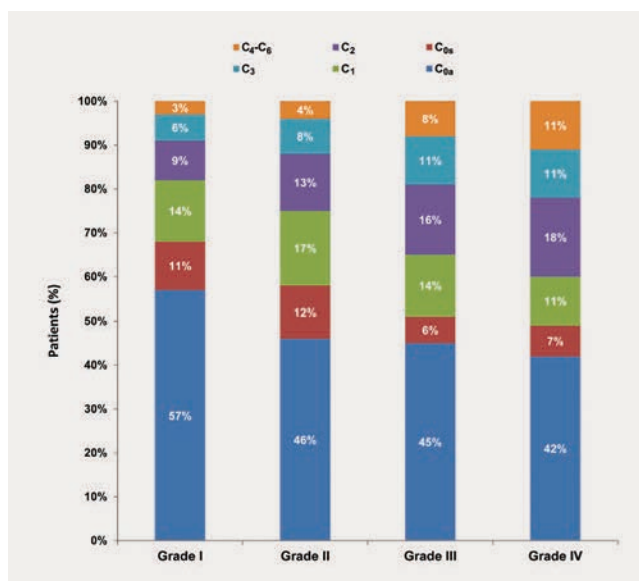


Figure 4. Influence of the severity of hemorrhoidal disease on chronic venous disease stages.

In patients with grades I, II, III, and IV hemorrhoidal disease, the proportion of patients with chronic venous disease was 43%, 54%, 55%, and 58%, respectively, with a clear increase with the severity of hemorrhoidal disease in the pooled analysis (Figure 4, page 95). In patients with recurrent hemorrhoidal disease, the proportion of patients with chronic venous disease was significantly higher than in those with no recurrent hemorrhoidal disease (58% vs 43%, respectively), suggesting a link between the recurrence of hemorrhoids and the presence of concomitant venous leg problems ($P < 0.0001$).

The pooled analysis showed that 99% of the patients were prescribed at least one treatment, of which 94% were prescribed a venoactive drug (93% received micronized purified flavonoid fraction [MPFF]), 71% a high fiber diet, 70% a topical cream, 26% painkillers, and 23% surgery (Figure 5). The choice of using a venoactive drug primarily in the management of hemorrhoids was common for all countries; nevertheless, there were differences regarding the implementation of other treatments.

Dietary fibers were mainly used in Pakistan, India, and Mexico, whereas the topical treatments were mostly preferred in Russia. The use of analgesics was very high in Pakistan (56%) when compared with other countries (2% to 35%). In Belgium and Slovenia, surgical treatments were performed in 56% and 43%, respectively, of the patients with hemorrhoids (Figure 6).

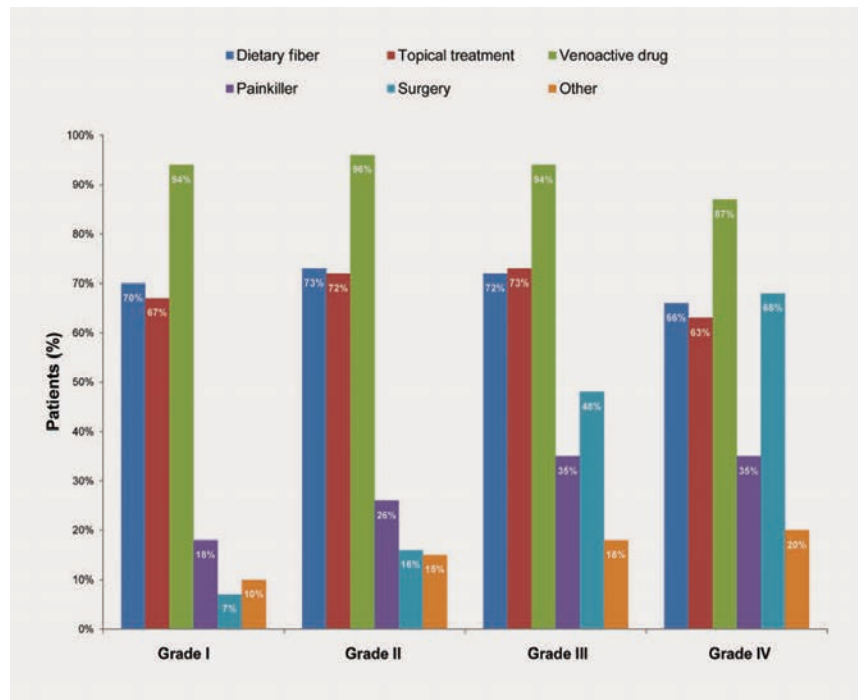


Figure 5. Prescribed treatments.

Conclusion

Hemorrhoidal disease is known to affect large numbers of individuals worldwide. CHORUS confirmed that hemorrhoidal disease is a condition that affects both sexes across a wide spectrum of age groups, but with peak presentation in those aged 35 to 50 years. CHORUS provides an overview of patient characteristics and hemorrhoidal management in clinical practice from different geographical zones worldwide, while demonstrating, for the first time, an association between hemorrhoids and chronic venous disease. Just over half of the subjects (51.2%) with hemorrhoidal complaints also presented with signs and/or symptoms of chronic venous disease, the majority (73.2%) with a CEAP classification of C_{0s} to C₂, and a greater proportion of patients with current venous leg problems had more severe grades of hemorrhoids. The proportion of patients with chronic venous disease increased with the severity and the recurrence of hemorrhoidal disease, which highlighted the importance of investigating the signs of chronic venous disease in this patient population during daily practice.

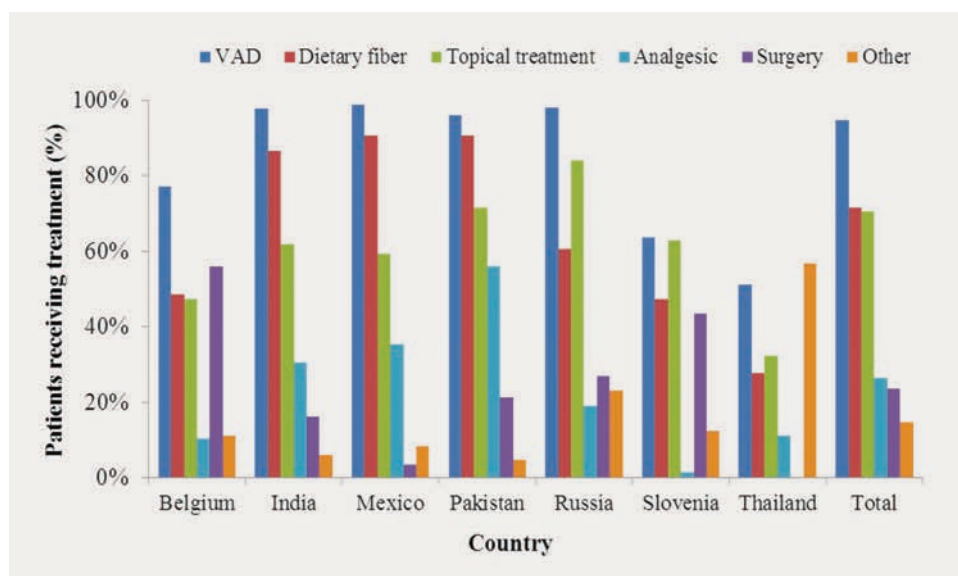


Figure 6. Type of treatment by country.

a venoactive drug, predominantly MPFF. MPFF is an effective treatment for acute hemorrhoidal attacks and it has been shown to serve as an effective adjuvant to surgery or other procedures in the management of hemorrhoidal disease.¹⁶ At the same time, MPFF is strongly recommended by the recent international chronic venous disease guidelines for the relief of chronic venous disease symptoms and signs at all CEAP stages, as well as for healing of venous ulcers as an adjunct treatment and for improving quality of life.¹⁷ Due to its beneficial effects on venous tone, the inflammatory processes,

and microcirculatory permeability, MPFF is able to address the underlying causes of both symptomatic hemorrhoids and chronic venous disease. Given that at least half of the patients in the current survey were suffering from both hemorrhoidal disease and chronic venous disease, the use of early pharmacological treatment with a venoactive agent, particularly with MPFF in this case, may play a significant role in preventing or slowing the development and recurrence of the signs and symptoms of both hemorrhoidal disease and chronic venous disease. ■

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