« At the crossroads of venous insufficiency and hemorrhoidal disease: Daflon 500 mg – Répercussions of venous insufficiency on everyday life »

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ABSTRACT

A research program has been developed to define an evaluation tool capable of assessing the impact of venous insufficiency and its treatments on the patient's everyday life. The methodology is described in the first part of this paper, followed by the results of the first phase of the research program, based on two surveys : a « qualitative » survey in a population of severely affected patients and a « quantitative » survey in a population of 150 patients.

INTRODUCTION

The quality of the dialogue between health authorities and the drug industry can be altered by the incompatibility of the arguments proposed. For example, health authorities very frequently stress the discrepancy between the rate of increase of health expenditure and the progress obtained in terms of prolonged life expectancy, while drug companies rightly emphasize that the current objectives of modern medicine consist of attenuating the consequences of disease and improving quality of life. The impossibility of demonstrating a positive action on health systems is due to the fact that the measuring instrument used is inappropriate and new tools need to be developed. Criteria other than physiological parameters must be defined to assess the subjective state of health and its improvement.

To our knowledge, the impact of the manifestations of venous insufficiency on the patient's everyday life has never been evaluated, despite the fact that this disease affects approximately one of every three adults. A research program has been developed to define an evaluation tool capable of assessing the repercussions of the course of the disease and the treatments prescribed on the patient's everyday life.

The methodology used is described in the first part of this paper, followed by the results of the first phase of the research program, based on two surveys : a « qualitative » survey in a population of severely affected patients and a « quantitative » survey in a population of 150 patients.

1. METHODS

1.1 Data Collection

1.1.1 Qualitative Survey

To ensure that the items of the questionnaire actually reflected the impact of venous insufficiency on hte patient's everyday life, twenty detailed, semistructured interviews, lasting one to one and a half hours, were conducted on 7 men and 13 women suffering from venous insufficiency in three regions with very different climatic and socioeconomic conditions : Paris, Strasbourg and Nice.

The interview guide was designed on the basis of preliminary information obtained from a review of the literature and by previous interviews with four expert clinicians (angiologists, dermatologists and phlebologists) and three general practitioners.

- *Dimensions of the repercussions*

Analysis of the content of these detailed interviews, presented in the second part of this report devoted to the results, demonstrated that none of the available indicators were able to integrate all

the dimensions of the repercussions of venous insufficiency. For example, SIP accurately assessed the repercussions of the disease in terms of mobility, sleep and restriction of leisure activities, in contrast with Ware's SF-36. However, in contrast to this latter test, it failed to evaluate the positive aspect of health, in particular, vitality and perception of the state of health. Obviously, none of the three indicators, SIP, NHP, of SF-36 was able to investigate the specific symptoms and signs of the disease.

- *Choice of descriptors*

For those dimensions effectively investigated by means of the existing indicators , the choice of items and their scoring were found to poorly reflect the specific impairments associated with venous disease. For example, the concepts of « standing about », particularly unpleasant for the patient, and « prolonged sitting » were never revealed. Moreover, the responses were very often expressed in the form « symptom present of absent », but such a dichotomy is unable to assess the degree of severity of the disease and its course.

This finding therefore confirmed the need to construct a specific indicator. Five dimensions were provisionally defined on the basis of this preliminary survey : symptoms and signs, their funcional repercussions, their psychological repercussions, their social consequences, and the impression of being in good or poor health. Forty-five descriptive items of the repercussions of the disease in relation to these dimensions were formulated on the basis of the exact words used by the patients, thereby constituting an « initial » questionnaire, used in the subsequent quantitative survey.

- *Calibration of the items*

Two types of questions were asked for each items : the first concerned the presence and severity of the impairment experienced and the second concerned the relative importance attributed to this item by the patient. This second score is essential to define on what basis the patients interviewed principally base their assessment of their quality of life. Lickert's 5-point scales were used in both cases.

1.1.2 Quantitative survey

This quantitative survey was conducted in a sample of 150 patients with venous insufficiency, with a dual objective :

- To select the most significant items
- To evaluate the ability of these items to measure differences as a function of the severity of the disease.

- *Stratification of the population*

It is obvious that, at this stage of the research, it would be unreasonable to try to measure the repercussions of the manifestations of venous insufficiency on the quality of life of the French population concerned. This would require a previously validated measuring instrument, which is only at the stage of construction and experimentation and the subject of the present investigation. Even when this prerequisite will have been satisfied, it will be essential to verify the representative nature of the sample in terms of sociodemographic data as well as the degree of severity of the disease.

No credible epidemiologic data concerning the prevalence of symptomatic venous insufficiency are available at the present time ; the only data concern varicose veins, lesions that are not systematically related and for which different treatment modalities may be applied. Not even a

recognized evaluation tool for the severity of these essentially functional manifestations is yet available : the presence of « objective » clinical signs always takes precedence over the description of « symptoms », which can be defined only by the patient. The Basel study[1] clearly illustrates this tendency. Although it provides a classification of the severity of varicose veins, now considered to be the reference, it also proposes the classification of chronic venous insufficiency. This classification relies on photographic observation of the signs present (dilated veins in the ankle region, pigmentation changes) rather than in terms of the functional symptoms reported by the patients in the interview, although stressing the « surprising », very high reproductibility of the results obtained.

The Basel study distinguishes the following three stages :

- ✓ Stage I : dilated subcutaneous veins, « corona phlebitica »
- ✓ Stage II : pigmentation changes with or without « corona phlebitica »
- ✓ Stage III : presence of open or treated ulcers.

In view of the low prevalence of open or treated ulcers and III, according to this definition, the very great majority of cases of chronic venous insufficiency are therefore described as being « minor », regardless of the functional complaints reported by the patients, of which the Swiss study attempts to measure not the severity, but principally their presence or absence.

In this survey, this stratification on the basis of the severity of the lesions was based on the description of the symptoms by the patient, their presence, their frequency, and/or their severity.

- *Recruitment of the study population*

The sociodemographic composition of the study population corresponded to that of the TMO[2] « heavy legs » study in terms of sex, age, and occupation.

A second aspect was the definition of the manifestations of venous insufficiency justifying inclusion of the patient. As in the « heavy legs » survey, inclusion was exclusively based on declarations of signs (varicosities and varicose veins, erythema, and color change) and/or symptoms (heavy legs, swelling, cramps, pain) in the absence of any interference by health professionals. In order to define as clearly as possible the range of manifestations, the description of the signs and symptoms was more detailed than that used in the TMO study, particularly in relation to varicose disorders. This may explain why the frequency of varicose veins in our study population was very much higher that that reported in the TMO study.

Lastly, the distribution of the sample according to the severity of the manifestations does not claim to be representative of the overall population of venous insufficiency patients for the reasons indicated above : our objective was to constitute groups that were sufficiently large to allow the observation of statistically significant differences in severity of the manifestations ; this objective was achieved, as indicated by the results of the analysis.

1.2 Data Processing

The qualitative survey investigated all dimensions related to quality of life as completely as possible. The questionnaire based on this preliminary survey therefore included a much greater number of items than would be suitable for the final questionnaire designed for use in a clinical trial.

1.2.1 Method of selection of the items

The quantitative survey was designed to select the relevant items for the final questionnaire.
These items were selected to be able to subsequently combine the variables selected into a single easy-to-use score. Guyatt[3] recommended two methods for this selection :

- A « rustic » method : the frequency, the mean importance experienced by the patient, and the product of the two, calculated for each item of impairment, the variables being selected by retaining only those items with the highest value for the product of the frequency and mean importance of the impairment.
- Factorial analysis (its principles are presented below)

We combined these two methods to select our variables.

Step one : principal component analysis (PCA)
In our study, we used PCA to detect and eliminate the redundant variables and, after identifying the relevant variables, to group them according to their contribution to the various dimensions.
The first step of selection was performed by PCA On the descriptive variables of the severity of the impairment. We preferred to analyze « severity variables » rather than « importance variables » (ie, describing the importance attributed to the impairment by the subject) for two reasons. First, the overlap between the variables may be observed both in terms of the severity of the repercussions and the importance attributed to them. Second, PCA must be applied to observations with no missing data; analyzing the importance attributed to an impairment inevitably involves missing data, for subjects not experiencing a particular symptom or sign are not concerned by its relative importance.

Step two : elimination of redundant variables
PCA identified the redundant variables ; the choice of variables for the final questionnaire was based on a second step : the item adopted was that associated with the greatest variation of the product of the frequency and the importance in relation to the severity of venous disease.

Step three : final selection of items
Lastly, the third step consisted of retained only nonredundant or isolated items when their frequency × importance product varied significantly in relation to the severity of venous disease. This final selection was performed as the items are designed to evaluate changes according to the stage of the disease and would appear to be useful only when they very considerably according to various degrees of severity of the disease.

1.2.2 Verification of the capacity to measure changes

- Assessment of the severity of venous disease

In order to try to assess the severity of the disease, we selected symptoms and staging of the varicose disease based on the Basel classification :

Symptoms
The symptoms evaluated in the study were heavy legs, leg cramps, swelling (ankles, legs), and leg pain and its severity. In order to try to assess the repercussions of the venous disease on the patient’s every life, we used severity of pain as the indicator, after confirming that it was correlated with the other symptoms (cf. Results). The severity of pain was scored according to a five-point scale ranging from « no pain » to « very severe pain ». Owing to the limited sample size, we classified our patients into three groups :

- I : no pain
- II : mild or moderate pain
- III : severe or very severe pain.

Stage of varicose disease
The Basel Classification proposed by Widmer distinguishes five subgroups based onb the presence of varicosities (small venules or burst vessels), varices of the secondary veins, or varices of the principal veins :
1 : no signs
2 : varicosities only
3 : varices of secondary veins only
4 : varicosities and varices of secondary veins
5 : varices of principal veins
We adopted this classification in our study. Hoever, as Widmer demonstrated the difficulty of establishing the diagnosis of varices of the secondary veins or varicosities and the virtual absence of complications associated with these two types of varices, we combined subgroups 2 and 3 and subgroups 4 and 5, resulting in the simplified classification :

- I : no signs
- II : varicosities only or varices of secondary veinis only
- III : varicosities and varices of secondary veins and/or varices of principal veins.

1.2.3 Verification of the « sensitivity » of the items

The items selected were combined into a single score based on equal weighting. To ensure that this score was « sensitive », ie, able to measure a change in the quality of life as a function of the severity of the disease, we tested whether this score differed significantly according to the various severity groups.

1.3 Statistical Analysis

The Chi^2 test was used to test the correlation between the various symptoms of the disease.

We used analysis of variance of their « state of health » according to the severity of the disease.

The Kruskall-Wallis nonparametric test was used to test whether the « single score » was significantly different accroding to the severity of the disease. This test was selected since it can be applied without making iany hypothesis concerning the distribution of this score. It consisted of classifying the scores according to their rank, then comparing the sum of the ranks according to the severity of the disease.

2. RESULTS

2.1 Description of the Study Population

2.1.1 Sociodemographic characteristics

One hundred fifty patients were recruited for this study with an equal distribution among Paris, Bordeaux and Rennes.

It will be recalled that the study population was structured for age, sex and occupation on the basis of the distribution observed in the TMO institute « heavy legs » survey :

- Female predominated (72%)
- The mean age of the patients was 47.5 ± 17.4 years with a minimum age of eighteen years and a maximum age of eighty-five years
- Working subjects predominated (61%).

Among the 91 working subjects, 18% were shopkeeper/sale assistants/hairdressers, 22% were secretaries of office employees and 11% were workers.
Fifty-one (56%) of the working subjects has an occupation that involved prolonged standing and 19 (21%) has an occupation requiring prolonged sitting. Occupations requiring prolonged standing concerned 94% of the shopkeepers/sales assistants/hairdressers and 70% of the workers, while the sitting position concerned 60% of the secretaries.

The distribution of the study population according to age, sex, and occupation is presented in Table I.

Table I : Characteristics of the Study Population

	Variables	**n**	**%**
Sex	Male	42	28
	Female	108	72
Occupation	Yes	91	61
	No	59	39
Type of Occupation	Shopkeepers/sales/hairdressers	16	
	Secretaries/office employees	20	
	Sedentary executives	6	
	Travelling salespeople	4	
	Workers	10	
	Restaurant employers/employees	2	
	Cleaners/domestic employees	8	
	Teachers	5	
	Nurses/dentists	4	
	Military	2	
	Musicians/artists	3	
	Others	11	
	Mean ± SD [min-max]	47.5 ± 17.4 [18-85]	

2.1.2 Presence and frequency of symptoms and signs of venous insufficiency

- Varicose disease

The presence or absence of clinical signs of venous insufficiency was assessed by the patient. About 65% of the patients reported more or less marked « small varicosities » (small venules or burst vessels).

Fifty-seven of the patients reported the existence of varices of secondary veins and 30% reported varices of principal veins (Cf. Table II).

Table II : Presence and More or Less Obvious Nature of the Various Forms of Varicosities Reported

Type of Varices	Sample Size	More or Less Obvious*		
Varicosities	150	1	2	3
Varices of secondary veins	150	64	54	32
Varices of secondary veins	150	106	22	22

** 1: absent, 2: present, but not obvious, 3 : present and very obvious*

Regrouping of the patients according to the severity of varicose disease, on the basis of the Basel study simplified classification, gave the following results :

- 21 patients with stage I disease, ie, no signs of varicose veins ; this group was composed of 5 men and 16 women with a mean age of 40.3 ± 21.3 years.
- 52 patients with stage II disease, ie, with varicosities only or varices of secondary veins only ; these patients had a mean age of 48.6 ± 17.4 years.
- 77 patients with stage III disease, ie, with varicosities and varices of secondary veins and/or varices of principal veins. The mean age in this group was similar to that of group II : 48.4 ± 16 years.

No significant age difference was observed between stages II and III in our study population. This result is in obvious contradiction with the results published in the Basel study, in which an almost linear relationship was observed between age and the stages of severity of the varicose veins, which may be explained by the different methodology adopted in the two studies. The technique used for the detection and characterization of the varicose veins in the Basel study was based on photographic documentation and a medical opinion, whereas in our survey, focused on the detection of functional disorders, it was based on the patient's declarations. It is not surprising, therefore, that this self-diagnosis of a clinical sign was less reliable. Many studies have demonstrated an inverse correlation between the physician's assessments of quality of life and the patient's own evaluation. The information asymetry with regard to clinical signs can be attributed to the patient : « the doctor knows how to interpret the signs, while the patient does not ». On the other hand, the asymetry in relation to the physical and psychological repercussions of the disease occurs in the other direction : only the patient has a clear perception of his or her symptoms and impairments.

Note also that the Basel study was based on a representative sample of the working population, with or without subjective complaints related to venous insufficiency, whereas our survey concerned only patients suffering from symptoms of venous insufficiency, whether or not they were working.

- Functional symptoms

Ninety-three percent of patients interviewed complained of varying degrees of heaviness of the legs, 65% reported swollen ankles, 67% suffered from cramps and 70% experienced pain in the legs (Table III).

Of the patients complaining of painful legs, 36 patients (24% of the study population reported severe of very severe pain (Table IV).

Table III : Frequency Distribution of the Symptoms

Symptoms	Sample Size	Frequency*				
		1	2	3	4	5
		n	n	n	n	n
Heavy legs	150	10	34	53	34	19
Swollen legs	150	53	24	31	33	9
Leg cramps	150	49	27	48	20	6
Painful legs	150	45	16	45	30	14

Table IV : Distribution of the Population According to the Severity of the Pain

Symptoms	Sample Size	Severity*				
		1	2	3	4	5
		n	n	n	n	n
Painful legs	150	45	21	48	25	11

** 1: no pain, 2: mild pains, 3 : moderate pain, 4 : severe pain, 5 : very severe pain*

2.2 Choice of the Criterion of Severity of the Venous Disorders

In order to define the criterion that most accurately described the severity of the symptoms we investigated possible correlations between the varicose disease or the severity of the pain and, first, the functional complaints (heaviness, cramps, swelling) and, second, two other variables reflecting the patient's own perception of his or her state of health. The first analysis investigated the subject's reactions toward venous insufficiency, « source of discomfort » or « real disease », while the second quantified the overall assessment of the state of health on a visual analogue scale from 0 to 100 (Table V).

Although none of the symptoms ware correlated with the varicose disease, 2 of 3 symptoms were correlated with the severity of pain :

- heavy legs ($P < 0.001$)
- cramps ($P < 0.01$)

Swollen ankles was not correlated with pain ($P = 0.11$, NS).

As illustrated in Table VI, the subjects who considered their venous symptoms to be a real disease were significantly ($P = 0.02$) more numerous among those subjects suffering from severe pain (stage III). In contrast, the degree of varicosity, according to our definition, did not modify the subjects'attitude toward venous insufficiency.

The subject's overall assessment of his or her state of health and decreased significantly according to the severity of pain ($P < 0.001$) but did not vary significantly in relation to the varicose disease (Table VII) . In the rest of the study, we used the severity of the pain to evaluate the severity of the venous disease, for the following reasons :

- The patient's symptoms and perception of his or her state of health were correlated with the intensity of leg pain.
- The subject's own assessment of a symptom appeared to be more reliable than his or her assessment of varicose disease, corresponding to clinical signs that can be accurately evaluated only by the physician.
- Lastly, the existence of a correlation between severity of the functional disorders and severity of the varicose disease is far from being demonstrated.

Table V : Distribution of the Patients According to the Type of Symptom, in Relation to the Stage of Varicose Disease and the Severity of Pain

Symptoms	**Varicose Disease**			**Severity of Pain**		
	I	II	III	I	II	III
	n	n	n	n	n	n
Heavy legs						
- Never	1	5	4	8	2	0
- Rarely	5	13	16	14	16	4
- Fairly often	9	17	27	15	30	8
- Regularly	6	11	17	8	14	12
- All the time or almost	0	6	13	0	7	12
- Total sample size	21	52	77	45	69	36*
Swollen legs						
- Never	8	19	26	19	24	10
- Rarely	3	10	11	8	15	1
- Fairly often	4	11	16	9	13	9
- Regularly	6	8	19	9	14	10
- All the time or almost	0	4	5	0	3	6
- Total sample size	21	52	77	45	69	36
Leg cramps						
- Never	7	18	24	14	27	8
- Rarely	4	8	15	11	10	6
- Fairly often	7	20	21	16	23	9
- Regularly	2	5	13	3	8	9
- All the time or almost	1	1	4	1	1	4
- Total sample size	21	52	77	45	69	36**

** $p < 0.001$ ** $p < 0.01$*

2.3 Selection of the items

2.3.1 Principal component analysis

Principal component analysis was performed on the 38 items describing the impairment experienced in relation to various activities ; the impairment affecting work with withdrawn from the analysis, for it concerned only the subgroup of working patients. PCA identified ten groups of redundant or similar items containing a total of twenty-eight items and concerning :

- walking : « walking 100m », « walking more than 1 km », « walking quickly »

- standing about : « waiting in line », « standing for a long time », « travelling on public transport »
- sports activities : « playing sport, « swimming »
- nighttime activities : « going out in the evening », « having guests at home », « going to parties », « going to the theatre »
- domestic activities : « doing certain household chores », « doing the shopping »
- vitality : « tiring rapidly », « tired at the end of the day », « tired legs », « feeling of general tiredness »
- going up one or several flights of stairs
- aesthetic impairment : « ashaimed to show one's legs », « problems dressing »
- enjoyment of life : « dancing », « impression of being handicapped », « absence of pleasure »
- anxiety : « fear of bumping legs », « must take precautions », « avoiding explosure to the sun.

Within these groups, the ten variables presenting high frequency x importance scores and varying according to the severity of pain were selected. PCA also revealed ten isolated or independent variables, seven of which were selected on the basis of the same criteria, while the other three variables (« sitting for a long time », « other people don't understand », « it can only get worse with age ») were aliminated because of the lack of variation of the frequency x importance product. Finally, the impairment experienced at work was reintegrated into the final questionnaire, which therefore included a total of eighteen variables.

Table VI : Distribution of the Venous Disorders by the Subject Accroding to the Severity of the Pain

Definition of the Venous Disorders	**Severity of the Pain**						
	I		II		III		
	n	%	n	%	n	%	Total
Source of discomfort	33	73	53	78	16	45	102
Disease	12	27	15	22	20	55	47
Total sample size	45	100	68	100	36	100	149

** $p < 0.001$*

Table VII : Subject's Overall Assessment of his or her State of Health According to the Stage of Varicose Disease and the Severity of the Pain

	I	II	III
	Mean ± SD	Mean ± SD	Mean ± SD
Varicose disease	63.4 ± 14.2	65.9 ± 19.9	62.4 ± 24.24
Severity of pain*	69.6 ± 19.4	66.9 ± 18.3	50.9 ± 24.2

** $p < 0.001$*

2.3.2 Grouping of the items by dimensions

The final eighteen items were submitted to another PCA in order to determine those items best able to explain the principal factors. PCA isolated four components whose specific values exceeded the threshold of 1 and accounted for 34%, 7.7%, 7.2% and 6.4% of the variance, respectively. All the items were positively correlated with the primary component, which was essentially physical and psychological. The second component was a vitality axis in which « playing sport » contrasted with « difficulty getting started in the morning ». The third axis essentially concerned irritability and the fourth axis only concerned esthetic aspects.

- Axis 1 :

Physical functioning
Going up several flights of stairs
Squatting/kneeling down
Standing for a long time
Walking quickly
Sleeping badly
Performing certain household tasks (ironing, cleaning floors or furniture, repairs)
Tiring rapidly
Psychological functioning
Feeling nervous/tense
Impression of being a dead weight
Impression of being handicapped
Always has to take precautions

- Axis 2 :

Vitality/energy
Interference with sports activities
Difficulty getting started in the morning

- Axis 3 :

Irratibility
Easily irritated

- Axis 4 :

Esthetic problem
Uncomfortable about showing one’s legs

- Other variables :

Interference with work
Going to parties/weddings
Car travel

2.4 Preliminary Verification of the Capacity to Assess Change

We combined these eighteen items selected into a single score. The Kruskall-Wallis test revealed a significant difference in the score as a function of the severity of pain : this score varied and increased as a function of pain ($P < 0.0001$) (Table VIII).

This score therefore appears to be able to measure the change in quality of life as a function of the severity of venous disease. This « sensitivity » needs to be confirmed by another study.

CONCLUSION

The semistructured interviews revealed the various dimensions of impairment. The descriptions of the items were based on the exact expressions used by the patients, which ensures the validity of the content of the first questionnaire used in the subsequent quantitative phase of the study. On the basis of the result of this second phase, principal component analysis confirmed the constructed validity of the tool.

The next steps in this research will be designed to confirm the ability of this tool to measure changes in the patient's condition by applying it repeatedly in two groups of patients : a « stable » group to verify its reproductibility and a group of subjects with a changing condition to confirm its sensitivity. The result of such a study, which could be conducted without a control group on a relatively small number of subjects, would establish an index of the capacity of this tool to measure a difference. The determination of the sample size required for a « quality of life » study could then be established on a rigorous basis.

REFERENCES

[1] Widmer LK, Stähelin HB (eds) : Peripheral venous disorders. Prevalence and socio-medical importance. Basel study III. Hans Huber Publishers, 1978.
[2] Etude « Jambes Lourdes ». Observatoire Santé. TMO Consultants, Paris, 1992.
[3] Guyatt GH : « Measuring disease specific quality of life ». Can Med Assoc J 1986, 136 ; 889.