Postpartum Varicose Veins: Supplementation with Pycnogenol or Elastic Compression—A 12-Month Follow-Up

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Abstract

This open registry aimed to evaluate the clinical evolution of postpartum varicose veins (VVs), in healthy women after the second pregnancy, how these veins regain shape and competence, and possible treatments. The registry included two groups of women: (1) those who used elastic compression stockings, and (2) who used an oral venotonic agent (Pycnogenol, 100 mg/d). A total of 12 evaluation targets were established. Minor symptoms were scored in an analogue scale line. A visual analogue scale line evaluated the overall satisfaction relative to elastic compression or Pycnogenol. Overall 133 women completed the registry evaluation with at least 3 months of follow-up. The resulting two registry groups were comparable. At 3 and 6 months in the Pycnogenol group the number of veins and incompetent sites were lower. At 6 months there were 13.3% of patients with edema in controls versus 3.2% in the Pycnogenol group. Spider veins decreased in Pycnogenol patients. Cramps and other minor symptoms were less common in the Pycnogenol group. In both groups there was a significant improvement at 6 months with better results in the Pycnogenol group. The need for treatment was limited with a decreased need for sclerotherapy, surgery, and conservative treatments in the Pycnogenol group. The overall satisfaction was higher among Pycnogenol patients, and compliance was optimal. Re-evaluation at 12 months indicated that the variations in VVs and spider vein clusters and the associated symptoms did not change. Most remodeling appeared to happen within 6 months after the pregnancy. It was concluded that the use of Pycnogenol improves signs/symptoms of postpartum VVs, and venous function and shape seem to return faster to prepartum, physiological pattern with its use.

Keywords

- varicose veins
- postpartum conditions
- edema
- women health
- compression stockings
- Pycnogenol
- supplement studies

Lower limb varicose veins (VVs) develop during the first pregnancy of some 30% of women who have no presence or history of VVs or thrombosis before pregnancy.[1–4] The number of VVs and the occurrence of new VV may increase with subsequent pregnancies.[3–6] The associated increased risk of superficial thrombosis and deep vein thrombosis (DVT) may be increasingly higher with repeated pregnancies but appears to be only partially associated with the development of VV that is a different problem than thrombosis.[1–7] The number of visible, primary VVs not associated with postthrombotic changes in the venous system that require medical attention and eventual treatments tend to increase with repeated pregnancies.[8–10]

In most healthy women, postpartum or "pregnancy" veins usually tend to disappear or reduce in size in the months following a pregnancy.[9–11] After 6 months most minor vein

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dilatations (visible at end pregnancy) may become almost invisible and clinically not relevant. However, in approximately 25% of women some VVs may be visible well after 6 months after the first pregnancy; and some patients, particularly those with symptoms such as edema, may need some form of management or ask for treatment within 12 months after delivery.[8,9]

If a postpartum VV is not reduced in size between 6 and 12 months after delivery, it is likely to remain and eventually progress.[1,9,10] "Pregnancy" VVs regain their original shape and competence, at least partially, particularly after the first pregnancy, in a period that varies between 3 and 6 months; and generally all or most improvements in vein size and visibility occur within 12 months of the end of pregnancy.[1–8] Rarely, pregnancy VVs may progress to chronic venous insufficiency (CVI), but in many women these veins are the first manifestation of varicosity that can eventually progress, if not properly managed, to CVI.

Hormonal aspects and hormonal pattern variations have important implications in dilatation and in determining the decreased venous wall tone during pregnancy.[8] However, hemodynamic factors (compression of veins of the lower abdomen) are of great significance as most postpartum VVs develop in the lower limbs while the hormonal alterations should affect all veins of the body.[1,8–11] Therefore, it is possible that hormonal more than hemodynamic factors (i.e., compression of the uterus on iliac veins) may be predominantly involved in the genesis of most "pregnancy" varicosities. The mechanisms of development of these veins are not completely clear and are likely multifactorial.[1,9,10] The disappearance of most veins after the end of the pregnancy may also be a consequence of hormonal changes in association with the improved hemodynamics at the level of intra-abdominal veins.[1]

This open registry was planned to evaluate the evolution of postpartum VVs in healthy women, after the second pregnancy, to observe how the VV may regain shape and competence, or may enlarge and remain visible and eventually produce clinical problems requiring treatment. The open registry study, organized as a supplement study,[12,13] included a group of women using elastic compression stockings as a control method and a group using an oral venotonic agent of a standardized French Pine bark extract (Pycnogenol, Horphag Research, Geneva, Switzerland).[14–25]

Materials and Methods

The management program was aimed at producing a faster regression of "pregnancy" VVs and spider vein clusters, also controlling associated signs and symptoms. Women were included between 4 and 8 weeks after delivery, within 3 months after they completed breastfeeding, or if they did not breastfeed their babies. They were included if the pregnancy had been uneventful, with a full term baby and no significant clinical problems reported during the pregnancy. Women were included after their second pregnancy, if the first pregnancy had been normal with a single, healthy, full term baby. Including women after the second pregnancy increased the possibility of evaluating a larger number of veins with larger dilatation and VV.

No women had a history of previous DVT or familiarity for DVT, and all blood tests were within the normal range at 3 months after delivery (when women were considered for inclusion). At least 2 years had passed from the first pregnancy before the second pregnancy had started. The new veins developing during pregnancy had first been noted between the third month and the end of the pregnancy. The body mass index (BMI) in these women was within normal values (< 25). No hormonal treatment had ever been used before pregnancy or was used in the 12 months of follow-up.

Women had a normal healthy life after pregnancy, and none started any contraceptive treatment before the sixth month after their last baby was born. No other clinical or metabolic condition was present in the inclusion period (within the third month after delivery).

Diagnostic Evaluation: Color Duplex

The venous system was evaluated according to well-defined methods[9–11] by an experienced angiologist or vascular surgeon with color duplex (Preirus, Hitachi, Japan). The main sapheno–femoral and external/posterior sapheno–popliteal junction were scanned and evaluated for competence with the patient standing. Also the long and short saphenous veins were scanned and perforating veins and incompetent varicose segments were scanned and photographically recorded on digital images. Ambulatory venous pressure (AVP)[1,9–11] was measured using a small (22 G) needle inserted in the distal long saphenous territory (foot) connected with a pressure transducer with a standard, 10 tiptoe, standing exercise. The AVP and the refilling time (RT, in seconds, as the time needed for the superficial venous system to refill at the end of the 10 tiptoe test) were recorded.

Both color duplex and AVP allowed the exclusion of subjects with more complex venous disease (i.e., arteriovenous communications or incompetence of the deep venous systems) as the study was exclusively focused on postpartum superficial vein incompetence. Any other vascular pathology was also excluded.

The main 12 evaluation targets, shown in ►**Table 1**, were the number of clinically important VVs (considering visible, incompetent veins with a length, on standing, of more than 4 cm), the points of major incompetence (reflux by duplex longer than 3 seconds on a compression-release maneuver), points of minor incompetence (reflux shorter than 3 seconds), and the presence of perimalleolar edema on prolonged standing in the evening (measured on an analogue scale line ranging from 0–5). Also, the presence of small, spider veins clusters, and leg cramps (considering the percentage of legs with the symptom) were considered. Other less important or common signs/symptoms were scored in a visual analogue scale line (VASL): heavier legs, pain on prolonged standing, restless legs, and bruises. Finally, the need (or patient's request) for treatment was considered: the need for sclerotherapy, surgery, and/or any medical or conservative treatment (including compression, pain killers, and anti-inflammatory agents) was recorded. A last item included a

Table 1 The main 12 clinical evaluation target items

Study targets	Evaluation
1. Average number of varicose veins (length > 4 cm)	Visual (number), photo
2. Points of major incompetence	Ultrasound (number)
3. Points of minor incompetence	Ultrasound (number)
4. Perimalleolar edema (0–5)	Visual + ASL
5. Spider veins clusters (average number in two legs)	Visual (number)
6. Cramps	Percentage of limbs with cramps
7. Occurrence of minor signs/symptoms (heavy leg, pain on standing, restless leg, small bruises)	ASL 0–5
8. Need for sclerotherapy (at 6 mo)	Clinical
9. Need for surgery	Clinical
10. Need for compression	Clinical
11. Need for medical treatment	Clinical
12. Overall satisfaction	VASL 0–10

Abbreviations: ASL, analogue scale line; mo, months; VASL, visual analogue scale line.

VASL (range 0–10) to evaluate the overall satisfaction relative to the two proposed control methods: elastic compression and Pycnogenol.

In these subjects the need for treatment and the request for treatment are individualized (i.e., if patients plan to have another pregnancy soon it may be suggested to postpone surgery).

Supplement Studies

Supplement studies[12,13] aim to define the field of activity of supplements and possible preventive applications. The best field of application for supplements is preclinical, borderline applications, or the supplementary management of risk conditions. Supplements—unless there are specific claims—are not generally used for treatment of signs/symptoms or clinical conditions. Generally, the aim of supplement studies is to produce supplementary data to be compared with "background" historical data (i.e., based on the best available management for comparable subjects) or to other management plans.[1,12]

In this study, supplementation with Pycnogenol was used according to the following rules:

(a) Supplementation was suggested to the evaluation subjects. The supplement was not prescribed and was suggested as an option to possibly improve the management of the condition.
(b) The supplementation was used in association with what was considered at the time the "standard or best-management/care" available for that condition according to international guidelines.
(c) The use of Pycnogenol should not have interfered with other treatments or preventive measures.
(d) The periods of follow-up were considered variable, possibly between the 3rd and 6th months after pregnancy and around 30 months.
(e) The type of evaluation was a registry.
(f) The supplement was available in the market and voluntarily acquired by the registry subjects. A quantity of product was made freely available for underprivileged subjects.

Characteristics of the Study

This study was basically a small-scale, independent, pilot registry study; Pycnogenol use was suggested, not prescribed. There was no defined group allocation or randomization organized by the investigators. Subjects decided on the basis of the preliminary briefing the group they would join. No placebo was used. The evaluation of the compliance concerning the use of the supplement was a significant value indicating how many subjects were willing to use the product. Patients were fully informed about treatment with either the supplement or with elastic compression stockings. A possible placebo effect was also explained and considered. Results were analyzed after a period of study of at least 3 months. No prescription or tests through the National Health Service were made. The analysis of data was managed by a group of external reviewers, not in contact with the registry subjects. Commercial sponsorship from the producers of the tested supplement was not available.

Pycnogenol in tablet form was used at a dosage of two 50 mg tablets daily for an average of 6 months. After 6 months all subjects using Pycnogenol decided to carry on with the supplement up to 12 months. Pycnogenol is a standardized extract from a French pine bark used in the recent past for several vein studies.[14–26] It has been shown that 100 mg of Pycnogenol may have better effects of 1 to 1.5 g of a commercial preparation of diosmin and esperidin.[24] Pycnogenol is very effective in acute models of venous edema[21,22] with a selective action of lower limb swelling and edema. Pycnogenol may also improve the healing of venous ulcers in severe models of CVI[15]; it is very effective in severe models of CVI as observed after a deep venous thrombosis in postthrombotic limbs[16] as seen in a recent study.

Elastic compression is effective in controlling edema and swelling and improving the tone of dilated or VVs.[27–31] Chronic compression may produce an improvement in vein wall function and reactivity and basically in the dynamic tone of the veins[31] restoring, at least partially, the original tone. Below-knee, medium-compression (Sigvaris Management AG, Winterthur, Switzerland), stockings were suggested and used as the standard compression in the months following pregnancy. These stockings have a mild-to-moderate compression (~22 mm Hg at the ankle) and are reasonably well tolerated in our climate, particularly in warmer months.

Thermography Patterns

Ultrafast thermography is made with the patient standing after 30 minutes resting and acclimatization in a room at

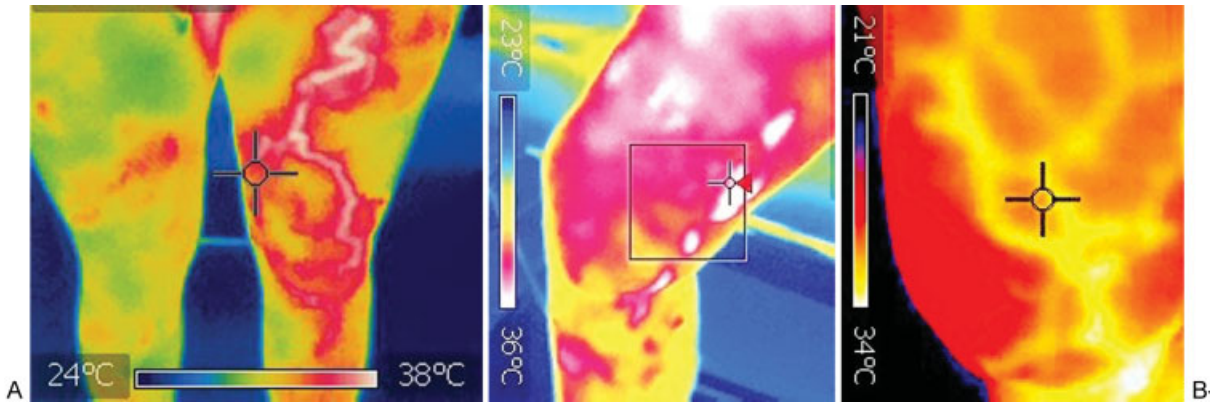

Fig. 1 Thermograms of three different patterns of postpartum varicose veins. (A) Diffuse pattern with small veins (anterior, accessory safenous system). (B) Dilatation of major vein trunks (long saphenous vein) associated with incompetence of the sapheno-femora junction. (C) Diffuse, extra-anatomical patterns, minor (< 2 mm in diameter) veins. All these veins, in these three cases, completely disappeared at 6 months.

standard temperature (22°C). Thermography patterns (►**Fig. 1**) were analyzed evaluating[32–37] the limbs with a FLIR (T440) as follows:

(a) The extension of higher temperature areas corresponding to the defined temperature of the VVs as observed in the standing leg image; and
(b) The number of major vein trunks visible at the internal (anterior surface of the leg and at the external–posterior leg surface).

Statistics

At least 25 subjects in each group (compression or Pycnogenol) were considered necessary to evaluate differences at 6 months in the registry, on the basis of observations from previous studies. The analysis of variance was used to compare the prevalence, progression, or regression of the VVs and spider veins clusters in the two groups. A SigmaPlot (Systat Software, Inc., San Jose, CA) software was used to perform all statistical analyses. All measurements were considered nonparametric and differences were evaluated with nonparametric tests (Mann-Whitney).[38,39] A visual analogue scale line according to Maxwell was used to evaluate nonquantifiable items (i.e., overall satisfaction, symptoms).[38]

Results

A group of 222 women was screened for VVs within 3 months after pregnancy, and 165 were considered eligible for this registry on the basis of normal BMI (< 25), absence of clinical or metabolic problems, and logistical considerations and availability for study and follow-up; 133 women completed the registry evaluation (at least 3 months of follow-up). The dropouts were a consequence of logistical problems resulting in failure (or late return) to be present at the 3-month controls. No medical problems were observed.

The resulting two registry groups were comparable for age and clinical problems (►**Table 2**). Also, at inclusion, the 12 investigation items were comparable in their distribution and values (►**Table 3**).

The number of VVs (average of the two limbs) at 6 months, the sites of incompetence, edema, cramps, and the most common signs/symptoms (comparable at inclusion in the two groups) were significantly lower in both group as the veins regained their shape and the venous system returned, at least partially, to its prepartum condition. However, at 6 months the number of veins in the Pycnogenol group was significantly lower ($p < 0.05$). Also the number of points of major and minor incompetence (detected by color duplex with the patient standing) was significantly lower ($p < 0.05$). Perimalleolar edema was also significantly less common and less severe in Pycnogenol subjects ($p < 0.05$). At 6 months there were 13.3% of patients with edema in controls versus 3.2% (one patient) in the Pycnogenol group ($p < 0.05$). The actual number of patients with edema is also shown in ►**Table 3**. The clusters of spider veins visible after pregnancy did not significantly change in control subjects but were significantly decreased in subjects using Pycnogenol ($p < 0.05$). Also the difference in leg cramps was significantly lower in the Pycnogenol group (4.6 vs. 12.5% in controls; $p < 0.05$).

Minor Signs/Symptoms

Minor signs or symptoms (particularly minor pain or discomfort on prolonged standing) were all significantly lower in the Pycnogenol group ($p < 0.05$). In both groups the trend indicated a significant improvement at 6 months.

The need for treatment in a nonthreatening condition such as postpartum VVs and VV in general is a complex negotiation between caregiver and patient. Young women tend to have a low level of acceptance even for small VVs that do not constitute a clinical problem. The progressive disappearance of at least some of the veins within 6 to 9 months after delivery suggests a late and conservative approach to sclerotherapy—or minor selective surgery—to treat these veins.

Social and cultural factors are more important than clinical considerations in most patients. However, specifically considering that the subject population lived in a seaside place where most social interactions, particularly with children, happen on the beach, young women are particularly sensitive

Table 2 Demographics of the two registry groups

Total	Completing 6 mo	Completing 12 mo	Compression only	Pycnogenol + compression
165	133 (A)		69	64
		98 (B)	42	56
Age (A)			31.6; 3.5	31.15; 3.1
(B)			31.7; 2	31.22; 2.9

Abbreviation: mo, months.
Note: A, group completing 6 mo; B, group completing 12 mo. The 32 subjects not completing at least 6 mo and the 35 subjects not completing 12 mo had only logistic and time problems and had to withdraw from the study for nonmedical problems

to even minor, visible alterations such as varicosities and tend to require treatment. In the registry subjects the request for sclerotherapy or minor surgery was significantly greater in controls in comparison with Pycnogenol patients ($p < 0.05$). Medical and conservative management (all minor interventions) included anti-inflammatory agents, compression, painkillers on demand, and physiotherapy, all suggested by the patients' physician without any intervention from the registry evaluators.

Finally, the overall satisfaction for the treatment used in the postpartum months was significantly higher ($p < 0.022$) in the Pycnogenol group. This was also associated with the obvious lower tolerability of stockings in the warmer periods (May–September) in comparison with the oral treatment with Pycnogenol.

Ambulatory Venous Pressure Measurements

The values of AVP (both the end-pressure at the end of the 10 tiptoe exercise test and the refilling time) were comparable at inclusion. The test indicated an exclusive incompetence of the superficial venous system with prolonged refilling time (the normal value for refilling the venous system is lower than 14 seconds after the end of the exercise test). At 6 months, the average RT was improved but not significantly different between the two groups; however 58 out 64 Pycnogenol patients were over the normal limit of 14 seconds in comparison with 32 out of 69 patients in the compression group ($p < 0.05$).

Compliance

It was optimal with Pycnogenol (96% of the tablets used according to schedule). Tolerability was also optimal. No patient in the Pycnogenol group had to stop treatment, while 35 out of 69 subjects in the control group had to stop using the compression stockings or only used them irregularly.

Re-evaluation

Re-evaluation at 12 months indicated that the variations in dimension and distribution of VVs and spider vein clusters and the associated signs and symptoms did not show statistically significant changes after 6 months. It seems that most remodeling to the original shape and function happens within 6 months after the end of the pregnancy. Minor, less significant changes are visible in the following months. Obviously the need for treatments at 12 months is influenced by the treatments given after the sixth month and basically includes requests from nontreated subjects with a persisting problem requiring management; therefore this difference was not evaluated. A higher request of medical management for persisting symptoms was observed in patients not using Pycnogenol ($p < 0.05$). APV was not repeated at 12 months.

Discussion

Postpartum VV and the less hemodynamically significant minor spider veins are a common observation (in some 20–33% of healthy women) in the year after a pregnancy. The dilated or VVs tend to decrease in size after pregnancy and some may completely disappear. Therefore, treatment and management after one or more pregnancies should consider timing and several other factors including the clinical importance of VV. The possible risks for VV thrombosis or hemorrhage after traumas are indications of nonconservative treatments with sclerotherapy or surgical techniques.[40]

Generally, it is better to delay invasive treatments for a few months (up to 6–9 months) to avoid treating veins that may spontaneously regress. Postpartum VV tend, at least partially, to regain the normal functions and shapes as seen in several studies, in particular using compression. Effective elastic compression is an important aid to regain tone. Regaining tone and muscular functions, most dilated or VVs may regress to the almost original shape and size. However, there is an evidence that some of these veins may further enlarge with subsequent pregnancies.

For VVs most treatments are individualized. The management of postpartum VV, at the moment, is not defined and depends on a complex interaction between patients (young women that do not easily tolerate even the appearance of VV, independently from their clinical value) and caregivers. It is also important to consider social and environmental conditions (i.e., in warmer climates and in warmer periods it is difficult to use elastic stockings with continuity).

Pycnogenol has shown important, multiple actions in VVs and in CVI as seen in several prospective studies. The effect of Pycnogenol on signs and symptoms and particularly on VV-associated edema seems to be very significant in several clinical contexts. Controlling edema also effectively controls the evolution of signs and symptoms and the progression to CVI and to the more severe stages of venous insufficiency.

Table 3 Clinical target points

Study targets		Inclusion	6 mo	12 mo
1. Average number of varicose veins (length > 4 cm)	Controls	4.9; 1.9	2.12; 2.1	2.2; 2.3
	PY	4.6; 1.1	1.3; 1.2[a]	1.3; 1.1
2. Points of major incompetence	Controls	2.1; 0.3	1.3; 0.2	1.2; 1
	PY	2.1; 0.8	0.9; 0.7[a]	1.1; 0.8
3. Points of minor incompetence	Controls	2.6; 1.1	0.9; 0.4	0.9; 1
	PY	2.7; 1.2	0.67; 0.3[a]	0.7; 0.4
4. Perimalleolar edema (0–5)	Controls	2.4; 0.5	1.8; 0.3	1.7; 0.5
	PY	2.42; 0.6	0.5; 0.3[a]	1.66; 0.5
5. Spider veins clusters (average number in two legs)	Controls	2.13; 0.5	2.3; 0.4	2.2; 0.4
	PY	2.2; 0.7	1.6; 0.5[a]	1.5; 0.4
6. Cramps (% of patients)	Controls	31.8; 3.4 (22/69)	12.5; 3.1 (8/69)	6/69
	PY	36.2; 3 (25/69)	4.6; 2.1 (3/64)[a]	2/64
7. Signs/symptoms (VASL 0–5)				
Heavy leg	Controls	2.1; 0.7	2.4; 1.2	2.3; 1
	PY	2.2; 1	1.1; 0.6[a]	1; 0.6
Pain on standing	Controls	1.6; 1	1.5; 1.2	1.4; 0.9
	PY	1.5; 0.5	0.5; 0.3[a]	0.4; 0.2
Restless leg	Controls	1.9; 1.1	1.8; 1.1	1.6; 0.4
	PY	1.8; 0.8	1.1; 0.5[a]	1; 0–4
Bruises	Controls	1.8; 0.5	1.7; 1.1	1.5; 0.5
	PY	1.9; 1.1	1; 0.6[a]	0.9; 0.3
8. Need for sclerotherapy	Controls		13/69	6/69
	PY		3/64[a]	1/64
9. Need For surgery	Controls		8/69	2/69
	PY		3/64[a]	1/64
10.Need for compression	Controls	58/69	24/69	28/69
	PY	57/64	9/64[a]	7/69
11. Need for medical or conservative treatments	Controls	18/69	16/69	14/69
	PY	18/64	6/64[a]	3/64[a]
12. Overall satisfaction (VASL 0–10)	Controls	–	6.4; 1.3	6.3; 2.1
	PY	–	8.2; 0.4[a]	8.1; 1
13. Ambulatory venous pressure (refilling time) (normal > 14 s)	Controls	10.3; 2.3	13.4; 3.1[a]	–
	PY	10.4; 1.1	14.5; 1.2[a]	–
14 Thermo				
Veins area (cm^2)	Controls	14.28; 2.2	7.3; 2.1[a]	6; 1.2[a]
	PY	14.33; 2.1	4.1; 1.2[a]	3.3; 1.3[a]
Number of trunks	Controls	6.9; 2.4	4.2; 2[a]	4.3; 2.1
	PY	6.9; 2.4	2.1; 1.1[a]	1.8; 1.3[a]

Abbreviations: mo, months; PY, pycnogenol subjects; s, seconds; VASL, visual analogue scale line.
Note: Blank cells (–) show standard management.
[a]$p < 0.05$.

Supplementation with Pycnogenol is very safe, as seen in many studies; this natural supplement appears to help the venous system in regaining faster and more effectively the original, prepartum circulatory physiology. Management with oral Pycnogenol controls both the minor signs/symptoms associated with postpartum VV and more significant symptoms as, for instance, cramps as seen in specific studies and swelling.

Limitations of this study are in its *supplement-study*, *registry design* based on voluntary use of the supplement and on its limited number of patients. A formal and larger double blind study – including more severe cases - could offer a better evaluation and a more definite evaluation of the efficacy of Pycnogenol in this common condition, affecting a significant number of women.

Conclusion

The very common problem of postpartum VV should be considered with attention as it constitutes an interesting model of acute development of varicosities and a model for VV regression that may even suggest some possible solution to promote vein varicosity regression and a faster recovery. A complex interaction between hormonal and dynamic factor is involved in postpartum VV, and future investigative models for the evaluation of these veins should also consider the hormonal pattern evolution.

At the moment, considering these observations, Pycnogenol appears to be a safe, effective, natural solution improving vein recovery and the problems associated with vein dilatations and varicosity. This study is still in progress and includes patients with a follow-up of 2 years.

Conflict of Interest
There was no conflict of interest.

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