



L. Cristaldi

**SUMMARY**

Chronic Venous Insufficiency (CVI) is due to a state of prolonged venous hypertension in the skin and subcutaneous tissue, predominantly in the lower limbs; the bicuspid venous valves are responsible for directing blood from the superficial veins of the lower limbs to the heart via the deep venous system, from the bottom up, against the force of gravity. In CVI, these valves are unable to perform this task, so there is a reversal of the flow (reflux) of blood from the Deep Venous System to the Superficial Venous System, which creates a continuous pressure on the walls of the veins that can lead, in an advanced phase of the disease, to the wearing out and dilation of the wall itself (varices) and to the leakage of fluid into the surrounding tissues (oedema).

– The aim of this clinical study is to verify whether the combined treatment with PRM medicines and Guna Collagen Medical Devices can provide more important and lasting clinical results than the treatment with phlebotonic drugs.

**KEY WORDS**

CVI, MD-MUSCLE, MD-TISSUE, ANTI AGE VEIN, GUNA MATRIX, GUNA LIVER

# TREATMENT OF CHRONIC VENOUS INSUFFICIENCY WITH GUNA COLLAGEN MEDICAL DEVICES AND PRM THERAPY

**VENOUS DISEASE IN MEDICINE**

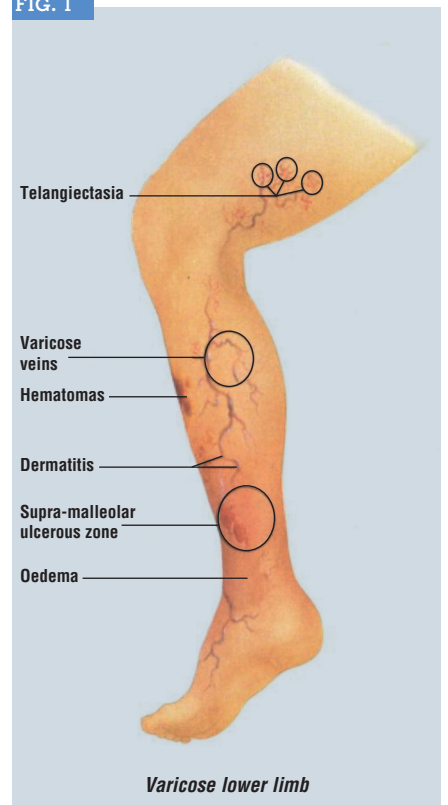
Venous disease is one of the oldest, most widespread medical conditions that affect humans. The first description of the disease appears in the Ebers Papyrus, considered to be the first Treatise on surgery and dating back to approximately 1550 BC (18<sup>th</sup> dynasty of Egypt).

– The first description of varicose vein surgery is attributed to Aulus Cornelio Celsus (1<sup>st</sup> century AD).

The only one of his four-part work *Artes* that has survived intact is *De Medicina*, in which the author gives a detailed discussion of Diet, Pharmacological Therapy and Surgery.

– In 1628, William Harvey (1578-1657), following the teachings of his master Gerolamo Fabrici d’Acquapendente (1533-1619), published the volume *Exercitatio Anatomica de Motu*

FIG. 1



**Truncal varicosis**

– Failure of the great saphenous vein and consequent varicosis of the branch in the anterior region of the leg.



**Reticular varicosis**



**Telangiectasia**

– Intracutaneous ectasia.



FIG. 2

*Cordis et Sanguinis in Animalibus*, in which he identified the structure and function of the venous valves and defined the physiological mechanisms of blood circulation.

**WHAT IS CVI**

**Chronic Venous Insufficiency (CVI)** is the result of prolonged venous hypertension in the skin and subcutaneous tissue, mainly affecting the lower limbs.

Under normal conditions, the venous bicuspid valves are responsible for directing blood upwards: from the superficial veins of the lower limbs towards the heart via the Deep Venous System, against the force of gravity.

– In CVI, these valves are unable to perform this task, so there is a reversal of the flow (reflux) of blood from the Deep Venous System to the Superficial Venous System, leading to **superficial venous hypertension**.

As a consequence, blood stagnates in the veins of the lower limbs and creates continuous pressure on their vein walls. In the advanced stages of the disease, CVI can lead to vein wall wear out and dilation (varicose veins) and to fluid leakage into the surrounding tissues (oedema), causing endothelial damage. CVI can be subdivided into:

– **organic**, caused by an actual disease of the veins (varicose veins, the re-

sults of venous thrombosis, etc.)  
 – **functional**, an expression of functional overload in the veins which, although normal, are stimulated to overwork (disorders of the sural pump due to problems with posture, lymphoedema, etc.) (FIG. 1).

**CVI – EPIDEMIOLOGY AND RISK FACTORS**

The prevalence of CVI is **10-15%** in adult men and **50-55%** in women.

– In the age range that goes up to 50-60 years old, the disease primarily affects females, while beyond this age-group there is no significant difference between men and women.

CVI is more common in individuals of Caucasian ethnicity due to a genetic predisposition associated with various environmental and social factors that lead to, or exacerbate, venous hypertension [(e.g. pregnancy, constipation, oral contraceptives, incorrect footwear, unsuitable clothing, a sedentary lifestyle, obesity, alcohol, smoking) and/or orthopaedic abnormalities (high arches or flat feet, postural disorders of the lumbar spine and/or knee)].

The phenomenon is increasing in highly urbanised and heavily industrialised populations.

CVI is a chronic progressive disease; in addition to the unquestionable aesthetic

implications, it must be considered a true social phenomenon, which causes ever-increasing costs for healthcare facilities.

**CVI – CLASSIFICATION AND STAGING**

In classifying and staging CVI, reference is made to the acronym **C.E.A.P.**, which was introduced in 1996 and later became established in literature.

– C.E.A.P. stands for components of venous disease: **C** = Clinic: clinical signs (grade 0-6); **E** = Etiology: etiological distinction into congenital, primary, secondary; **A** = Anatomy: vein segments affected, perforating veins, superficial veins, deep veins; **P** = Pathophysiology: pathophysiological dysfunction, reflux, obstruction, reflux, and obstruction.

• The clinical classification is as follows:

**C0s**: no visible or palpable clinical signs of venous disease

**C1**: telangiectasia (small intracutaneous reticular varicose veins <1 mm) and reticular (varicose veins hypodermic <3 mm)

**C2**: varicose veins; subcutaneous >3 mm

**C3**: oedema; fluid retention

**C4a**: dystrophic lesions of venous origin (dyschromia, eczema, hypodermatitis)

**C4b**: dystrophic lesions of venous origin

(hypodermatitis, lipodermatosclerosis, *atrophie blanche*)

**C5:** C4 + healed ulcer

**C6:** C4 + open ulcer.

## CVI – CLINICAL SIGNS

Varicose veins are the most common manifestation of superficial venous disease.

From a morphological point of view, the following types of varicose can be distinguished (FIG. 2):

- **Truncal varicosis**

Great saphenous vein, small saphenous vein

– Complete truncal varicosis: venous reflux starts from the first valve, at the junction of the venous trunk (*crosse*).

– Incomplete truncal varicosis: insufficiency of the main venous trunk with sufficient *crosse*, and venous reflux affecting another vessel.

– Collateral varices: inflow through insufficient lateral branching.

– Varices from perforating vein: insufficient inflow through a perforating vein.

- **Reticular varicosis**

Subcutaneous tortuous vein which belongs to neither the main trunk nor the collateral branches; diameter: <3 mm.

- **Telangiectasia**, Intracutaneous ectasia.

## PHLEBOEDEMA

A slight swelling of the limbs in the evening is not uncommon.

After a long day of work, the volume of the leg can increase by up to 100 ml; after a long flight, with no movement, this can be as much as 200 ml.

Oedema that does not disappear spontaneously within a few hours, or after a walk, is considered pathological.

Bilateral and poorly symptomatic types of oedema are mostly systemic (cardiac, renal, hepatic).

Phleboedema is always associated with disorders and/or clinical signs such as dilated superficial veins, varicose veins, and cutaneous dystrophy.

Chronic phleboedema is only partially

reversible. It results in an induration that can be detected on palpation and affects all structures in the integument, a condition defined as **lipodermatosclerosis (LDS)**.

LDS can develop into atrophy.

The leg has the appearance of an upside-down bottle of *champagne*.

In some cases, a secondary lymphoedema develops (FIG. 3), presenting acral thickening of the epidermal fold, hyperkeratosis and papillomatosis.

## CUTANEOUS DYSTROPHIES

Cutaneous dystrophy mainly refers to damage caused by chronic venous hypertension, or failure to lower the pressure in the veins when walking.

It is localised in the area of the primary varices, particularly in regions with insufficient perforating veins, in the leg and the distal foot.

– The clinical picture becomes rapidly dominated by secondary disorders: allergic inflammation and irritation in the case of chronic oedema and loss of epidermal barrier function, microvascular thrombosis, local ischaemia and reperfusion, intoxication due to accumulation of Iron, etc.

The pathophysiology can be recognised from the clinical picture: dermo-epidermitis, hypodermatitis, hyperpigmentation, and ulceration. Reorganisation of



FIG. 3

the epidermal vessels can partly be thought of as a consequence of the reparative response: telangiectasia of the thighs, retromalleolar and paraplantar varices, and loss of capillaries in atrophic areas with capillary expansion. *Atrophie blanche* is a result of *capillaris alba* and eventually of an acute, intensely painful circumscribed ischaemia, associated with inflammation or microvascular thrombosis.

The *ulcus cruris* occurs spontaneously due to minor traumas which often go unnoticed. Some ulcers can be healed by compressive therapy, while others persist for years (FIG. 4).

## JOINT DYSFUNCTIONS

Joint dysfunction is an inevitable consequence of CVI.

Of particular importance is the functional limitation in the mobility of the ankle joint, initially associated with



FIG. 4

FIG. 5



pain, then subsequently aggravated by a narrowing of the joint capsule. This leads to the so-called phlebological equinism, with a resulting difficulty in walking (FIG. 5).

Patients normally compensate for the problem by wearing high-heeled shoes.

The lesion causes a vicious circle, in which the pump function of the calf muscles is severely compromised.

### ACUTE VENOUS DISEASES – CLINICAL SIGNS

#### VARICOSE HAEMORRHAGE

The rupture of varicose veins is a dramatic, albeit harmless, complication of a particular form of varicosis: thin-walled intracutaneous venous aneurysms can develop painless fissures due to minor trauma.

The raised venous pressure, lack of musculature in the vascular walls, and small size of the opening often result in extensive bleeding.

The acute phase can be resolved by elevating the lower limb and applying a compression bandage.

– The most effective treatment for these varicose veins is sclerotherapy with effective eccentric compression.

#### PHLEBITIS

The term phlebitis (FIG. 6) refers to a series of disease patterns that differ from a nosological and clinical point of view.

The occurrence of a reddish thrombus in a varicose vein is inevitable in cases of varicose thrombosis, with little inflammation in the venous wall but intense inflammation in the surrounding area.

The inflammation of a superficial non-varicose vein affects the entire vascular wall, and the surrounding area to a much lesser extent; the thrombus is reduced or absent.

In varicothrombosis, a thrombus tends to grow and become stratified, with possible development in the Deep Venous System; phlebitis in a non-varicose vein tends to migrate, occasionally passing into a different venous segment (migrating phlebitis).

The autonomous development of deep vein thrombosis and oligosymptomatic pulmonary embolism are not uncommon in both forms of venous inflammation.

– Frequent ultrasound examinations are prescribed in both cases.

In the case of varicothrombosis, removal of the thrombus by incision or heat procedure on the varicose veins generally leads to rapid improvement.

FIG. 6



#### DEEP VENOUS THROMBOSIS

The signs of acute venous thrombosis depend on the patient's situation and the extent of the thrombosis itself.

– In bedridden patients, the signs are so subtle that diagnosis is often delayed.

Typical warning signs are cyanosis, dilated superficial veins and raised skin temperature.

Ambulatory patients rapidly show signs of compartment syndrome: hardening of the affected parts (sole of the foot, calf), tenderness in the muscles, reduced mobility, pain when placing the foot on the ground, walking, or during active or passive flexion and extension of the foot.

Obvious oedema, i.e. a difference between the circumference of the calf and that of the contralateral of >3 cm, is only to be expected in cases of ascending thrombosis (FIG. 7) if the thrombosis has reached the common femoral vein.

On the other hand, descending thrombosis typically causes rapid, major swelling, and is not generally characterised by compartment syndrome in the calf.

## MATERIALS AND METHODS

The patients in our case study were examined from a clinical and instrumental point of view both at the start and end of treatment.

– The following criteria were considered in the assessment:

gender, age, weight, height, family history of CVI, family history of venous thromboembolic disease, oestrogen-progestin therapy, hormone replacement therapy, pregnancy, work activity, weight gain, history of deep vein thrombosis (DVT) or superficial vein thrombosis (SVT).

The objective assessment was carried out through careful analysis of the lower limbs (condition of the skin, examination, palpation).

The subjective assessment was carried out using a VAS representing the pain level, on which the patient places a point corresponding to the degree of pain.

The Trendelenburg manoeuvre enables the formulation of a clinical diagnosis of insufficiency of the large and small

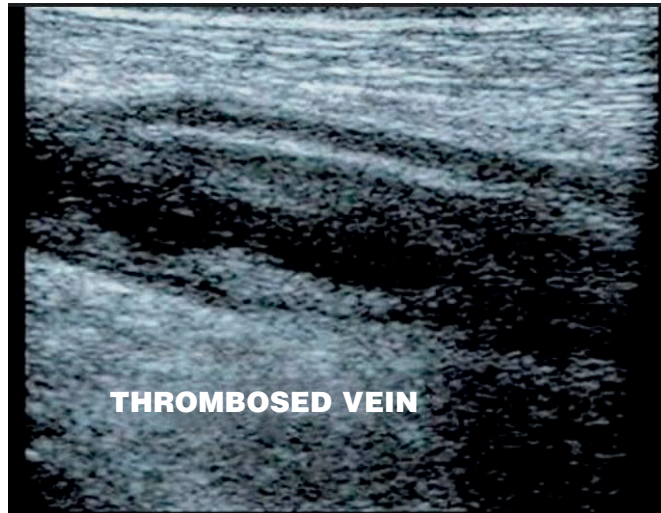


FIG. 7

saphenous veins in the region of the valves at the cross of the perforating veins.

A haemodynamic study using colour doppler echocardiography is performed to assess the level of venous incontinence and the reduced rate of flow in the iliac, femoral, and popliteal veins.

- Nineteen patients with a C.E.A.P. classification, 13 female and 6 male, were enrolled in the study. 2-3.

The patients, aged between 35 and 55 years old, were monitored from March to June 2021.

– Inclusion criteria: F and M patients with a clinical and instrumental diagnosis of CVI, C.E.A.P. 2-3.

– Exclusion criteria: pregnancy; breastfeeding; current or previous DVT within one year of diagnosis; destructive or ablative treatment of the saphenous axis; other ongoing therapies for the same disease.

All the patients were given the following therapy:

- Outpatient treatment: **MD-Muscle** 1-2 vial(s) + **MD-Tissue** 1-2 vial(s). Treatment by injection in acupoints M5, M6, M9, M10 (see page 60) and parallel to the varicose vessel using 30G x 4 mm needles, 1/week.
- Home therapy: **Anti Age Vein**, 5 pellets x 2/day; **Guna Liver**, 5 pellets/day; **Guna Matrix**, 30 drops/day diluted

in 1.5 litres of drinking water throughout the day for 90 days.

- 18 - 21 mm/Hg elastic-compression stocking.

Patients were also monitored from the nutritional point of view.

They were encouraged to consume foods rich in substances recommended for this disease: cherries, berries, blueberries, blackberries, and currants (rich in proanthocyanidins, anthocyanidins and bioflavonoids that boost the resistance of small vessels, counteracting the permeability of the capillaries and inflammatory reactions in the connective tissue).

Buckwheat, a source of flavonoids, was also included in the diet.

This food is rich in rutin, a glycoside of quercetin, which has properties that strengthen the capillary wall.

Foods containing rutin can prevent the onset of bleeding and improve microcirculation, with pronounced anti-inflammatory, antioxidant properties. In addition to rutin, buckwheat contains other flavonoids (vitexin and isovitexin).

– Chilli, ginger, garlic, and onion were also recommended.

Due to their ajoene and adenosine content, garlic and onion are particularly effective as thromboxane inhibitors.

Apples, oranges, grapefruit, and lemon were also recommended for their rutin content, and fresh pineapple, rich in

bromelain, as an ingredient that supports fibrin metabolism.

The diet also included natto, a soy-based food rich in probiotics, vitamin K2 and nattokinase, an enzyme that reduces the formation of blood clots and dissolves those already formed, and omega-3 fatty acids, which lower cholesterol and stimulate the release of blood thinning enzymes.

Finally, grape seed oil, rich in polyunsaturated fatty acids (which have a laxative and cholesterol-lowering effect); associated with the anthocyanosides in leaves, it helps protect the blood vessels and improves elasticity in the tissues due to its ability to stabilise elastin and collagen.

– Foods whose consumption was reduced or ruled out included pepper, aubergines, tomatoes, potatoes, dairy products, and red meat (saturated fats), to avoid overloading the liver and strengthen the integrity of the connective tissue and the muscle components of the venous walls.

### THERAPEUTIC PROPERTIES OF THE PRM MEDICINAL PRODUCTS USED

– **Anti Age Vein** is the PRM medicinal product indicated in venous stasis, venous varices, thrombophlebitis, phlebothrombosis, and haemorrhoids.

– **Guna Matrix** is a medicinal product specifically formulated for its pronounced detoxification effect on the ECM (extra-cellular matrix).

Its composition facilitates a coordinated action targeted at the deactivation, cleavage, and centrifugation of ECM toxins.

The primary effect of the medicinal product is exerted on the ECM, with a secondary effect on the kidneys (where it channels the toxin load removed by the ECM).

– **Guna Liver** is an effective medicinal product in diseases affecting the organs of the digestive system; it is a co-adjuvant in the treatment of liver disorders. Guna Liver contains active ingredients that help relieve gastroenteritis, meteorism, liver disease, and chronic vomiting.

– **Guna MD-Muscle** and **Guna MD-Tissue** are injectable medical devices made with Type I collagen of porcine origin.

- MD-Muscle contains Collagen, Heparin, NaCl, and Water for injection.
- MD-Tissue contains Collagen, Ascorbic Acid, Magnesium Gluconate, Pyridoxine hydrochloride, Riboflavin, Thiamine hydrochloride, NaCl, and Water for injection.

### WHY USE GUNA COLLAGEN MEDICAL DEVICES

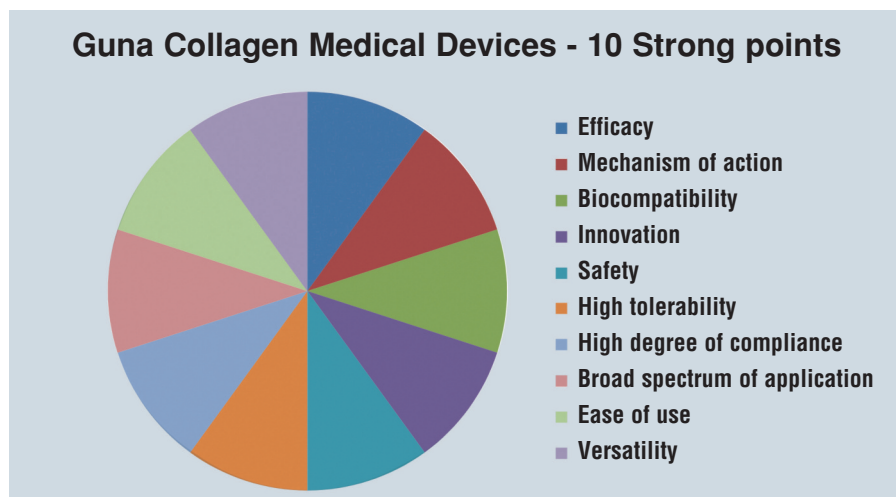
The advantages of the Guna Collagen Medical Devices are (TAB. 1):

- **Efficacy:** they restore and strengthen damaged anatomical structures; improving mobility and function, and acting directly on pain.
- **Mechanism of action:** they perform supportive actions in their specific areas of use.
- **Biocompatibility:** total compatibility between type I collagen of porcine origin and human collagen.
- **Innovation:** the collagen used is the outcome of innovative production processes developed in the Guna Laboratories.
- **Safety:** chemical and physical properties that ensure safety in clinical use.
- **High tolerability:** no side effects, allergic reactions, or problems due to drug interactions have been recorded so far.
- **High degree of compliance:** due to the mechanism of action and the absence of side effects, the treatment is well tolerated and satisfies patient expectations.
- **Broad spectrum of application:** they can be used in the treatment of various diseases in various fields of medicine.
- **Ease of use:** they can be used for subcutaneous, intra-dermal, local intramuscular, peri- and intra-articular injections.
- **Versatility:** they can be administered individually or in combination with one another; they are not contraindicated in patients receiving drug therapy, before or after surgery.

**MD-Muscle** and **MD-Tissue** were used in this study to manage the repair and remodelling of the venous vessels, essential to the functional recovery phase. The main difference between the venous and the arterial wall are that the former has more elastin and less collagen.

– Collagen Medical Devices act as bioscaffolds.

TAB. 1



The deposition of newly synthesised collagen fibrils in the damaged region, secondary to the loco-regional infiltration of Collagen Medical Devices, produces a significant improvement in the mechanical qualities of the injured tissue; the anisotropic properties of the tissue are particularly well-restored.

Anisotropy is a mechanical property of collagen that describes the ability of its fibres to propagate the tensile forces to which they are subjected in a single preferred direction.

– This property, which is fundamental to many biological functions, is gradually lost when the collagen fibres are damaged due to ageing, wear, or trauma, particularly when the H+ bonds between the collagen fibres, essential to their orientation, are distorted. The optimal formation and distribution of collagen fibre is not only essential to structural integrity and functionality; it also plays a central role in transmitting tensile forces to the fibroblasts.

## RESULTS

All patients reported heaviness in the lower limbs, which disappeared within 3 weeks after starting treatment.

At the start of the treatment, one male patient reported a sense of tension and weight in the calves, particularly after long periods sitting or standing, with ankle oedema in the evenings, itching and noticeable varices.

– After one month of treatment the pain and swelling disappeared; after 3 months the varices were much less evident.

All the 13 female patients, had pain, swelling, reticular varices and noticeable varices.

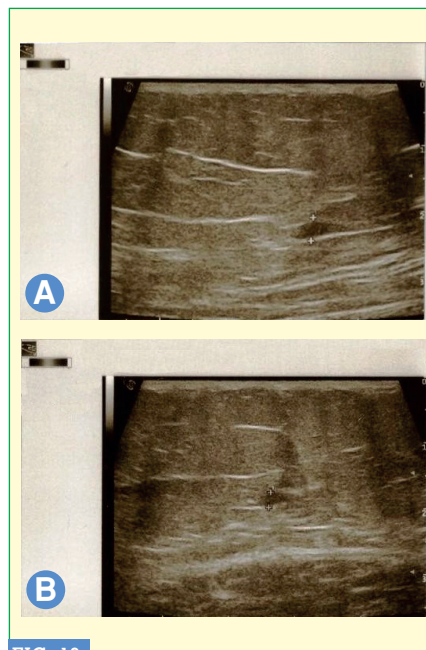
– After only 1 month of treatment the pain and swelling disappeared; 3 months after the start of treatment the varicose veins were much less evident.



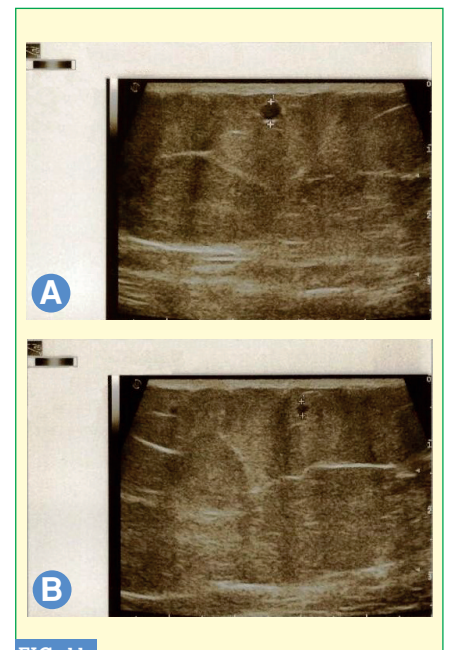
**FIG. 8**  
Start of the treatment.



**FIG. 9**  
End of the treatment.



**FIG. 10**  
Male patient before the treatment (A) and after the treatment (B).



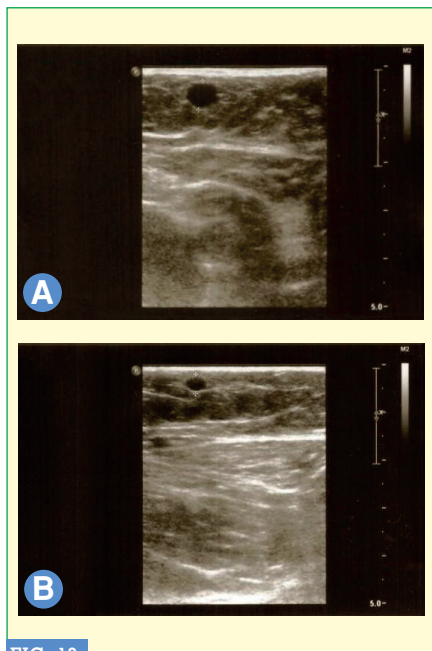
**FIG. 11**  
Female patient before the treatment (A) and after the treatment (B).

## CONCLUSIONS

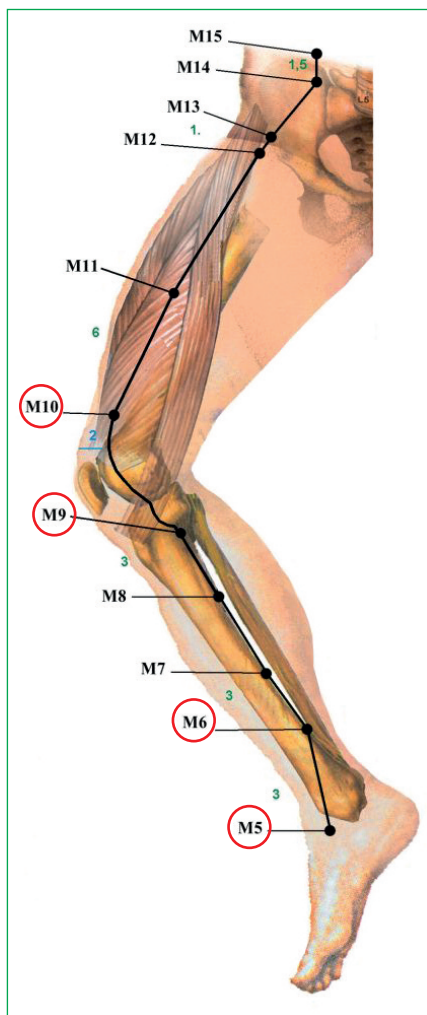
This clinical study showed a clear improvement in symptoms (**pain, swelling, and heaviness**); the **reduced size** of the

**varices** was also appreciated.

– Moreover, owing to the observance of dietary instructions, the patients lost 10-20% of their body weight. Due to the synergistic combination of



**FIG. 12**  
**Female patient. VGS before the treatment (A) and after the treatment (B).**



<http://freeyouenergy.it/lelemento-terra-meridiano-dello-stomaco-della-milza/>

PRM medicinal products - Guna Collagen Medical Devices, the treatment proposed here proved effective in treating the symptoms of CVI in patients with a C.E.A.P. classification 2-3 (FIGS. 8-12). ■

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**author**

**Dr. Lidia Cristaldi**  
 – Specialist in Angiology  
 – Azienda USL Bologna Hospital for Rare Diseases Polyclinic Mengoli; Reference Centre for Diseases of the Circulatory System; Reference Operative Unit; Territorial Angiology  
 Cesena, Italy