Ultrasound-Guided Injection of Polidocanol Microfoam in the Management of Venous Leg Ulcers

Juan Cabrera, MD, PhD; Pedro Redondo, MD, PhD; Antonio Becerra, MD; Celia Garrido, MD; Juan Cabrera, Jr, MPharm; Maria Antonia García-Olmedo, MPharm; Alejandro Sierra, MD, PhD; Pedro Lloret, MD; Miguel A. Martínez-González, MD, PhD, MPH

Background: Venous leg ulceration is a frequent and severe complication of lower limb venous insufficiency. Compression therapy is associated with a protracted course of healing and multiple recurrences. Minimally invasive surgery (subfascial endoscopic perforating surgery) is only possible in a subset of patients with leg ulcers. Low-cost and noninvasive therapeutic procedures are needed as alternative treatments.

Objective: To evaluate the efficacy and safety of sclerosant in microfoam in treating venous leg ulceration.

Design: A retrospective study of medical records, pretreatment and posttreatment color photographs, and echo Doppler in patients with venous leg ulceration. All patients were evaluated at 6 months after therapy; 70% were also evaluated at 2 years, 25% at 3 years, and 14% at 4 or more years after treatment. They were assessed for complete (100%) ulcer healing, time to wound closure, and recurrence.

Setting: Private vascular surgery clinic in Granada and dermatology department at a hospital in Pamplona, Spain.

Patients: Over 115 months, 116 consecutive patients (mean age [range], 57 [25-85] years) treated with ultrasound-guided injection of polidocanol microfoam (UIPM).

Interventions: To reduce venous hypertension, UIPM was used to selectively and progressively sclerose sources of incompetence. The number of sessions per patient varied between 1 and 17 (mean, 3.6).

Main Outcome Measures: Complete ulcer healing, defined as full reepithelialization of the wound with absence of drainage. Recurrence was defined as epithelial breakdown in the healed limb.

Results: At 6-months’ follow-up, treatment with UIPM achieved complete healing in 83% of patients (96/116), with median time to healing of 2.7 months; 7 patients were never cured, and 1 patient was lost to follow-up. There were recurrences in 10 patients.

Conclusions: The use of UIPM to selectively and progressively sclerose incompetent veins produced by venous hypertension is highly effective to achieve a stable ulcer healing with minimal invasion, even in elderly patients. Recurrences are easily treatable with this approach. This technique may become a first-line treatment in the management of leg venous ulcers.

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VENOUS ULCERS CONSTI-
tute approximately 80% of all leg ulcers. Venous leg ulcers have been estimated to afflict 0.2% to 1% of the total population and 1% to 3% of the elderly population in the United States and Europe. Venous ulceration (VU) is a debilitating problem associated with a major financial burden, including medical care costs and the considerable loss of work hours. The treatment of venous ulcers has been estimated to represent 1.3% of the total United Kingdom health care budget. Venous blood flows through perforator veins following the pressure gradient between elevated hydrostatic pressures in superficial veins and rhythmically decreased mean pressures in deep calf veins. Abnormal function of the deep or superficial venous system will commonly result in increased venous pressure, volume, and refill time. Venous hypertension (VH) is the underlying cause of VU, although the pathogenic steps involved are not fully understood. Different mechanisms are implicated: dysfunction of valves in superficial and/or perforator veins because of congenital or acquired incompetence; dysfunction of valves in the deep system due to congenital absence, inherent weakness, or thrombotic damage; deep venous outflow obstruction; and muscle dysfunction or calf muscle pump failure. Reflux may result from pri-
mary valvular insufficiency of the deep or superficial system or from secondary deep valvular insufficiency. The incidence of ulceration is linearly related to increases in ambulatory venous pressure above 30 mm Hg. Rapid reflux is also associated with a higher incidence of ulceration.

The primary role of the treatment of chronic VU is to reverse the effects of VH. For decades, the hallmark of treatment has been compression therapy. Wound care with previous debridement and systemic therapy with hemorheologic and venotonic agents may be useful as adjuvants to standard compression therapy. However, the results of these approaches are often discouraging, with delayed healing and multiple recurrences.

In 1938, Linton described the interruption of incompetent perforator veins to mitigate the effects of VH. This approach used subfascial perforator ligation via a long vertical incision directly into the fascia. DePalma performed modified infrasfacial and extrafascial dissections to interrupt perforator veins. Over the past 2 decades, however, the emergence of minimally invasive surgical techniques has led to debate about the most appropriate surgical therapy for severe chronic venous insufficiency and venous ulcers. Subfascial endoscopic perforator surgery has become the surgical technique of choice for perforator ablation. Nevertheless, the efficacy of perforator ablation remains highly controversial, regardless of the technique used. Furthermore, this approach cannot be adopted in all cases. Venous ulcers vary in size and location, but most are usually found on the medial malleolus on the distal aspect of the lower leg. Ulcers within 10 cm of the sole of the foot are frequently chronic, long-standing lesions that present low surgical accessibility and are usually refractory to conventional treatments.

Several novel approaches to venous ulcers have been proposed, including the use of topical granulocyte-macrophage colony-stimulating factor, tissue-engineered skin equivalent, and hyperbaric oxygen. These new techniques have not become standard procedures because they are relatively expensive and still require further evaluation.

We present the first series of chronic venous leg ulcers treated with a novel procedure, the ultrasound-guided injection of polidocanol microfoam (UIPM). This is a highly effective, minimally invasive technique, able to achieve the selective and permanent disappearance of the sources and transmission routes of VH. After this treatment, a short-term complete closure of leg ulcers is observed, together with a stable scarring process. Moreover, when the outcome is not successful, the treatment can be easily repeated.

### METHODS

#### PATIENTS

Between July 1993 and January 2003, we treated 151 ulcers in 116 consecutive patients (39 men and 77 women [age range, 25-85 years]) with chronic venous leg ulceration using UIPM. All had been diagnosed as having VU by the referring center and had been previously treated with conservative therapy (occlusive dressing and/or compression bandaging). Twenty patients also had undergone surgery at other institutions and experienced recurrences. To be included in the study, the ulcers had to be of 1-month duration or more. Mean (range) duration was 62 (1-480) months. Venous insufficiency was characterized in all patients by a clinical examination and venous Doppler examination. Patients were classified into the following mutually exclusive categories, according to the vein segments showing insufficiency: exclusively saphenous (n = 34); exclusively deep vein (n = 2); exclusively perforator vein (n = 8); saphenous + perforator (n = 41); saphenous + deep vein (n = 9); perforator + deep vein (n = 11); and all 3 segments (n = 11). A further classification separated patients with some degree of deep vein incompetence (n = 33) from those with only perforator and/or superficial incompetence (n = 83).

All patients exhibited a moderate to severe dermatosclerosis and absence of significant arterial insufficiency (defined by an ankle brachial index >0.65). Baseline characteristics of the patients, number of treatment sessions, and outcomes are given in Table 1 and Table 2.

All the assessments were performed by at least 1 investigator (J.C.) who also evaluated each patient before treatment and at each of the initial posttherapy visits. All 116 patients were evaluated at 6 months after therapy, 70% were evaluated at 2 years, 25% at 3 years, and 14% at 4 or more years after the therapy. All patients signed their informed consent.

Complete ulcer healing was defined as full reepithelialization of the wound with absence of drainage. Recurrence was defined as epithelial breakdown in the healed limb.

#### MICROFOAM

Polidocanol sclerosant in microfoam form was administered in direct ultrasound-guided percutaneous injections. The polidocanol microfoam is composed of carbon dioxide microbubbles of small diameter with sufficient stability to be injected into the vessels. The combination with gas greatly increases the volume and creates an enormous increase in surface area compared with the liquid. Sclerotherapy sessions were normally given every 2 to 4 weeks at the beginning of the treatment and reduced in frequency as the patient improved. Polidocanol was injected at concentrations of 0.27% to 1%, depending on the size of the vein and the hemodynamic characteristics of the treated area. The maximum recommended dose to treat varicose veins is 6 mL of 3% polidocanol in liquid form.

The precise procedure to prepare the microfoam is the subject of a confidential agreement with a third party who is the proprietary. It is, however, based on the procedure described in granted European and US patents EP 656203 and US 5676962, respectively.

#### TECHNIQUE

Sclerotherapy was performed in a treatment room without anaesthesia. The technique consists in nonsurgical elimination of
superficial reflux pathways and incompetent perforator veins. By means of Doppler ultrasound, we identified the valveless vessels in connection with the ulcer and thus potentially responsible for the local VH. Color duplex scanning has 100% specificity and the highest sensitivity of all available diagnostic tests to identify incompetent perforator veins. Duplex scanning localizes venous obstruction and reflux in specific anatomic segments of superficial, deep, and perforator veins.\textsuperscript{14,15} Polidocanol microfoam was injected under ultrasound guidance into the original source of reflux—the saphenous or perforator veins or both. We injected those vessels that were potentially responsible for the VH. We injected a variable microfoam volume according to the size of the vein to be occluded; the injected volume ranged from 20 to 30 mL for saphenous veins to 1 to 4 mL for isolated valveless perforators.

The access route was variable depending on the size of the vein. Cannulation was performed in larger veins and direct needle was used for smaller veins. The volume of 1% polidocanol microfoam necessary to fill the proximal saphenous segment was then injected. The ultrasound transducer (probe), placed at the saphenous-femoral confluence, shows the arrival of the injected microfoam. The microfoam is then directed distally, using a finger to block the proximal saphenous vein. Perforator veins are selectively sclerosed by direct ultrasound-guided injection, placing a 23-gauge or 25-gauge needle in a superficial segment that is connected to but distant from the perforator vein. The injection of 0.27% to 0.37% polidocanol microfoam into this area allows control over the volume and avoids an extension of its action to the deep venous system (DVS). Ultrasound was used to visualize microfoam during the procedure. Selective digital or transducer compression was performed to avoid the entrance of microfoam into the DVS. Another way of protecting the DVS was by injecting the microfoam with the limb elevated (safety angle). This position creates a gradient where the DVS has a higher blood pressure, thus avoiding the entrance of microfoam in the DVS. The treatment is complemented with compression bandaging (Struva 23–mm Hg stocking; Medibayreuth, Barcelona, Spain). This stocking was maintained 7 or 15 days after the injection.

\subsection*{Statistical Analysis}

Time to healing was calculated from the date of the first UIPM treatment session. Kaplan-Meier estimates were used for time-to-event data. The unit of analysis was the individual patient (n = 116), regardless of the number of their ulcers. Fourteen patients had more than 1 ulcer; for the analyses we considered the largest ulcer (square centimeter) or, in the assessment of chronicity, the ulcer of the longest duration. We used a Cox proportional hazards model (with patients as units of analysis) to identify variables independently related to therapeutic success. Regardless of the statistical significance, these estimates were adjusted for age and sex. Adjusted hazard ratios and their respective 95% confidence intervals were computed as estimates of relative risk. We compared our results with those of a previously reported\textsuperscript{2} control group with similar characteristics to our series, although their ulcers generally carried a better theoretic prognosis because of their smaller size (1.05 ± 1.61 vs 9.3 ± 2.25 cm\textsuperscript{2}) and shorter duration (33.3\% vs 36.2\% with >2 years evolution). This group had received only compression therapy and showed 49% complete healing at 6 months, were used as expected events.

\renewcommand*\arraystretch{1.25}

\begin{table}[ht]
\centering
\begin{tabular}{|c|c|c|}
\hline
Characteristic & % & \textit{P} Value (vs Reference Series\textsuperscript{*}) \\
\hline
Overall & 86 & <.001 \\
Sex & & \\
M (n = 39) & 81 & <.001 \\
F (n = 77) & 89 & <.001 \\
Age, y & & \\
<50 (n = 35) & 90 & <.001 \\
50-65 (n = 44) & 88 & <.001 \\
>65 (n = 37) & 80 & .001 \\
Ulcer chronicity, mo & & \\
\leq 6 (n = 44) & 81 & <.001 \\
>6-12 (n = 16) & 83 & .002 \\
>12-24 (n = 14) & 83 & .001 \\
>24-72 (n = 18) & 86 & .02 \\
>72 (n = 24) & 66 & .19 \\
Ulcer area, cm\textsuperscript{2} & & \\
\leq 2 (n = 55) & 71 & .001 \\
>2 to \leq 6 (n = 24) & 88 & <.001 \\
>6 (n = 72) & 81 & <.001 \\
Localization & & \\
Exclusively saphenous (n = 34) & 90 & <.001 \\
Exclusively perforator vein (n = 8) & 85 & .04 \\
Exclusively saphenous and perforator (n = 41) & 94 & .001 \\
Exclusively saphenous and deep vein & 85 & .03 \\
(n = 11) & & \\
Deep vein ± perforator (n = 13)\textdagger & 79 & .04 \\
All 3 segments (n = 11) & 64 & .33 \\
Previous surgery & & \\
No (n = 96) & 88 & <.001 \\
Yes (n = 20) & 77 & .06 \\
\hline
\end{tabular}
\caption{Percentage of Patients Completely Healed by 6 Months (Kaplan-Meier Estimates)}
\end{table}

\*\textit{P} values were determined using the \textit{χ}\textsuperscript{2} test. The results in control patients of the study by Falanga et al.,\textsuperscript{9} who received only compression therapy and showed 49\% complete healing at 6 months, were used as expected events.

\textdaggerThere were only 2 patients with exclusively deep vein incompetence. We merged them with 11 cases with incompetence of both perforator and deep veins.

\textsuperscript{*}For this analysis, always considering the individual patient (not the ulcer) as the unit of analysis. \textit{P}.<.05 was considered statistically significant.

\subsection*{Results}

Sclerosis of incompetent trunk veins was followed up at 2 to 4 weeks with further injections to sclerose tributaries and residual incompetent perforators under ultrasound guidance. The process continued until all identifiable incompetence was eliminated. Standardized photographs were taken at each visit. The number of sessions per patient varied between 1 and 17 (mean, 3.6). Nineteen patients received more than 5 sessions. All data were evaluated from the photographs by 3 independent investigators (J.C., A.B., and P.R.).

Perforating veins were present in most patients, usually close to the ulcer. Microfoam was injected in the superficial venous system close to perforating veins. Two weeks later, the treated perforating vein could be observed with ultrasound, but it was not compressible and no flow was noticeable with Doppler exploration. Treat-
ment with UIPM achieved complete healing in 86% of patients at 6 months (Table 2), with an 8-week median time to healing; 7 patients were never cured and 1 patient was lost to follow-up (Figures 1, 2, and 3). We observed a lower success rate in ulcers of longer duration and in patients with incompetent DVS (Table 2) (Figure 4). However, incompetence in the perforator veins was associated with a worse prognosis than when it was found exclusively in the saphenous veins. The worst results (64% complete healing at 6 months) were found when all 3 segments were affected (Table 2).

In comparison with the controls of a previously reported series,9 we obtained a significantly better outcome at 6 months in all subgroups except for ulcers open for longer than 12 years (n=24), in which our success rate was 66% (of patients). In comparison with the success rate (63%) reported by the earlier study9 in the active treatment arm also showed a highly significant advantage for

Figure 1. A 57-year-old woman with a varicose ulcer in the distal aspect of her leg before treatment (A) and 2.5 months after 3 sclerotherapy sessions (B).

Figure 2. A 59-year-old woman with multiple ulcers in her right ankle and left leg and abundant varicose veins before the start of treatment (A) and 4 months after 4 sclerotherapy sessions (B).
our overall results ($\chi^2$ test, $P<.001$). We observed statistically significant advantages for men ($P=.03$) and women ($P=.001$); for patients younger than 65 years ($P=.01$); for ulcers with diameter greater than 2 cm\(^2\) ($P=.001$); for ulcers open for less than 24 months ($P=.05$); for patients without involvement of the DVS ($P=.001$); and for patients with no previous surgery ($P=.001$). However, these comparisons likely underestimated the real effectiveness of UIPM because they were always referred to the percentage of complete healing in the whole active treatment series of that report\(^9\) and not to the success rate in specific subgroups with a poorer prognosis.

In the multivariate Cox model, the presence of deep vein incompetence and an ulcer of long duration were identified as independent predictors of failure to achieve complete healing, although the independent contribution of the latter variable was small (hazard ratio, 1.02 for each additional year the ulcer had been open) (Table 3). When we further subclassified the patients into 6 groups according to the localization of the incompetence, the Cox proportional hazards model found no statistically significant differences among these groups because of their smaller sample size (data not shown).

There were recurrences in 10 patients. The recurrence rates in patients are exhibited in Table 4 (for the analysis by lesion area, the ulcers and not the patients were considered as units of analysis). The 24-month recurrence rate was 6.3% overall and was below 8.5% across all subgroups except for older patients, the largest ulcers, ulcers of the longest duration, and patients with deep vein incompetence (Table 4).

No major complications were noted. No patient had thrombosis of the DVS, a pulmonary embolism, or neurological lesions. Pigmentation was seen in 20% of the patients, but it spontaneously resolved in 90% of them after 6 months. Transient visual disturbances (<2 minutes) were observed in 2 patients. Two patients developed temporary dry cough (<1 minute). Signs and symptoms compatible with superficial phlebitis were seen in 10% of the patients. The aim of the treatment with an sclerosant is to induce an inflammation in the endothelium; thus, in our opinion, phlebitis cannot be considered an adverse effect.

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**Table 3. Independent Predictors for Failure to Achieve Complete Healing of Ulcers**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only saphenous ± perforator</td>
<td>1 (Reference)</td>
<td></td>
</tr>
<tr>
<td>Deep vein incompetence ± saphenous</td>
<td>1.76 (1.12-2.78)</td>
<td>.01</td>
</tr>
<tr>
<td>Ulcer chronicity for each 12-mo period</td>
<td>1.02 (1.01-1.05)</td>
<td>.04</td>
</tr>
</tbody>
</table>

*Cox proportional hazards model, age- and sex-adjusted. A higher hazard ratio is associated with a higher probability of failure to achieve complete healing.*

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**Figure 3.** A 63-year-old woman with a large-sized ulcer in her right ankle before the start of treatment (A) and at 10 months after 7 sclerotherapy sessions (B).

**Figure 4.** Cumulative incidence of complete healing according to ulcer chronicity and to localization of venous incompetence. Kaplan-Meier estimates (patient as the unit of analysis).
Despite the high prevalence of venous ulcers, they are often neglected or inadequately managed. To our knowledge, we describe herein the first series of patients with chronic leg ulcers to undergo UIPM, a relatively inexpensive and minimally invasive technique. We obtained a high success rate, which exceeded those previously reported for conservative or newly developed nonsurgical therapeutic approaches.8,10,16 Despite the similarity of patient characteristics in the previously reported control series8 with our patients, we acknowledge that a threat to validity (ie, a bias) may exist in the comparisons vs this group. However, this bias would likely operate against our results because in that series8 the ulcers had a better theoretical prognosis owing to their smaller size and shorter duration. In spite of this potential bias, which may operate against our findings, we have found better results in our series. Thus, in any case, this possible bias enhances our favorable findings. Moreover, we also found successful our comparisons (even using subgroups of patients) with respect to the group that exhibited the better prognosis (active treatment) in the series reported by Falanga et al9 and not only with respect to their control group.

Skin closure occurs rapidly when the VH is improved. Superficial vein reflux is present in 88% of limbs with venous ulcers, while DVS reflux alone is only seen in 12%. These data may have substantial clinical implications, since reflux in the superficial system can be easily eliminated by excision of the affected veins.11 On the other hand, perforator incompetence, caused by primary valvular incompetence or by previous deep venous thrombosis, contributes to ambulatory VH and to the development of chronic VU. Although isolated perforator incompetence is seen in only 5% of patients with VU, it occurs in conjunction with superficial reflux (without deep reflux) in 32% of patients, and incompetent calf perforator in conjunction with either superficial or deep reflux has been reported in 73% of limbs with VU.10 Therefore, the ablation of superficial and perforator vein incompetence provides clinical and hemodynamic improvement in patients with chronic VU.10 Several studies indicate that subfascial endoscopic perforator surgery is as effective as open perforator ablation during early follow-up, with the additional benefit of significantly fewer wound complications, thereby establishing it as the procedure of choice for perforator vein surgery when indicated.20,21 Although early reports have been enthusiastic, failure of ulcer healing or recurrence after subfascial endoscopic perforator surgery has ranged from 2.5% to 22%, suggesting a need to reevaluate the indications and techniques of this procedure. In addition, the retromalleolar space and inframalleolar perforators are not accessible with the subfascial endoscopic perforator surgery approach. A recent study found that 50% of incompetent perforators within 10 cm of the sole of the foot, identified preoperatively by duplex ultrasound, were missed at subfascial endoscopy.22 Small interconnected collaterals between the perforators and the skin frequently convey the VH to the skin area, and surgical procedures are inherently unable to close these vessels. Thus, small interconnected collaterals can often remain open after surgical closure of the perforator, probably leading to a new increase in venous pressure and eventual recurrence of the ulcer. Besides cost issues, a painful postoperative evolution and a high risk of postoperative sensitivity disorders (20%) are further drawbacks of endoscopic surgery.23

Darke and Penfold24 used surgical saphenous ligation without perforator ligation for patients with leg ulcers in whom saphenous and perforator incompetence were the only identifiable abnormalities. They found complete healing in 90% (48/53) of their assessed patients after a mean follow-up of 3.4 years, although they had substantial losses to follow-up. Our results in this subtype of patients (94% complete healing at 6 months; Table 2) using a considerably less invasive procedure compares favorably with their reported success rate.

Sclerotherapy appears to be a promising alternative approach to venous ulcers. However, studies of the sclerosing treatment of venous ulcers are scarce and usually report the combined application of surgery and sclerotherapy.25,26 The use of color duplex scanning would be incorporated into the assessment in all ulcerated limbs. If color venous duplex imaging can accurately demonstrate patients with superficial venous reflux and incompetent perforator veins, it may be possible to improve ulcer outcome by sclerotherapy treatment. Theoretically, sclerosing treatments are optimal to close small collaterals. In fact, our present results confirm that UIPM can achieve this, thus accelerating ulcer closure and preventing recurrences caused by the reappearance of VH.

The common sclerosants (absolute ethanol and sodium tetradecyl sulfate) are potentially dangerous and require the use of tourniquets and compression to minimize the passage of sclerosing agent into the systemic circulation. When sclerosing liquids are used, the dosage

### Table 4. Percentage of Recurrences After 24-Month Follow-up (Kaplan-Meier Estimates)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>% Recurrence at 24 Months</th>
<th>Follow-up, Median (Range), mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>6.3</td>
<td>20.4 (1-113)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M (n = 36)</td>
<td>6.6</td>
<td>20.8 (3-101)</td>
</tr>
<tr>
<td>F (n = 73)</td>
<td>5.6</td>
<td>18.8 (1-113)</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50 (n = 32)</td>
<td>0</td>
<td>20.0 (4-98)</td>
</tr>
<tr>
<td>50-65 (n = 43)</td>
<td>8.0</td>
<td>24.1 (2-113)</td>
</tr>
<tr>
<td>&gt;65 (n = 34)</td>
<td>10.5</td>
<td>18.8 (1-101)</td>
</tr>
<tr>
<td>Ulcer chronicity, mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤6 (n = 44)</td>
<td>8.2</td>
<td>19.3 (3-101)</td>
</tr>
<tr>
<td>&gt;6-12 (n = 15)</td>
<td>0</td>
<td>20.5 (6-100)</td>
</tr>
<tr>
<td>&gt;12-24 (n = 14)</td>
<td></td>
<td>19.1 (3-98)</td>
</tr>
<tr>
<td>&gt;24-72 (n = 14)</td>
<td></td>
<td>19.0 (5-62)</td>
</tr>
<tr>
<td>&gt;72 (n = 22)</td>
<td>14.6</td>
<td>20.9 (1-113)</td>
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<tr>
<td>Ulcer area, cm²</td>
<td></td>
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<tr>
<td>≤2 (n = 42)</td>
<td>0</td>
<td>29.8 (4-101)</td>
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<tr>
<td>&gt;2 to ≤5 (n = 24)</td>
<td></td>
<td>18.5 (5-88)</td>
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<tr>
<td>&gt;5 (n = 65)</td>
<td>11.3</td>
<td>15.2 (1-113)</td>
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<td>Localization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only saphenous ± perforator (n = 79)</td>
<td></td>
<td>2.1</td>
</tr>
<tr>
<td>Deep vein incompetence ± saphenous perforator (n = 30)</td>
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<td>3.5</td>
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<tr>
<td>Previous surgery</td>
<td></td>
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</tr>
<tr>
<td>No (n = 92)</td>
<td>6.3</td>
<td>20.6 (1-113)</td>
</tr>
<tr>
<td>Yes (n = 17)</td>
<td>5.9</td>
<td>17.4 (2-60)</td>
</tr>
</tbody>
</table>

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is difficult to control because of their progressive dilution and irregular distribution in the vessels. It is also impossible to control the postinjection distribution of liquid sclerosants, whose spread cannot be visualized on ultrasound examination. Sclerosing liquids cannot be manipulated after injection, and there is no control over the duration of the sclerosant-endothelium contact. In contrast, a sclerosant in microfoam form displaces the blood from the lesion, permitting homogeneous contact between the sclerosant and the endothelium, facilitating endothelial destruction. We recently published encouraging results using this treatment in 50 patients with venous vascular malformations. Since the 1950s, the intravenous injection of carbon dioxide at doses of 50 to 100 mL has been used as a contrast for radiographic and hemopericardium diagnoses and in echocardiography. Carbon dioxide is non-toxic and large amounts can be administered. When the carbon dioxide is mixed into the surfactant liquid sclerosant, the area of liquid sclerosant with the appropriate coadjuvants, microbubbles of reduced diameter can be obtained of sufficient stability to be injected into the vessels. The area of liquid on their surface is enormous increased in inverse proportion to the diameter of the bubble. Alongside the high blood solubility and pulmonary diffusibility of the gas used, this increased surface area also facilitates its metabolism.

This new form of sclerotherapy showed a high degree of success in the present series of patients, who reported no discomfort. The technique was well tolerated both locally and generally, with no major complications. The best response vs other subgroups was observed in patients with incompetent superficial venous system. In summary, UIPM of superficial and perforating valveless veins is a well-tolerated and effective outpatient procedure. Major advantages include a great increase in action of the sclerosant agents in this novel pharmaceutical form, selective effect on endothelium, visibility on ultrasound examination, predictability of outcome, high success rate, and low frequency of recurrence. To our knowledge, this is the first series of patients with venous ulcers of the legs treated with sclerosants in microfoam form. This minimally invasive procedure may become the treatment of choice for venous ulcers in the future.

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From the Vascular Surgery Clinic, Granada, Spain (Drs J. Cabrera, Becerra, and Garrido, Ms García-Olmedo, and Mr J. Cabrera Jr); and Departments of Dermatology, University Clinic (Drs Redondo, Sierra, and Lloret), and Epidemiology and Public Health (Dr Martínez-Gonzalez), Medical School, University of Navarra, Pamplona, Spain. Dr J. Cabrera and Mr J. Cabrera, Jr have a financial interest in the commercial development of the patented microfoam. The microfoam presented in the study was made of the subject of a patent application by the authors in 1993, and they have subsequently assigned the patents to BTG International Limited. Provensis Ltd, a subsidiary of BTG, has developed the patented microfoam concept into a pharmaceutical product, Varisolve, which is currently used in clinical trials in Europe and the United States.

This study was presented at the UIP (International Union of Phlebology) World Congress Chapter Meeting; August 27, 2003; San Diego, Calif.

Corresponding author and reprint requests: Pedro Redondo, MD, PhD, Department of Dermatology, University Clinic of Navarra, PO Box 4209, 31080 Pamplona, Spain (e-mail: prendon@unav.es).

REFERENCES