Outcome of Ultrasound-guided Sclerotherapy for Varicose Veins: Medium-term Results Assessed by Ultrasound Surveillance

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Objective. To estimate medium-term success after a technique for ultrasound-guided sclerotherapy for superficial chronic venous disease.

Design. A prospective study in a single unit with ultrasound surveillance after treatment.

Materials. Results after 1189 treatment sessions for 807 venous saphenous veins and related tributaries or non-saphenous tributaries in 489 patients.


Results. Primary and secondary success rates at 36 months for all veins were 52.4% (95%CI 46–58%) and 76.8% (95%CI 71–82%). Cox regression analysis for primary success for all veins showed significantly worse results for saphenous veins compared to tributaries (HR 3.72 95%CI 1.9 to 7.3). Cox regression for all saphenous veins showed independently worse results for patients less than 40 years age (HR 2.16 95%CI 1.27–3.66), small compared to great saphenous veins (HR 1.58 95%CI 1.11–2.24), veins greater than 6mm diameter compared to smaller veins (HR 2.22 95%CI 1.40–3.50), liquid compared to foam sclerotherapy (HR 2.20 95%CI 1.28–3.78), lower volumes of sclerosant compared to volumes greater than 12 ml (HR 0.51 95%CI 0.33–0.81) and highly diluted compared to concentrated sclerosant (HR 2.05 95%CI 1.21–3.46) with worse results using highly diluted or undiluted 3% sclerosant compared to a 1.5% concentration. There were no significant differences for primary success for saphenous veins for date of procedure, sex, side, primary or recurrent varicose veins, or commercial type of sclerosant.

Conclusions. Ultrasound-guided sclerotherapy gives satisfactory results if it is accepted that treatment may need to be repeated to achieve secondary success. Results provide a basis for further research to explore factors that might affect outcome. Younger patients with larger diameter saphenous veins may warrant alternative forms of treatment, particularly for small saphenous reflux.

Keywords: Sclerotherapy; Ultrasound; Veins; Varicose; Saphenous.

Introduction

Many phlebologists now favour ultrasound-guided sclerotherapy to treat varicose veins but there are few published reports of the outcome. Earlier studies have presented results for liquid and foam sclerotherapy.1–7 Various techniques are advocated but there is little objective evidence that any one has an advantage over others in clinical practice. This paper presents a prospective observational study of a technique for ultrasound-guided sclerotherapy in a single unit with surveillance by serial ultrasound scans. Results were assessed by life table analysis to allow assessment of medium-term success rates and Cox regression analysis for the influence of covariates that might influence outcome. The aim was to determine whether results suggested ways to improve outcome and indicate directions for future research to evaluate best patient selection and treatment methods.

Materials and Methods

Patients and veins treated

This was a prospective study to determine outcome assessed by ultrasound surveillance. Only patients...
who presented for their first endovenous treatment by ultrasound-guided sclerotherapy were analysed. Patients treated with follow-up ultrasound-guided sclerotherapy after endovenous laser therapy were not included. The treatment period was from early 1999 to mid 2005. There were 1189 treatment sessions for 807 saphenous veins and related tributaries as well as non-saphenous varices in 677 lower limbs of 489 patients. Of the 1189 treatment sessions, success was achieved with one sclerotherapy session in 767 (65%), two sessions in 153 (26%) and three or more sessions in 34 (9%), an average of 1.49 sessions per venous system treated. Of the 807 saphenous veins and related tributaries as well as non-saphenous varices initially successfully treated, subsequent failure due to development of reflux in the treated veins as shown by ultrasound resulted in the patient returning for a second series of treatments for 113 (14%) and for a third series in 15 and fourth for 5 (2%). The authors decided not to record clinical success or failure or other indicators of outcome such as quality of life or cost-benefit analysis.

The patients’ ages ranged from 19 to 92 (median 53) years with 401 women (82%) and 88 men. The clinical CEAP category was determined for each limb. For limbs with saphenous reflux, the clinical CEAP category was C2-3 in 569 (90%) and C4-6 in 62 limbs (C4-39, C5-21, C6-2). Primary varicose veins were present in 516 limbs (82%) and recurrent varicose veins after previous saphenous vein surgery in 115 limbs.

Reflex was present in the great saphenous vein or tributaries in 454 limbs (56%) including 5 where reflex was present in the anterior accessory saphenous vein rather than the great saphenous vein. The small saphenous territory was involved in 177 limbs (22%) including 8 with involvement of the thigh extension or vein of Giacomini, and tributaries alone without reflux in either saphenous system in 176 limbs (22%). There were 60 limbs where both the great and small saphenous veins were treated.

Pre-operative ultrasound assessment

All patients were studied before the procedure by qualified vascular sonographers in the unit as previously described. Scans were performed with the patient standing and the limb relaxed. Reflux was defined as retrograde flow lasting for greater than 0.5 seconds in the affected vein. Reflux at the saphenofemoral junction was elicited with the Valsalva manoeuvre and at the saphenopopliteal junction by a calf compression-release manoeuvre. The scan assessed all deep, superficial and perforating veins. The diameter of incompetent saphenous trunks was measured.

Techniques for treatment

The sclerosant drugs used and their preparation varied from patient to patient according to the size and extent of the varicose veins and the attitude of the treating surgeon (KM). This provides an opportunity to compare success rates for different treatment techniques. The drug used was either sodium tetradecyl sulphate or polidocanol and these were not used in combination in any patient. No more than 4 ml of 3% sodium tetradecyl sulphate or 2 mg/kg of 3% polidocanol was used at any one treatment session as recommended by the Australian Therapeutic Goods Administration (TGA). In the first year, liquid sclerosant at a 3% concentration was used for 98 treatment sessions. From early 2000, foamed sclerosant was used for all procedures. Sclerosant foam was prepared from 0.6–3% sclerosant liquid, using saline dilution, to provide greater volumes of foam for more extensive varicose disease. Foam was made by a modification of the Tessari method with two parts of sclerosant combined with three parts of air mixed between two syringes connected by a two-way tap with a 5 micron filter in the system. Initially, no limit was placed on the maximum volume of foam given at one session although it is now restricted to no more than 20 ml of foam. The volume injected per session ranged from 3–40 ml foam (median 5 ml).

Injections were given as far distally and away from connections between superficial to deep veins as was possible while patients lay supine. The aim was to find a “strategic vein” that appeared from the preoperative scan to provide the best avenue for foam to fill the full length of the venous system to be treated. If scanning showed that sclerosant had not filled the veins then it was gently massaged along their length until it appeared at the appropriate saphenous junction. Usually, only one injection was required to fill the vein. Further injections at the proximal limit were performed if necessary. The sonographer followed the passage of foam and applied pressure to saphenous junctions or large perforators with the probe as foam approached.

The vein was usually viewed in the longitudinal axis and injection made with a 5 ml or 10 ml syringe and 1.5-inch-long 25-gauge needle. Injections were given into a prominent tributary where this was technically easier in 223 procedures (24%). Tributaries were injected either with or without ultrasound.
guidance. Foam was often seen to pass from one saphenous system to the other through communicating veins.

Following completion of injections, compression was applied with a two layer bandage if there were prominent superficial tributaries, or a class II thigh-length stocking if superficial veins were not prominent. Each patient was then immediately mobilised and asked to walk for about 15 minutes. Initial compression was maintained for three days and then changed to a compression stocking in all patients, worn just through the day and removed at night and for the morning shower. Compression was maintained for two to three weeks depending on the degree of reaction in the superficial veins. Ambulation was encouraged during the first 2 weeks.

Post-operative ultrasound surveillance

All patients were assessed by an ultrasound scan at 3–5 days after every treatment session to assess the effect of treatment, to detect residual patent veins requiring further treatment, and to detect deep vein thrombosis. Ultrasound scans and clinical review were then repeated at 6 weeks, 6-monthly for two years and then annually to determine whether treated veins were absent, occluded, patent or refluxing. Reflux in non-treated veins was also recorded.

Statistical analysis

Data were entered prospectively into an Excel spreadsheet and statistical analysis was performed with Stata software. Primary success was defined as persistent occlusion or absence of reflux in the treated venous segment. Secondary success was defined as persistent occlusion or absence of reflux in the treated venous segment after further ultrasound-guided sclerotherapy for primary failure. The time for commencement of surveillance was the date at which the last treatment session was performed that achieved occlusion of the treated venous system. The time to failure was the interval at which reflux was noted on the follow-up scan at the next scheduled appointment. If the patient had missed a scheduled appointment then the time to failure was dated back to that missed appointment.

Univariate life table analysis using Kaplan-Meier curves was performed for primary and secondary success for all veins and for tributaries without saphenous reflux, great saphenous reflux with or without tributaries, and small saphenous reflux with or without involvement of the thigh extension or tributaries.

Multivariate Cox regression analysis was used to estimate hazard ratios for covariates that might affect outcome for all veins and for all saphenous veins. The covariates studied were age and sex, right or left side, date of procedure, primary or recurrent varicose veins, vein treated, representative diameter of the vein, technique of injection into tributaries or the saphenous trunk, use of foam or liquid, sodium tetradecyl sulphate or polidocanol, concentration of sclerosant, and volume of liquid or foam infused. Specific covariates for great saphenous veins were the extent of involved vein above and below knee and the source of reflux from the deep system through the saphenofemoral junction or other sites such as low abdominal or pelvic veins or perforators. For covariates with continuous rather than categorical data, an arbitrary point was taken to separate approximately equal subgroups.

To avoid linearity assumptions, we categorized continuous covariates. We selected categories based on quartiles of the variable’s distribution, independent of its association with the outcome variable. We used a likelihood-ratio $\chi^2$ test to assess the contribution of each predictor variable in a final model. The unit of analysis for Cox proportional hazard regression was the vein. We used the Huber/White sandwich estimator of variance to accommodate clustering of veins within the same patient. Each vein inherited the higher-level characteristics of its ‘parent’ limb and patient within the regression model.

Results

Primary and secondary success rates

Primary and secondary success rates at three years for all veins were 52.4% (95%CI 46 to 58%) and 76.8% (95%CI 71 to 82%) respectively (Fig. 1).

Covariates affecting primary success rates

All veins

Cox regression analysis for all veins treated showed significantly worse primary success rates for saphenous veins compared to tributaries alone (HR 3.72 – 95%CI 1.9 to 7.3). Primary success rates at three years from life table analysis were 83.4% (95%CI 69 to 91%) for tributaries, 53.1% (95%CI 45 to 60%) for great saphenous veins, and 36.1% (95%CI 25 to 48%) for small saphenous veins (Fig. 2).
Cox regression analysis for all saphenous veins and related tributaries showed worse primary success rates for patients less than 40 years age (HR 2.16 95%CI 1.27–3.66 compared to patients 50–59 years). In relation to veins, there were worse results for small compared to great saphenous veins (HR 1.58 95%CI 1.11–2.24) and veins >6 mm diameter (HR 2.22 95%CI 1.40–3.50 compared to veins <5 mm diameter). For the technique of injection, there were worse results for liquid compared to foam sclerotherapy (HR 2.20 95%CI 1.28–3.78), smaller volumes of sclerosant compared to volumes >12 ml (HR 0.51 95%CI 0.33–0.81 and highly diluted compared to more concentrated sclerosant (HR 2.05 95%CI 1.21–3.46), (Table 1). In addition, hazard ratios suggest better results for patients older than 70 years compared to patients aged 50–59 years (HR 0.63 – 95%CI 0.35–1.14), and CEAP category C4-6 compared to C2-3 (HR 1.57 – 95%CI 0.91–2.73). Other covariates studied showed little influence on outcome.

Subsequent arbitrary subdivision of success rates for each of the sclerosant concentrations used showed best results for a 1.5% solution compared to either stronger or weaker concentrations (Fig. 3).

Postoperative complications

Deep vein thrombosis was detected by the routine early postoperative scan after 16 procedures. There were 9 occlusive posterior tibial vein thromboses and 7 partially occlusive femoropopliteal thromboses which represented 1.8% and 1.4% of the 489 patients respectively. All were asymptomatic and resolved with a short period of treatment with subcutaneous low molecular weight heparin therapy. Follow-up scans showed persisting reflux after recanalisation in the posterior tibial segment in 5 limbs. All deep vein thromboses followed use of foam and the volume infused ranged from 5–35 ml (median 14 ml). No clinical episodes of pulmonary embolism or other cardiovascular complications were observed. Three

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patients with a prior history of migraine headaches developed visual aura during mobilisation after injection, all typical of previous symptoms, and all settled within 20 minutes without headache or residual neurological deficit. No other neurological symptoms were observed. No other complications occurred.

Discussion

Ultrasound-guided sclerotherapy has gained great popularity but there has been little objective clinical appraisal of its results compared to other forms of treatment, or factors that might influence outcome to help select the most suitable patients.

Ultrasound surveillance provides the most stringent test for success after any treatment for varicose veins. It is also important to determine factors such as clinical recurrence rates, patient satisfaction, quality of life and cost-effectiveness but these were not assessed in this study. Ultrasound surveillance has been used by van Rij and colleagues to determine outcome after surgery, with success at three years in 79% of limbs after great saphenous surgery and 49% of limbs after small saphenous surgery. It has also been used to determine success after radiofrequency closure for great saphenous reflux and after endovenous laser therapy for great and small saphenous reflux. However, there are few studies after ultrasound-guided sclerotherapy. Kanter and Thibault reported cumulative success of 76% at two years from an early experience with liquid sclerosant while Belcaro and colleagues showed 56% success at 10 years with foam sclerotherapy.

In our study, most veins were obliterated with one treatment session, in agreement with the experience of Cabrera and colleagues. Primary success rates at three years for saphenous veins determined by ultrasound are little better than 50% so that patients should be warned that repeat treatment may be required at some time in the future. The improved secondary success rates might have been higher if all patients had agreed to repeat treatment.

We could find no compelling clinical evidence to favour any technique for preparation of the sclerosant or its administration. Accordingly, we chose to use various techniques in an attempt to select the best methods. In Australia, the regulatory authority (the Therapeutic Goods Administration) recommend that no more than 4 ml of a 3% solution of sodium tetradecyl sulphate and 2 mg/kg of polidocanol should be used at any one treatment session and this recommendation was followed. The most commonly used technique in Australia is to administer a 3% solution of either sclerosant but we elected to dilute this to increase the volume of foam in many patients. It was considered that inclusion of a 5 micron filter in the system increased foam stability.

When saphenous veins were considered in this study, no significant independent influence on outcome was demonstrated for date of procedure, sex, side, primary or recurrent varicose veins, or commercial type of sclerosant. Treatment was more likely to be effective for older patients, great saphenous compared to small saphenous veins, foamed sclerosant rather than liquid independent of experience, 1.5% sclerosant rather than more diluted or undiluted 3% sclerosant, larger volumes of sclerosant, and smaller compared to larger diameter veins. There were other covariates where hazard ratios suggested better outcome such as clinical C2 rather than C4-6. Others have reported better outcome for small compared to large diameter veins although satisfactory results for large veins have also been reported. Other findings are not necessarily intuitive so that their main value is to point to fields for further research. For example, it is not clear why outcome should be influenced by age or concentration of sclerosant, while we find it difficult to explain the marked difference in results between the great and small saphenous veins.

The use of foam compared to liquid is strongly supported in the contemporary literature. Concerns have been expressed regarding the maximum volume of foam that should be used at one session and a European consensus group and a German national group have established guidelines but these have not yet been subjected to scientific analysis. No conclusive evidence is available that larger volumes are
associated with any increased risk to the patient other than the possible slightly increased likelihood of deep vein thrombosis observed in the present study.

The only complication observed in this study was deep vein thrombosis which occurred in 3.2% of patients. This is somewhat higher than reported in other studies but this may reflect an aggressive policy to scan the deep veins within a few days after treatment for every session which detected asymptomatic thrombosis. This rate is similar to that described with ultrasound evaluation after surgery for varicose veins. Neurological complications have been reported but were not observed in this series.

The findings from this study support the use of ultrasound-guided sclerotherapy for varicose disease with or without saphenous reflux provided patients are warned of the possible need for repeat treatment to achieve secondary success. Results are not as good for large diameter veins or disease in younger patients, particularly for the small saphenous vein. The most effective concentration of sclerosant was 1.5%. Patients should be of the risk of deep vein thrombosis.

References