Eur J Vasc Endovasc Surg (2019) 58, 401–408

A Randomised Controlled Trial Comparing Three Different Radiofrequency Technologies: Short-Term Results of the 3-RF Trial

Isaac K. Nyamekye *, **Nikesh Dattani, Wendy Hayes, Daniel Harding, Sarah Holloway, Jeremy Newman**

Department of Vascular Surgery, Worcestershire Royal Hospital, Worcester, UK

WHAT THIS PAPER ADDS

This paper demonstrates a clear difference between radiofrequency thermal ablation outcomes, with endovenous radiofrequency (EVRF) having significantly greater early failures (6 months) than Venefit and radiofrequency induced thermal therapy (RFITT). The paper also demonstrates the safety of the routine practice of starting ablation within 5 mm of the saphenofemoral junction (SFJ). The commonly cited (but little evidenced) $\geq$ 2 cm clearance from the SFJ is not backed by research studies and exposes patients to long-term risk of recurrence from junctional tributaries. It is hoped that this paper will stimulate research directed at this aspect of thermal ablation treatment.

Objective: To date there has been no comparison of outcomes of endovenous radiofrequency (RF) devices. The 3-RF trial is the first randomised controlled trial of three commercially available RF ablation technologies.

Methods: Patients were recruited [182/302 patients with great saphenous vein (GSV) incompetence] into a prospective double blind randomised trial of Venefit, radiofrequency induced thermal therapy (RFITT), and endovenous radiofrequency (EVRF). The primary outcome measure was GSV closure (total/partial/failed) at six months. Secondary outcome measures included ablation times, complications, pain scores, analgesia requirements, and quality of life (QoL) scores to 12 months.

Results: Patients treated [180: Venefit (57), RFITT (64), EVRF (59)] were matched for age, sex, and vein characteristics. At six months, complete GSV closure was significantly better after Venefit and RFITT treatment (100% and 98%, respectively) compared with EVRF treatment (79%, $p < .001$). Mean treatment time was significantly faster for RFITT than for Venefit and EVRF ($p < .0001$). Euroqol 5D (EQ5D) visual analogue score (VAS) did not differ between groups at any time point. The only difference between groups in EQ5D domain scores was for the pain/discomfort domain at two weeks when significantly fewer EVRF patients reported no problems compared with Venefit and RFITT. This difference had disappeared at six and 12 months. The Aberdeen Varicose Vein Questionnaire (AVVQ) improved for all groups at six and 12 months compared with pre-treatment levels; however, there was no significant difference between groups.

Conclusion: Compared with Venefit and RFITT, EVRF was associated with significant failure of truncal ablation at six months; however, clinical outcomes did not differ significantly at 12 months. clinicaltrials.gov identifier: NCT02441881, NHS Health Research Authority (Hampstead Research Ethics Committee) number: 14/LO/1232.

Keywords: Closurefast, Endovenous radiofrequency, Radiofrequency induced thermal therapy, Thermal ablation, Varicose veins
Article history: Received 22 August 2018, Accepted 28 January 2019, Available online 24 July 2019

INTRODUCTION

The most commonly used radiofrequency (RF) ablation is the Venefit procedure, employing the Closurefast catheter (Closurefast, Venefit, VNUS Medical Technologies, Inc., Sunnyvale, CA, USA).[1] In 2013 when this 3-RF trial was conceived there were two alternative radiofrequency devices available: radiofrequency induced thermal therapy (RFITT, Olympus Surgical Technologies Europe, Hamburg, Germany) using the Celon ProCurve S1200-15 applicator, and endovenous radiofrequency (EVRF, F Care Systems, Antwerp, Belgium) using the RF CR.45i applicator.[2,3] Both applicators have smaller treatment tips than Closurefast and offer the potential to treat long and short vein segments, and incompetent perforators, with a single applicator.[2–5] These three radiofrequency technologies also differ in their method of energy transfer from applicator tip to vein wall.[5] These differences introduce the possibility that the devices may differ in effectiveness of treatment.

* Corresponding author. Department of Vascular Surgery, Worcestershire Royal Hospital, Charles Hastings Way, Worcester, WR5 1DD, UK.
E-mail address: i.nyamekye@nhs.net (Isaac K. Nyamekye).
Twitter: isaacnyamekye@veindoc1

https://doi.org/10.1016/j.ejvs.2019.01.033

Table 1. Radiofrequency energy delivery protocols in the 3 RF randomised controlled trial

GSV diameter	<6 mm		6–8 mm		>8 mm	
GSV segment	Proximal 10 cm	Distal GSV	Proximal 10 cm	Distal GSV	Proximal 10 cm	Distal GSV
Venefit – cycles	× 2	× 1	× 2	× 2	× 3	× 3
Venefit and RFITT – catheter passes	× 2	× 2	× 3	× 2	× 3	× 3
EVRF – catheter passes	× 2	× 2	× 3	× 2	× 3	× 3

Energy delivery was optimised depending on the diameter of the vein, with treatments repeated as above. More treatment was given to proximal trunks (10 cm) up to the maximum number of repeats used. EVRF = endovenous radiofrequency; GSV = great saphenous vein; RFITT = radiofrequency induced thermal therapy.

Venefit has the most published evidence (ablation rates of 94–98%)[6–9] and marketing of other devices has, to some extent, been done on the back of Venefit's results. For RFITT, early anatomical studies reported ablation rates of 88.7–88.9% at one year.[10–12] However, greater energy delivery using slower applicator pullback increases closure rates to 98%.[10] The present authors' technique of re-treating vein segments also demonstrated superior great saphenous vein (GSV) ablation (98%) at 12 months.[13] The only publication on effectiveness of EVRF showed modest ablation rates of 89.2% at one year; however, complication rates were low.[14]

These three radiofrequency devices were directly compared in a randomised controlled trial.

METHODS

Study design

A prospective double blind randomised trial was performed to compare the outcomes of endovenous radiofrequency treatment of the GSV (with saphenofemoral incompetence) in patients with primary varicose veins. This study was conducted in a single centre and the senior author, a radiofrequency technologies enthusiast and experienced with all three devices prior to commencement of the trial, performed all procedures. The primary outcome measure was GSV closure at six months. Secondary outcome measures included speed of treatment, complications, patient recorded pain scores and tablet counts (self assessed in the first week), GSV closure at two weeks, and patient reported quality of life (QoL) at two weeks, six months, and 12 months. Patients and clinicians (vascular scientist and clinical staff) assessing and recording outcomes were blinded to the treatment performed. This trial was conducted according to the Helsinki Declaration in a UK NHS hospital vascular unit, with national ethical committee approval (NRES Committee London–Hampstead 14/LO/1232). The trial was registered on the clinicaltrials.gov register (NCT02441881) and performed without commercial or other funding. All patients were already scheduled to undergo NHS funded treatment. Postage for questionnaires was funded from the lead author's general amenities fund. The Worcestershire Acute Hospitals NHS Trust sponsored the study.

Recruitment

Adults (aged $\geq$ 18 years) with symptomatic varicose veins who had no significant arterial disease and who were able to give consent were included. Patients who had tortuous, kinked, or recurrent GSVs or those with deep venous disease (incompetence or occlusion) on duplex were excluded. Active thrombophlebitis, pregnancy, and the presence of an indwelling pacemaker or defibrillator were also exclusions.

Consecutive patients who were scheduled to undergo GSV endovenous thermal ablation treatment for CEAP C2-C5 venous disease under the care of a single surgeon, were invited to participate in the study. All patients had undergone prior clinical and duplex assessment (Toshiba Viamo Ultrasound, Tokyo, Japan or Sonosite M-Turbo Bothell, Washington, USA) to demonstrate SFJ incompetence and significant GSV reflux (>1 s). After detailed explanation of the study, consenting patients were enrolled and asked to complete quality of life (QoL) questionnaires (Euroqol 5-Dimensional [EQ-5D] and the Aberdeen Varicose Vein Questionnaire [AVVQ]) prior to intervention. Patients with bilateral disease were enrolled but only one leg could be randomised and only single leg treatment was performed on the study treatment day.

Randomisation, performed on the day of treatment to Venefit, RFITT, or EVRF, was performed by a computerised research random number generator (https://www.randomizer.org) set to generate a number of one, two or three for Venefit, RFITT, and EVRF, respectively. Patients, the vascular scientist who undertook post-procedural imaging, and clinicians undertaking assessments were blinded to the radiofrequency device used.

Interventions

All procedures were performed using tumescent local anaesthesia (TLA) and without sedation. A detailed description of the technique can be found in a previous publication.[15] Selective thromboprophylaxis was managed according to a thromboprophylaxis protocol.[16] All procedures were performed under duplex ultrasound control.

Specific aspects of each radiofrequency technique have been described in detail elsewhere.[5] Treatments were performed from the lowest point of tuncal reflux and the applicator tip was positioned within five mm of the saphenofemoral junction prior to commencing treatment (acknowledging this practice differs from instructions for use for all three devices). The method of applicator withdrawal is device specific and additional energy delivery, achieved by repeating treatment, was based on pre-treatment vein diameters[5] (Table 1).

Table 2. Patient numbers, age, great saphenous vein (GSV) characteristics, and treatment duration

	Venefit (n=57)	Venefit and RFITT (n=64)	EVRF (n=59)
Men - n (%)	28 (49)	26 (40)	17 (29)
Age - years	55.7 ± 17.1	52.8 ± 14.3	51.8 ± 14.8
GSV Diameter - mm	7.1 ± 1.8	7.1 ± 1.4	6.6. ± 1.8
Ablation length - cm	37.3 ± 11.8	33.2 ± 9.7	34.7 ± 11.1
Ablation time - min	4.88 ± 1.9[a]	3.32 ± 1.1[a]	6.8 ± 3.1[a]
Total treatment time - min	20.43 ± 5.2[a]	18.87 ± 4.7[a]	23.55 ± 7.2[a]

Data are presented as mean ± standard deviation unless indicated otherwise. For the three groups, age, sex, GSV diameter, and treated GSV length were not statistically significantly different at alpha level of .05. EVRF = endovenous radiofrequency; GSV = great saphenous vein; RFITT = Radiofrequency induced thermal therapy; y = years.
[a] Ablation times ($p < .0001$) and total treatment time ($p < .0001$) were statistically significantly different between the groups.

For Venefit the standard 7 cm heating element Closurefast catheter was used with the pre-set 20 s cycle, and additional energy cycles were given segmentally. RFITT treatment was delivered by slow continuous applicator withdrawal (<1 cm/1.5 s) guided by the device's acoustic feedback signal. Additional energy delivery was given by repeated withdrawal over 5—10 cm lengths.[13] EVRF treatment was administered by slow stepwise applicator withdrawal timed to the generators audible beeps and withdrawing the tip by 5 mm on each (higher pitched) third beep. Additional energy was given by repeat withdrawal. No additional phlebectomies or foam sclerotherapy were performed in patients during the study period.

Treated diameter and length, duration of ablation, and total treatment time were recorded on a trial proforma.

Post-operative management

Treated legs were dressed by application of a rolled dressing pad (Zetuvit R E, Hartmann, Paul-Hartmann-Stasse 12, Heidenhelm, Germany) over the treated vein (to capture TLA seepage) and secured with Peha-haft compression bandaging (Selles Medical Ltd, Hull, UK). Bandages were exchanged for thigh length RAL class II compression hosiery (Medi UK Ltd, Hereford, UK) after 48 h, with instruction for this to be worn for a minimum of two weeks. All procedures were ambulatory and patients were discharged home within 30 min of returning to the ward, with instructions advising immediate and frequent ambulation. No analgesia was prescribed but patients were advised, if required, to take paracetamol, then add cocodamol and then ibuprofen as required. They were asked to score the worst level of pain experienced on each of the first seven post-operative days onto a simple 10 cm visual analogue pain chart together with the daily number of analgesic tablets taken. Patients were given a comprehensive patient information sheet outlining their expected post-operative progress, the analgesia advice, and contact information for the research nurse and the vascular ward, should any adverse events arise.

Assessments

Follow up was at two weeks, six months (clinical, duplex, and QoL questionnaires), and 12 months (postal QoL questionnaires alone). A maximum of two reminders were sent to non-attendees/non-responders. Two week and six month duplex scans assessed GSV closure. Unblinding for all patients and data analysis was done only after study completion.

Primary outcome

Primary outcome was GSV closure at six months. Failure was defined as any segment of treated trunk greater than five cm in length and demonstrating patency (compressible) and any flow or reflux (and more than two cm from the saphenofemoral junction) irrespective of clinical outcome. Two different failure types were characterised as follows: partial failure, incomplete recanalisation anywhere in the treated vein but with a separate segment of treated vein still present; complete failure, failure throughout the treated vein trunk irrespective of vein diameter.

Secondary outcomes

Secondary outcomes were ablation time, total treatment time (from initial infiltration of local anaesthesia prior to access needle puncture to completion of post-procedure bandaging), complications, pain scores and tablet counts, GSV closure at two weeks, and Aberdeen Varicose Vein Questionnaire (AVVQ) and Euroqol 5D (EQ5D) scores up to 12 months. For EQ5D scores, the percentage of patients scoring 1 (no problems) was compared between devices.

Statistical analysis

From existing non-randomised data, a six month difference in failure of ablation between Venefit, RFITT, and EVRF of 15% was predicted. At 80% power (α-error 5%, β-error 20%), sample sizes of 53 patients per treatment group and a minimum of 159 patients were calculated to detect this difference. Because varicose vein studies with relatively high proportions of patients of working age, have high rates of loss to follow up, a 10% dropout rate was assumed. This gave a minimum recruitment target of 176.

Data were tabulated onto a Microsoft Excel spreadsheet (Microsoft, CA, USA) and statistical analyses performed using GraphPad Software Inc (GraphPad, La Jolla, CA, USA). Descriptive data were reported as mean (SD) and

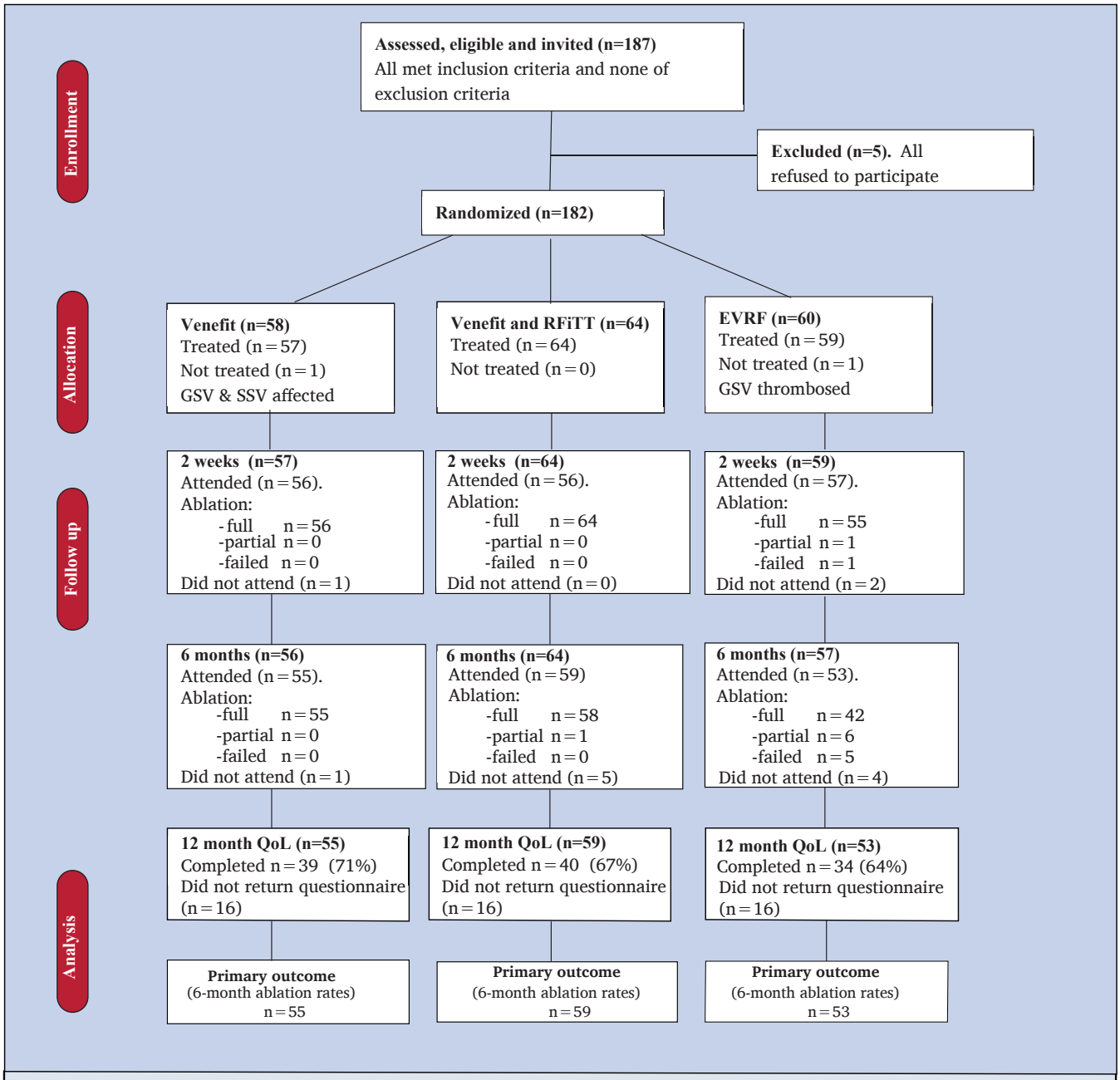

Figure 1. CONSORT diagram showing the flow of patients through the 3-RF randomised controlled trial. EVRF = endovenous radiofrequency; GSV = great saphenous vein; QoL = quality of life; RFITT = radiofrequency induced thermal therapy; GSV = great saphenous vein; SSV = small saphenous vein.

continuous data was compared using the ANOVA test to compare the means of the three treatments. Significance was set at a p value of < 0.05.

RESULTS

Demographic data

Three hundred and two patients were assessed and 187 patients, selected for their non-tortuous veins, were enrolled. One hundred and eighty two patients were randomised between September 2014 and September 2016. Randomised patients had a mean age of 53 years (range 20—80 years), and 61% were women. All fell within CEAP classes 2—5. Groups were well matched and there were no differences in vein characteristics (Table 2).

Primary outcome

Details of treatment groups are given in the consort diagram (Fig. 1). Direct comparison of devices showed that closure rates differed significantly at six months. EVRF treated patients had 11 (21%) failures (six [11%] partial and five [10%] complete) compared with 0 (0%) failures for Venefit and one (2%) partial failure for RFITT ($p < .001$). All recanalisations identified in partial ablations were in the GSV segment that was immediately distal to the SFJ, and refluxing vein lengths ranged from 5 to 20 cm.

Table 3. Secondary outcome of the 3-RF randomised controlled trial: 7 day pain score and tablet counts

	Number completing score	Total pain score for 7 d		Total tablet count for 7 d	
		Median	Range	Median	Range
Venefit	53 (out of 57)	3	0–27	0	0–24
Venefit and RFITT	59 (out of 64)	2.5	0–43	0	0–34
Endovenous radiofrequency	55 (out of 59)	5	0–44	0	0–35

There was no statistically significant difference between devices for pain or tablet count during the first week at alpha level of .05. d = days; GSV = great saphenous vein; RFITT = radiofrequency induced thermal therapy.

Secondary outcome

Mean time for ablation (and total treatment time) differed significantly between groups, with RFITT having the shortest and EVRF the longest times ($p < .00001$, Table 2). No patients developed deep venous thromboembolism, skin burns, wound infections, post-operative paraesthesia, or skin discolouration. One patient developed asymptomatic endovenous heat induced thrombosis (EHIT) grade 2 following EVRF treatment. This incidental finding on two week duplex imaging was managed conservatively (without any additional medication) and had resolved without incident on the six month imaging. Two week vein closure rates did not differ significantly.

There was no significant difference in pain score or tablet count between groups (Table 3). A significant minority of patients, after each treatment, recorded pain scores of zero during the first seven days (12, 25, and 20 patients for Venefit, RFITT, and EVRF, respectively) and a majority took no analgesia (28, 42, and 37 for Venefit, RFITT, and EVRF, respectively).

QoL questionnaire return rates were 98% pre-operatively, 98% at two weeks, 92% at six months, and 63% at 12 months. EQ5D questionnaire-VAS average scores across the complete dataset were 0.82 pre-procedure compared with 0.83 at two weeks, 0.84 at six months, and 0.84 at 12 months, and there were no between group differences (Table 4). There was no significant difference between treatments for the domains of Mobility, Self care, Usual activity, and Anxiety/depression (data not shown). For the Pain/discomfort domain, there was a difference between groups at two weeks, with significantly fewer patients reporting no problems (score 1) after EVRF compared with Venefit and RFITT (Fig. 2). This had disappeared at six and 12 months (Table 4).

Overall, for the Aberdeen Varicose Vein Questionnaire (AVVQ) 87.9% of patients reported an improvement in scores. Average pre-procedure scores for Venefit, RFITT, and EVRF of 15.32, 15.61, and 17.58 improved to 7.53, 9.6, and 10.97, respectively, at 12 months (Fig. 3). However, there was no significant difference in AVVQ scores between groups.

DISCUSSION

All treatments in this study were commenced with the catheter/applicator tip positioned within 5 mm of the SFJ. The authors acknowledge that this clearance distance from SFJ prior to commencing treatment is an ongoing area of controversy. Venefit's manufacturer recommends "at least 2 cm clearance from the saphenous junction" (but no maximum clearance is advised), and 2 cm has been adopted for RFITT and EVRF (although, interestingly, the recently introduced second generation RFITT recommends only a 1 cm clearance). The stated aim of placing the catheter tip 2 cm below the saphenous junction is to reduce the risk of endovenous heat induced thrombosis (EHIT). However, no studies have specifically assessed this recommendation and there is evidence that this policy risks increasing future recurrence from communicating junctional tributaries.[17] The "SFJ clearance distance" was reviewed in publications that used the Closurefast catheter (and its predecessor ClosurePlus) (unpublished data). Starting distances for treatment were <2 cm in 12%, 2 cm in 17%, and 2–3 cm in 37% of publications. In 15% of publications the start point was merely stated as "distal to a junctional tributary," and no reference distance was given in 19% of publications. No good negative correlation was found between reported EHIT rates and increasing distance distal to the SFJ, and increasing starting distance distal to the SFJ did not offer protection from EHIT. It is postulated that leaving ≥2 cm of GSV untreated at the SFJ may encourage thrombus formation and propagation in the residual low flow sump that cannot always be prevented by slow prograde flow in patent small tributary veins (as theorised by others). This is clearly an area in need of further study by EHIT enthusiasts. The senior author has routinely treated from within 5 mm of the SFJ, aiming to leave as little sump as possible. On clinical review at six weeks (the present authors do not perform early control duplex), EHIT has not presented a single clinical problem in >1500 GSV radiofrequency thermal ablations performed since 2010.

The two week GSV closure rates of 100% for Venefit and RFITT and 98% for EVRF compare favourably with published immediate ablation rates of 90–100%. At six months, Venefit and RFITT ablations of 100% and 98% were also comparable to reported short-term ablations of up to 97% at three months and closure rates of 94–97% at 12–14 months.[6,8,9,13] However, EVRF delivered significantly inferior ablation rates (only 79% ablation) at six months. This occurred despite careful use of repeat treatments to deliver additional energy at the treatment tip. The actual amount of energy reaching the vein wall cannot be reliably

Table 4. Secondary outcome of the 3-RF randomised controlled trial: Euroqol 5D visual analogue score (EQ5D VAS) and pain discomfort domain score

	Mean EQ5D VAS ± SD			Pain Discomfort domain score (% indicating 1 = no discomfort)		
	Venefit	Venefit and RFITT	EVRF	Venefit	Venefit and RFITT	EVRF
Baseline	83.0 ± 12.7	82.4 ± 13.8	82.9 ± 12.7	22.6	22.8	23.1
2 wk	84.1 ± 13.0	82.2 ± 12.3	81.8 ± 15.7	32.4[a]	28.4[a]	16.7[a]
6 mo	85.0 ± 10.0	85.1 ± 11.6	81.7 ± 16.0	62.8	59.8	41.9
12 mo	85.1 ± 11.6	82.2 ± 16.7	83.6 ± 14.7	49.4	53.3	40.8

EQ5D VAS scores did not differ significantly between groups at any time point. EVRF = endovenous radiofrequency; mo = months; RFITT = radiofrequency induced thermal therapy; VAS = visual analogue score; wk = weeks; SD = standard deviation.
[a] There was a difference between groups for the pain and discomfort domain at two weeks, with fewer patients reporting no problems after EVRF compared with Venefit and RFITT ($p < .05$). This had disappeared at six and 12 months.

calculated as it is influenced by factors such as contact between catheter tips and vein wall, residual luminal blood, and, for the continuous withdrawal devices, coagulum formation. EVRF also had significantly longer treatment times than Venefit and RFITT. However, this was not translated into differences in patient reported pain scores, analgesic use, complication rates, or QoL score between the three devices during the study period. Interesting, at two weeks, significantly fewer patients reported no problems in the EQ5D Pain and Discomfort domain after EVRF compared with Venefit and RFITT. This is difficult to explain because no difference was shown in pain scores during the first week.

Two practical issues were encountered with the pullback device applicators (RFITT and EVRF). For RFITT, overly slow pullback led to increased impedance and ultimately triggered the device's auto-stop function to stop treatment. This necessitated applicator removal for cleaning of coagulum that had formed at the bipolar tip, before treatment could continue. The number of removals for cleaning in the study was not specifically recorded; however, it occurred on at least one occasion during about a third of treatments. During stepwise EVRF pullback there was frequent applicator tip adherence to the vein wall (despite strict compliance with the manufacturer's withdrawal method). This required a tugging motion to free the tip to allow pullback to continue. This was a relatively predictable occurrence in most cases. EVRF has no auto-stop feature and treatment could, apparently, be continued as "stickiness" reduced with treatment progression. Removal of the applicator tip revealed tissue (presumed to be endothelium) adherent to the tip. Despite assurances from the manufacturer that this would not affect RF conduction (and therefore effectiveness of treatment), the present experience suggests otherwise. It seems likely that initial applicator tip adherence reduces effectiveness of energy transfer to the vein wall as treatment progresses. It is hypothesised that this may have contributed to the poorer outcome for truncal ablation with EVRF.

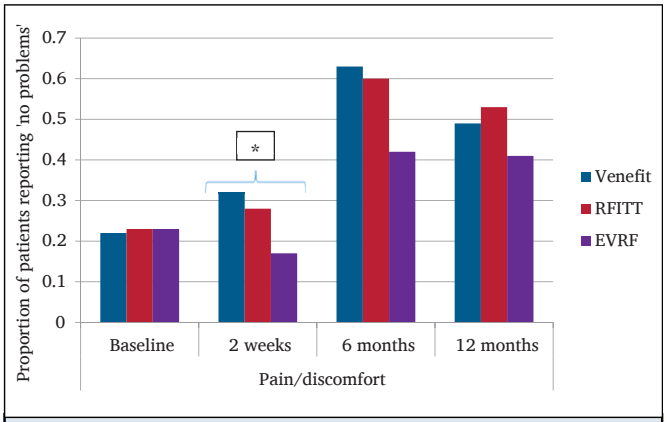

Figure 2. Pain Discomfort domain. There was no difference in proportion of patients reporting "no problems" between treatment groups at baseline, six months or 12 months. However at two weeks fewer patients reported symptoms after endovenous radiofrequency (EVRF) (*$p < .05$). Within groups, compared with baseline, significantly fewer patients reported symptoms at six months for all groups. However, by 12 months this remained significant for Venefit and Venefit and radiofrequency induced thermal therapy (RFITT) ($p < .05$), but not for EVRF ($p > .05$).

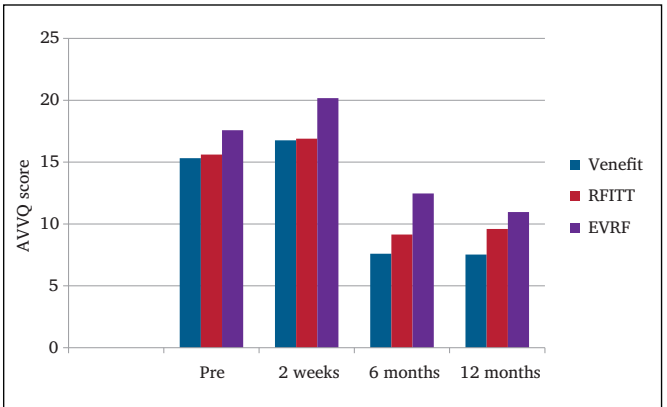

Figure 3. Changes in Aberdeen Varicose Vein Questionnaire (AVVQ) scores for Venefit, Venefit and radiofrequency induced thermal therapy (RFITT), and endovenous radiofrequency (EVRF). Average pre-procedure AVVQ scores for Venefit, RFITT, and EVRF of 15.32, 15.61, and 17.58 improved statistically significantly to 7.6, 9.15, and 12.47 (<0.05) at six months. This reduction in symptom scores remained statistically significant for all three interventions at 12 months. There was no difference between the three treatment groups at $p < .05$.

Effective thermal closure of larger veins might be expected to be more challenging compared with smaller veins. Radiofrequency therapy has been shown to effectively ablate large diameter veins (>12 mm diameter) and additional energy delivery aids closure of these larger veins.[18,19] For Venefit, up to three treatment cycles per segment (permitted on IFU) has been shown to effect quicker and greater shrinkage of larger GSVs without an increase in side effects.[8] The aim was to increase the likelihood of successful vein closure by employing similar repeat treatments for all devices, including Venefit; however, there were differences in outcomes despite these manoeuvres for additional energy delivery.

The possibility of treatment failure and potential for late recanalisation are recognised after all endovenous thermal ablation procedures. The early and significant failure with EVRF reported here, even in the hands of an experienced endovenous operator, is a concern and should caution practitioners seeking to adopt this particular radiofrequency technology. The present results suggest that EVRF treatment requires further objective evidence of equivalent effectiveness to Venefit and now RFITT before it can be recommended for standard clinical care. Effective thermal ablation results in fibrosis, with the vein trunk eventually becoming indistinguishable from other soft tissue on ultrasound. Treatments that cause thrombosis rather than fibrosis could result in early recanalisation and such an outcome might explain the early failures seen at the relatively short time point of six months. It is planned to obtain ethical approval to further evaluate patient outcomes by extending the study to three years. However, the high dropout rate already experienced at the 12 month postal questionnaire follow up (and reports from other similar studies) suggests this may not yield useable results.[6]

In the European Society of Vascular Surgery (ESVS) guidelines on chronic venous disease (CVD) written by Wittens et al., radiofrequency ablation is cited as one of the two most frequently used endovenous modalities when treating superficial venous incompetence in truncal saphenous veins. Because of the limited evidence available for other types of RF device, the guidance addresses only the Closurefast catheter (and its predecessor) used in the Venefit procedure.[20] The 3-RF Trial has shown that the guidance given for Closurefast can probably be applied equally to RFITT, but not to EVRF. As the ESVS guidelines have done for lasers, and because of the differences shown in this paper, future versions of the ESVS CVD guideline should aim to distinguish between different types of available RF treatment.

Limitations

The methodology of using a single surgeon in a single centre might be viewed both as a weakness, but also a strength. This would clearly be a weakness if the aim was attempting to teach a technique because it would negatively impact the generalisability of the results. However, in this head to head study of three devices, it is believed to have strengthened the results. It eliminated differences in technique that invariably exists between centres and between clinicians, and that might otherwise have biased treatment outcomes. The authors believe the methodology, including absence of any secondary treatments during the study period, limited influence on outcomes as far as possible, to the RF devices themselves.

In recruiting the study population 120 patients (38%) were excluded because of tortuosity or kinking in the GSV during the screening process. This was because the repeat treatment technique used for the pullback devices might not have been possible. These patients all had Venefit treatment where proximal repositioning is never used, including occasional catheter placement using the over the wire technique.

Venous studies are typically limited by a paucity of long-term outcomes due to the number of patients lost to follow up and this study is no exception. The loss of only 12 patients (6.7%) at six months was less than had been accounted for in the power calculation and compares favourably with other studies that deliberately selected short follow up times of six weeks and three months, because of fear of dropouts. Dropouts in these studies were still 12% and 13% respectively.[6,21] Although obtaining 12 month duplex results was desirable this was not possible as the study had no specific funding for this test. Also by 12 months, the high dropout rates (only 63.1% questionnaire returns) suggests that funding for duplex at this time point might not have yielded meaningful results.

CONCLUSIONS

Radiofrequency technology is a proven, efficacious and safe treatment modality for truncal venous reflux ablation however available devices do not have equivalent effectiveness for GSV truncal vein ablation. Whilst Venefit and RFITT had similar outcomes for vein closure at six months, EVRF was significantly inferior. However, this did not translate into difference in QoL results at up to 12 months. These ablation results should inform existing users of EVRF to take special measures to follow patients and to audit their outcomes.

A broader point of the paper is to caution against the introduction and marketing of new technologies into clinical practice without controlled comparison with existing proven treatments.

ACKNOWLEDGEMENTS

The authors are most grateful for the significant contributions made by Alexandra Wagstaff and Kristin Cooper, without whom the 3-RF Trial could not have been delivered.

CONFLICTS OF INTEREST

I. Nyamekye has lectured on and demonstrated Venefit for its former owner Covidien and RFITT for Olympus for which expenses and honoraria were paid. He currently acts as an endovenous consultant for Olympus.

FUNDING

None.

REFERENCES

1 Ltd. CUC. *Instructions for Use: ClosureFAST Catheter (Package Insert)*. 2014.
2 Olympus Winter & ibe GmbH H, Germany. *Instructions for Use: CelonProCurve Catheter*. 2014.
3 F Care Systems A, Belgium. *Instructions for Use: CR45i EVRF Catheter (Package Insert)*. 2014.
4 van den Bos R, Arends L, Kockaert M, Neumann M, Nijsten T. Endovenous therapies of lower extremity varicosities: a meta-analysis. *J Vasc Surg* 2009;**49**:230–9.
5 Goodyear SJ, Nyamekye IK. Radiofrequency ablation of varicose veins: best practice techniques and evidence. *Phlebology* 2015;**30**: 9–17.
6 Nordon IM, Hinchliffe RJ, Brar R, Moxey P, Black SA, Thompson MM, et al. A prospective double-blind randomized controlled trial of radiofrequency versus laser treatment of the great saphenous vein in patients with varicose veins. *Ann Surg* 2011;**254**:876–81.
7 Creton D, Pichot O, Sessa C, Proebstle TM. Radiofrequency-powered segmental thermal obliteration carried out with the ClosureFast procedure: results at 1 year. *Ann Vasc Surg* 2010;**24**: 360–6.
8 Choi JH, Park HC, Joh JH. The occlusion rate and patterns of saphenous vein after radiofrequency ablation. *J Korean Surg Soc* 2013;**84**:107–13.
9 Bisang U, Meier TO, Enzler M, Thalhammer C, Husmann M, Amann-Vesti BR. Results of endovenous ClosureFast treatment for varicose veins in an outpatient setting. *Phlebology* 2012;**27**: 118–23.
10 Braithwaite B, Hnatek L, Zierau U, Camci M, Akkersdijk G, Nio D, et al. Radiofrequency-induced thermal therapy: results of a European multicentre study of resistive ablation of incompetent truncal varicose veins. *Phlebology* 2013;**28**:38–46.
11 Tesmann JP, Thierbach H, Dietrich A, Grimme H, Vogt T, Rass K. Radiofrequency induced thermotherapy (RFITT) of varicose veins compared to endovenous laser treatment (EVLT): a non-randomized prospective study concentrating on occlusion rates, side-effects and clinical outcome. *Eur J Dermatol* 2011;**21**: 945–51.
12 Boon R, Akkersdijk GJ, Nio D. Percutaneus treatment of varicose veins with bipolar radiofrequency ablation. *Eur J Radiol* 2010;**75**: 43–7.
13 Newman JE, Meecham L, Walker RJ, Nyamekye IK. Optimising treatment parameters for Radiofrequency Induced Thermal Therapy (RFITT): a comparison of the manufacturer's treatment guidance with a locally developed treatment protocol. *Eur J Vasc Endovasc Surg* 2014;**47**:664–9.
14 Spiliopoulos S, Theodosiadou V, Sotiriadi A, Karnabatidis D. Endovenous ablation of incompetent truncal veins and their perforators with a new radiofrequency system. Mid-term outcomes. *Vascular* 2015;**23**:592–8.
15 Nyamekye IK. A practical approach to tumescent local anaesthesia in ambulatory endovenous thermal ablation. *Phlebology* 2019;**34**: 238–45.
16 Goodyear SJ, Nyamekye IK. Rational anti-DVT prophylaxis for ambulatory varicose veins procedures. In: Greenhalge RM, editor. *Vascular and endovascular challenges update*; 2016. p. 541–9.
17 Proebstle TM, Möhler T. A longitudinal single-center cohort study on the prevalence and risk of accessory saphenous vein reflux after radiofrequency segmental thermal ablation of great saphenous veins. *J Vasc Surg Venous Lymphat Disord* 2015;**3**:265–9.
18 Calcagno D, Rossi JA, Ha C. Effect of saphenous vein diameter on closure rate with ClosureFAST radiofrequency catheter. *Vasc Endovasc Surg* 2009;**43**:567–70.
19 Garcia-Madrid C, Pastor Manrique JO, Sanchez VA, Sala-Planell E. Endovenous radiofrequency ablation (venefit procedure): impact of different energy rates on great saphenous vein shrinkage. *Ann Vasc Surg* 2013;**27**:314–21.
20 Wittens C, Davies AH, Bækgaard N, Broholm R, Cavezzi A, Chastanet S, et al. Editor's choice - management of chronic venous disease: clinical practice guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2015;**49**:678–737.
21 Shepherd AC, Gohel MS, Brown LC, Metcalfe MJ, Hamish M, Davies AH. Randomized clinical trial of VNUS ClosureFAST radiofrequency ablation versus laser for varicose veins. *Br J Surg* 2010;**97**:810–8.