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Quality-of-Life (QOL) and Patient-Reported Outcome Measures (PROMs) Following Intervention for Chronic Venous Disease

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Introduction

Lower extremity chronic venous disease affects a considerable percentage of the population. Approximately 25 million people in the United States have varicose veins and the annual prevalence of venous thromboembolism (including both deep vein thrombosis and pulmonary embolism) is approximately one million people [1]. Although the majority of patients with lower extremity chronic venous disease are asymptomatic, a number of serious complications can occur, including venous leg ulcers, acute and chronic venous thromboembolism (that can cause pulmonary embolism), chronic thromboembolic pulmonary hypertension and death [2].

A serious and common complication/manifestation of lower extremity chronic venous disease is the formation of venous leg ulcerations. Venous leg ulcers affect approximately 600,000 individuals in the United States and place a burden on patients in terms of quality of life (QoL), pain and social isolation [3, 4]. In addition to the psychosocial consequences of these complications, lower extremity chronic venous disease is associated with high costs, which are estimated between $150 million and $1 billion per year in the United States [3, 4].

The management of chronic venous disease may be conservative/non-invasive and invasive. Graduated compression stockings and a number of venotropic drugs (e.g. flavonoids [e.g. daflon], naftidrofuryl, naftazone, hydroxyethylrutosides [e.g. venoruton], etc.) have been shown to be effective in the control of venous disease (reduction of pain and swelling) [1, 2]. The traditional surgical management (high venous ligation and stripping in combination with ambulatory/transilluminated powered phlebectomies) has been largely replaced by the endovenous techniques (endovenous laser ablation [EVLA], radiofrequency ablation [RFA], liquid/foam/glue sclerotherapy, cyanoacrylate embolization and mechanochemical ablation) [1–3]. A description/comparison of the various techniques available is beyond the scope of this article and is presented in greater detail elsewhere [5].

Non-invasive hemodynamic measurements and ultrasonic anatomic evaluation can be used to objectively assess the effect of intervention on venous insufficiency (such as venous filling index

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[as measured by air-plethysmography] that measures the global venous reflux) [1–3]. Besides these objective outcomes, however, there is also the perceived satisfaction/symptom relief as experienced by the patient. Patient-reported outcome measures (PROMs) provide a means by which the impact of varicose veins or their treatments can be measured on the patient's QoL [6]. Several questionnaires have been developed to assess the impact of chronic venous disease and venous leg ulcers. The items in these questionnaires aim to capture the patient's experience using psychometric analyses and to explore their relationship with each and their overall ability to detect change [6]. The effect of venous interventions on quality of life can be assessed by general and specific assessments. Disease-specific quality-of-life instruments can be divided in PROMs and physician-reported outcome measurements.

The reliability of a PROM is its ability to produce the same results when measurements are repeated in populations with similar characteristics [6]. PROMs commonly use more than one item to measure a single dimension that is important to the patient [6]. These items need to be reliable, valid and internally consistent [6]. A brief description of the available PROMs to assess chronic venous disease is presented.

PROMs to Assess Chronic Venous Disease

Five questionnaires have been developed for patients with venous leg symptoms or signs, but without ulcers (Table 21.1), namely:

1. **The Freiburg Life Quality Assessment (FLQA) questionnaire** [7]**:** The FLQA consists of 93 items and differentiates between limitations in QoL in seven scales: physical complaints, everyday life, social life, emotional status, treatment, satisfaction and general health [7].
2. **The Specific Quality of life and Outcomes Response—Venous (SQOR-V) questionnaire** [8]**:** This questionnaire consists of 46 items with special attention to the patients' main complaints with relevance for venous disorders [8].
3. **The ChronIc Venous Insufficiency Questionnaire (CIVIQ)** [9]**:** This is a 20-item questionnaire which explores four dimensions: psychological, physical, social functioning and pain [9].
4. **The Aberdeen Varicose Vein Symptom Severity (AVVSS) Score or Aberdeen Varicose Vein Questionnaire (AVVQ)** [10]**:** This questionnaire is devoted exclusively to

Table 21.1 Available questionnaires with patient-reported outcome measures (PROMs) to assess chronic venous diseases

Questionnaire	Dimensions (number of items)
Freiburg Life Quality Assessment questionnaire [7]	Physical complaints (14), everyday life (10), social life (6), emotional status (9), treatment (4), satisfaction (7), VAS General Health (1), VAS Skin condition (1) and VAS Quality of Life (1)
Specific Quality of life and Outcomes Response—Venous questionnaire [8]	Discomfort, Appearance, Restriction of movements, Risk, Emotional Problems, Physical impact, Psychosomatic impact, Global Score
Chronic Venous Insufficiency Questionnaire (CIVIQ) [9]	Physical repercussions (e.g. standing/squatting/kneeling, walking quickly/climbing stairs, travelling), psychological repercussions (e.g. anxiousness, tiredness, embarrassment), pain repercussions (e.g. pain, interference with work/sleep), social repercussions, overall quality of life score
Aberdeen Varicose Vein Questionnaire [10]	Functional status (physical/social functioning, role limitations attributed to physical/emotional problems), wellbeing (mental health, energy/fatigue, pain), overall evaluation of health (interference with work/leisure, concern)
Venous insufficiency epidemiological and economic study on quality of life [11]	Symptoms (10), limitations in daily activities (9), time of greatest intensity (1), change over the past year (1), psychological impact (5)

VAS visual-analogue scale

the QoL measurement of patients suffering from varicose veins. It includes information on four important health factors: pain and dysfunction, cosmetic appearance, extent of varicosity and complications [10].

5. **The VEnous INsufficiency Epidemiological and Economic Study on Quality of Life (VEINES-QoL)** [11]**:** This is a scientifically sound, patient-reported outcome score that evaluates quality of life and symptoms across a range of conditions (e.g. telangiectasias, varicose veins, edema, skin changes, leg ulcers) in chronic venous disorders of the leg [11].

Besides these five questionnaires, there are another four scales dedicated to patients with venous leg ulcers, namely:

1. **The Venous Leg Ulcer Quality of Life (VLU-QoL) questionnaire** [12]**:** This questionnaire consists of 34 items on three domains: Activities (12 items), Psychological (12 items) and Symptom Distress (10 items). This questionnaire is a useful tool to assess the outcomes of treatment from the patients' point-of-view [12].
2. **The Leg and Foot Ulcer Questionnaire of Hyland (LFUQ)** [13]**:** This questionnaire measures functional limitations and emotional reactions to quantify QoL deficits. Functional limitations and emotional reactions are inter-correlated to evaluate the effect of venous leg ulcers on the patient's global QoL [13].
3. **The Sheffield Preference-based Venous leg Ulcer Questionnaire with five Dimensions (SPVU-5D)** [14]**:** This is a questionnaire consisting of 16 disease-specific items and life-satisfaction questions. It assesses the level of pain and discomfort, as well as the psychological effects of venous ulcerations [14].
4. **The Charing Cross Venous Leg Ulceration Questionnaire (CCVUQ)** [15]**:** This questionnaire assesses four important health domains: social function, domestic activities, cosmetic appearance and emotional status [15].

Finally, the Short Form 36-Item (SF-36) and 12-Item (SF-12) health surveys [6] are tools that assess QoL in association with:

1. **The Venous Clinical Severity Score (VCSS)** [16]**:** VCSS assesses venous disease severity using several characteristics, including pain, varicose veins, edema, pigmentation, inflammation, induration, number and size of ulcers, ulcer duration and use of compression (Table 21.2) [16].
2. **The Clinical, Etiologic, Anatomic, Pathophysiologic (CEAP) score** [17]**:** The CEAP classification for chronic venous disorders was developed in 1994 by an international ad hoc committee of the American Venous Forum. The CEAP classification provides a descriptive classification of chronic venous disease (Table 21.2) [17].

The above-mentioned questionnaires and PROMs have been used to compare the various interventions for the treatment of chronic venous diseases and assess their efficacy from the patient's perspective. A comparison of the various methods used in randomised controlled trials with respect to the QoL of the patient using PROMs is presented in Table 21.3. The different comparisons that have been assessed are presented below.

Table 21.2 Available questionnaires to assess quality-of-life in patients with chronic venous diseases

Questionnaire	Dimensions (number of items)
Venous Clinical Severity Score [16]	Absent/Mild/Moderate/Severe classification in pain, varicose veins, venous edema, skin pigmentation, inflammation, induration, number and size of active ulcers, ulcer duration, compression
Clinical, Etiologic, Anatomic, Pathophysiologic score [17]	Clinical classification (8), Etiologic classification (4), Anatomic Classification (4), Pathophysiologic classification (4)

Table 21.3 A list of all randomized controlled trials, questionnaires used and outcomes

Study (year)	# Limbs	Follow-up (month)	Instrument	Design	Comparison	Outcome
Lurie (2003) [18]	86	4	CIVIQ2-QoL	Prospective multicenter RCT	44 RFA vs. 36 L&S	Global score (72 h): 13.3 (SE: 3.1) vs. −3 (2.3); $p < 0.0001$ Global score (1 week): 3.7 (2.5) vs. −9.2 (2.3); $p < 0.0001$
Lurie (2005) [19]	65	24	CIVIQ2-QoL	Prospective multicenter RCT	36 RFA vs. 29 L&S	Global score at 1 and 2 years; $p < 0.05$
Subramonia (2010) [20]	88	1	AVVSSS	Prospective 2-center RCT	47 RFA vs. 41 L&S	Mean improvement in global QoL score: −9.12 vs. −8.24; $p = 0.532$
Rasmussen (2013) [21]	580	36	AVVSSS	Prospective 2-center RCT	148 RFA vs. 144 EVLA vs. 144 UGFS vs. 142 L&S	RFA AVVSSS: 18.74 (8.63) to 4.43 (6.58); $p < 0.0001$ EVLA AVVSSS: 17.97 (9.00) to 4.61 (5.8); $p < 0.0001$ UGFS AVVSSS: 18.38 (9.07) to 4.76 (5.71); $p < 0.0001$ L&S AVVSSS: 19.3 (8.46) to 4.00 (4.87); $p < 0.0001$
Rasmussen (2007) [22]	137	6	VCSS, SF-36, AVVSSS	Prospective 2-center RCT	69 EVLA vs. 68 L&S	EVLA VCSS: from 2.8 (1–8) to 0.4 (0–7); $p < 0.001$ EVLA L&S: from 2.4 (2–12) to 0.2 (0–2); $p < 0.001$
Rasmussen (2011) [23]	580	12	VCSS, SF-36, AVVSSS	Prospective 2-center RCT	148 RFA vs. 144 EVLA vs. 144 UGFS vs. 142 L&S	The VCSS, AVVSSS and SF-36 all improved significantly after the procedure ($p < 0.001$) with no significant difference between them
Christenson (2010) [24]	200	24	VCSS, SF-36, AVVSSS	Prospective single-center RCT	100 L&S vs. 100 EVLA	The VCSS, AVVSSS and SF-36 all improved significantly after each procedure with no significant difference between the groups
Biemans (2013) [25]	223	12	CEAP, CIVIQ, EuroQoL	Prospective 2-center RCT	78 EVLA vs. 77 UGFS vs. 68 L&S	The CIVIQ and EuroQoL improved in all groups at 3 months and showed no significant difference between the groups.
Pronk (2010) [26]	130	12	CEAP, EuroQoL	Prospective single-center RCT	62 EVLA vs. 68 L&S	Although pain scores were higher after EVLA up to Day 14 ($p = 0.01$), no differences were noted between the procedures at 1 year ($p = 0.87$)
Flessenkamper (2013) [27]	449	42	CEAP	Prospective multicenter RCT	159 L&S vs. 142 EVLA vs. 148 EVLA + L&S	The CEAP classification improved in all groups already at 2 months and showed no significant difference between the groups.

Table 21.3 (continued)

Study (year)	# Limbs	Follow-up (month)	Instrument	Design	Comparison	Outcome
Mozafar (2014) [28]	65	18	CEAP, AVVSSS	Prospective single-center RCT	30 EVLA vs. 35 L&S	The CEAP classification improved in both groups significantly and showed no between-group difference.
Roopram (2013) [29]	175	1.5	AVVSSS, EuroQoL	Prospective 2-center RCT	118 EVLA vs. 57 L&S	Both groups showed significant improvement ($p < 0.001$) with no between-group difference.
Brittenden (2019) [30]	595	60	AVVSSS, EuroQoL	Prospective multicenter RCT	162 EVLA vs. 219 UGFS vs. 214 L&S	The AVVSSS and EuroQoL improved in all 3 groups and showed no difference between the groups.
Carradice (2011) [31]	280	12	VCSS, SF-36, AVVSSS	Prospective single-center RCT	140 EVLA vs. 140 L&S	The VCSS, SF-36 and AVVSSS improved in both groups with no between-group difference.
Samuel (2013) [32]	106	12	VCSS, SF-36, AVVSSS	Prospective single-center RCT	53 EVLA vs. 53 L&S	The VCSS, AVVSSS and SF-36 improved in all groups with no significant between-group difference
Darwood (2008) [33]	80	3	AVVSSS, VCSS	Prospective single-center RCT	54 EVLA vs. 26 L&S	The VCSS and AVVSSS improved in both groups with no significant between-group difference
Bountouroglou (2006) [34]	60	3	AVVSSS, VCSS	Prospective single-center RCT	30 UGFS vs. 30 L&S	The VCSS and AVVSSS improved in both groups with no significant between-group difference
Campos (2015) [35]	58	12	AVVSSS, VCSS, VDS	Prospective single-center RCT	29 UGFS vs. 29 L&S	The VCSS, VDS and AVVSSS improved in both groups with no significant between-group difference
Shadid (2012) [36]	430	24	VCSS, EuroQoL	Prospective 3-center RCT	230 UGFS vs. 200 L&S	The VCSS and EuroQoL improved in both groups with no significant between-group difference
Michaels (2006) [37]	217	24	SF-36, EuroQoL	Prospective 2-center RCT	160 L&S vs. 57 UGFS	The SF-36 and EuroQoL improved in both groups with no significant between-group difference
Wozniak (2015) [38]	102	36	VCSS	Prospective single-center RCT	52 thermal ablation vs. 50 L&S	The VCSS scores improved significantly ($p < 0.05$) in both groups with no between-group difference
Lattimer (2013) [39]	90	15	AVVSSS, VCSS, STS	Prospective single-center RCT	44 EVLA vs. 46 UGFS	The AVVSSS, VCSS and STS were all reduced from baseline ($p < 0.0005$) with no between-group difference
Shepherd (2015) [40]	110	6	AVVSSS, VCSS	Prospective single-center RCT	54 EVLA vs. 56 RFA	The VCSS and AVVSSS improved in both groups with no significant between-group difference

(continued)

Table 21.3 (continued)

Study (year)	# Limbs	Follow-up (month)	Instrument	Design	Comparison	Outcome
Nordon (2011) [41]	159	3	AVVSSS, EuroQoL	Prospective single-center RCT	80 EVLA vs. 79 RFA	The AVVSSS and EuroQoL improved in both groups with no significant between-group difference
Carradice (2009) [42]	50	12	AVVSSS, VCSS	Prospective single-center RCT	25 EVLA alone vs. 25 EVLA plus phlebectomies	VCSS and AVVSSS were lower in EVLA plus phlebectomies vs. EVLA alone in 3 months (for both, $p < 0.0001$) but at 1 year there were no differences
Liu (2011) [43]	134	60	CEAP	Prospective single-center RCT	74 EVLA vs. 60 EVLA + stab avulsions	There was no difference in pain between groups after Day 5 onwards.
Theivacumar (2008) [44]	68	3	AVVSSS	Prospective single-center RCT	23 EVLA AK vs. 23 EVLA ABK vs. 22 EVLA BK + UGFS	There was significant improvement in AVVSSS ($p < 0.001$) in all groups with no difference between groups at 3 months
van den Boss (2014) [45]	227	3	VCSS, AVVSSS	Prospective single-center RCT	110 EVLA vs. 117 thermal ablation	The VCSS and AVVSSS improved in both groups with no significant between-group difference
Morrison (2015) [46]	222	3	AVVSS, EuroQoL, VCSS	Prospective single-center RCT	108 cyanoacrylate embolization vs. 114 RFA	VCSS, AVVSS and EuroQoL improved significantly ($p < 0.01$) for both procedures with no between-group difference at 3 months.
Gibson (2018) [47]	222	24	AVVSS, EuroQoL, VCSS	Prospective single-center RCT	108 cyanoacrylate embolization vs. 114 RFA	VCSS, AVVSS and EuroQoL improved significantly ($p < 0.01$) for both procedures with no between-group difference at 24 months.

L&S ligation and stripping, *RFA* radiofrequency ablation, *EVLA* endovenous laser ablation, *UGFS* ultrasound-guided foam sclerotherapy, *AVVSSS* Aberdeen varicose vein symptom severity score, *VCSS* venous clinical severity score, *VDS* venous disability score, *STS* saphenous treatment score, *AK* above-knee, *ABK* above-below-knee, *BK* below-knee, *VSDS* venous segmental disease score, *CXVUQ* disease specific ulcer questionnaire

Comparison of Surgical vs. Endovenous Interventions

These include the following comparisons: (a) high ligation and stripping vs. RFA, (b) high ligation and stripping vs. EVLA, (c) high ligation and stripping vs. sclerotherapy, and, (d) high ligation and stripping vs. thermal ablation.

High Ligation and Stripping vs. RFA

One randomised controlled trial (RCT) measured quality of life using the CIVIQ-2 score at baseline, 1-week and 2-year follow-up [18]. There was a marked difference in perceived pain already at 72 h in favour of RFA compared with high ligation and stripping (-1.77 ± 0.6 vs. 2.9 ± 0.7, respectively; $p < 0.0001$). This difference

persisted at 1 week postoperatively (−2.4 ± 0.6 vs. 1.2 ± 0.7, respectively; $p < 0.0001$) and was coupled with a significantly better global QOL (pain, physical, social and psychological) score (−9.2 ± 2.3 vs. 3.7 ± 2.5, respectively; $p < 0.0001$) [18]. The differences in pain and global QOL scores disappeared at 3 weeks after treatment, but then surprisingly reappeared in favour of the RFA group at 1 year postoperatively and remained significant at 2 years [19].

Two RCTs compared QoL after RFA vs. surgery using the AVVSS score [20, 21]. The first RCT showed improvement in QoL after both surgery and RFA, with no difference between the two groups [20]. The second RCT similarly showed no difference between the two groups at 3 days, 1 month, 1 year and 3 years [21]. This RCT also reported less pain on the visual analog scale (VAS) in the RFA group at 10 days post-operatively compared with the high ligation and stripping arm [21]. In conclusion, it appears that there may be an early advantage with RFA compared to the traditional open surgery in QoL that in subsequent assessments is no longer measurable.

High Ligation and Stripping vs. EVLA

Three studies including a total of 780 patients compared high ligation and stripping vs. EVLA [22–24]. All three studies used the AVVSS score, the VCSS and several domains of the Medical Outcomes Study Short Form-36 QoL scores [22–24]. The AVVSS score, VCSS and Short Form-36 scores improved after both procedures. None of the studies found any significant difference in any of the clinical severity scores and QoL between groups (Fig. 21.1). Similarly, when the CEAP score was used (n = 4 studies; 867 patients), no difference could be demonstrated at 12 months following the intervention (Fig. 21.2) [25–28]. Another four studies reported AVVSS

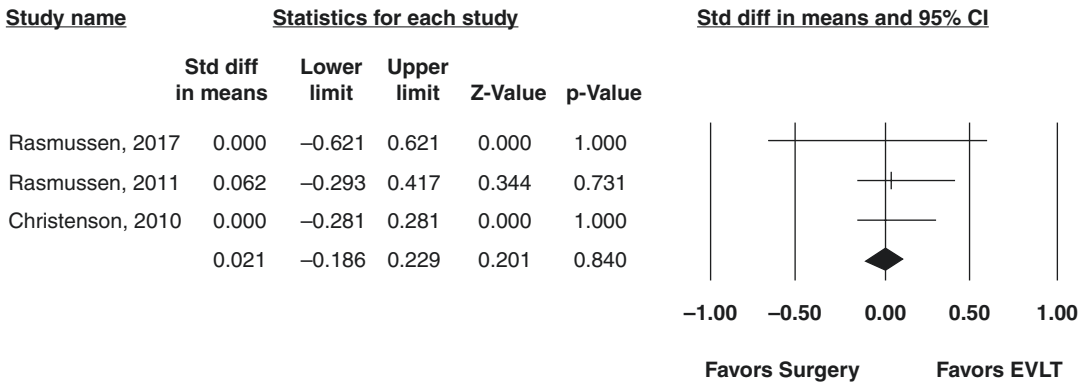

Fig. 21.1 Forest plot of long-term VCSS effects for high ligation and stripping vs. EVLA

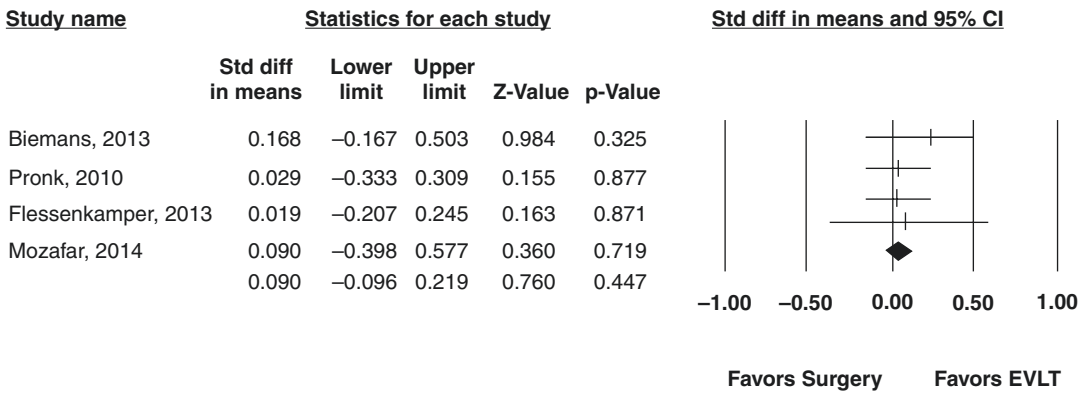

Fig. 21.2 Forest plot of CEAP effects for high ligation and stripping vs. EVLA

and EuroQoL-5D scores at various time-points post-intervention [25, 29–31]. Once again, disease-specific QoL did not differ between surgery and EVLA up to 5 years post-procedurally [25, 29–31].

Finally, six studies (n = 663 patients) evaluated long-term QoL using the AVVSS score (Fig. 21.3) [23, 24, 28, 31–33]. Like before, after the periprocedural period no long-term difference was found between the two treatment strategies. The early benefits associated with EVLA as demonstrated with PROMs were virtually abolished after the first month following the intervention [23, 24, 28, 31–33].

High Ligation and Stripping vs. Sclerotherapy

Five studies reported VCSSs at various time after high ligation and stripping vs. sclerotherapy [23, 30, 34–36]. One of these studies reported a significant improvement in mean scores from baseline to 1-year follow-up for both sclerotherapy (from 12.26 ± 3.05 to 4.26 ± 3.05, respectively; $p < 0.001$) and surgery (from 12.5 ± 1.64 to 3.39 ± 1.57, respectively; $p < 0.001$), but without any significant difference between groups [35]. Another study reported a significant improvement from baseline to 6-month VCSS scores for both treatment groups (sclerotherapy: from 4.9 ± 2.6 to 1.6 ± 1.7, respectively; $p < 0.001$; surgery: from 5.1 ± 2.5 to 1.4 ± 1.7, respectively; $p < 0.001$) without between-group difference [30]. The other three studies also reported improvements in VCSS scores at different time points [23, 34, 36]. One of these three studies demonstrated an additional improvement in CEAP score, as well [34].

Three of these five studies also reported AVVSS scores at various time points ranging from baseline to 3 years post-intervention [23, 30, 35]. All three studies showed decreased scores at 3 years, thus indicating an improvement in symptoms, but no difference between groups. Finally, three studies (n = 900 patients) explored the long-term change in QoL as measured by EuroQoL-5D (Fig. 21.4) [25, 30, 37]. Once again, these studies did not demonstrate any difference between the two modalities. The early advantage in pain and discomfort with foam sclerotherapy compared with open surgery was abolished completely at 1 month following the procedure.

High Ligation and Stripping vs. Thermal Ablation

Only one study reported VCSS scores after endovenous thermal (steam) ablation (n = 52 patients) vs. high ligation and stripping (n = 50 patients) [38]. This study showed that the mean VCSS scores were reduced from 7.25 to 1.78 in the

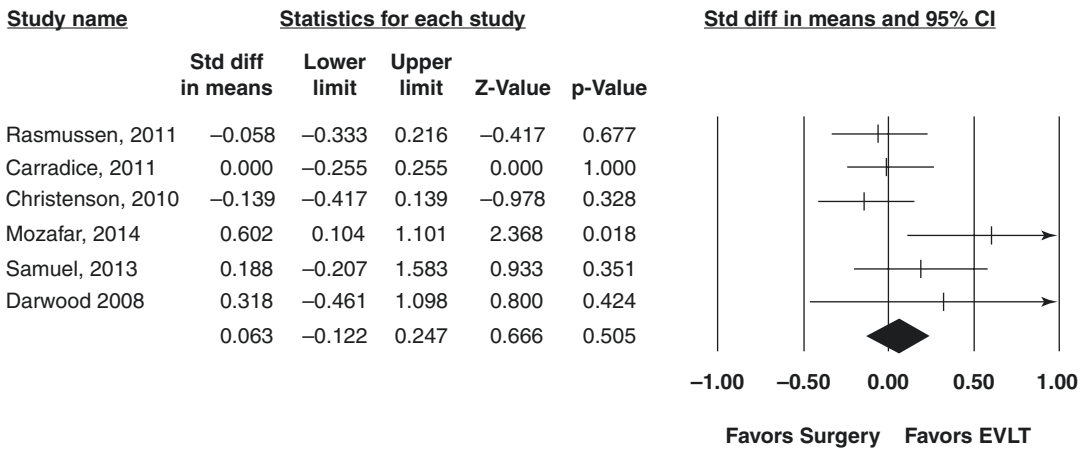

Fig. 21.3 Forest plot of long-term AVVSS score effects for high ligation and stripping vs. EVLA

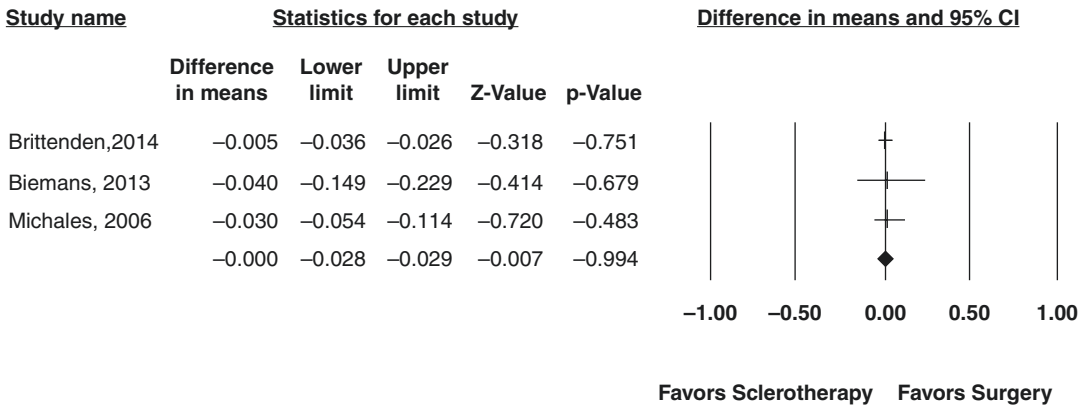

Fig. 21.4 Forest plot of QoL effects for high ligation and stripping vs. sclerotherapy

endovenous thermal ablation group and from 8.28 to 2.2 in the surgical group (for both interventions, $p < 0.05$), but without any between-group difference in QoL [38]. The conclusion reached was that endovenous thermal ablation is safe and comparable with surgery.

Comparison Between Different Endovascular Interventions

Sclerotherapy vs. EVLA

Three RCTs reported information on QoL following EVLA vs. endovenous foam sclerotherapy [23, 30, 39]. These studies provided AVVSS scores at 6 weeks [30], 3 months [39], 6 months [30], 15 months [39] and 3 years [23] for each group. In one study, there was a statistically significant between-group difference regarding effect size in the adjusted data for AVVSS scores at 6 weeks in favour of the EVLA group ($p = 0.032$) [30]. However, this difference did not persist beyond the 3 months. In another study from the Imperial College, London, UK [39], both the VCSS and AVVSS scores were significantly reduced compared to baseline ($p < 0.0005$), but without any statistical difference between the groups [39].

RFA vs. EVLA

Two RCTs reported AVVSS scores for EVLA vs. RFA [40, 41]. At 6 weeks the mean between-group change of AVVSS scores was 0.2 in the EVLA group and −0.3 in the RFA group [40]. At 3 months the mean within-group change of AVVSS scores was −11.2 in the EVLA group and −10.3 in the RFA group [41]. There was no statistically significant between-group difference ($p = 0.12$), but AVVSS scores improved within each group at 3 months [41].

Despite the lack of difference in AVVSS scores, these studies showed that there was a statistically significant between-group difference with regards to the 10-point VAS pain scores at 7 [41] and 10 [40] days. The first study reporting median pain scores at 7 days showed a statistically significant difference in favor of the RFA group with a median pain score of 13.5 in the EVLA group and 0 in the RFA group ($p = 0.001$) [41]. In the other study, the RFA group similarly reported better improvement in the pain score compared with the EVLA group at 10 days (12.3 vs. −6.3, respectively; $p = 0.01$) [40]. However, with the introduction of the higher frequency laser equipment (1470-nm), there are no longer any differences in pain scores at 3 and 10 days, 1 month and 1 year [48].

RFA Plus Phlebectomies vs. EVLA Plus Phlebectomies

One good-quality RCT [22] (n = 762 patients) reported comparisons of EVLA plus phlebectomies vs. endovenous RFA plus phlebectomies. Patients in the RFA group reported significantly less postoperative pain than those in the EVLA group (Mean ± SD: 1.21 ± 1.72 vs. 2.58 ± 2.41; p < 0.001) [23]. The scores improved significantly in both groups from 1 month after the procedure, with no difference between groups thereafter. The mean AVVSS scores at 3 years presented in the RCT did not differ between groups (4.61 vs. 4.43, for the EVLA plus phlebectomies vs. the RFA plus phlebectomies groups, p = not significant) [23]. The same applied to the mean VCSS scores (0.34 vs. 0.44, for the EVLA plus phlebectomies vs. the RFA plus phlebectomies groups, p = not significant) [23].

EVLA vs. EVLA Plus Phlebectomies

Two RCTs compared EVLA vs. EVLA plus phlebectomies [42, 43]. In the first RCT, the VCSS at 3 months was lower with EVLA plus phlebectomies compared with EVLA alone (0 vs. 2, respectively; $p < 0.001$) [42]. The AVVSS scores were also lower for the EVLA plus phlebectomies group at 6 weeks (7.9 vs. 13.5, respectively; $p < 0.001$) and 3 months (2.0 vs. 9.6, respectively; $p = 0.015$). However, there were no differences in either VCSS or AVVSS scores at 1 year [42].

The second RCT reported the number of patients with pain at 1 and 4 weeks for each group [43]. The EVLA alone group reported fewer patients with pain compared with the EVLA plus phlebectomies group at 1 week (11 vs. 22 patients, $p = 0.002$). However, no patients in either group reported pain at 4 weeks [43].

EVLA vs. EVLA Plus Sclerotherapy

One small single-centre RCT from the UK reported a comparison of EVLA above the knee (n = 23 patients) vs. EVLA above and below the knee (n = 23 patients) vs. EVLA above the knee plus foam sclerotherapy (n = 22 patients) [44]. The median AVVSS scores improved significantly in all groups. There was a significant between-group difference in terms of patient satisfaction at 6 weeks in favor of EVLA above the knee plus foam sclerotherapy ($p = 0.015$) [44].

EVLA vs. Thermal Ablation

One RCT reported a comparison of EVLA vs. endovenous thermal (steam) ablation in 237 patients with symptomatic lower extremity chronic venous insufficiency/reflux and varicose veins [45]. Both groups showed improvement in AVVSS scores at 12 weeks postprocedure, but no statistically significant between-group difference was noted [45]. Similarly, VCSS scores improved in both groups but the improvement in between-group comparison was not significant ($p = 0.242$) [45].

Cyanoacrylate Embolization vs. RFA

One multicentre (n = 10) RCT from the U.S. reported a comparison of cyanoacrylate embolization vs. RFA using AVVSS scores on 242 patients with symptomatic lower extremity chronic venous insufficiency/reflux and varicose veins [46]. At 1 month, AVVSS scores improved significantly both in the cyanoacrylate group and in the RFA group, without any statistically significant between-group difference [46]. There was also no difference in postoperative pain between the two groups according to the 10-point VAS score ($p = 0.36$) [46]. In the subsequent report of the 2-year results, there was once again no difference in patients' QoL through 24 months [47].

The conclusion reached was that both cyanoacrylate embolization and RFA of the great saphenous vein are safe and durable up to 2 years [47].

Recurrence Rates Following Different Interventions

A key parameter in selecting the appropriate intervention for the management of lower extremity chronic venous disease is recurrence rates. In the earlier mentioned RCT comparing EVLA vs. RFA vs. ultrasound-guided foam sclerotherapy vs. surgical stripping, there was no difference in varicose vein recurrence rates at 3 years between the procedures (20% vs. 14.9% vs. 19.1% vs. 20.2%, respectively; p = 0.66) [21]. There were more patients in the sclerotherapy group presenting with reflux in the groin compared with the other groups (p = 0.34) and more reoperations performed in the sclerotherapy group compared with the EVLA, RFA and surgical groups (31.6% vs. 12.5% and 11.1% and 15.5%, respectively; p < 0.0001). However, patients undergoing sclerotherapy were only give a single injection of foam and were not seen again [21]. This is an inadequate method to offer foam sclerotherapy, as approximately 20–30% of patients require additional foam in tributaries at 6 weeks to complete their treatment. Nevertheless, the VCSS, SF-36 and AVVSS QoL scores all improved significantly in all the groups with no difference between the various procedures [21].

Other RCTs similarly demonstrated no significant difference in recurrence rates between the various modalities despite a slightly higher incidence of great saphenous vein reflux [39, 49, 50]. Nevertheless, this slightly higher reflux rate was not related to deterioration in QoL indicating that this reflux was largely asymptomatic [39].

The Finnish Venous Study was a randomized trial comparing the effect of ultrasound-guided foam sclerotherapy vs. EVLA with phlebectomies vs. surgery on the QoL of patients receiving treatment for great saphenous varicose veins [49]. It showed significant improvement in AVVSS QoL scores postoperatively in all groups, with no significant differences between them [49]. In contrast, a similar randomized trial from the Netherlands and Belgium [50] demonstrated a significant deterioration in CIVIQ scores in the sclerotherapy group compared with the EVLA group (p = 0.013). However, the CIVIQ scores for the conventional surgery group did not differ from those in the EVLA and the sclerotherapy group, and the EuroQoL-5D scores improved equally in all groups [50]. The extended 5-year results of the Finnish Venous Study similarly showed a sustained improvement in AVVSS scores from baseline for all procedures, with no significant difference in terms of QoL between the procedures at 5 years [51].

Conclusions

The effect of several procedures on QoL has been extensively investigated for patients with lower extremity chronic venous disease (Fig. 21.5).

Although no long-term difference is seen in effectiveness between RFA and high ligation and stripping, RFA is associated with less periprocedural pain, faster improvement in symptom scores and QoL. Among patients undergoing endovenous interventions, RFA, EVLA and sclerotherapy all demonstrate improvement in QoL and standardized symptom scores. When compared with patients offered EVLA, those treated with foam sclerotherapy had significantly less periprocedural pain, while patients treated with RFA had significantly less periprocedural pain but also less short-term improvement in VCSS. Patients treated with foam sclerotherapy demonstrate significant improvement in standardized symptom scores and QoL compared with placebo. Similarly, patients treated with high ligation plus stripping demonstrate improved long-term symptoms and QoL compared with those patients managed with compression therapy alone. Endovascular techniques have a sig-

Fig. 21.5 Summary and concluding remarks

Quality-of-life (QOL) and Patient-Reported Outcome Measures (PROMs) following intervention for Chronic Venous Disease

- Venous leg ulcers affect patients in terms of quality-of-life(QoL), pain and social isolation
- Patient-reported outcome measures (PROMs) provide a means by which the impact of varicose veins or their treatments can be measured on the patient's QoL
- PROMs explore several dimensions in patients' QoL, including psychological effects, physical effects, social well-being, pain and cosmetic appearance
- Radiofrequency ablation has an early advantage over high ligation and stripping but this disappears at 3-4 weeks after treatment
- Endovenous laser ablation, thermal ablation and sclerotherapy have no significant difference in PROMs compared with surgery
- There is no difference in varicose vein recurrence rates between any procedures

nificant early improvement of the quality of life in patients who are treated for chronic venous insufficiency compared to open traditional surgery (saphenofemoral ligation and saphenectomy). This early advantage is lost with intermediate and long-term follow-up compared to the quality of life in patients treated with saphenofemoral ligation and long saphenous vein stripping. As the long-term results are comparable irrespective of the technique that is used for the management of the patient, the choice of the intervention will depend on patient's preference, local expertise, the configuration of the varicose vein and the diameter of the saphenous trunk.

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