Studiekarakteristieken bij module behandeling van stamvarices bij UCV

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Montminy 2018 a. Cikrit 1988 b. Darke 1992 c. Wolters 1996 d. Pierik 1997 e. Pierik 1997 f. Bello 1999 g. Glovkiczki 1999 h. Murray 1999 i. Nelzen 2000 j. Barwell 2000 k. Lawrence 2001 l. Iafrati 2002 m. Kalra 2002 n. Tawes 2003 o. Zamboni 2003 p. Bianchi 2003 q. Adam 2003 r. Al-Mulhim 2003 s. Barwell 2004/Gohel 2007 t. El-Hafez 2005 u. Masuda 2006 v. Magnusson 2006 w. Obermayer 2006 x. Ting 2006 y. Lin 2006 z. Viarengo 2007 aa. Sharif 2007 bb. Darvall 2009 cc. Pang 2010 dd. Rathod 2010 ee. Teo 2010 ff. Nelzén 2011 gg. Figueiredo 2012	Type of study SR of RCTs / cohort / case-series studies Literature search up to January 2017 Setting and Country: USA Source of funding: MM, AJ and SR received funding. Inclusion criteria SR: - RCT and observational studies - Participants with a healed or active medial VLU (C5-C6). - Minimum of 20 patients with clinical, ethology, anatomy and pathophysiology clinical class C5 to C6 score. SVR search: - All techniques of GSV, SSV and varicose vein ablation. IPV search: - IPV only intervention. Exclusion criteria SR: - Articles not yet published *49 studies included*	Important patient characteristics at baseline: Total N: 5488 patients N, mean age Reported per study, see below *Sex:* not reported Groups not comparable at baseline.	1 surgical ablation group: 1.1.surgical SVR ablation (with) compression *Studies*: O, S, UU, 1.2 surgical SVR ablation with(out) IPV ablation *Studies*: FF, J, T, V, B, F, Q, R, SS, E, G, P, W, X, D, H, I, L, M, N 2. Foam sclerotherapy group *Studies*: QQ, BB, CC, GG, JJ, OO, PPRR, VV, WW 3. ELVT group Studies: Z, AA, DD, EE, KK, TT. 4. RFA group Studies: LL, MM, HH, II 5. IPV group C, NN, K, U	Intervention was compared to compression, surgical intervention of there was no comparison	End-point of follow-up: Mean FU: 12 months – 5.5 years For how many participants were no complete outcome data available? Not reported	See the results per article below. These results (comparative studies) were used for this guideline.	

hh. Harlander -Locke 2012 ii. Harlander -Locke 2012 jj. Kalkarni 2013 kk. Murli 2013 ll. Rueda 2013 mm. Alden 2013 nn. Kiguchi 2014 oo. Williamss on 2014 pp. Lloret 2015 qq. Campos 2015 rr. Garcarek 2015 ss. Kanchan abat 2015 tt. Shi 2015 uu. Van Gent 2006-2015 vv. Howard 2016 Grover 2016							
Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison / control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comments**
Puggina, 2020	Type of study: RCT Setting: Prospective, open-label, randomized controlled trial, single centre Country: Brazil Source of funding: government research funding agency (FAPESP). Inclusion criteria: - Age 18-80 yr - ≥ 1 active VLU - ≥ 1 saphenous and ≥ 1 perforating vein insufficiency in previous duplex. - ABPI > 0.8 Exclusion criteria: - evidence of significant arterial obstruction.	N total at baseline: 56 Intervention: 27 Control: 29 Important prognostic factors[2]: *For example age ± SD:* *I: 53.48 ± 12.73* *C: 54.06 ± 11.70* *Sex:* *I: 25.9% M* *C: 27.6% M* Groups were comparable at baseline.	RFA + compression (two layer compression bandages)	Compression (two layer compression bandages)	Length of follow-up: Mean FU I: 74 weeks Mean FU C: 67 weeks Loss-to-follow-up: Number: 1 (1.8%) Reasons: death from a comorbid condition. Incomplete outcome data: Outcome data complete	1. Ulcer recurrence rate at 12 months: **I**: 3.7% **C**: 44% (HR 0.083; 95% CI 0.011 – 0.0632; p < 0.001) 2. Ulcer healing rate **At 6 weeks** NS difference (HR 1.176; 95% CI 0.412 – 3.353; p = 0.762) **At 12 weeks** NS difference (HR 1.259; 95% CI 0.649 – 2.444; p = 0.496) **At 24 weeks**	

	- Previous personal history or current evidence of occlusion. - obstruction/previous deep venous thrombosis in the leg with ulcer shown on ultrasound. - evidence of previous superficial thrombophlebitis in the target saphenous vein. - pregnancy - contra-indications for surgery - suspicion of other causes of ulceration in leg - inability to walk or severe ankle ankylosis - no evidence of insufficiency of at least 1 saphenous vein and perforating vein in the leg with VLU, saphenous vein diameter >12 mm.					NS difference (HR 1.390; 95% CI 0.768 – 2.516; p = 0.277) 3. ulcer healing velocity (secondary) Higher in intervention group (0.739, ± 0.498 cm2 per week) compared to control group (0.495, ± 0.409 cm2 per week). (p = 0.049) 4. venous clinical severity score (VCSS) (secondary) I: 8.74 ± 3.04 C: 11.79 ± 3.47 (MD 3.05, BI 95% 1.30-4,80; p=0.001)	
Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison / control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comments**
Zhou, 2021	Type of study RCT Country: China Source of funding: not reported Inclusion criteria: - patients with superficial venous swelling, hyperpigmentation and other clinical symptoms. - patients diagnosed with unilateral varicose veins - patients with increased diameter of vein, no deep vein thrombosis,	N total at baseline: 89 Intervention: 42 Control: 47 Important prognostic factors[2]: *For example age ± SD:* *I: 52.7 ± 3.6* *C: 52.0 ± 2.6* *Sex:* *I: 52.4% M* *C: 66.0% M* Groups were comparable at baseline.	Great saphenous vein high ligation + cinnamyl alcohol foam hardening. The cinnamyl alcohol (1%) and air were mixed in a ratio of 1:4. After high ligation of the great saphenous vein, lauric alcohol foam sclerosant (5 mL) was infused into the trunk of the vein. Finally, bleeding was drawn back at each puncture point, and	Great saphenous vein high ligation. Patients underwent high ligation of the main great saphenous vein.	Length of follow-up: 3 months Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	ulcer healing: C: 31.67 (SD 7.86) days. I: 19.33 (SD 3.35) days. (MD 12.34; 95% BI 9.74-14.94; p < 0.001). VAS scores Before treatment no SD (p= 0.861). After treatment SD (p< 0.001). Lower in intervention group (p< 0.001)	Not all patients received a physical examination. Small group of patients.

	and smooth blood circulation. - patients informed and agreed to this experiment. Exclusion criteria: - patients with deep vein thrombosis and other venous diseases by preoperative angiography - patients with varicose veins due to malignancies - patients who could not clearly describe their status. - patients with sclerosis contraindications or allergies.		then 1.2 mL of sclerosant was injected, by which the total volume of injection was less than 20 mL, and pressure bandage (elastic bandage) was applied after puncture			Secondary effects I: 7.14% (3 patients) C: 17,02% (8 patients) (p= 0.201) Recurrence rate I: 2.38% C:10.64% (p= 0.146)	
Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison / control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comments**
Zamboni 2003	Type of study: prospective randomised study. Country: Italy Source of funding: Not mentioned Inclusion criteria: - C6 Exclusion criteria: - ABI <0.9 - age > 80 years - diabetes - unable to walk - ulceration <2cm^2/>12	N total at baseline: 45 I: 21 pt. C: 24 pt.	2 types of surgical techniques depending on location RPV - I: classic high ligation of the SFJ/SPJ completed by flush ligation and division from the saphenous trunk and insufficient tributaries. - II: flush ligation + disconnection from the saphenous trunk of the insufficient tributaries which contained the identified RPV.	Compression Foam dressing, zinc oxide, inelastic bandage. Once the ulcers were healed elastic stockings (20-30mmHg) were prescribed.	Length of follow-up: 3 years Loss-to-follow-up: None. Incomplete outcome data: Not reported	Ulcer healing rate and time to ulcer healing: - 100% intervention group (median 31 (17-53) days) - 96% comparison group (median 63 (21-80) days) (p <0.005) Ulcer healing: RR=1,04; 95% BI 0,96-1,13 Time to heal: MD 32 dagen; 95% BI 19,9-44,0; p< 0,005 Recurrence rate - 9% intervention group (n=2) - 38% compariso	

						n group (n=9) (RR 0,254; 95% BI 0,62-1,05; p< 0,05).	
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Barwell 2004/ Gohel 2007 (ESCHAR trial)	Type of study: RCT Setting: Specialist nurse led leg ulcer clinics in three UK vascular centres. Country: UK Source of funding: NHS Executive South and West Research and Development Directorate, Southmead Hospital Research Foundation, and Medical Research Council. Inclusion criteria: - open or recently healed leg ulceration (within 6 months) >4 weeks. - >0.85 SVR and/or DVR Exclusion criteria: - Duplex scanning impossible. - Multilayer compression therapy not practical Unable or unwilling to give informed consent. Deep venous occlusion Unfit for surgery. Malignant ulceration.	N total at baseline: 500 I: 242 pt. C: 258 pt. Baseline characteristics: Age ± SD: I: 74 (60-80) C: 72 (60-79)	Superficial venous surgery + compression Depending location reflux: I: saphenofemoral junction disconnection, stripping long saphenous vein, calf varicosity avulsions. II: saphenopoplitteal junction disconnection, calf varicosity avulsions.	Compression Open ulceration: multi-layered compression bandaging Healed ulceration: class 2 elastic stocking.	Length of follow-up: 1,5 yrs. – 4 yrs. Loss-to-follow-up: 54 pt. (27 intervention group, 27 control group). Incomplete outcome data: Not reported	Ulcer healing rates 3yr: - 89% comparison group - 93% intervention group (p 0.737) Recurrence rate 12 months - 28% comparison group - 12% intervention group (p <0.0001) Recurrence rate 4 years - 56% comparison group - 27% intervention group (p <0.01) Ulcer-free time: - 71% comparison group - 78% intervention group (p 0.007))	Forty seven patients randomised to compression plus surgery did not attend for surgery and three randomised to compression requested surgery. % recurrence rate 4 years modified in later version.
Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison / control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comments**

Van Gent 2005/2015	Type of study: A prospective, randomized, multicentre trial Country Netherlands Source of funding: The study was sponsored by Ziekenfondsraad/ Ontwikkelingsgnk (Dutch government; project OG98-045) Inclusion criteria: - C6, medial/lateral - both primary and secondary causes of leg ulcers were included. Exclusion criteria: - ABI < 0.8 Total or partial occlusion of the deep venous system. - Former subfascial ligation of perforating veins - Severe neurologic or muscular pathology. - Immobility.	N total at baseline: 200 I: 97 C: 103 Baseline characteristics: Age ± SD: I: 64 ± 15 C: 68 ± 14 Sex: I: M:F = 2:3 C: M:F = 2:3	SEPS ± GSV or SSV ligation and stripping I: SEPS + (when indicated) surgery of the superficial venous system. II: flush saphenopoplitteal ligation and/or saphenofemoral ligation and limited stripping of the long saphenous vein.	Compression Standardized ambulatory compression therapy	Length of follow-up: 2006: Intervention: 29 months Compression: 26 months 2015: 97 months Loss-to-follow-up: 4 pt. directly after randomization (3 intervention group, 1 control group). Cause unknown. Incomplete outcome data: Not reported	2006: Healing rate (not sign.) - 83% intervention group - 73% comparison group Recurrence rate (not sign) - 22% intervention group - 23% comparison group Ulcer-free rate at mean FU (not sign.) - 72% intervention group - 53% comparison group 2015: Using the "last-observation carried-forward technique", ulcer free rate was significantly (P=.007) higher in the surgical group (58.9%), compared to the compression group (39.6%). Ulcer recurrence was 48.9% for the surgical group and 94.3% for the compression group.	
Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison / control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comments**
Nelzen 2011	Type of study: RCT Country: Sweden	N total at baseline: 75 I: 37 C: 38	GSV or SSV ligation and stripping and SEPS	GSV or SSV ligation and stripping only	Length of follow-up: 32 months (14-57) Loss-to-follow-up:	Ulcer healing after 12 months: - 91.9% intervention group	

	Source of funding: not reported Inclusion criteria: - open or healed venous ulcer at least 6 weeks (C5-C6) - ABI > 0.8 - Age 30-78yr. - Duplex scan showing incompetence of the SV and 1 or more medial lower leg Ips with a diameter greater than 2 mm. Exclusion criteria: - incompetence of the popliteal vein - Severe CV disease - Malignancy - Renal failure - Expected survival less than 5 years. - Dementia	Baseline characteristics: age ± SD: 57 (28-78)			Not reported Incomplete outcome data: Not reported	- 92.1% comparison group Recurrence after 12 months: - 5.4% intervention group - 5.3% comparison group Mean time to ulcer healing for 22 patients with C6 lesions was similar after the two procedures	
Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison / control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comments**
Barwell 2000	Type of study: Prospective cohort study Country: UK Source of funding: not reported Inclusion criteria: - C6 > 4 weeks - C5 healed in the last 6 months - ABI > 0.85 - Isolated SVR Diagnosis: reflux >1 sec	N total at baseline: 236 limbs I: 131 C: 105 Baseline characteristics: Age ± SD: 77 (27-97) group1, 70 (29-92) group2	SVR ablation (GSV, SSV, 4 perforators only)	No surgery	Length of follow-up: Not reported Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Ulcer healing rate at 12 and 24 weeks respectively - 50% and 72% intervention group - 62% and 74% comparison group P 0.67 Recurrence rate at 1, 2 and 3 years respectively - 14%, 20% and 26% intervention group - 28%, 30% and 44% comparison group P 0.03	

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el-hafez 2004	Type of study Case series Source of funding: not reported Inclusion criteria: - C6 not responding to conservative treatment > 6 months. - 2-7 cm diameter Exclusion criteria: - ABI <0.9	N total at baseline: 36 pt Baseline characteristics: Age ± SD: 42 (29-61)	GSV stripping and tributaries ligation	GSV and tributaries ligation	Length of follow-up: Not reported Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Ulcer healing rate at 12 months: - 70% intervention group - 84.6% comparison group P < 0.05 Postoperative complications were significantly reduced in group with ligation only compared to group with ligation and stripping (P<0.05)	

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Pierik 1997 (2)	Type of study: RCT Country: Netherlands Source of funding: not reported Inclusion criteria: - C6 Exclusion criteria: - ABI <0.8	N total at baseline: 39 pt Baseline characteristics: Age (SD) I: 70 (36-89) C: 64 (33-89)	Linton	SEPS with/without surgical SVR ablation.	Length of follow-up: 21 months (16-29) Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Ulcer healing rate: - 90% open group - 85% endoscopic group NS No recurrences were noticed in either group.	

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Gloviczki 1999	Type of study: Registry in 17 centres in the United States and Canada Country: USA Source of funding: not reported Inclusion criteria:	N total at baseline: 146 pt Baseline characteristics: Age ± SD: 56 (27-87)	SEPS + stripping	SEPS	Length of follow-up: 24 months (1-53) Loss-to-follow-up: Not reported Incomplete outcome data: not reported	Cumulative ulcer healing - 88% 1 year; 90% in limbs with reflux alone and 56% in those limbs with deep venous obstruction.	

	- advanced CVI (C5-C6)					- 95% 2 years <u>Cumulative ulcer recurrence</u> - 16% 1 year - 28% 2 years; PTS limbs had a higher 2-year cumulative recurrence rate (46%) than did those limbs with primary incompete nce	
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Campos 2015	<u>Type of study</u> RCT <u>Country</u>: Brazil <u>Source of funding</u>: authors received no financial support for this study. <u>Inclusion:</u> - primary CVI - SVR - GSV diameter of 0.7-1.4 - Active ulcer (max 5 cm diameter). - ABI 0.9-1.3 <u>Exclusion:</u> - history of DVT - DVR - superficial thrombosis - Diabetes - thrombophilia - pregnancy - allergy to polidocanol	<u>N total at baseline</u>: 56 pt, 58 limbs I: 29 limbs C: 29 limbs <u>Baseline characteristics:</u> Age ± SD: - surgery: 47 - UGFS: 52	GSV UGFS Polidocanol foam was prepared by using 2 10-ml syringes that were connected by a 2-way stopcock connector. 1 was filled with 8ml air. After aspiration of 2ml 3% polidocanol the syringes was rapidly/alternately pumped. In each procedure 8-10ml of 3% polidocanol was injected. A compressive bandage was applied and kept in place for 72 hr after surgery. Afterward, the patients wore a 30-mm Hg elastic stocking above the knee for >8 hr/day.	Surgery Surgery consisted of: GSV stripping, phlebectomy of tributaries and ligation of perforating veins. A compressive bandage was applied and kept in place for 72 hr after surgery. Afterward, the patients wore a 30-mm Hg elastic stocking above the knee for >8 hr/day.	<u>Length of follow-up:</u> Mean 502 days <u>Loss-to-follow-up:</u> Not reported <u>Incomplete outcome:</u> Not reported	<u>Ulcer healing</u> I: 21/23 (91,3%) C: 28/28 (100%) P 0.19 (RR 6,04; 95% BI 0,30-119,89; p= 0,24) The mean time to ulcer healing was 37.1 SD 22.1 days in the surgical treatment group and 56.4 SD 39.4 days in the foam sclerotherapy group (P.008) <u>Recurrence rate</u> I: 1/23 (4,3%) C: 2/29 (6,9%) (RR 0,63; 95% BI 0,06-6,53; p= 0,699) <u>*VCSS after FU*</u> I: 4,26 (SD 3,14) C: 3,39 (SD 1,57) NS (p=0,58)	

						VCSS decrease after therapy: I: 65,2% decrease C: 72,8% decrease	
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Viarengo 2007	Type of study: RCT Country: Brazil Source of funding: not reported. Inclusion: - C6 - varicose veins Exclusion: - previous GSV ablation - acute DVT or superficial thrombophlebitis - occlusion of the femoral or iliac vein presenting with PTS Coagulation disorders - PAD - degenerative systemic diseases - pregnancy - unable to ambulate	N total at baseline: 52 pt I:27 C:25 Baseline characteristics: Age ± SD: - I: 57 - C: 61	EVLT and compression Dressings at home following the routine adopted in the preoperative period, in a manner similar to that of the control group.	Compression Dressings at home, followed by the use of an elastic support (hose or an elastic bandage)	Length of follow-up: Not reported Loss-to-follow-up: Not reported Incomplete outcome: Not reported	ulcer healing rate at 12 months: - 81.5% intervention (n=22) - 24% control (n=6) P 0.0001 Recurrence rate - 0% intervention - 44% control (n=4) p-value unknown.	
Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison / control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comments**
Rueda 2013	Type of study: Retrospective cohort study Country: USA Source of funding: not reported. Inclusion: - C6	N total at baseline: 64 pt I: 23 C: 41 Baseline characteristics: Age ± SD: - I: 60 (35-87) - C: 59 (30-83)	RFA IPV + compression All patients were placed in elastic compression garments. Following this intervention, most patients are placed in 20-30 mmHg compression garments.	SEPS + compression All patients were placed in elastic compression garments. Following this intervention, most patients are placed in 20-30 mmHg compression garments.	Length of follow-up: 37 months Loss-to-follow-up: Not reported Incomplete outcome Not reported	Ulcer healing rate at 12 months: - 88% SEPS - 100% RFA IPV P = NS Ulcer recurrence rate - 17% SEPS (n=7) - 23% RFA IPV (n=6) P = NS	

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Alden 2013	Type of study: Retrospective cohort study Country: USA Source of funding: not reported Inclusion: - C6 - at least 2 visits with adequate data	N total at baseline: 86 pt I: 48 ulcers C:47 ulcers Baseline characteristics: Age: - I: 67 - C: 71	SVR ablation (RFA stripping/ligation) + compression (UGFS of IPV a second time). 2- and 4-layer systems. Unna boots, short stretch bandages, and gradient compression hose were also used.	Compression 2- and 4-layer systems. Unna boots, short stretch bandages, and gradient compression hose were also used.	Length of follow-up: Not reported Loss-to-follow-up: Not reported Incomplete outcome: not reported	Ulcer healing rate - faster in the intervention group compared with compression group (10% vs 4% per week. P = 0.001) Recurrence rate - fewer recurrences at 1-year FU in the intervention group compared with the compression group (27.1% vs 48.9%. P0.015)	