Appendix 1 Table of included studies with moderate risk of bias / Bilaga 1 Tabell över inkluderade studier med måttlig risk för bias

Sammanfattning av studier med måttlig risk för bias

Author, year Country Ref # Study design	Population	Intervention	Results	Risk of bias	Notes
Szolnoky, 2009 Hungary [1] CCT	n=38 women (76 legs) with lipedema Age: median years (range) Complex decongestive physiotherapy (CDP): 54.83 (31 to 76) Moisturizers: 51.27 (29 to 66)	CDP vs moisturizers during a 5 day course CDP (n=21) MLD using Vodder's method performed by trained physiotherapist 30 min / day + moisturizers (non-ionic hydrophyl ointment) + multi-layered short-stretch bandaging + walking exercises 2 x 30 min / day + IPC (pressure 30 mmHg, 30 min / day) Moisturizers (n=17) Moisturizers (non-ionic hydrophyl ointment, same as above) applied 1x / day + no other intervention	After a 5-day-course: Capillary fragility[1]: Mean number of petechiae (SD) before / after treatment CDP: 13.95 (10.17) / 8.78 (6.88) MC: 12.38 (9.35) / 12.15 (8.73) Leg volume[2]: liters (SD) before / after treatment CDP: 16.5 (2.0) / 15.6 (1.9) MC: 15.6 (2.0) / 15.5 (1.8) Adverse effects: not reported	Moderate (risk of selection bias, information bias, detection bias and conflict of interest)	1-Capillary fragility evaluated with vacuum suction method (VSM) using Parrot's angiosterrometer: reclined rest before measurement, 30mmHg negative pressure applied for 1 minute, number of petechiae (broken capillaries) counted under magnification 2-Leg volumes were measured with Kuhnke's disc method
Di Renzo, 2021 Italy [2] CCT	n=29 women Lipedema: n=14 Control: n=15 Patient Characteristics at baseline: Age: not reported BMI Kg/m2: mean (SD) Lipedema: 35.50 (12.17) Control: 27.52 (5.22) Age of onset, time since symptom debut, comorbidities other than	Modified Mediterranean diet therapy (mMeD) for 4 weeks All participants provided with a personalized mMeD with 20% caloric restriction based on each patient's calculated energy requirements. Daily menus of 5 meals per day were supplied. Monitored by telephone interview once a week Program duration: 4 weeks	Follow-up directly after 4 weeks program Biometrics BMI (kg/m2): mean (SD) before /after Lipedema: 35.50 (12.17) / 34.36 (11.84) Control: 27.52 (5.22) / 26.38 (4.99) QoL with EQ-5D: mean total score (SD) before / after Lipedema: 8.3 (1.8) / 6.9 (1.4) Control: no clinically relevant change, data not shown Perceived level of health with EQ-5D	Moderate (risk of selection bias, detection bias)	

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	those excluded, and previous treatments not reported.		VAS (1-100): mean score (SD) before / after Lip: 64.7 (18.3) / 69.9 (18.3) Control: no clinically relevant change, data not shown Adverse effects: not reported		
Szolnoky, 2011 Hungary [3] CCT	38 women (76 legs) with lipedema Treated = 19 women (38 legs) Control = 19 women (38 legs) Mean age: years (range) Treatment: 53.89 (31 to 68) Control: 55.7 (42 to 80) BMI: not reported Comorbidities: not reported	CDP vs Control CDP: MLD (30 min./ day) + IPC (30 mmHg, 30 min. / day) + walking (2 x 30 min. per day) + moisturizers + multi-layered short-stretch bandaging Control: moisturizers (same as above) + no treatment with physiotherapy or compression Treatment length = 5 days	After a 5-day course: Pain[1] Descriptive scale (1 to 4): CDP: change significant for all adjectives (data available in study) Control: change not significant for any adjective (data available in study) NAS (0 to 10): mean (SD) before/after CDP: 5.89 (1.868) / 3.34 (2.561) Control: 5.37 (1.95) / 4.74 (1.91) Wong Baker Faces scale (0 to 10): mean (SD) before/after CDP: 5.26 (2.423) / 3.05 (3.009) Control: 5.16 (2.34) / 4.95 (2.147) Mean leg volume reduction[2] CDP: 5.6% (2.78) Control: "no significant change" Adverse effects: not reported	Moderate/high (risk of selection bias, information bias, detection bias and conflict of interest)	1 - Pain measured with 3 scales: Descriptive: Adjectives describing pain: pressing, dull, heavy, pulling, torturing, enervating, violent, unbearable, exhausting, stabbing; rated as none = 1, mild=2, moderate=3, severe=4 NAS= 0 to 10 (none to worst possible pain) Wong Baker Faces scale (VAS 0 to 10, no pain at all to the worst pain imaginable) 2 - Leg volume measured with Kuhnke's disc method
Szolnoky, 2008 Hungary [4] RCT	n=23 women (46 legs) with lipedema[1] Group 1 = 13 women Group 2 = 10 women	CDP vs CDP + IPC CDP	Follow-up = end of treatment (assumed)	Moderate (risk of selection bias, information	1- Baseline patient characteristics are provided for the two groups, but it is not clear which group is which

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	Mean age: years (range) Group 1: 51.3 years (32 to 65) Group 2: 50.0 (44 to 80) BMI: not reported Comorbidities: patients were screened for deep vein thrombosis (excluded), otherwise not reported	MLD performed by trained physiotherapist using Vodder's method for 60 min / day + moisturizers + multi-layered short-stretch bandaging Total treatment time = 60 min / day CDP + IPC MLD performed by trained physiotherapist using Vodder's method for 30 min / day + moisturizers + multi-layered short-stretch bandaging + IPC[2] for 30 min / day (pressure 30 mmHg) Total treatment time = 60 min / day Both groups: Wore grade II or II medical compression stockings between treatments. Treatment length = 5 days	Leg volume[3]: mean volume (ml) before / after CDP: Left: 17976.15 (4960.8) / 16866.46 (4474.2) Right: 17760.08 (4692.9) / 16998 (4516.9) CDP + IPC: Left: 15396.4 (2284.9) / 14024.5 (2821.2) Right: 15331.8 (2767.5) / 14240 (2907.9) Adverse effects: not reported	bias, detection bias and conflict of interest)	2-Lympha Press Plus machinery (Mego Afek, Israel) 3-Leg volume measured with Kuhnke's disc method
Schneider, 2020 Germany [5] RCT	31 women with lipedema Lost to follow-up: 1 person stopped treatment after first session for personal reasons n=30 Mean age (range) = 53.2 yrs. (23–75) Mean weight (SD) = 91.2 kg (20.4)	MLD vs MLD + vibrotherapy (V)[1] MLD: n=15 MLD + V: n=15 30-minute sessions were delivered by experienced physiotherapists 2x / week, for 3 weeks (6 sessions in total)	Follow-up: immediately after last treatment Health related QoL 5-point Likert scale (anchors very bad, bad, moderate, good, and very good)[2] Domain: score (SD) before / after Physical performance (range 0 to 32): MLD: 15.0 (6.6) / 17.5 (5.9) MLD+V: 16.9 (4.4) / 21.9 (3.5) Cohen's d = 0.7 (95% CI 0.1 to 1.2) Ability to relax (range 0 to 32):	Moderate (risk of selection bias, information bias, conflict of interest)	1-Vibrotherapy: Patient receives mild, vertical, low frequency impulses during MLD treatment (Cell connect Impulse). 2-Measured with Quality of Life with Chronic Disease tool PLC with 6 dimensions, 4 of which considered here (1) physical performance (2) ability to relax (3) ability to

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	Comorbidities: none had acute health threatening disease, drug addiction, mental illness (exclusion criteria) Previous treatment: 16/30 compression bandaging was worn 3 to 24 hours / day 17/30 women were under regular medical treatment, duration 3 to 26 years		MLD: 17.3 (5.0) / 18.3 (5.8) MLD+V: 19.7 (3.3) / 23.5 (3.0) Cohen's d = 1.1 (95% CI 0.4 to 1.9). Positive mood (range 0 to 20): MLD: 8.7 (4.0) / 9.9 (3.8) MLD+V: 10.6 (3.0) / 13.5 (2.3) Cohen's d = 0.5 (95% CI –0.01 to 0.9) Negative mood (range 0 to 32): MLD: 19.6 (6.3) / 19.9 (7.3) MLD+V: 21.6 (4.0) / 25.6 (4.5) Cohen's d = 0.8 (95% CI 0.1 to 1.6) Expectations[3] Scale 5–20 Mean expectation (SD) before / after MLD: 13.6 (3.9) / 12.3 (2.9) MLD+V: 12.2 (SA 3.3) / 16.8 (2.1) Cohen's d = 1.8 (95% CI 1.2 to 2.3) Circumference (cm) Location: mean (SD) before /after Forefeet MLD: 23.8 (1.6) / 23.6 (1.5) MLD+V: 22.9 (1.3) / 22.3 (1.4) Ankles MLD: 26.6 (2.3) / 26.4 (2.1) MLD+V: 25.5 (2.5) / 24.3 (1.9) Calves MLD: 42.1 (4.1) / 41.5 (4.2) MLD+V: 42.8 (3.6) / 41.0 (3.2) Thighs MLD: 58.2 (8.0) / 57.7 (7.9) MLD+V: 61.8 (9.8) / 59.2 (9.6) Adverse effects: not reported		communicate (4) sense of belonging, measured with a 5-point-Likert-scale with the anchors very bad, bad, moderate, good, and very good. 3-Expectations: Asked to predict improvement in the following domains: (1) bodily impairments; (2) physical quality of life; (3) well-being; and (4) symptom-related stress measured with 4-point-Likert-scale with the anchors not at all, hardly, somewhat, and very much

RCT =Randomized controlled trial; **CCT** = Controlled clinical trial; **CI** = confidence interval; **MLD =** Manual lymph drainage, aims to remove excessive interstitial fluid by gentle, pumping, circular movements using low pressure; **CDP =** Complex decongestive physiotherapy; **BMI** = Body mass index, **QoL** = Quality of life

Referenser

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