Objective. In systemic sclerosis (SSc; scleroderma) patients in edematous phase, hand edema is often present. Manual lymph drainage (MLD) stimulates the lymphatic system and reduces edema. Our aim was to evaluate the efficacy of MLD in reducing edema and in improving functionality of the hands and perceived quality of life (QOL) in SSc patients in edematous phase.

Methods. Of 35 SSc patients with edematous hands, 20 were treated with MLD according to the Vodder technique once a week for 5 weeks (intervention group), and 15 served as the observation group. Patients were evaluated at enrollment, at the end of treatment (T1), and after 9 weeks of followup (T2) by volumetric test (assessing hand volume), the Hand Mobility in Scleroderma (HAMIS) test, and 4 visual analog scales (VAS; scored 0–10) evaluating the perception of hand edema and pain and their interference on daily activities. QOL and disability were assessed by the physical synthetic index (PSI) and mental synthetic index (MSI) of the Short Form 36 (SF-36) and by the Health Assessment Questionnaire (HAQ).

Results. In the intervention group, hand volume, the HAMIS test, and the 4 VAS were improved significantly at the end of treatment ($P < 0.001$). The results were maintained at T2 ($P < 0.001$). The HAQ and the PSI and MSI of the SF-36 also improved significantly at T1 ($P < 0.001$), but only PSI improvement was maintained at T2 ($P < 0.001$). In the observation group, no improvement at T1 and at T2 was observed.

Conclusion. In SSc, MLD significantly reduces hand edema and improves hand function and perceived QOL.
Manual Lymph Drainage in Systemic Sclerosis

Significance & Innovations

- To our knowledge, this is the first study assessing the effects of manual lymph drainage (MLD) on the hands of systemic sclerosis (SSc) patients in edematous phase.
- MLD (executed for 5 weeks) was able to reduce hand volume, improve hand function and patients’ self-perception of hand disability, and ameliorate global disability and perceived quality of life in SSc patients.
- All of the improvement obtained in hands by MLD was maintained after 9 weeks of followup.
- Based on these data, although preliminary, MLD may be introduced in the management of SSc patients in edematous phase.

PATIENTS AND METHODS

Forty consecutive white female SSc patients (mean ± SD age 50.17 ± 15.69 years and mean ± SD disease duration 8.0 ± 3.9 years), classified according to American College of Rheumatology criteria (18), with edematous hands and fingers were enrolled from the outpatient clinic of the Department of Biomedicine, Division of Rheumatology of the University of Florence and agreed by written informed consent to participate in the study, which was approved by our institutional ethics committee. Exclusion criteria were ongoing infections and thrombosis. Patients with hand fibrosis and/or finger contractures were also excluded from the study.

All of the patients underwent a clinical examination and were assessed according to international guidelines (19). No patient was experiencing arthritis or myositis.

The sample size calculation performed for the present study was based on the changes in volumetry of hands with SSc after treatment with MLD obtained in preliminary experiences of our group, and with a desired power of 0.80 and an alpha level of 0.05. The sample size required was 28 patients, to be allocated, after randomization with an allocation ratio of 1:1, to treatment with MLD (intervention group [IG]) or to the observation group (OG; n = 14 patients each). Given the probable attrition rate due to allocation in the control group, a total of 40 patients were enrolled and randomized.

After baseline assessment, the patients were randomly allocated to IG (20 patients) or OG (20 patients). Randomization was performed by using a random number sequence prepared by an independent person not connected with the study, who also provided sequentially numbered and sealed envelopes. The results of the randomization were unknown until the patient accepted or refused to participate in the study.

Patients in the IG were treated with MLD and patients in the OG were considered as controls. The study had a total duration of 14 weeks: 5 weeks of rehabilitation and 9 weeks of followup.

Patients in the IG were treated with MLD for a period of 5 weeks, 1 session a week (lasting 1 hour). All MLD treatments were performed by the same physiotherapist (MP). OG patients, allocated to a “waiting list,” were asked to maintain their lifestyle for the entire duration of the study and to refrain from starting any new regular physical activity or exercise programs unrelated to the study or other nonpharmacologic interventions for SSc.

In both groups, all of the patients continued their pharmacologic treatments (alprostadil-α-cyclodextran, prostacyclin, calcium-channel blockers, topical glyceryl trinitrate, endothelin receptor antagonists, proton-pump inhibitors, steroids, cyclophosphamide, azathioprine, and methotrexate) with no changes throughout the study and were asked to refrain from starting any new pharmacologic therapy for SSc.

Patients. All of the patients underwent a clinical evaluation (15); interstitial lung disease was examined by standard chest radiographs, high-resolution computed tomography, respiratory functionality tests, and bronchoalveolar lavage; pulmonary arterial hypertension was examined by color Doppler echocardiography; heart involvement was defined if pericarditis, arrhythmia, or left ventricular congestive heart failure was present; esophagus involvement was defined by the presence of hypomotility at barium radiography and/or manometry; global skin involvement was assessed by the modified Rodnan skin thickness score (20); and a partial skin score of the upper extremities was also assessed. The presence of fingertip ulcers at the hands, Raynaud’s phenomenon, and tenderness at the metacarpophalangeal and interphalangeal joints and wrists (range 0–22) was also recorded, as well as the vasoactive drugs assumed by the patients.
Assessment. All of the patients were evaluated at enrollment (T0), at the end of the treatment (T1), and after a followup of 9 weeks (T2).

Hands volume was assessed by a volumetric test performed by slowly dipping the hand in a cylinder full of water. The patients immersed the upper extremity into the water-filled cylinder by placing the hand up to the wrist perpendicular to the bottom of the cylinder with contact of the metacarpophalangeal joints of the fingers with the projecting part of the cylinder. Then, the quantity of the water overflowed from the cylinder into a beaker with graduated markings, was measured twice for each hand, and a mean of 2 consecutive measurements was calculated (21) (Figure 1).

All of the volumetric examinations were made between 9:00 AM and 12:00 PM in order to avoid the diurnal variation of dermal edema. The intraclass correlation coefficient (ICC) was used to assess the intra- and interobserver variability of the method. The intraobserver variability was significantly low (ICC 0.997, 95% confidence interval [95% CI] 0.984–0.999), as was the interobserver variability (ICC 0.995, 95% CI 0.977–0.999).

Hands function was evaluated by the Hand Mobility in Scleroderma (HAMIS) test, assessed in both hands (22). The HAMIS test is a performance-based test, found to be a reliable and valid tool to assess hand function in SSc patients, composed of 9 items, evaluating in both hands: finger flexion and extension, abduction of the thumb, dorsal extension and volar flexion of the wrist, pronation and supination of the forearm, and the ability to make a thumb pincer grip and to make finger abduction. The different performance areas of the HAMIS test are composed of different-sized grips and different movements, all related to tools and movements that are part of daily occupations. Each exercise is graded on a 0–3 scale (where 0 = normal function and 3 = inability to perform the task), with a total possible score of 27 for each hand (22).

Patient perception of hand disability was scored by 4 visual analog scales (VAS; range 0–10, where 0 = best condition and 10 = worst condition) by which the patient self-evaluated the entity of hand edema, pain, and the

**Figure 1.** Execution of the volumetric test. A, A patient before placing the hand into the water-filled cylinder. The wrist is marked with a red pen. B and C, frontal and lateral view of the patient with the hand immersed in the cylinder; the water is overflowing from the cylinder into a beaker with graduated markings, where the water is measured.

**Figure 2.** Procedure of manual lymph drainage (MLD). MLD is applied first at the terminus (A), the triangular area at the base of the neck, above the clavicles, where the lymph returns to the circulatory system by flowing into the subclavian veins, then to the neck (B) and head (C) lymphatic skin vessels and lymph nodes and then, following a centrifugal direction, at the upper extremity (axilla, arm, elbow, forearm, wrist, hand, and fingers; D–H), starting from the less edematous side. In a subsequent phase, lymph nodes of the wrist, elbow, axilla, and neck are treated in a centripetal direction.

Figure 2. Procedure of manual lymph drainage (MLD). MLD is applied first at the terminus (A), the triangular area at the base of the neck, above the clavicles, where the lymph returns to the circulatory system by flowing into the subclavian veins, then to the neck (B) and head (C) lymphatic skin vessels and lymph nodes and then, following a centrifugal direction, at the upper extremity (axilla, arm, elbow, forearm, wrist, hand, and fingers; D–H), starting from the less edematous side. In a subsequent phase, lymph nodes of the wrist, elbow, axilla, and neck are treated in a centripetal direction.
interference of edema and pain on the daily activities in the previous week.

QOL and disability were evaluated by the physical synthetic index (PSI) and mental synthetic index (MSI) of the Short Form 36 (SF-36) (23) and by the Health Assessment Questionnaire (HAQ) (24), both autoadministered to the patients.

Volumetric and HAMIS tests were assessed at each time point (T0, T1, T2) by a physiotherapist blinded to group allocation and to treatment of the SSc patients (SM). VAS and the HAQ and SF-36 questionnaires were autoadministered and returned in a sealed envelope by the patients to the same physiotherapist.

**MLD.** MLD was applied by a trained operator (MP) according to the Vodder method by using manual adapted pressure with repetitive and pumping, circular, and spiral movements. MLD mobilizes the skin over the underlying tissues with a pressure increase (30 torr), followed by a loosening phase. By stimulating the musculature of lymphatic vessels, these changes in pressure create a pumping effect, elicit the flow of the lymph, and drain the excess of fluid from the tissues. The strokes are performed constantly and rhythmically (7–9).

The MLD was applied first at the “terminus” (the triangular area at the base of the neck, above the clavicles, where the lymph returns to the circulatory system by flowing into the subclavian veins) (Figure 2A) with light massage strokes. Then, the neck (Figure 2B) and head (Figure 2C) lymphatic skin vessels and lymph nodes were massaged. Subsequently, the axillary lymph nodes were treated and a light massage was directed from the proximal site of the arm to the wrist, following a centrifugal direction in the upper extremity, with the aim of opening the lymphatic vessels. The treatment was performed by stimulating sequentially the lymphatic vessels of the arm, elbow, forearm, and wrist. This procedure was followed by the treatment of the dorsal and, then, of the palmar side of the hand and fingers (Figures 2D–H). Afterward, the upper extremity was treated in a centripetal direction by massaging the lymph nodes of the wrist, elbow, and axilla, and reaching again to the neck, with the aim of draining the content of the lymphatic vessels into the circulatory system. MLD sessions were performed in both upper extremities, starting from the less edematous side, and lasted for approximately 60 minutes.

**Statistical analysis.** Data are shown as the mean ± SD and as numbers and percentages. Student’s t-test, chi-square test, and Fisher’s exact test, when appropriate, were used to compare for group characteristics at T0. Student’s t-test was also used to evaluate differences in groups at T1 and T2. For outcome measures, analysis of variance for repeated measures with Bonferroni test for the post hoc analysis was used to detect effects of treatment. The intra- and interobserver variability of hand volumetry was assessed by the ICC. Data analysis was performed using the SPSS statistical package for Windows.

**RESULTS**

After baseline evaluation and randomization, 5 of the 20 SSc patients assigned to the OG withdrew because they did not accept their group allocation. Therefore, a total of 35 SSc patients participated in the study: 20 in the IG and 15 in the OG.

In both groups, the enrolled patients were similar in their baseline characteristics and in the vasoactive drugs assumed (Table 1). None of the patients dropped out of the study and no side effects were observed in the IG after the application of MLD.

**Effects of MLD on hand volume.** In the SSc patients in the IG, MLD application at the upper extremities reduced volume assessed by hand volumetry at the end of the treatment (T1) in respect to T0 (P < 0.0001) (Figure 3).

At the followup evaluation (T2), the reduction of hand volume obtained by MLD was maintained with respect to T0 (P < 0.0001) and remained stable with respect to T1 (P = not significant [NS]).

In the SSc patients in the OG, at T1 hand volume was unchanged with respect to T0 (P = NS) and remained stable at T2 versus T0 and versus T1 (P = NS for both comparisons) (Table 2).

**Effects of MLD on hand function and hand disability.** In the SSc patients in the IG, MLD treatment of the upper extremities improved hand functionality and patient perception of hand disability. At T1, the HAMIS test and the 4 VAS (evaluating hand edema, pain, and the interference of edema and pain in daily activities) improved significantly (P < 0.0001 with respect to T0).

At T2, the improvements obtained by MLD with respect to T0 were maintained for all of the items assessed (P < 0.0001 for hand volume, the HAMIS test, the VAS assessing hand edema and pain, and the VAS evaluating interference of hand edema in daily activity; P < 0.001 for the VAS assessing interference of hand pain in daily activity) and remained stable in respect to T1 (P = NS).

In the SSc patients in the OG, at T1 none of the items assessing hand function and patient perception of hand disability was changed significantly with respect to T0 (P = NS for all of the comparisons at T1 versus T0). All of the items remained stable at T2 versus T0 and T1 (P = NS for both comparisons) (Table 2).

**Effects of MLD on disability and QOL.** In the SSc patients in the IG, MLD treatment of the upper extremities ameliorated the overall perception of disability and QOL. At the end of the treatment (T1), the HAQ (P < 0.001) and the PSI and MSI of the SF-36 (P < 0.0001 for both) improved significantly with respect to baseline (T0).

At the followup evaluation (T2), only PSI improvement was maintained with respect to T0 (P < 0.0001 at T2 versus T0), whereas the MSI and HAQ returned to their baseline values (T2 versus T0: P = NS in both cases).

At T1 versus T2, the values of the HAQ and MSI worsened (P < 0.05 and P < 0.0001, respectively), while PSI scores remained stable (P = NS).

In the SSc patients in the OG, at T1 the HAQ and the
MSI and PSI of the SF-36 remained unchanged with respect to the baseline values ($P = NS$ for all of the comparisons at T1 versus T0). All of the items remained stable at T2 with respect to T0 and T1 ($P = NS$) except for the PSI, which was impaired versus T0 ($P < 0.05$), but was not different with respect to T1 ($P = NS$) (Table 2).

### DISCUSSION

With the present study that, to the best of our knowledge, is the first assessing the effect of MLD in SSc, we demon-
strate that MLD is effective in the treatment of hands of SSc patients in edematous phase by reducing hand volume and improving hand function and self-perceived edema and pain. The reduction of hand volume and the improvement in function were also maintained at followup. These results are implemented by the amelioration of overall disability and QOL in patients treated with MLD.

In the early phase of SSc, hand edema and puffy fingers are the first objective signs of the disease after the onset of Raynaud’s phenomenon (2). At high-frequency ultrasound, dermal thickness of the dorsal side of the second finger is significantly higher in the edematous phase than in the fibrotic phase (25).

In SSc patients, hand involvement leads to notable difficulties in ADL (26). Therefore, techniques aiming to improve hand function may be of pivotal importance in reducing the disability due to hand impairment (27) since the earliest phases of the disease.

Previous experiences showed the usefulness of MLD in the treatment of lymphedema in psoriatic arthritis (28) and in treating edema and pain in reflex sympathetic dystrophy (29). In patients with fibromyalgia syndrome, MLD reduced pain intensity and improved pain pressure threshold, QOL, and disability (30).

Our SSc patients had objective evidence of puffy hands and fingers as shown by volumetry; perceived their hands as disabled, edematous, and painful; and regarded edema and pain as obstacles and interferences in their ADL. Accordingly, self-perceived disability and QOL were impaired, as shown by the high values of HAQ and by the low values of the PSI and MSI of the SF-36 found in our patients.

Our results demonstrate that, in SSc patients with edematous hands, MLD was capable of reducing hand volume and improving hand function, self-perceived edema, and pain.

The efficacy of MLD on hand edema in SSc patients may be due to its action on some contributors of SSc tissue edema, such as vasculopathy of blood (14) and lymphatic (9–11) microvessels, autonomous nervous system activity (15), and inflammatory changes (16). MLD, by stimulating lymphatic vessels (6,8), may contribute to mobilizing edema and removing the excess of interstitial fluid. Moreover, it may modulate sympathetic nervous activities and increase parasympathetic nervous activities, thus leading to blood vessel vasodilation (6) and to improvement in circulation, and may reduce chronic inflammatory processes (8).

The amelioration in the hand functionality and performances due to MLD in our patients is reflected by the reduction in the HAMIS test scores. The HAMIS test, specifically designed to evaluate SSc patients’ hand function and manual ability in ADL, has already been shown as a reliable outcome measure to followup physiotherapeutic treatments. In a study of our group, the HAMIS test was able to evaluate the improvement in SSc patients’ hands due to a combined rehabilitation protocol based on connective tissue massage, Mc Mennell joint manipulation, and home exercises (31).

In our patients, MLD also reduced self-perceived pain and interference in daily activities related to pain, probably because it contributes to reducing the compression on the skin and subcutaneous nervous fibers due to interstitial edema and to draining algogenic molecules into the lymphatic vessels (8).

The improvement in HAQ and SF-36 scores after the application of MLD reflects how hand functionality, having a prominent role in the execution of ADL, may be
a fundamental determinant in the perception of global disability and in QOL in patients with SSc (28). However, different from the amelioration obtained at the hands, maintained after a period of followup, the improvement reached at the end of the treatment in the measures assessing global disability and QOL were not confirmed after a followup period.

The loss of significance at followup of HAQ improvement is not completely unexpected. As this tool does not specifically assess hand disability, the effects of MLD on its score could be the first not to be maintained.

The improvement of MSI was also not confirmed at followup. The latter result may address the importance for patients with SSc to execute a rehabilitation program performed under the guide of a physiotherapist, underlining the pivotal role that these figures may have not only on the physical problems, but also on the psychological aspects of SSc patients.

It is known that commonly used pharmacologic therapy and physiotherapeutic techniques have only some efficacy in treating edematous hands and puffy fingers in SSc patients and in ameliorating hand function and disability in this phase. This evidence stresses the importance of the results obtained with MLD in our study.

Given the important results obtained by MLD in SSc patients in hand volume, perceived edema and pain, hand function, and QOL, specific home decongestive exercises, as seen in postmastectomy lymphedema, should be added...

Table 2. Hand characteristics and quality of life at baseline (T0), at the end of treatment (T1), and at followup (T2) in the intervention group (IG) and in the observation group (OG)*

<table>
<thead>
<tr>
<th></th>
<th>T0, mean ± SD</th>
<th>T1, mean ± SD</th>
<th>T2, mean ± SD</th>
<th>T0–T1, P</th>
<th>T0–T2, P</th>
<th>T1–T2, P</th>
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</thead>
<tbody>
<tr>
<td>Hand volume, cm³</td>
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<tr>
<td>IG</td>
<td>340.0 ± 59.51</td>
<td>310.7 ± 51.84</td>
<td>316.6 ± 61.76</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>NS</td>
</tr>
<tr>
<td>OC</td>
<td>343.7 ± 51.25</td>
<td>345.3 ± 46.56</td>
<td>350.2 ± 46.90</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>IG vs. OG, P</td>
<td>NS</td>
<td>&lt; 0.05</td>
<td>&lt; 0.01</td>
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<tr>
<td>HAMIS test, right hand</td>
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</tr>
<tr>
<td>IG</td>
<td>8.15 ± 4.28</td>
<td>4.75 ± 3.22</td>
<td>5.7 ± 4.27</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>NS</td>
</tr>
<tr>
<td>OC</td>
<td>8.4 ± 5.14</td>
<td>8.53 ± 4.53</td>
<td>8.93 ± 4.7</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>IG vs. OG, P</td>
<td>NS</td>
<td>&lt; 0.01</td>
<td>&lt; 0.05</td>
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<tr>
<td>HAMIS test, left hand</td>
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<tr>
<td>IG</td>
<td>8.1 ± 4.14</td>
<td>4.35 ± 3.17</td>
<td>5.5 ± 4.25</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>NS</td>
</tr>
<tr>
<td>OC</td>
<td>8.33 ± 4.80</td>
<td>8.47 ± 5.41</td>
<td>8.73 ± 5.06</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>IG vs. OG, P</td>
<td>NS</td>
<td>&lt; 0.01</td>
<td>&lt; 0.05</td>
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<tr>
<td>Hand edema†</td>
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<tr>
<td>IG</td>
<td>6.95 ± 1.47</td>
<td>2.64 ± 1.89</td>
<td>3.26 ± 2.03</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>NS</td>
</tr>
<tr>
<td>OC</td>
<td>6.34 ± 1.52</td>
<td>6.83 ± 1.7</td>
<td>7.09 ± 1.56</td>
<td>NS</td>
<td>&lt; 0.05</td>
<td>NS</td>
</tr>
<tr>
<td>IG vs. OG, P</td>
<td>NS</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
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<tr>
<td>Interference of hand edema in daily activity†</td>
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<tr>
<td>IG</td>
<td>4.26 ± 2.46</td>
<td>1.98 ± 1.79</td>
<td>2.32 ± 1.8</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>NS</td>
</tr>
<tr>
<td>OC</td>
<td>4.54 ± 2.53</td>
<td>4.13 ± 2.26</td>
<td>4.63 ± 2.35</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>IG vs. OG, P</td>
<td>NS</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
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<tr>
<td>Hand pain†</td>
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<tr>
<td>IG</td>
<td>3.78 ± 2.6</td>
<td>1.52 ± 2.07</td>
<td>1.84 ± 2.29</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>NS</td>
</tr>
<tr>
<td>OC</td>
<td>3.62 ± 2.77</td>
<td>3.78 ± 2.44</td>
<td>4.01 ± 2.37</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>IG vs. OG, P</td>
<td>NS</td>
<td>&lt; 0.01</td>
<td>0.01</td>
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<tr>
<td>Interference of hand pain in daily activity†</td>
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<tr>
<td>IG</td>
<td>3.43 ± 2.44</td>
<td>1.69 ± 2.19</td>
<td>2.0 ± 2.17</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.001</td>
<td>NS</td>
</tr>
<tr>
<td>OC</td>
<td>3.73 ± 2.59</td>
<td>3.86 ± 2.68</td>
<td>4.14 ± 2.46</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>IG vs. OG, P</td>
<td>NS</td>
<td>0.01</td>
<td>0.01</td>
<td></td>
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<tr>
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<tr>
<td>IG</td>
<td>1.56 ± 0.82</td>
<td>0.88 ± 0.7</td>
<td>1.4 ± 0.82</td>
<td>&lt; 0.001</td>
<td>NS</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>OC</td>
<td>1.47 ± 0.90</td>
<td>1.49 ± 0.81</td>
<td>1.53 ± 0.94</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>IG vs. OG, P</td>
<td>NS</td>
<td>0.05</td>
<td>NS</td>
<td></td>
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<tr>
<td>SF-36 PSI</td>
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<tr>
<td>IG</td>
<td>38.77 ± 7.91</td>
<td>44.79 ± 8.27</td>
<td>44.10 ± 7.25</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>NS</td>
</tr>
<tr>
<td>OC</td>
<td>39.19 ± 6.95</td>
<td>38.95 ± 7.35</td>
<td>37.01 ± 5.34</td>
<td>&lt; 0.05</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>IG vs. OG, P</td>
<td>NS</td>
<td>&lt; 0.05</td>
<td>&lt; 0.01</td>
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<tr>
<td>SF-36 MSI</td>
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</tr>
<tr>
<td>IG</td>
<td>38.21 ± 6.69</td>
<td>44.43 ± 6.84</td>
<td>39.72 ± 5.82</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>NS</td>
</tr>
<tr>
<td>OC</td>
<td>37.15 ± 6.38</td>
<td>38.76 ± 6.46</td>
<td>37.30 ± 6.41</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>IG vs. OG, P</td>
<td>NS</td>
<td>0.01</td>
<td>NS</td>
<td></td>
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</tr>
</tbody>
</table>

* NS = not significant; HAMIS = Hand Mobility in Scleroderma; HAQ = Health Assessment Questionnaire; SF-36 = Short Form 36; PSI = physical synthetic index; MSI = mental synthetic index.
† Assessed by visual analog scale (range 0–10).
to MLD in order to maintain the beneficial effects of MLD over time (7). These additional techniques may also potentially be helpful in maintaining in a mid- and/or long-term period the improvements obtained in general disability and in self-perceived QOL.

Our study has 2 main limitations. It is conducted on a relatively short period (14 weeks, with 5 weeks of treatment and 9 of followup) and on a relatively low number of SSC patients, which did not permit a disease subsetting.

In conclusion, the application of MLD is effective in the treatment of the hand in edematous SSC by reducing hand volume, edema, and pain, and improving hand function and perceived QOL. A study on a larger cohort of patients and with a longer followup is needed to assess the effect of MLD on disease subsets as well, and to verify if the technique could be of help in preventing the transition from hand edema to fibrosis.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Del Rosso had full responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Maddalı Bongi, Matucci Cerinic.

Acquisition of data. Maddalı Bongi, Del Rosso, Passalacqua, Miccio.

Analysis and interpretation of data. Maddalı Bongi, Del Rosso, Passalacqua, Matucci Cerinic.

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