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Rehabilitation in systemic sclerosis: proposed personalised rehabilitation programme

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ABSTRACT. Background: *Systemic sclerosis is a multisystem autoimmune disease that causes chronic widespread obliterative vasculopathy of the small arteries associated with various degrees of tissue fibrosis. The prognosis of the disease depends largely on the visceral involvement; however musculoskeletal involvement is an important factor to functional disability. Suffering from a chronic auto-immune disease, such as Systemic Sclerosis, compromises the quality of life and the work ability. The rehabilitative treatment may be a viable option for improving the quality of life, but there are few studies to support this hypothesis in adequate population. (Rehabilitation is still an under- studied field of research).*
Aim: *Proposed personalised rehabilitation programme, with a multilocalized, multidisciplinary approach specifically designed for patients with Systemic Sclerosis.*
Design: *Retrospective study.*
Setting: *Rehabilitation Institute, inpatients.*
Population: *Forty-three patients affected by systemic sclerosis.*
Methods: *Patients underwent a rehabilitation programme of 3 weeks. Three cycles of rehabilitation in 3 consecutive years were administered. The priority outcome measure was the Health Assessment Questionnaire-Disability Index (HAQ-DI). The effectiveness of treatment cycles repeated at 1-year intervals was also compared to the first cycle.*
Results: *Each treatment had an acute beneficial effect, leading to an improvement in the disability score after each of the three cycles (admission vs discharge: 1.2±0.6 vs 0.8±0.6, p<0.0001, 1.3±0.6 vs 1.0±0.6, p<0.0001 and 1.4±0.7 vs 1.1±0.7, p<0.0001). The improvement in HAQ-DI scores after repeated cycles was progressively lower, but the difference in efficacy was not statistically significant (p=0.38 and p=0.17 for the comparison between the second and the first and the third and the first cycles respectively).*
Conclusions: *The multilocalized, multidisciplinary protocol developed by our rehabilitation team led to a significant reduction in disability perceived by patients, independently of the disease duration. The beneficial effects at the end of the first cycle were reproduced in the subsequent cycles. Nevertheless, there was a tendency of progressive efficacy reduction in following cycles, due to increased disability caused by disease stage.*
Impact of rehabilitation: *We believe that our results demonstrate the utility of personalised, multilocalized, multidisciplinary rehabilitation treatment in slowing the evolution of systemic sclerosis.*

Key words: systemic sclerosis, HAQ-DI, rehabilitation.

RIASSUNTO. *Introduzione:* La sclerosi sistemica è una malattia autoimmune multi sistemica che causa una cronica e diffusa vasculopatia obliterante delle piccole arterie

Introduction

Systemic sclerosis is a chronic, progressive, autoimmune disease of the connective tissues, characterized by functional changes in the capillary microcirculation and increased production and deposition of collagen in the connective tissues. These changes affect the skin, causing progressive cutaneous fibrosis and damage to numerous internal target organs, including the lungs, heart, kidneys and gastrointestinal tract with different expression of damage to the organs (1,2).

The appearance of Raynaud's phenomenon of the hands is often the first sign of the disease and can precede other manifestations by many years. With the progression of the disease there is involvement of the skin and tendons. The hand assumes classical claw-like appearance: flexion of the metacarpal-phalangeal joints is lost, the proximal interphalangeal joints remain in fixed flexion, while the distal interphalangeal joints are often fixed in semiflexion; the thumb loses mobility in abduction, flexion and opposition (3-5).

The involvement of the face, altering the mimica and individual's physiognomy, has an important psychological impact. Often also affects the oral cavity and temporomandibular joint. The consequences (reduced movements of the mouth, thinned lips, and decreased tongue volume) create difficulties in feeding and ensuring correct oral hygiene, thus worsening the patient's quality of life considerably (6).

Besides impairments in body functions and structures, Systemic Sclerosis may also have a negative influence on the level of activity and participation, such as fitness to work (7,8).

Working is one of the most important activities of daily life, providing income, structure, social interaction and the opportunity to learn, among other things. Therefore, limitations in work capacity or the inability to work have a major impact on the individual (8,9).

Although musculoskeletal involvement is one of the main causes of disability (10), and has a strong psychological impact (11), the prognosis of the disease depends specially from the visceral involvement.

Recent improvements as the earlier diagnosis and treatment of systemic sclerosis have led to longer survival for affected patients, but the extreme variability in the

associata a vari gradi di fibrosi tissutale. La prognosi dipende in gran parte dal coinvolgimento viscerale; tuttavia l'interessamento muscolo-scheletrico è un fattore importante di disabilità funzionale, compromettendo la qualità della vita e le capacità lavorative. Dato il coinvolgimento progressivo e invalidante di tutti i tessuti, il trattamento riabilitativo rappresenta un valido alleato nell'offrire al paziente la migliore qualità di vita possibile. In letteratura sono presenti pochi studi a sostegno di questa ipotesi.

Obiettivo: Proporre un programma riabilitativo personalizzato, multi distrettuale condotto con approccio multidisciplinare specificamente progettato per i pazienti affetti da sclerosi sistemica.

Disegno: Studio retrospettivo.

Popolazione: Quarantatré pazienti affetti da sclerosi sistemica ricoverati nella nostra struttura riabilitativa specialistica.

Metodi: I pazienti sono stati sottoposti, per tre anni consecutivi, a un programma riabilitativo individuale della durata di tre settimane. L'outcome è stato l'Health Assessment Questionnaire-Disability Index (HAQ-DI) somministrato all'inizio e alla fine dei tre cicli di riabilitazione.

Risultati: Ogni trattamento ha determinato un miglioramento significativo del punteggio di disabilità al termine di ognuno dei tre cicli (ingresso vs dimissione: 1.2 ± 0.6 vs 0.8 ± 0.6, $p<0,0001$, $1,3\pm0,6$ vs $1,0\pm0,6$, $p<0,0001$ e $1,4\pm0,7$ vs $1,1\pm0,7$, $p<0,0001$). Tuttavia questo miglioramento si è progressivamente ridotto nei cicli successivi al primo con una differenza di efficacia, comunque, non statisticamente significativa ($p=0,38$ e $p=0,17$ per il confronto tra il secondo e primo ciclo e tra terzo e primo ciclo, rispettivamente).

Conclusioni: Il protocollo riabilitativo multi distrettuale, multidisciplinare sviluppato dal nostro team ha portato ad una significativa riduzione della disabilità percepita dai pazienti, indipendentemente dalla durata della malattia. Gli effetti benefici riscontrati al primo ciclo si sono ripetuti nei successivi. Tuttavia è stato evidenziato un trend di progressiva riduzione di efficacia nei cicli successivi, parallelamente al crescere della disabilità percepita.

Impatto riabilitativo: Crediamo che i nostri risultati dimostrino l'utilità del trattamento riabilitativo personalizzato, multi distrettuale, condotto con un approccio multidisciplinare nel migliorare la qualità della vita dei pazienti con sclerosi sistemica, nonostante questa sia una patologia cronica progressiva altamente disabilitante.

Parole chiave: sclerosi sistemica, HAQ-DI, riabilitazione.

clinical expression and evolution of the disease prevents the development of a standard therapeutic protocol valid for all types of patients (12).

Although pharmacological treatment is fundamental, personalised rehabilitation treatment, planned with appropriate, integrated multilocalized programmes, could be a valid aid in giving patients the best possible quality of life (13,14). However, the efficacy of the various rehabilitation methods and techniques in this context has been little studied so far. The few published works suggest that specific rehabilitation programmes can prevent or reduce disability caused by involvement of the skin joints and muscles, but these studies were performed on limited numbers of patients, and analysed only short-term efficacy in a single body segment (15-20). To the best of our knowledge, there are no published studies with a mid to long term follow-up of a large series of patients.

The first aim of this study was to assess the effectiveness of a multilocalized, multidisciplinary rehabilitation programme specifically designed for patients with systemic sclerosis. The results were measured as decreased functional disability, determined at the end of a single course of treatment and after repeated cycles at 1-year intervals for an overall study period of 2 years. The second aim was to determine whether the repeated cycles of rehabilitation treatment after 1-year intervals had the same effectiveness as the first cycle.

Materials and methods

Study population

This retrospective study was based on patients with systemic sclerosis admitted to Montescano Rehabilitation Centre between January 2008 and December 2012 for 3-week cycle of multidisciplinary treatment. Patients were submitted to 3 rehabilitation cycles. One a year, for total observation period approximately 2 years.

During the period of inpatient rehabilitation, all our patients could see the effectiveness of the pharmacological treatment plans, scheduled by the referring rheumatologists.

The main used drugs were: NSAIDs and corticosteroids to control pain and edema of the suffering tissues, Bosentan to control pulmonary hypertension, Iloprost prescribed as periodical infusion, suggested by doctors to control skin injuries, Ace-Inhibitors to control hypertension, Biological Drugs for the most aggressive therapy forms.

Inclusion criteria: age between 18 and 75 years, no changes of pharmacological anti-rheumatic treatment during rehabilitation period. Exclusion criteria: the presence of severe co-morbidities that would cause serious difficulties in accomplishing physiotherapeutic activities.

The study was approved by the local Ethics Committee.

Protocol

All patients took part in the multilocalized, multidisciplinary rehabilitation programme specifically designed for systemic sclerosis. Each cycle of treatment lasted 3 weeks and the patients were admitted to hospital in order to follow it. (Hospitalization)

Besides the rehabilitation physician, other specialists were included in this programme: nursing staff, rehabilitation therapists, and speech therapists. Occupational therapists, psychologists and nutritionists were involved in selected cases.

The programme consisted of individual sessions witch lasted 280 minutes each day from Monday to Friday. Different districts were involved, concentrating on rehabilitation exercise of the hand, feet and face, global exercises for the back and limb girdles combined with respiratory kinesiotherapy, cardio-respiratory training exercises, speech therapy and use of instrumental physical- therapies.

The programme was personalised, considering the general clinical characteristics of the patient, stage of the disease, districts involved.

Detailed daily treatment protocol:

Connective tissue massage: specific manual technique in order to improve skin elasticity and softness, increasing

the circulation and improving tissue metabolism, as well as having a muscle relaxant effect (21-23). This massage was administered to the face and neck, the limbs and the back. Each session lasted an average of 60 minutes (Fig. 1a-f).

Mc-Mennel joint manipulation: technique of joint manipulation that had a goal to improve joint play and lubrication, induce a trophic effect on cartilage, increase elasticity of the capsule ligaments and reduction of pain (24). This treatment was administered to the wrists and small joints of the hands and feet. Each district was treated for an average of 15 minutes (Fig. 2a-c).

Kabat technic administrated to the face: this technique of neuromotor facilitation was used to improve facial expressions, restore skin elasticity and improves movements of the temporo-mandibular joint (25) and can be combined, if necessary, with *swallowing exercises* with the purpose of improving the coordination of swallowing movements. Each session, 30 minutes average, was performed individually with the assistance of speech therapist (Fig. 3a-f).

Global kinesiotherapy of the back and limb: this rehabilitation technique, practise with the goal to improve mobility, muscle strength and flexibility, combined with
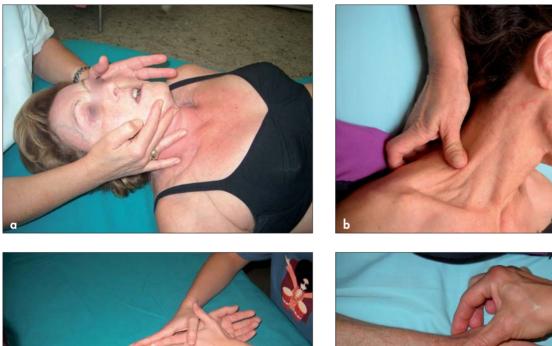

Figure 1. *Connective tissue massage of the face and neck (a,b), forearm and hand (c,d), whole back (e,f)*

Figure 2. *Mc-Mennel joint manipulation of the wrists (a) and small joints of the hands (b) and feet (c)*

breathing exercises in order to increase elasticity of the chest cage, respiratory dynamics and lung volumes. Each session of exercises of the global kinesiotherapy protocol, combined with breathing exercises, lasted an average of 30 minutes (Fig. 4a, b).

Aerobic training: this was designed to increase the resistance, reduce muscle fatigue and increase the cardiovascular and pulmonary capacity. Exercises with bicycle ergometer, tread-mill, bicycle or training steps were used with intensity, duration and frequency of the exercises es-

tablished considering the clinical conditions of the patients (Fig. 5a, b).

Proprioceptive training: was included in the programme to improve balance and neuromotor coordination. The training was performed using proprioceptive mono or bipodalic platforms for an average of 20 minutes (Fig. 6a, b).

Physical treatments (Radar Med, Marconi Pulse, TENS, static ultrasound or ultrasound in water, interferential stimulation): were used with the aim to relieve joint and muscle pain as well as reducing oedema and inflammation process. The physical treatments were administered in different body districts affected by the disease for an average of 60 minutes (Fig. 7a-c).

Outcome

The primary outcome measure was the HAQ-DI (26) score (Italian version) (27). This questionnaire consists of 20 questions on the ability to perform certain activities, each valued on a scale with four levels from 0 (no difficulty) to 3 (unable to do). The questions are divided into eight categories. The highest score in a sub-category determines the value for that category. The use of aids/devices or physical assistance increases raw scores of 0 or 1 to 2, while raw scores of 2 and 3 are not changed. The values of each category are summed and divided by eight to calculate the overall index of functional disability (HAQ-DI from 0 to 3). Decimal values from 0 to 1 indicate mild to moderate disability, values from 1 to 2 indicate moderate to severe disability, while values from 2 to 3 indicate severe to very severe disability.

Statistical analysis

Descriptive statistics are reported as means ± standard deviations. Intra-group comparisons were performed with Student's t-test for paired data for continuous variables and by the chi-squared test for dichotomised variables.

Repeated measures analysis of variance was used to study the effect of rehabilitation treatment on HAQ-DI values, with two repeated measurements (admission and discharge), for all three cycles of rehabilitation. The same method was applied to evaluate the effect of the rehabilitation programme on each of the eight categories making up the HAQ-DI.

In order to determine if the expected beneficial effects of the treatment were maintained over time, we studied the tendency of HAQ-DI scores over time by repeated measures analysis of variance, with three measurements, at the enrolment time in the three considered cycles, which gives a follow-up of 2 years. Finally, using the same statistical approach, we compared the changes in the HAQ-DI scores (differences between scores at discharge and on admission) in the three cycles.

The relationships between duration of disease and both HAQ-DI score on first admission and change in score following the rehabilitation treatment were investigated using Spearman's correlation coefficient.

The relationships between age the change in HAQ-DI score following the rehabilitation treatment and between duration of disease and both HAQ-DI score on first ad-
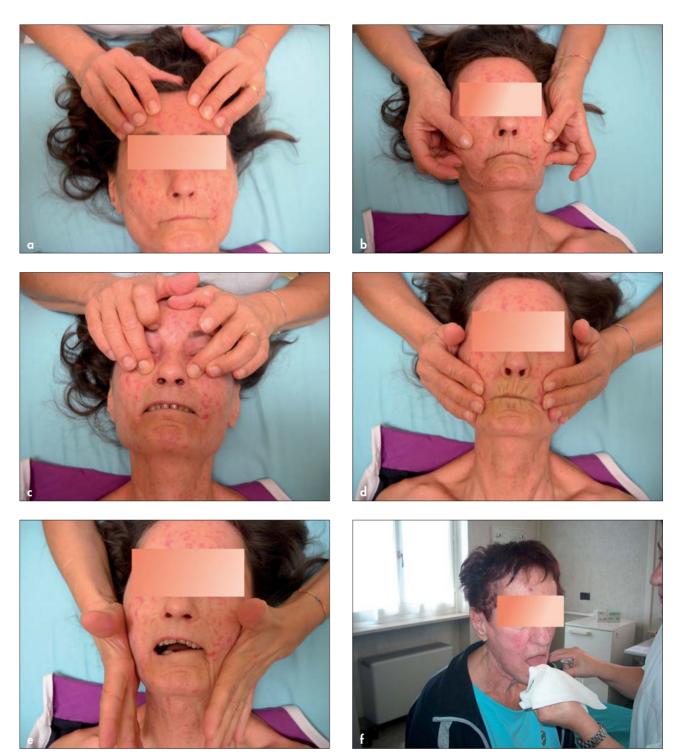
Figure 3. *Technique of neuromotor facilitation with Kabat's method for the face involvement (a-e) and swallowing exercises (f)*

mission and change in score were investigated using Spearman's correlation coefficient.

P values <0.05 are considered statistically significant. All analyses were performed using SAS/STAT version 9.2 software (SAS Institute Inc., Cary, NC, USA).

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Results

Between January 2008 and December 2012, 43 patients with systemic sclerosis, hospitalized in Rehabilita-
tion Unit of Montescano Scientific Institute, were recruited for rehabilitation protocol.

The demographic and clinical characteristics of the treated patients are presented in Table I. The period between the first and second admission was 11.9 ± 2.0 months, while the time elapsed between the second and third admissions was 12.3 ± 2.2 months.

The HAQ-DI scores on admission and at discharge for all the three admissions considered are reported in Table II.

Figure 8 shows the time course of the HAQ-DI scores for each of the six assessments made.
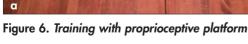
Figure 4. *Global kinesiotherapy of the back and limb girdles with breathing exercises*

Figure 5. *Aerobic training with bicycle ergometer (a) and tread-mill (b)*

Figure 6. *Training with proprioceptive platform*

The observed trend is that the outcome improved at the end of each of the three rehabilitation cycles (discharge vs admission, p<0.0001 all).

The repeated measures analysis of variance of HAQ-DI scores for the three following admissions revealed a significant effect of time (p=0.027), indicating that the patients functional ability was decreased over the 2-year period of assessment. At the second admission, after 1 year,

the scores values were slightly worsened than those at the first admission, although the difference was not statistically significant (p=0.16); the second cycle of rehabilitation restored the scores, with a significant improvement compared to the first admission (p=0.011).

The trends were slightly different in the second year: at the third admission the scores were significantly worse (p=0.017) than at the time of the first admission. At the end

Figure 7. *Physical treatments with Radar Med (a), Marconi Pulse (b) and ultrasound in water (c)*

for all categories except category 6: p=0.017 and p=0.033 in the second and third cycles, respectively).

Age was not related to the improvement in HAQ-DI score (p=0.86, p=0.42 and p=0.43 for the first, second and third rehabilitation cycle, respectively). We noted a significant correlation between duration of disease prior to rehabilitation and the HAQ-DI score at the first admission (r=0.43, p=0.0046), but not between duration of disease and improvement conferred by the first cycle of rehabilitation (r=-0.16, p=0.32).

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Discussion

Various rehabilitation methods and techniques were insufficiently investigated in systemic sclerosis patients. Studies were focused on the analysis of the short-term effects on single districts in small cohorts of patients. However, the few studies published in the literature suggest that a specific rehabilitation programme integrated with pharmacological treatment can improve the quality of life in patients with systemic sclerosis, reducing the disability caused by the involvement of the skin and joints.

Since there are no international recognised guidelines for musculoskeletal rehabilitation for patients with systemic sclerosis, in this study we developed a personalised rehabilitation treatment, with a multilocalized, multidisciplinary approach specifically designed for patients with this disease. We have considered the effectiveness of rehabilitation at the end of a single cycle of treatment and in the long-term treatment.

The retrospectively analysed results from a cohort of 43 patients, homogeneous in clinical disease appearance, showed that the rehabilitation protocol designed by our team led to a significant reduction in the functional disability at the end of the first cycle of treatment. Whose results were confirmed in the following cycles. The three cycles effect were statistically equal, although the trend to a progressive efficacy reduction in the following cycles. The fact that the scores for each category of the HAQ-DI, that analyses different aspects of the disease, improved after the treatment cycles, confirms the validity of the multilocalized approach.

We discovered that despite the significant correlation between functional disability and duration of the disease, the treatment effects were independent of the disease duration. This finding suggests that even patients affected by the disease for many years could benefit from rehabilitation treatment.

Our study indicates that rehabilitation treatment conducted with a multidisciplinary and multilocalized approach can have a fundamental role in improving the quality of life in patients with systemic sclerosis, without regard for the stage of the disease. In fact the treatment proposed in our study can slow the natural evolution of systemic sclerosis, despite this being a chronic, progressive, severely disabling disease.

Our study did not include interventions during the period between rehabilitation cycles. This leads us to consider that the maintenance of the benefits obtained with each cycle could be improved by educating the patients

of the second cycle of rehabilitation, the HAQ-DI score did not differ significantly from the baseline value (p=0.31).

As far as concerns the effect of repeated cycles of treatment, the improvement in HAQ-DI scores was progressively less, but the difference in efficacy was not statistically significant (p=0.38 for the comparison between the second and first cycles; p=0.17 for the comparison between the third and first cycles).

Considering the individual categories composing the HAQ-DI, the scores for each of these improved significantly at the end of each cycle of rehabilitation (p<0.002

Table I. *Demographic and clinical characteristics of the patients at each admission*

Characteristics	Admission I (T0)	Admission II (T2)	Admission III (T4)
Gender (F/M)	43/0		
Age	58±11		
Duration of disease (years)	12.8±10.1		
Musculoskeletal involvement, n. (%)			
Raynaud's phenomenon	43 (100%)	43 (100%)	43 (100%)
Chondrocalcinosis	5 (12%)	6 (14%)	9 (21%)
Active ulcers of the digits	8 (19%)	6 (14%)	7 (16%)
Sequelae of past ulcers	6 (14%)	14 (33%)[†]	16 (37%)[†]
Flexion contractures (claw hands)	7 (16%)	9 (21%)	11 (26%)
Amputation of digits	3 (7%)	3 (7%)	3 (7%)
Gastrointestinal involvement, n. (%)	23 (53%)	25 (58%)	25 (58%)
Pulmonary involvement, n. (%)			
Pulmonary fibrosis	15 (35%)	18 (42%)	18 (42%)
Pulmonary hypertension	4 (9%)	8 (19%)	8 (19%)
Concomitant autoimmune disease, n. (%)			
Sjogren's syndrome	1 (2%)	1 (2%)	1 (2%)
Autoimmune thyroiditis	2 (5%)	2 (5%)	2 (5%)
Dermatomyositis/polymyositis	2 (5%)	2 (5%)	2 (5%)
Rheumatoid arthritis	1 (2%)	1 (2%)	2 (5%)
Primary biliary cirrhosis	2 (5%)	2 (5%)	2 (5%)

[†]: p<0.05 compared to T0

Table II. *Mean ± standard deviation (SD) of the HAQ-DI scores at the six observation times considered: on entry to hospital and at discharge for each of the three admissions*

	T0 Mean ± SD	T1 Mean ± SD	T2 Mean ± SD	T3 Mean ± SD	T4 Mean ± SD	T5 Mean ± SD	T0-T1 P	T2-T3 P	T4-T5 P
HAQ-DI	1.2±0.6	0.8±0.6	1.3±0.6	1.0±0.6	1.4±0.7	1.1±0.7	P<0.0001	P<0.0001	P<0.0001

HAQ-DI Health Assessment Questionnaire-Disability Index
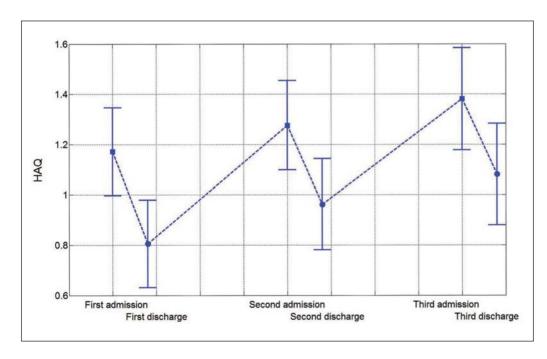

Figure 8. *Time course of the HAQ-DI scores at the six observations considered*

on correct behavioural strategies, hygiene, and specific regime of exercises to carry out autonomously at home.

Despite the lack of a control group, which is a limitation of our study, we believe that, given the degenerative nature of systemic sclerosis, obtained results demonstrate the utility of rehabilitation treatment. In the future, further studies will be conducted in order to identify the best rehabilitation strategies to propose, considering the cost-benefit ratio.

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