

Ocena wpływu terapii manualnej na sprawność funkcjonalną rąk chorych z twardziną układową – opis przypadku

Evaluation of the manual therapy effect on hand functional efficiency in the patients with systemic sclerosis – case description

Mateusz W. Romanowski^{1,3(A,E)}, Maja Špiritović^{2(B,E)}, Agata Zdanowska^{3(B,F)}, Anna Kwaśniewska^{3(C,F)}

¹Klinika Reumatologii i Rehabilitacji, Uniwersytet Medyczny w Poznaniu, Polska/
Department of Rheumatology and Rehabilitation, Poznan University of Medical Sciences, Poland

²Instytut Reumatologii i Klinika Reumatologii, Uniwersytet Karola, Praga, Czechy/
Institute of Rheumatology and Clinic of Rheumatology, Charles University, Prague, Czech Republic

³Wielkopolski Ośrodek Reumatologiczny w Sremie, Polska/Rheumatological Centre in Srem, Poland

Streszczenie

Twardzina układowa jest przewlekłą, układową chorobą tkanki łącznej, którą charakteryzuje uszkodzenie naczyń krwionośnych, obecność autooprzeciwciał oraz postępujące włóknienie skóry i narządów wewnętrznych prowadzące do ich niewydolności. Utrata ruchomości w stawach ręki oraz nadgarstka, które bardzo często dotykają chorych z twardziną układową, znacznie pogarszają ich jakość życia. Niefarmakologiczne leczenie twardziny układowej obejmuje: fizjoterapię, edukację, nowe metody terapeutyczne. Indywidualnie dobrana terapia przeciwdziała oraz zmniejsza dysfunkcje w obrębie stawów, tkanek miękkich oraz skóry, może poprawiać wydolność narządów wewnętrznych. Terapia manualna doskonale uzupełnia kompleksowe leczenie tej grupy chorych poprzez oddziaływanie na receptory: Golgiego, Ruffiniego, Paciniego oraz śródmiąższowe. Techniki z zakresu terapii manualnej ukierunkowane na skórę, powięź, mięśnie, stawy poprawiają sprawność ręki oraz zmniejszają odczucie bólu chorych z twardziną układową. Zastosowane techniki manualne (rolowanie skóry, masaż głęboki powięzi powierzchownej oraz mięśni odpowiedzialnych za wyprost w stawie nadgarstkowym, poizometryczną relaksację mięśni, mobilizację w kierunku grzbietowym w stawie promieniowo-nadgarstkowym, mobilizację boczno-boczną w stawach międzypaliczkowych) w przeprowadzonym badaniu poprawiły sprawność funkcjonalną ręki we wszystkich badanych parametrach (Cochin Hand Scale, Hand Mobility in Scleroderma, finger-to-palm-distance).

Słowa kluczowe:

Twardzina układowa, terapia manualna, terapia tkanek miękkich, fizjoterapia

Abstract

The systemic sclerosis is chronic systemic disease of connective tissue that is characterized by damage of blood vessels, presence of autoantibodies and progressing skin and internal organs fibration, leading to their failure. The loss of mobility in hand and wrist joints, which often affects patients with the systemic sclerosis, significantly worsens their life quality.

Non-pharmacological treatment of the systemic sclerosis includes: physiotherapy, education, new therapeutic methods. Individually selected therapy counteracts and diminishes dysfunctions in the joints area, soft tissues and skin, and may improve efficiency of internal organs.

Manual therapy perfectly complements comprehensive in this group of patients, by influencing the following receptors: of Golgie, Ruffini, Pacini and interstitial. The manual therapy techniques directed to the skin, fascia, muscles, joints, improve hand efficiency and decrease pain in patients with systemic sclerosis. Application of manual techniques (skin rolling, deep massage of superficial fascia and muscles responsible for straightening the wrist joint, postisometric muscle relaxation, mobilization in ridge direction in radiocarpal joint, side-to-side mobilization in finger joints) performed in the study improved hand functional efficiency in all tested parameters (Cochin Hand Scale, Hand Mobility in Scleroderma, finger-to-palm-distance).

Key words:

systemic sclerosis, manual therapy, soft tissue therapy, physiotherapy

Introduction

The systemic sclerosis is chronic systemic disease of connective tissue that is characterized by damage of blood vessels, presence of autoantibodies and progressing skin and internal organs fibrination, leading to their failure [1]. Hand function impairment very often applies to the patients with systemic sclerosis. and it includes: hand deformations, loss of mobility in metacarpophalangeal joints and interphalangeal joints, nearer and farther, loss of abduction movements, loss of thumb bending and opposing, loss of wrist mobility in all planes. Dysfunction from forearm side are present mainly at acute form of this disease and it includes: muscles, fascia and skin [2].

Depending on dermal changes location, type and degree of take up of individual organs and systems, rate of change development, usually two main clinic forms of the systemic sclerosis are distinguished: diffuse form and limited form [3]. In the systemic sclerosis limited form skin changes are limited to distal sections on the limbs and face, clinical course is usually quite slow, serious organ complications typically occur at later stage of the disease, and general prognosis is quite good. The diffuse form is characterized by large dermal changes that cover not only distal limb parts, but also shoulders, tights and/or trunk. The clinical course of diffuse form is usually dynamic, especially during first years of the disease, and serious organ complications appear in the first stages of the disease. Prognoses in the systemic sclerosis diffuse form are worse than in the limited form (3). Raynaud's phenomenon appears in 95% of patients with the systemic sclerosis and it is often the first symptom that may be visible before other symptoms (Tab. 1).

Tab. 1 Algorithm for diagnosing Raynaud's phenomenon [5]

1. Does cold affect your fingers, like e.g. cold water, cold can?

Answer:

- A. Yes (go to question no. 2)
- B. No – Raynaud's phenomenon is unlikely

2. How does cold affect your fingers?

Answer:

- A. They change colour (Raynaud's phenomenon is likely - go to question no. 4)
- B. They stiffen (Raynaud's phenomenon is unlikely - go to question no. 3)
- C. I don't understand; what do you mean? (Raynaud's phenomenon is unlikely)

3. Do your fingers change their appearance when they are cold?

Answer:

- A. They do (Raynaud's phenomenon is likely - go to question no. 4)
- B. They swell (Raynaud's phenomenon is very unlikely)

4. What colour?

Answer:

- A. White (Raynaud is very likely)
- B. Blue (Raynaud is very likely)
- C. Czerwony (prawdopodobieństwo Raunauda)
- D. Inny (mało prawdopodobne że występuje syndrom Raynauada)

Frequency of the systemic sclerosis occurrence fluctuates from 50 to 300 cases per million. Women obviously more frequently suffer from the systemic sclerosis than men and this relation is from 3:1 to 14:1 [4].

Complications related with the course of systemic sclerosis are: acute pains in connection with ischaemia or ulceration, dermal changes, changes in joints and soft tissues that may restrict mobility in upper and lower limb joints, problems with swallowing and/or heartburn, breathlessness, pain in chest area, palpitation, dry cough, muscle strength weakening [1].

Non-pharmacological treatment of the systemic sclerosis includes: physiotherapy, education, new therapeutic methods [6]. Authors agree that individually selected therapy counteract and decrease the joints dysfunction and the skin stiffness in patients with the systemic sclerosis. In the literature we find only a few reports on non-pharmacological treatment [7]. The following are used in treatment of the systemic sclerosis: exercises that increase mobility range in hand joints, exercises that improve mouth opening span, stretching exercises, strengthening exercises, manual therapy (massage with mobilization of hand joints) [7]. The research concerning effect of the manual therapy on hand dysfunctions in patients with the systemic sclerosis took place in 2009 and it was first randomized research that proved its effectiveness.

The manual therapy is widely used by physiotherapists, osteopaths and chiropractors, in particular at ailments related with the spine. However, it must be noted that the techniques used by professional therapists basically take effect on musculoskeletal system, and their application allows to cure many dysfunctions of motor organ system. Almost 90% patients with the systemic sclerosis complain of ailments from the musculoskeletal system at certain stage of the disease. That is why, the manual therapy may be successfully included in the comprehensive treatment of patients with systemic sclerosis.

Manual therapy for patients with systemic sclerosis

The therapist that work manually with a patient that suffer from systemic sclerosis has many manual techniques to disposal, which are selected individually to each patient. In order to diagnose the patient the manual therapist should each time interview the patient, evaluate her or him visually, perform palpation, evaluate mobility of joints and slide play, examine muscles and fascia move. Selected manual techniques are mentioned and described in Tab. 2, and their complement may be: postisometric muscle relaxation, feedback inhibition, myofascial relaxation or skin rolling. Immediate purpose of manual techniques is to lower pain and to fight with the effects of static overload, muscle irritation and connective tissue irritation. To long-term purposes we may classify correct length and elasticity of contracted muscles and fasciae, recovering correct mobility range in joints [8]. Among therapeutic effects of manipulation and mobilization we may mention: recovering correct mobility, joint play normalization, causing reflex effect that affects all around-joint structures, leading to their relaxation. Reflexive muscle hypotony, increased skin sensitivity to wrinkling and tensioning, changes in periosteum points, reduced tissue tension [8]

Tab. 2 Types of techniques used in manual therapy [9]

Techniques used in manual therapy	Definition	Desired results
work with joint		
<ul style="list-style-type: none"> • manipulations 	<ul style="list-style-type: none"> • passive motion in joint lead beyond normal motion range 	<ul style="list-style-type: none"> • increase motion range • decrease muscular tension
<ul style="list-style-type: none"> • mobilizations 	<ul style="list-style-type: none"> • passive motion in joint lead within normal motion range 	<ul style="list-style-type: none"> • decrease pain
soft tissue techniques		
<ul style="list-style-type: none"> • classic massage 	<ul style="list-style-type: none"> • set of motions that apply compression on skin and soft tissues 	<ul style="list-style-type: none"> • blood circulation improvement
<ul style="list-style-type: none"> • deep massage 	<ul style="list-style-type: none"> • set of motions that apply deep compression on skin and soft tissues 	<ul style="list-style-type: none"> • decrease muscular tension • relaxation
<ul style="list-style-type: none"> • trigger points therapy 	<ul style="list-style-type: none"> • deep compression on area of local pain 	<ul style="list-style-type: none"> • release tissue adhesions
<ul style="list-style-type: none"> • shiatsu massage 	<ul style="list-style-type: none"> • rhythmical compression with fingers 	<ul style="list-style-type: none"> • increase motion range
techniques directed on nervous tissue		
<ul style="list-style-type: none"> • neuromobilizations 	<ul style="list-style-type: none"> • tensioning, nerve activation to restore nerve system plasticity 	<ul style="list-style-type: none"> • increase motion range • decrease pain

Very important element of the therapy used for patients with systemic sclerosis is paying attention to the fascia and remembering its variable role in correct motor system functioning. Techniques directed to the fascia should be always included in the manual therapy for patients with systemic sclerosis. Working with the fascia in classic approach consists in finding place, where its mobility is reduced, and in determining direction of limited mobility. Manoeuvre that we perform as a diagnostic motion for the fascia relocatibility is also a motion that we may used as a therapeutic treatment. First, it is required to reach the motion limit, and then to keep

this position until we feel relaxation. In this approach, the fascia mobilization is continued until the point of physiological barrier is reached. However, it must be remembered that the latest research brought many essential facts about the fascia. Among them, that the fascia includes four types of nerve endings:

- Golgi receptors [I b];
- Ruffini receptors [II];
- Pacini receptors [II] (lamellated corpuscles, paciniform);
- Interstitial receptors [III and IV] [10].

Golgi receptors are present in ligaments, articular capsules (10%) and around muscular tendon connections (90%). Pacini receptors are located in deep parts of articular capsules, deep spine ligaments, in palms, foot soles, in peritoneum, connective tissues around muscles. Ruffini receptors are found in particular in tissues subject to regular stretching: external layers of articular capsules, dura mater, joint circumferential ligaments. Interstitial receptors partly function as pain receptors, they react to stretching the fascia and skin (10). Each of the receptors react to specific type of manual technique that affects the particular receptor. It is presented in Tab. 3.

Tab. 3 Types of receptors with manual technique that best affects the particular receptor

Fascia receptor types	Manual technique types
<ul style="list-style-type: none"> • Golgi receptors 	<ul style="list-style-type: none"> • Post-isometric relaxation • Local strong compression
<ul style="list-style-type: none"> • Pacini receptors 	<ul style="list-style-type: none"> • Sudden change of compression and vibrations • Manipulation type "high velocity thrust" • Oscillation techniques
<ul style="list-style-type: none"> • Ruffini receptors 	<ul style="list-style-type: none"> • Constant compression - particularly lengthwise and lateral stretching • Slow and deep techniques on soft tissues
<ul style="list-style-type: none"> • Interstitial receptors 	<ul style="list-style-type: none"> • Fascia and skin stretching

Case description

Female patient, 44 years, in whom the systemic sclerosis was diagnosed 7 years ago. She was directed to stay at the rheumatology ward by her attending physician - rheumatologist, due to stiffness and reduced mobility in hand joints, wrists. The patient has Reynaud phenomenon.

For 5 years she has been rehabilitated during outpatient physiotherapy, usually once a year, at the rheumatology ward she was the second time.

The patient had no therapeutic puncture of her joint in 2 months before treatment at the centre. She had no changes in using symptomatic medicines, immunosuppressive, in the period of last 3 months. During the therapy no changes were made in pharmacological treatment.

Measurement techniques

Cochin Hand Scale (CHS) is a questionnaire that evaluates the hand functional efficiency in patients with the systemic sclerosis. The patient assesses 18 everyday activities in the scale from 0 (no difficulty) to 5 (impossible to perform). Maximally 90 points may be reached, while the higher score, the less hand efficiency [11].

Hand Mobility in Scleroderma (HAMIS) – HAMIS includes 9 tests to evaluate the effect of systemic sclerosis on limiting the range of hand joint, wrist mobility. Each task is scored from 0 (possible to perform) to 3 (impossible to perform). Maximal result is 27 for one hand and 54 for both. The higher score, the lesser hand and wrist efficiency [12].

Finger-to-palm in extension (FTPinE) The distance was measured from the tip of middle finger in extension from further lateral line ("distal palmar crease") [13]. Measurement was made for right and left hand.

Finger-to-palm in flexion (FTPinF) - The distance was measured from the tip of middle finger in bend to further lateral line („distal palmar crease”) [13]. Measurement was made for right and left hand.

The patient stayed at the ward for 2 weeks. The procedure was not performed on Saturday and Sunday. Evaluation was made before treatment (day 1) and after its finish (day 10). On the last day (day 10) the patient had no treatment.

Used therapy

The manual therapy included 9 sessions lasting 40 min (20 min left hand, 20 min right hand). The therapy was performed by duly qualified therapist with five years of experience. The patient was given no other treatment during her stay. In the research the following manual therapy techniques were used:

1. Skin rolling – we hold skin between the thumb and the index finger and gently roll forward (Fig. 1). At the moment when therapist feels restriction in the area of soft tissues, he should stop rolling and only keep position on the mobility barrier and wait for tissues relaxation.
2. Deep massage of superficial fascia and muscles responsible for extension in the wrist joint. Fig. 2 present the work in direction of tissue stretching that is the technique when the therapist performs simultaneous deep massage motion with slow, active palm bend.



Fig. 1. Skin rolling

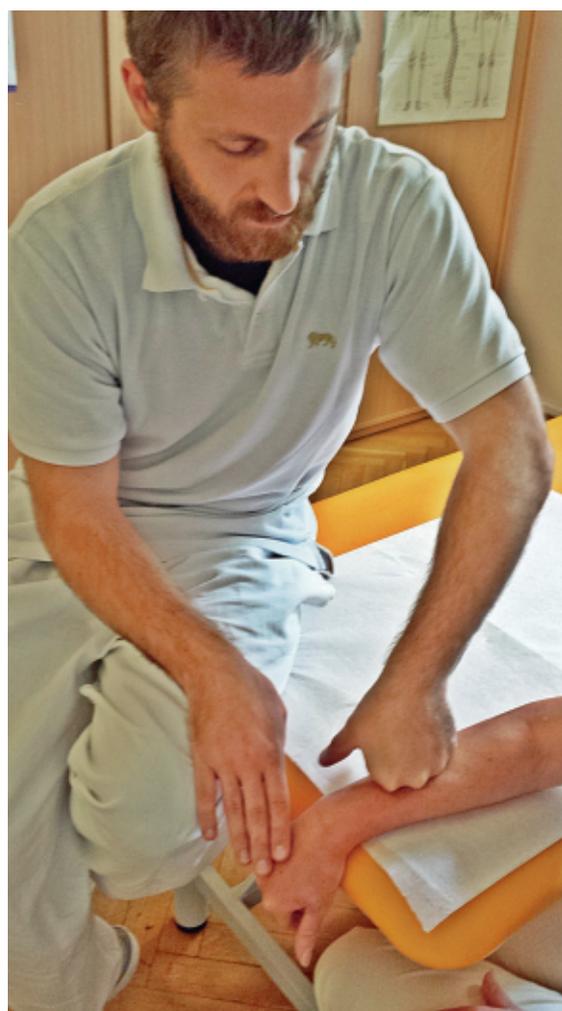


Fig. 2. Work in direction of tissue stretching



Fig. 3. Post-isometric muscle relaxation

3. Post-isometric muscle relaxation that increase mobility range in the joint by reducing pathologic muscle tension. The technique allows influencing both the muscles, and the fascia and joints, it is effective method to overcome muscle contracture and has analgesic effect. For muscles palmar bending the carpal joint, the therapist stabilizes the patient's forearm with one hand, and holds the patient's hand with the other (Fig. 3). The therapist performs passive palmar bending in the carpal joint to the first stretch feeling in the patient. The patient is asked to make extension movement with minimal force against the resistance applied by the therapist. The muscles tensioning lasts 10 s, then the therapist passively increases the palmar bend to the first stretch feeling in the patient. The new position is kept for 30 s. The activity is repeated four times.

4. Mobilization in tergal direction in radiocarpal joint. The therapist stabilizes distal part of radial bone in supination with one hand, the hold is located near the joint gap. The second hand is put on the row nearer to the wrist bone and the mobilization is performed in tergal direction (Fig. 4).

5. Side-side mobilization in interphalangeal joints. The therapist holds with his thumb and index finger the closer finger joint, stabilizing it, then with the index finger and thumb of the other hand mobilizes the distal finger joint in relation to proximal in the above mentioned directions. The hold must be placed possibly close to the joint gap (Fig. 5).



Fig. 4. Mobilization in tergal direction in radiocarpal joint



Fig. 5. Side-side mobilization in interphalangeal joints

Results

In the research improvement was achieved in all used tests [Tab. 4]. The hand functional efficiency evaluated with CHS questionnaire improved from 35 to 21. Mobility range assessed with HAMIS tests improved from 15 to 9 (right hand), and from 17 to 8 (left hand). Distance from the middle finger in extension to further lateral line (FTPinE) increased for right hand from 10.0 cm to 12.0 cm, and for left hand from 9.5 cm to 11.5 cm. Distance from the middle finger in extension to further lateral line (FTPinF) was improved and decreased for right hand from 3.5 cm to 3.0 cm, and for left hand from 3.5 cm to 2.5 cm.

Tab. 4. Results of made tests before and after therapy

Test	Before therapy		After therapy	
CHS	35		21	
	right	left	right	left
HAMIS	15	17	9	8
FTPinE (cm)	10.0	9.5	12.0	11.5
FTPinF (cm)	3.5	3.5	3.0	2.5

CHS – Cochin Hand Scale
HAMIS – Hand Mobility in Scleroderma
FTPinE finger-to-palm in extension
FTPinF finger-to-palm in flexion

Discussion

Used manual therapy in presented research caused improvement of hand functional efficiency in the patient with systemic sclerosis, as evaluated by the tests: Cochin Hand Scale, Hand Mobility in Scleroderma, finger-to-palm-distance.

The hand dysfunction characteristic for the systemic sclerosis sufferers significantly hinders performance of everyday activities. Tasks and motions that patients should do with their upper limbs are much more precise and complex, comparing to the function of lower limbs. Raynaud phenomenon, stiffness, decreased hand gripping force are elements that most worsen life quality in this group of patients [14]. For that reason just the therapy directed to improve hand efficiency, increase hand and wrist mobility range, increase the gripping force, is so essential in treating patients with the systemic sclerosis.

So far, only small number of researches concerned the subject of non-pharmacological treatment of patients with the systemic sclerosis. We have found no research that would describe the use of similar manual therapy in patients with the systemic sclerosis. That is why, it seems that more important is the fact that our research clearly indicates that the manual therapy really improves hand functional efficiency, increases mobility of hand and wrist joints. This in turn may lead to life quality improvement in patients from this group, by easier and more efficient performance of everyday activities.

In the literature we find studies that in accordance with our research confirms effectiveness non-pharmacological treatment of patients with the systemic sclerosis. Antonioli et al. [15] demonstrated that 2 weeks daily individual rehabilitation of patients with the systemic sclerosis improves their life quality, increases hand efficiency. Thai massage in combination with thermotherapy and stretching exercises cause significant hand efficiency measured with HAMIS test [2]. Exercises that increase the range of mobility in hand and wrist joints, as well as mobilization of the hand and wrist joints with "Mc Mennell" technique in combination with massaging this area, suit well for rehabilitation of patients with the systemic sclerosis [16]. Bongi et al. [16] also notice that in case of patients with the systemic sclerosis comprehensive rehabilitation is more effective form of therapy than only motorial exercises at home.

The manual therapy is non-invasive form of treatment that uses basically the therapist's hands and fingers in order both diagnose the patient and to perform therapy. Usually the techniques are directed to soft tissues and, what is important, they may be used as the only form of treatment or in combination with other treatment [17]. Researches indicate that the manual therapy may be successfully used in patients with motor organ dysfunctions [18]. Such disorders are characteristic to patients with the systemic sclerosis and its effectiveness was confirmed by our research. I must be also mentioned that the patient felt no pain during the therapy. She describe her feelings as pleasant, definitely within the limits of her pain tolerance.

We are aware of limitations in our research, but the method of therapy that we described encourages further studies on this subject, during which as we think the following issues should be addressed.

1. Evaluation of long-term effect of the manual therapy on the patients with systemic sclerosis. Is it an effective form of therapy only at the moment when it is performed, or is its effect longer?

2. Conduct research on larger group and check of the achieved results correlate with results obtained in this research.
3. Measurement techniques used to evaluate this group of patients should be uniformed to allow comparing different forms of the therapy. It should also be considered if for better objectification of results, the patient clinical condition evaluation should not be made by two independent therapists.
4. In this research, the manual therapy was performed exclusively in upper limbs area, it would be very interesting to assess the manual therapy effect on the temporomandibular joint and mouth opening range in patients with the systemic sclerosis.
5. Should the non-pharmacological treatment of patients with the systemic sclerosis include also other therapy forms or if eventual combination of therapeutic methods in order to achieve possibly best results is justified?

Non-pharmacological treatment of the systemic sclerosis needs further researches. Presented results demonstrate that hand functional efficiency in such patients may be improved due to the manual therapy.

Adres do korespondencji / Corresponding author

dr Mateusz W. Romanowski,

Klinika Reumatologii i Rehabilitacji,
Uniwersytet Medyczny w Poznaniu,
ul. 28 Czerwca 1956 r. nr 135/147, 61-545 Poznań,
e-mail: mateuszromanowski@onet.pl

Piśmiennictwo/ References

1. Samborski W, Brzosko M. Reumatologia praktyczna. Wydawnictwo Wolters Kluwer Polska. Warszawa 2011.
2. Vannajak K, Boonprakob Y, Eungpinichpong W, i wsp. The short-term effect of gloving in combination with Traditional Thai Massage, heat, and stretching exercise to improve hand mobility in scleroderma patients. *J Ayurveda Integr Med.* 2014; 5(1):50-5.
3. Kowal-Bielecka O, Kuryliszyn-Moska A. Twardzina układowa. *Reumatologia* 2012; 50, 2: 124–129
4. Gabrielli A, Avvedimento E, Thomas Krieg T. Mechanisms of Disease Scleroderma. *N Engl J Med* 2009;360:1989-2003.
5. Richter JG, Sander O, Schneider M, Klein-Weigel P. Diagnostic algorithm for Raynaud's phenomenon and vascular skin lesions in systemic lupus erythematosus. *Lupus.* 2010; 19(9):1087-95.
6. Kowal-Bielecka O, Landewe R, Avouac J, i wsp. EULAR recommendations for the treatment of systemic sclerosis: a report from the EULARS scleroderma Trials and Research group (EUSTAR) *Ann Rheum Dis* 2009 ;68:620–628.
7. Poole J. Musculoskeletal rehabilitation in the person with scleroderma. *Curr Opin Rheumatol.* 2010; 22(2):205-12.
8. Śliwiński Z, Sieroń A. Wielka fizjoterapia. Wydawnictwo Elsevier Urban & Partner. Wrocław 2014.
9. Bialosky JE, Bishop MD, Price DD, i wsp. The mechanisms of manual therapy in the treatment of musculoskeletal pain: a comprehensive model. *Man Ther.* 2009;14(5):531-8.
10. Schleip R, Findley TW, Chaitow L, i wsp. Powięź. Badanie, profilaktyka i terapia dysfunkcji sieci powięziowej. Wydawnictwo Elsevier Urban & Partner. Wrocław 2014.
11. Brower LM, Poole JL. Reliability and validity of the Duruoz Hand Index in persons with systemic sclerosis (scleroderma). *Arthritis Rheum* 2004;51:805–9.
12. Sandqvist G, Eklund M. Validity of HAMIS: a test of hand mobility in scleroderma. *Arthritis Care Res* 2000;13:382–7.
13. Torok KS, Baker NA, Lucas M, Domsic RT, Boudreau R, Medsger TA. Reliability and validity of the delta finger-to-palm (FTP), a new measure of finger range of motion in systemic sclerosis. *Clinical and experimental rheumatology.* 2010;28(2 Suppl 58):S28-S36.
14. Sandqvist G, Eklund M, Akesson A, Nordenskiöld U. Daily activities and hand function in women with scleroderma. *Scand J Rheumatol* 2004; 33:102 – 107.
15. Antonioli CM, Bua G, Frigè A, i wsp. An individualized rehabilitation program in patients with systemic sclerosis may improve quality of life and hand mobility. *Clin Rheumatol.* 2009;28(2):159-65.
16. Bonghi SM, Del Rosso A, Galluccio F, i wsp. Efficacy of connective tissue massage and Mc Mennell joint manipulation in the rehabilitative treatment of the hands in systemic sclerosis. *Clin Rheumatol.* 2009 ;28(10):1167-73.
17. Kim C-G, Mun S-J, Kim K-N, i wsp. Economic evaluation of manual therapy for musculoskeletal diseases: a protocol for a systematic review and narrative synthesis of evidence. *BMJ Open* 2016;6:e010556.
18. Southerst D, Yu H, Randhawa K, i wsp. The effectiveness of manual therapy for the management of musculoskeletal disorders of the upper and lower extremities: a systematic review by the Ontario Protocol for Traffic Injury Management (OPTIMA) Collaboration. *Chiropractic & Manual Therapies* (2015) 23:30.