

**ELABORATION AND ADMINISTRATION OF NEW MEASURES OF
DISEASE COURSE AND OUTCOME IN PATIENTS WITH
SYSTEMIC SCLEROSIS AND
IDIOPATHIC INFLAMMATORY MYOPATHIES**

PHD THESIS

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Introduction

Connective tissue diseases or systemic autoimmune diseases are autoimmune disorders with chronic inflammation affecting the internal organs and also the musculoskeletal system. These diseases of unknown pathogenesis are characterized by chronic inflammation damaging tissues and organs, leading to disability and chronic functional disorders.

The course of these autoimmune diseases is often variable. The intensity of the inflammation and the severity of the damage may vary in different organs, which must be considered when choosing adequate therapy. As the real cause of the systemic autoimmune diseases is only partially understood, therapy can aim the reduction of the inflammation and the maintenance of a good functional state of the organs. During the active period of the disease an effective antiinflammatory therapy is needed followed by early rehabilitation and regular control. For the adequate harmonization of these tasks a regular disease-activity and organ-state monitoring is indispensable. In chronically ill patients, the social problems and difficulties in everyday activities become more and more frustrating. Complaints of the patients are not only directly related to organ damage but also indirectly to the problems occurring in family life and social life. These problems can be revealed and characterized using the quality of life questionnaires which would allow us to find the right way to provide help. It is hard to decide what to measure and how to measure. Theoretically there are several possibilities: physical examination, instrumental and laboratory measurements, the use of questionnaires, etc.

Our aim was to define the most important prognostic factors as well as find and adapt the most useable methods in the treatment and follow-up of patients with inflammatory myopathies based on our clinical observations, experiences and on data found in the literature.

Objectives

1. To study the survival and risk factors of a personal series of 366 consecutive patients with systemic sclerosis (SSc). To compare the causes of death related to SSc using Hungarian and international data of the last ten years.
2. To adapt and validate the Hungarian version of the Disabilities of the Arm, Shoulder, and Hand (DASH) and the shorter QuickDASH Outcome Measures and to establish their validity in patients with systemic sclerosis (SSc).
3. Hungarian adaptation of the Scleroderma Health Assessment Questionnaire (sHAQ) and perform a psychometric study on our scleroderma patients.
4. To study the effect of physical exercise 2-3 weeks after an acute flare of dermato/polymyositis (DM/PM).

Patients and Methods

1. In the study of investigation the causes of death and the factors of the survival 366 patients with SSc were enrolled. Female/male ratio was 314/51. The mean (\pm SD) age of the patients was 56.8 ± 12.2 years. The mean follow up was 7.8 ± 5.9 years, the mean disease duration was 13.5 ± 10.7 years.

Kaplan-Meier survival curves were calculated to estimate the 5 and 10 year survival rates. Log rank tests were performed to establish differences in survival of subgroups. Items with a significant effects on survival with univariate method were entered into the **Cox proportional hazards model**. To establish the minimum set of predictive variables, backward stepwise selection was performed by the Cox proportional-hazards model.

2. In the cross-cultural adaptation and validation of the DASH questionnaire study 128 consecutive patients, 116 female and 12 male were enrolled. There were 87 patients with limited cutaneous (lcSSc) and 41 with diffuse cutaneous systemic sclerosis (dcSSc), and their mean age was 55.7 ± 11.7 (\pm SD) years.

The main part of the DASH questionnaire, called “the DASH disability-symptom” (DASH-DS) contains 30 questions: 21 about the degree of difficulty in performing various physical activities, 5 regarding severity of symptoms of pain, tingling, weakness and stiffness, and 4 dealing with problems affecting social activities, work and sleep, and with psychological impact. The DASH also contains two optional 4-item parts concerning ability

to work (DASH-W) and ability to perform sports, or play musical instruments (DASH-SM). Each item has 5 response choices (1-5) ranging from "no difficulty" or "no symptom" to "unable to perform the activity" or "very severe symptom". The scores for all items are used to calculate final score ranging from 0 (no disability) to 100 (severest disability).

The QuickDASH questionnaire contains only 11 items of the DASH-DS but has the same optional modules intended to measure symptoms and functions in workers, sportsmen and artists who require a high degree of physical performance.

The Hungarian adaptation of the DASH questionnaire was performed by using the „**forward/backward translation method**”.

We applied the Outcome Measures in Rheumatoid Arthritis Clinical Trials (**OMERACT**) **filter** during the validation procedure for truth, discrimination and feasibility.

Truth: Concurrent validity was assessed by searching for correlations between the different parts of the DASH and other well known instruments. All patients had a physical examination by a physician and two physical therapists and had to complete the Short Form Health Survey (SF-36) questionnaire, a measure of health related quality of life, and the modified Health Assessment Questionnaire developed for patients with SSc (sHAQ).

Structural validity: To support the hypothesized scale structure of the questionnaire a principal component analysis with orthogonal (varimax) rotation was performed

Discriminant validity explores the ability of the questionnaire to discriminate between groups of patients with different symptom severity. DASH score of lcSSc and dcSSc patients were compared first, then all patients were divided into groups based on presence/absence of arthralgia/arthritis, or contractures of the hands or shoulders.

Floor and ceiling effects were considered if more than 15% of respondents achieved the highest or lowest possible score.

Sensitivity to change From December 2006 to March 2007, 76 patients (67 female, 9 male, mean age 56.6 ± 11.6 years, 50 patients with lcSSc and 26 with dcSSc) filled out the same questionnaires again after 12 months. Changes between baseline and 12 months in DASH and other measures were tested with paired t tests by the comparing of changes in HAQ-DI. Sensitivity to change was estimated using the standardized response mean (SRM, as the ratio of the mean to the standard deviation of the change), the effect size (ES, as the ratio of the mean change to the standard deviation of the first measure) and the responsiveness statistic (RS, as the ratio of the mean change to the standard deviation of change in patients that remain stable over time).

Feasibility: 20 consecutive SSc patients (17 female, 3 male, mean age 56.0 ± 8.7 (\pm SD) years) were given the Hungarian DASH Pre-final questionnaire for self-testing.

3. We performed the **adaptation and validation of sHAQ for systemic sclerosis patients** into Hungary. The validation was performed together with the DASH and QuickDASH questionnaires. The Hungarian adaptation of the original HAQ was done by Rojkovich et al with our participation in 1998, therefore this validated version was used in our current project. The sHAQ 5 Visual Analog Scale (VAS) was also adapted to Hungarian language with appropriate cultural differences using the „**forward/backward translation method**” as mentioned above.

The psychometric assessment of sHAQ was done applying the „OMERACT filter” recommendations as detailed at the DASH validation method.

The standard disability index of the Health Assessment Questionnaire (HAQ-DI) is a self-administered questionnaire, which contains 20 items (each scored 0-3), divided into 8 domains of daily activity. The highest score of the 2 (or 3) questions in each domain are added then divided by 8 to determine the HAQ-DI, calculated as a continuous variable, which ranges from 0 (no disability) to 3 (severe disability). When for one of the 20 items, the patient needs an aid or a help of somebody, the domain is automatically rated 2. Additionally, a pain visual analog scale (VAS) is completed by the patient, on which the patient rates pain on a 15 cm line, which is then converted to a continuous scale from 0 to 3.

The **sHAQ contains additional visual analog scales (VAS)** to assess the following SSc symptoms: Raynaud’s phenomenon, digital tip ulcers, gastro-intestinal symptoms, lung symptoms and the overall severity of the disease from the patient’s perspective. Patients are asked: “In the past week how much have your - Raynaud’s phenomenon, digital ulcers, gastro-intestinal, lung, overall scleroderma - symptoms interfered with your activity?” The anchors of the line are “does not interfere” and “very severe limitations”. The length of each VAS is 15 cm. The patient’s value on each of the 5 VAS can be calculated multiplied by 0.2 the value of the length (cm) from the basic point to obtain scores ranging from 0 to 3.

4. In the study of the effect of physical exercise following acute disease exacerbation in patients with dermatomyositis twenty-one consecutive cases (16 women and five men) with DM/PM were selected for the training program. The mean disease duration of the patients was 46 ± 45 months. Patients were divided into two groups. The “**early recovery group**” consisted of 10 patients, six with DM and four with PM. Their mean

age was 50.6 ± 14.2 years. These patients had had acute phase of the disease two-three weeks before they entered the study. All of them had stabilized creatinine phosphokinase (CK) levels for at least two weeks, and no muscle pain was observed. Furthermore according to the general evaluation of the physician these patients were considered to be in the post-acute phase of the disease. The “**chronic stage group**” included 11 patients: six with DM and five with PM. Their mean age was $44,1 \pm 14,6$ years, all with symptoms that had not changed considerably during the last three months.

Clinical and laboratory assessments: in addition to the overall clinical evaluation, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and CK were measured weekly. The ten-point visual analogue scale (VAS) was used to evaluate changes in pain and fatigue. Disability was measured using the Health Assessment Questionnaire (HAQ) and Functional Independence Measure (FIM).

Strength measurement: the muscle strength of each patient was measured at the beginning and at the end of the three-week therapy using a Modus M393 (Germany) type dynamometer fitted with a band. With the patients sitting we measured the strength of the quadriceps group in 90-degree knee flexion (band on the ankle), the arm abductor group with extended elbow (band held in hand), and the forearm flexor group with an elbow in 90-degree flexion (band held in hand). A special dynamometer Aesculap AD 141 (Germany) was used for measuring the strength of the palm and finger flexor muscles at the grasp.

To evaluate the changes in the respiratory function three parameters were measured using a Piston PDD 301 type (Hungary) **spirometer**: forced vital capacity (FVC), forced expiratory flow $FEF_{(25-75\%)}$ and forced expiratory volume 1s to FVC (FEV_1/FVC) ratio.

The exercise program: For five days out of the week in a three-week period, patients received special physical therapy. In the morning muscles and joints were relaxed and prepared for the physical training by a warm mud (38°C) treatment on the neck and shoulders for 15 minutes or by a gentle massage with hands. In the afternoon patients received a relaxing thermal bath with carbon dioxide (36°C). The daily (40-60 minutes) physical training was guided by a physical therapist. The first part was a series of **assisted bending and stretching exercises** of all the joints. The second part consisted of **isotonic muscle training** first for the trunk, then for the neck, dorsal muscles and abdominal region, and finally for the muscles of the upper and lower limbs. Patients were requested to continuously repeat simple isotonic movements until they felt fatigue. The numbers of repetitions completed by each patient were counted weekly. During the daily training the patients repeated each movement for the given muscle groups until they had reached 65-70% of the

maximal repetitions, then they had a three minute rest after which they were encouraged to perform the same series of exercises before going on for the next muscle group. If the given muscles were too weak to work against gravity the patients were treated in sling suspension type Pannonia 2000 (Hungary). Depending on the strength of the patients a weight of 500 gramms was used either to add to gravity or to provide some resistance. The third part was **respiratory training** to teach the patients how to breathe efficiently by letting them put their own hands on their abdomen and on different parts of their rib cage and thereby feel and control the movements.

Statistical analysis: For the measurement of muscle strength the percentages were calculated and one-tailed paired t-tests were performed. The exact Wilcoxon signed rank test was used to test changes in HAQ, FIM and VAS.

Results

1.1. In addition to the well known factors influencing the outcome (diffuse subset, internal organ involvements, age, inflammatory signs) the coexistence of scleroderma and malignancy also causes a poor outcome.

Cause of death 93 patients died during the 22-year of follow-up. 86 deaths were caused by SSc. In 8 cases more than one organ insufficiency was the cause of death. **65% of the deaths were attributed to cardiorespiratory manifestation** of disease. Interstitial lung involvement in 20 cases, pulmonary arterial hypertension on 7 cases, heart involvement in 26 cases, cardio-respiratory involvement in 3 cases (clearcut distinction was not possible, this category probably includes cases with pulmonary arterial hypertension) caused fatal outcome. Renal involvement in 16 patients caused death. **Tumour associated early death was found in 12 cases (14%).** Watermelon stomach as a cause of death due to severe bleeding was related to the fatal outcome in 4 cases. GI-tract-related death (malabsorption/dysmotility, bleeding from watermelon stomach) was found in 8 cases. In 2 cases severe infection was detected as the cause of death.

Kaplan-Meier **cumulative five year overall survival rate** was 84 %, and the ten year survival was 72.6 % (Table 2). In dcSSc, the five and ten year survival was 67% and 48.6%, respectively. In lcSSC we found 90.5% and 81.8% five and ten year survival rates, respectively (p<0.001). Male patients had 78.3% and 66 % while females showed 84.9% and 73.6% five and ten year survival rates, respectively (NS).

1. 2. Fatal bleedings due to gastrointestinal teleangiectasis and death related to pulmonary arterial hypertension (PAH) became more frequent in the past 20 years.

In our country watermelon stomach as documented finding started to appear only in the last 10 years. The frequency of PAH has a growing tendency with the appearance of better diagnostic tools.

1. 3. In the multivariate Cox proportional hazards model kidney involvement, coexistence of a malignancy, increased ESR, the presence of diffuse scleroderma and elderly age at the onset of disease caused unfavourable outcome.

Kaplan-Meier univariate analysis showed that renal, cardiac involvement, pigmentation disturbances, malabsorption, a forced vital capacity < 50%, diffuse scleroderma, coexistence of an early malignancy, anaemia and increased ESR were unfavourable prognostic signs of disease, whereas the presence of anticentromere antibody positivity caused a favorable outcome.

We entered into the Cox proportion-hazards model the items with significant effect on survival in univariate analysis, and we also added to the variables the gender and age at onset. Diffuse SSc, age at onset of the disease, renal involvement, increased ESR and paraneoplastic syndrome (coexistence of SSc and a malignancy) were independent prognostic factors.

1. 4. The most frequent simultaneous malignancies in systemic sclerosis were lymphomas, leukaemia, breast-, lung- and colorectal cancers.

We diagnosed in 16 cases out of 366 patients malignant tumours in the first 4 years after the onset of SSc. The mean age of the patients with tumours at the onset of scleroderma was 57,5 (50 - 68) years (median, upper-lower quartiles), significantly higher, than the one of patients without malignancies. We could not determine any other different clinical signs comparing patients with and without tumours using statistical analysis by Fischer-test.

2. 1. The cross-cultural adaptation into Hungarian of the Disabilities of the arm, shoulder, and hand (DASH) Questionnaire was successfully performed using the forward/backward translation method.

The original and also the Hungarian DASH and QuickDASH versions can be seen on the website <http://www.dash.iwh.on.ca>.

Feasibility: 20 consecutive SSc patients (17 female, 3 male, mean age 56.0 ±8.7 (±SD) years) were given the Hungarian DASH Pre-final questionnaire for self-testing. The

average time needed to fill out the whole questionnaire was 9 min 15 s \pm 1 min 48 s. No patients had difficulty completing the DASH questionnaire.

128 patients completed successfully the DASH-DS but out of the 128 SSc patients only 48 (37.5%) filled out the optional Work module the DASH-W. The patients who filled out the DASH-W had better DASH-DS scores than those who did not ($p < 0.05$, by Mann-Whitney U test). Only 8 patients (6.3 %) filled out the optional DASH-SM.

2. 2. The Hungarian version of the DASH and the shorter QuickDASH are sensitive questionnaires, suitable for a reliable follow-up of upper limb function in systemic sclerosis.

Truth: Concurrent validity: The DASH-SM, the QuickDASH-SM and the DASH-W scores showed strong correlations with the HAQ-DI, the sHAQ index and the physical dimensions of the SF-36 (all Spearman's rho-s were between 0.42 and 0.86). All VAS answers of the sHAQ indicated significant correlations with the DASH-DS and QuickDASH-DS, the strongest correlations were seen in the answer to the question concerning how overall scleroderma problems had interfered with the patient's activity during the last week.

Structural validity: Unidimensionality of the DASH-DS, the QuickDASH-DS, the DASH-W and also the DASH-SM components were confirmed by principal component analysis, respectively.

Discriminant validity There was no significant difference between groups of lcSSc and dcSSc patients neither in DASH scores, nor in HAQ-DI, nor in sHAQ, or Rodnan's skin scores. On the contrary, patients with hand and/or shoulder contractures, or with symmetric tender or swollen joints had significantly higher DASH and QuickDASH scores compared to patients without these abnormalities.

Reliability: Out of 45 patients, there were 43 who completed all three DASH questionnaires for the test-retest reliability. Three repeated measures were performed, the period between two consecutive tests was one week. The intraclass correlation coefficient (ICC) for DASH-DS was 0.89 (95%CI 0.82-0.93) and 0.87 (95%CI 0.79-0.92) for QuickDASH-DS. ICC for DASH-W (n=9) and DASH-SM (n=6), only the second and third measures were available for analysis) were 0.65 (95%CI 0.28-0.89) and 0.88 (95%CI 0.43-0.98). All ICC values indicated good reproducibility.

Internal consistency was assessed with Cronbach's alpha. The alpha coefficients in the DASH sections were between 0.94-0.97. No item was found to substantially change the internal consistency.

Sensitivity to change The SRM of DASH was 0.64 among the scleroderma patients with worsening HAQ status.

3. 1. **The sHAQ showed the strongest correlation with outcomes of the musculoskeletal damage and the increased numbers of affected organs exhibited worsening condition.**

Feasibility: During the tryout period the patients did not suggest alternative wording or other modifications, therefore the Hungarian version of sHAQ was confirmed.

Truth: Concurrent validity: sHAQ score showed strong correlations with the physical dimensions of the SF-36, and there were only weak correlations with the Role-Emotional or with the Mental Health. We also found strong correlations between sHAQ scores and clinical data of physical function, and there were no correlations between the sHAQ scores and the modified Rodnan skin score, or FVC or the DLCO values of the patients. Separately analyzing the VAS-data we found significant correlations between VAS answers assessing the respiratory function, and the FVC or the DLCO.

Discrimination validity: Among patients with dcSSc the indexes of sHAQ and HAQ showed higher (worse) values than the lcSSc patient group ($p < 0.05$). Skin ulcers, significant knee-extensor muscle weakness or hand-contracture correlated with higher HAQ-DI and sHAQ scores. The VAS scores of patients were coherent with the organ damage, respectively. Patients with more affected lung scored higher pulmonary VAS values than the group without it. Similarly, the presence of oesophageal lesions or finger ulcerations yielded significantly higher GI-VAS or skin ulcer-VAS scores. The increasing value of the HAQ-DI and sHAQ along with the increased numbers of organs affected was consistent with worsening condition (ANOVA, $p < 0.001$).

Reproducibility was excellent of both the HAQ-DI (0.96) and sHAQ (0.91) showing high ICC values. The single VAS scores had less but still good reproducibility ICC values (Raynaud-VAS ICC=0.74, skin ulcer-VAS ICC=0.79, GI-VAS ICC=0.79, pulmonary-VAS ICC: 0.88, SSc-sum-VAS ICC=0.83).

The **internal consistency** of sHAQ did not change after adapting to Hungarian conditions (Cronbach alfa: 0.91). Eliminating single domains did not result significant changes in the alpha value (0.90-0.91).

Ceiling-floor effect: The best functional state 0 value of HAQ-DI was found in 10 cases of the patient group of lcSSc and only 2 cases in the dcSSc group. However, the value

of 3 representing the worst functional state was found in only one dcSSc patient. In comparison, the index of sHAQ resulted a single lcSSc patient with maximal score (0). There was no maximal score among the dcSSc patient group and neither any worst value (3) was calculated in the total SSc group of patients.

4. 1. As laboratory parameters stabilize two-three weeks after an acute exacerbation of dermatomyositis and polymyositis physical therapy is safe and beneficial.

During the investigation period all patients remained in clinically inactive stage and serum muscle enzyme levels also remained stable. None of the patients experienced any significant changes in muscle pain, but their feeling of fatigue decreased significantly according to the VAS scale. No significant differences were found between the left and right limbs concerning the changes in muscle strength.

In the early recovery group of patients muscle strength improvement was achieved in the shoulder abductors by $34\pm 27\%$ ($p<0.05$), while the two other proximal muscle groups (the elbow flexors and knee extensors) did not show significant changes. For the proximal muscles this comes to an average of $17\pm 31\%$ ($p>0.05$) improvement. As for the distal muscles the hand flexors became stronger by $37\pm 23\%$ ($p<0.05$).

In the chronic stage group the average improvement of strength was $46\pm 34\%$ ($p<0.05$) for the proximal muscles (the shoulder abductors, the elbow flexors and knee extensors) and $37\pm 29\%$ ($p<0.05$) for the distal muscle group (the hand flexors) (Table 1). Significant FVC improvement $17\pm 21\%$ ($p<0.05$) was found in the early recovery group, but no other respiratory parameters were affected.

4.2. For measuring disability changes in dermatomyositis and polymyositis the HAQ is more sensitive and more suitable than FIM.

Clinically we observed functional improvement in four patients from the early recovery group who were unable to sit and stand up alone at the beginning of the therapy. By the end of the training they were able to get up without any external help, indicating that the muscles of the trunk have become stronger. The massage, the warm mud and bath helped the patients to experience less muscle rigidity and increased joint flexibility.

HAQ indexes showed some improvement in almost every case in both groups ($p<0.05$), FIM scores did not show significant changes in either of the groups.

Discussion

The aim of our work was to find – using our follow-up data of patients with systemic sclerosis (SSc) and with idiopathic inflammatory myopathy (IIM) – the most important risk factors and prognostic factors as well as develop and adapt easy-to-use methods for the care and follow-up of such patients.

Analyzing data of 366 SSc patients we defined the most important prognostic factors like involvement of the kidneys, the heart and skin, older age at the beginning of SSc, and permanently high erythrocyte sedimentation rate. According to the present study a **simultaneous malignant tumour predicts a shorter survival**. The SSc associated early tumors diagnosed within a four-year interval after the onset of SSc are mainly breast tumours, haematological or lung tumours according to previous studies and our observations. This makes it **important to search for malignant tumours during the first years of SSc**, especially in patients older than 50 years.

The Hungarian adaptation and validation of the DASH was done on a group of 128 SSc patients. At the onset of SSc the contractures affect the upper limbs, especially the fingers. The follow-up of the contractures of the joints of the fingers cannot be achieved by angular measurements, this is why there are different methods developed to assess the function of the hands. Self assessment questionnaires have the advantage of simplicity, but need linguistic and cross cultural adaptation.

The DASH and the QuickDASH are widely used in orthopaedics, traumatic surgery and rheumatology to assess upper-limb function. Data gained during the validation process with the help of our SSc patients prove that the Hungarian adaptation of the DASH and QuickDASH can be considered successful.

The different parts of the DASH questionnaire can differentiate and follow the functional damage of the upper limbs. We demonstrated that the DASH and QuickDASH similarly to the HAQ well known in rheumatology are sensitive and reliable tools to assess upper limb functional damage.

Though the **QuickDASH is shorter and simpler**, it is still as **sensitive and reliable** as the original, longer DASH version, so the QuickDASH is more suitable for the everyday practice. Based on the results we emphasize that the damage of the upper limbs is the major cause of disability in case of SSc patients.

Our further aim was to perform the Hungarian adaptation and a **psychometric study on 123 SSc patients with the sHAQ**, the HAQ self assessment questionnaire modified for

use in SSc. The completed sHAQ contains questions also about the state of the skin, lungs, oesophagus, stomach and the overall state. Our results prove a successful Hungarian adaptation of the sHAQ. The sHAQ showed a worse state parallel with multiple organ manifestations and correlated with the SF36 physical dimension scores and HAQ-DI scores. According to our calculations the sHAQ had the strongest correlation with the damage of the musculoskeletal organs and there was no correlation with the state of the skin, lungs or heart. The sHAQ VAS scores must be followed one by one as they provide pieces of quick information on the changes of the vascular symptoms, or state of the skin, lungs, heart, stomach and the general state of the disease.

We examined the effect of physiotherapy in PM and DM patients shortly after the acute phase of the disease. In inflammatory myopathies physiotherapy during the acute phase can lead to necrosis of the inflamed muscles. During remission the lack of physiotherapy, the inactivity and corticosteroid therapy will enhance muscle atrophy and the development of joint contractures. Earlier, physiotherapy was started only at the late remission with already necrotized muscles. PM and DM patients received physiotherapy with massages and mud treatment for three weeks shortly after the active period with the usual corticosteroid and cytostatic medication still in progress. We measured the changes in the muscle state and respiratory function.

The early physiotherapy did not induce reactivation of the myositis. Muscles became slightly stronger, **the FVC, which is related to muscle function got significantly better** while FEF and FEV/FVC did not change. Greater vital capacity was very promising and reduced fatigue on the VAS scale. Based on the findings that 2-3 weeks after the acute symptoms of myositis when the CK in the serum does not rise, muscles stop losing force, the erythrocyte sedimentation rate and the C-reactive protein level return to normal physiotherapy has no considerable risk.

For the follow-up of the functional parameters **HAQ is better** than FIM.

New results

1. 1. Analyzing survival data of Hungarian SSc patients we found that the factors of the highest risk for survival are kidney involvement, malignant tumour diagnosed around the onset of SSc, permanently high erythrocyte sedimentation rate, diffuse involvement of the skin and older age. We were the first to point out that the SSc associated malignant tumours are also significant causes of death along with renal, pulmonary and cardiac manifestations.

1. 2. We proved that fatal bleeding of abnormal gastric vessels „watermelon stomach” and pulmonary arterial hypertension gained a greater proportion of the causes of death. The explanation is the longer survival, and the development in the diagnosis of PAH.

2. 1. Our group was the first to use the DASH questionnaire and prepare its Hungarian adaptation with forward and backward translation.

2. 2. We validated the DASH and the QuickDASH questionnaires first in the world on SSc patients. We stated that both the DASH and the QuickDASH are reliable questionnaires in SSc to assess function. Both questionnaires are sensitive enough to verify upper limb functional damage as a result of SSc. In a follow-up study we proved that similarly to the HAQ questionnaire the DASH and QuickDASH questionnaires are appropriate to indicate worsening or change in the functional state.

3. 1. We were the first in Hungary to adapt and validate the modified HAQ (sHAQ) for SSc patients. We found the strongest correlation between the sHAQ and the physical status or the musculoskeletal manifestations.

3. 2. During the common investigation of the DASH and the sHAQ we emphasised the significance of the fact that the DASH indexes show a strong correlation with the sHAQ index and with the physical function cores of the SF36 quality of life questionnaire.

4. 1. We proved that in PM and DM 2-3 weeks after the active symptoms as laboratory signs of inflammation stabilize controlled physiotherapy is safe to start and may result in better muscle strength, vital capacity and function.

4. 2. We stated that HAQ is superior FIM for following functional changes.

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