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Spinal Mobility Measurements and Functional Indices in Ankylosing Spondylitis and Other Spondyloarthropathies



ACADEMIC DISSERTATION

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List of original publications

This thesis is based on the following original publications, referred to as I-VI in the text:

- I. Viitanen J, Heikkilä S, Kokko ML, Kautiainen H. Clinical assessment of spinal mobility measurements in ankylosing spondylitis: a compact set for follow-up and trials? *Clin Rheumatol* 2000;19:131-7.
- II. Heikkilä S, Viitanen J, Kautiainen H, Kauppi M. Sensitivity to change of mobility tests; effect of short-term intensive physiotherapy and exercise on spinal, hip, and shoulder measurements in spondyloarthropathy. *J Rheumatol* 2000;27:1251-6.
- III. Heikkilä S, Viitanen J, Kautiainen H, Kauppi M. Evaluation of the Finnish versions of the functional indices BASFI and DFI in spondylarthropathy. *Clin Rheumatol* 2000;19:464-9.
- IV. Heikkilä S, Viitanen J, Kautiainen H, Kauppi M. Does improved spinal mobility correlate with functional changes in spondyloarthropathy after short-term physical therapy? *J Rheumatol* 2000;27:2942-4. [letter]
- V. Heikkilä S, Viitanen J, Kautiainen H, Kauppi M. Functional long-term changes in patients with spondylarthropathy. *Clin Rheumatol* 2002;21:119-22.
- VI. Heikkilä S, Ronni S, Kautiainen H, Kauppi M. Functional impairment in spondyloarthropathy and fibromyalgia. *J Rheumatol* 2002;29:1415-9.

Abbreviations

AS	ankylosing spondylitis
BASDAI	Bath ankylosing spondylitis disease activity index
BASFI	Bath ankylosing spondylitis functional index
BAS-G	Bath ankylosing spondylitis patient global score
BASMI	Bath ankylosing spondylitis metrology index
BASRI	Bath ankylosing spondylitis radiology index
CI	confidence interval
CRP	C-reactive protein
DFI	Dougados functional index
DMARD	disease modifying antirheumatic drug
ES	effect size
ESR	erythrocyte sedimentation rate
ESSG	European Spondylarthropathy Study Group
FM	fibromyalgia
HAQ	health assessment questionnaire
HAQ-S	health assessment questionnaire for spondyloarthropathies
Hb	haemoglobin
HLA	human leukocyte antigen
ICC	intraclass correlation coefficient
ILAR	International League of Associations for Rheumatology
IQR	interquartile range
NSAID	nonsteroidal anti-inflammatory drug
OMERACT	outcome measures in rheumatoid arthritis clinical trials
PsA	psoriatic arthritis
RA	rheumatoid arthritis
ReA	reactive arthritis
ROM	range of motion
SD	standard deviation
SpA	spondyloarthropathy
VAS	visual analogue scale
WHO	World Health Organization

Introduction

In Finland 15 000 people are receiving drug reimbursement for different kinds of chronic spondyloarthropathies (SpAs) (Amor et al. 1990, Dougados et al. 1991) and the annual incidence of SpA in Finland is 800 (Kaipiainen-Seppänen and Aho 2000). In this country there is an active practice in drug treatment and rehabilitation. The Rehabilitation Institute of the Finnish Rheumatism Association rehabilitates SpA patients on three-week inpatient courses.

In ankylosing spondylitis (AS) (van der Linden et al. 1984) limitation of the spinal mobility is a combination of structural damage and disease activity (van der Heijde and van der Linden 1998): inflammation is responsible not only for the subjective clinical symptoms of pain and stiffness, but also for reduction in spinal mobility. Ankylosis is responsible for reduction in spinal and thoracic mobility leading to impaired daily activities and lowered respiratory capacities. Abnormal posture may be caused by both inflammation and ankylosis. In rare instances ankylosis may even occur in the absence of clinical symptoms (Dougados et al. 1998).

The measurement of symptoms and signs of AS is difficult. The International Assessment in AS Working Group (van der Heijde et al. 1997) has pointed that the studies concerning AS are not comparable, because every investigator can select many measures. The International AS Working Group (van der Heijde et al. 1999a) has subsequently developed and recommended core sets for different treatment settings: symptomatic therapy, disease modification, physiotherapy, and clinical practice. These are now accepted as the World Health Organization (WHO)/International League of Association for Rheumatology (ILAR) core set for the assessment of AS (van der Heijde et al. 1997). The domains for physical therapy are function, pain, spinal mobility, patients' global assessment and stiffness.

No consensus has so far been achieved on the assessment methods of other SpAs than AS, such as psoriatic arthritis (PsA) and reactive arthritis (ReA); and mostly an overlap of measures used for rheumatoid arthritis (RA) and for AS is used (van der Heijde and van der Linden 1998). In a large multicentre trial on AS, PsA and ReA all patients fulfilled the European Spondylarthritis Study Group (ESSG) (Dougados et al. 1991) classification criteria for SpA and the subgroups were analysed according to the

presentation of the disease: axial involvement only, oligoarticular and polyarticular disease (Dougados et al. 1995). Dougados (1995) emphasised that we still need to be more problem-oriented and less disease-oriented. If the aim of the study is to focus inclusion on a particular subgroup of patients it seems more logical to specify a clinical presentation (e.g. axial involvement) than diagnosis of a disease belonging to a subgroup of SpA (e.g. AS). While SpAs comprise a group of so many various diseases, the disease spectrum is also wide, from acute to chronic manifestations, mostly mild to moderate. Symptoms and signs may come from many organs (urogenital, respiratory tract, gut, skin, entheses, peripheral joints, sacroiliac joints, spine, eye and heart), but may not be present in all patients (Angulo and Espinoza 1998).

The specific instruments for spinal mobility accepted by WHO/ILAR are modified Schober, chest expansion and occiput-to-wall distance. Although lumbar spinal flexion, extension and lateral bending together with chest expansion are the mobility criteria for AS, the knowledge of their clinimetric properties remains insufficient (Percy 1986, Wright 1991). The previous compact set mobility measurements made in the Rehabilitation Institute of the Finnish Rheumatism Association (Viitanen 1996) did not include the lateral bending measurement of the thoracolumbar spine, and the rotation of the thoracolumbar spine was made with a special instrument, which is troublesome in clinical practice. The most popular spinal mobility measurements change only a little during the short-term rehabilitation (Laurent et al. 1991, Viitanen et al. 1992). More information is needed to find out the most sensitive spinal mobility measurements to show the efficacy of the treatment (Dagfinrud and Hagen 2002).

In the domain of function the Outcome of Measures in Rheumatoid Arthritis Clinical Trials filter (OMERACT) (van der Heijde et al. 1999b) has concluded that both the Bath Ankylosing Spondylitis Functional Index (BASFI) (Calin et al. 1994) and the Dougados Functional Index (DFI) (Dougados et al. 1988, Dougados et al. 1990) can be used. Other functional indices exist e.g. a Dutch version (Creemers et al. 1994) and the Health Assessment Questionnaire for Spondyloarthropathies (HAQ-S) (Daltroy et al. 1990). More information about the minimum required methodological steps in the translation and cross-cultural adaptation of different measurements is needed (Ferraz 1997). The functional indices BASFI and DFI accepted by WHO/ILAR should be used in Finland.

There may be other rheumatic diseases whose symptoms, especially in the early phases, resemble those of SpAs. Fibromyalgia (FM) (Wolfe et al. 1990) is a syndrome characterised by generalised pain and widespread tenderness on palpation in specific areas of the musculoskeletal system, including the cervical and lumbosacral areas. Some questionnaires have been reported to be feasible with AS and FM patients (Bakker et al. 1994, Bakker et al. 1995).

Classification of a patient as having AS is clearly important in directing attention to proper posture and using exercise (Viitanen et al. 1992, Viitanen et al. 1995d). While the therapeutic options for patients with refractory axial involvement are very limited (new drug treatment trials are going on) (Dougados 2001), it is beneficial to maintain as much mobility as possible and the best possible posture during the process of ankylosis. Nowadays patients with severe forward stooped posture are rarely seen.

In this dissertation SpAs with spinal involvement were included and the measures of AS were applied. The main concern was restricted to musculoskeletal manifestations only, and manifestations in other organs were not described. The lateral bending of the thoracolumbar spine and the Pavelka method (Pavelka 1970) made with a tape for measuring the thoracolumbar rotation would merit investigation as a part of a compact set of mobility measurements and their sensitivity to change due to rehabilitation. The aim of this study was to validate the internationally recommended functional indices with disease activity, spinal mobility and radiology, in order to establish whether cultural differences diminish their value. Because assessment of functional changes and limitations of spinal range of motion (ROM) due to the disease is of special interest in rheumatological rehabilitation (van der Heijde et al. 1999a), one goal of the study was to investigate how improvements in these assessments during the inpatient course correlate with each other. There are only few follow-up studies on function (Ward and Kuzis 1999), and in this study the three-year follow-up of these functional indices was described for the first time. No previous comparison of the indices (BASFI, DFI and HAQ-S) between SpA and FM patients has been made.

Review of the literature

1 General aspects of spondyloarthropathy

1.1 History and diagnostic criteria

Bony ankyloses of the spine have been observed in prehistoric men and the kings of Egypt about three thousand years B.C. suffered from AS type axial disease. Around the end of the 19th century descriptions of AS were made by Srümpel, Marie and Bechterew (Ott 1979). In the 1950s the problem involved the identification of AS among the whole group of rheumatic diseases and the distinction between AS and RA was not yet clear. The AS criteria of Rome 1961 (Gofton et al. 1966) and New York 1966 (Bennett and Burch 1968) were improvements since they included bilateral radiological sacroilitis, low back pain and spinal movement restrictions (Moll and Wright 1973). The modified New York criteria for AS (van der Linden et al. 1984) (Table A in Appendix 1) require radiological sacroilitis leading to delay of the diagnosis, but this is not needed in SpA.

The concept of SpA introduced by Moll et al. (1974) is unique in that, although based on clinical grounds, it tends to put together several previously well recognised separate diseases. The term SpA is a popular working concept (Dougados 1993). Two main sets of classification criteria have been proposed by Amor et al. (1990) (Table B in the Appendix 1) and the ESSG (Dougados et al. 1991) (Table C in the Appendix 1). The several previously defined disorders that here form the composition called SpA include AS, both an adult and a juvenile subgroup, ReA, PsA, and enteroarthritis due to ulcerative colitis and Crohn's disease. Patients with these disorders usually fulfil both sets of above mentioned criteria. Otherwise unclassified peripheral arthritis linked to the human leukocyte antigen (HLA)-B27 (Meyer et al. 1982) is also often considered to be undifferentiated SpA (Zeidler et al. 1992). The Italian Society of Rheumatology 1998 classification of rheumatic diseases has replaced the term SpAs with that of enthesoarthritis (Marcolongo 1999).

A committee of the European League Against Rheumatism has recommended that the term 'spondylarthropathy' (without the letter "o" in the middle) should be avoided and the term 'spondyloarthropathies' is most widely used (Khan 1996).

1.2 Epidemiology

The prevalence of AS in Finland has been estimated to be 0.15–1% (Julkunen and Korpi 1984, Julkunen et al. 1989, Kaipiainen-Seppänen et al. 1997). There was a strong association between HLA-B27 and AS, and the prevalence of AS closely paralleled the frequency of HLA-B27 in most populations that have been studied (Khan 1995). The prevalence of HLA-B27 was 12–18% in Finno-Ugric populations. The prevalence of HLA-B27 among western European populations ranged 6–9%, but it varied between 10 to 16% in the northern parts of Norway and Sweden and in Iceland; the prevalence of AS was 0.2% in Western Europe and up to 1.4% in the latter areas respectively. The reported absolute risk of HLA-B27 positive persons developing AS has varied from 1.3 to 6.7% (Gran and Husby 1993). There could also be discrepancy between the association of HLA-B27 and AS, suggesting the presence of some non-HLA-B27 protective factor (Brown et al. 1997), and HLA-B27 contributed only 16–50% of the total genetic risk for the AS and related SpAs indicating that other genes must be involved (Reveille et al. 2001).

The association of HLA-B27 varied among different SpAs, from about 50% in the case of psoriatic and enteropathic spondylitis, 80% in ReA to over 95% in primary AS (Khan 1998). There are only few studies about epidemiology of SpA. A study of the epidemiology of SpA in the population of Berlin (Braun et al. 1998) showed that the prevalence of SpA was 1.9%, with a background HLA-B27 frequency of 9.3%, AS being the most frequent SpA subtype.

In Finland during 1995 the incidence for AS, PsA, chronic ReA and other SpAs was 6-7, 6-7, 2-3 and 3/100 000 respectively; and the mean age at the time of diagnosis was 40, 44, 40 and 41 years, respectively (Kaipiainen-Seppänen and Aho 2000). The incidence of SpAs remained similar during the period 1980–1995. The gender distribution in Finland varied among different SpAs: about 30% of AS patients were women, the male:female ratio for PsA was 1.3:1 and about two thirds of chronic ReA cases were female (Kaipiainen-Seppänen 1997).

The gender ratios varied a lot in different studies all over the world, although male predominance was common among SpAs (Gran and Ostensen 1998). The reports of the outcome by gender also varied. The functional outcome was better in female than male patients (Jimenez-Balderas and Mintz 1993) but similar in men and women (Gran and Skomsvoll 1997) without evidence for differences in reduction of spinal mobility

between the two genders. However, a radiologically totally obliterated sacroiliac joint and a higher incidence of radiological spinal involvement occurred significantly more often in men than in women (Kidd et al. 1988).

The age at disease onset did not differ significantly between men and women and the delay of the diagnosis was getting shorter (Feldtkeller et al. 2000), but there has been a relatively greater degree of underdiagnosis of SpA among female than male patients in the past. The speed of spinal progression was slower in female patients, but in terms of pain and the need for drug therapy, female patients were in a significantly worse situation compared to men. The average age at disease onset was 26 years and average age at diagnosis 35 years. The male to female ratio was 2:1 depending on the date of diagnosis.

1.3 Ethiopathogenesis

The prototype of the group of SpAs is AS. The cause of AS remains unclear. There is ongoing discussion about the evidence that this disorder or any of the SpAs is an autoimmune disease attributable to cross-reactivity between bacteria and HLA-B27 (Ringrose 1999). The pathogenesis of ReA has been extensively reviewed (Yu 1999, Toivanen and Toivanen 2000). Differences in endogenous peptide presentation by HLA-B27 subtypes may be relevant in the ethiopathogenesis.

An enthesal-associated pathology could explain spinal and much of the synovial joint inflammation in patients with AS and related SpA. The concept of inflammatory arthritis in general must be extended to view the role of enthesal or capsular changes in disease pathogenesis. The enthesis is the point of insertion of the tendon, ligament, joint capsule, or fascia to bone, and its inflammation (enthesitis) is the cardinal feature of SpA (Schweizer and Resnick 1994). Histology studies have demonstrated soft tissue inflammation and bone destruction at the site of enthesal insertion to bone (Ball 1971). Recent magnetic resonance imaging studies have drawn attention to enthesitis as a possible unifying inflammatory lesion in the musculoskeletal manifestations of SpA (McGonagle et al. 1998a, McGonagle et al. 1998b). Bone oedema at the sacroiliac joint as the earliest lesion in AS (Braun and Sieper 1996) is also postulated to be secondary to enthesitis in circumferential capsular attachments and at the intraosseous ligament (Marzo-Ortega et al. 1998).

1.4 Clinical manifestations

The typical postural and mobility changes in AS depend on arthritis in the costovertebral (Pascual et al. 1992) and apophyseal joints (Simkin et al. 1988) and enthesitis and calcifications of the spinal anterior and posterior ligaments (Adams et al. 1980). The musculoskeletal manifestations of SpA include spinal symptoms, extraspinal joint disease and enthesiopathic lesions. The clinical symptoms of these are back pain at night, back stiffness in the morning, asymmetric synovitis/oligoarthritis predominant in the lower limbs, buttock pain in alternating gluteal areas, sausage-like digit or toe, heel pain and other enthesopathies. Inflammation may lead to general symptoms, and patients may suffer from sleep disturbances and fatigue (van der Linden 1997). Pain in coughing and difficulties in breathing deeply are typical. It is easier to be in the forward-bowed position with a risk of developing kyphosis. Progression is usually slow and fluctuating, but a minority of patients has a severe continually active disease. AS is associated with osteoporosis and loss of bone mass occurs mainly in patients with persistent active disease suggesting strongly that inflammatory activity itself plays a role in this bone mineral pathology (Gratacos et al. 1999). Manifestations of other than musculoskeletal or complications like secondary amyloidosis were not described in this connection.

The clinical criteria of inflammatory spinal pain are insidious in onset, in a patient younger than 40 years, persisting for at least three months, associated with morning stiffness and improving with exercise (Calin et al. 1977). Nowadays sacroilitis is not always detected by magnetic resonance imaging in patients with inflammatory back pain leading to confusion about the conception of the inflammatory spinal pain (Brandt et al. 1999).

On population level, the disease spectrum may range from very mild undifferentiated SpA to incapacitating AS. Axial manifestations are seen in over half of the patients with undifferentiated SpA and ReA (Boyer et al. 1999). Male gender and hip involvement are related to more severe spinal disease (Calin et al. 1999a). The ankylosed spine is at increased risk for fractures, which may remain occult (Finkelstein et al. 1999).

1.5 Treatment

The treatment includes pharmacological and non-pharmacological therapies. The objectives are to relieve symptoms (e.g. pain and stiffness) and to reduce and/or prevent inflammation, cartilage breakdown, ankylosis and development of abnormal posture. The management of SpAs is related more to their clinical presentation i.e. axial versus peripheral involvement, than to the precise diagnosis (Dougados 2001).

Traditional disease modifying antirheumatic drugs (DMARD)s (Clegg et al. 1999, Sampaio-Barros et al. 2000, Scarpa and Mathieu 2000, Toussirot and Wendling 2001) and also other drugs (Leirisalo-Repo 1998, Breban et al. 1999, Yli-Kerttula et al. 2000, Maksymowych 2001) with new agents (van den Bosch 2000, Baeten 2001) were prescribed for patients with peripheral inflammatory articular involvement. The question still remains whether there is place for DMARDs in the treatment of the axial involvement of SpA? (Dougados 2001). Sulphasalazine is the single drug sufficiently studied to try to answer to this question (Dougados et al. 1986, Feltelius and Hallgren 1986, Nissilä et al. 1988, Dougados et al.1995, Clegg et al. 1996) and in daily practice, sulphasalazine can be proposed to patients with symptomatic refractory axial involvement. Future studies are needed, (and are ongoing) to confirm the results of the promising preliminary studies on pamidronate, thalidomide and tumour necrosis factor alpha blockers (Dougados 2001).

Nonsteroidal anti-inflammatory drugs (NSAID)s are considered the cornerstone of drug therapy for SpA and their intake is restricted to painful periods. Glucocorticoids may be administered locally or systemically. When given orally glucocorticoids probably do not arrest the progression of the disease process in AS, but in a few cases, pulse therapy using high dose methylprednisolone may temporarily control painful acute attacks (Peters and Eijstrup 1992).

Non-drug therapy includes: education of patients to increase compliance; daily exercises, after muscle-warming in a hot shower, e.g. swimming, extension promoting exercises or sporting activities to counteract the kyphotic effects of pain and fatigue on posture and reduce stiffness, but avoiding vigorous or contact sports if the spine has become fused or osteoporotic; prone lying for 30 minutes a day to reverse the tendency for kyphosis and flexion contractures of the hip joints; sleep on firm mattress with only a small neck support pillow; supportive measures and counselling; avoidance of smoking; patient support groups and family counselling (van der Linden 1997).

Occasionally lumbar osteotomy is needed for correction of thoracolumbar kyphotic deformity with impaired forward vision in AS (van Royen and de Gast 1999).

Rehabilitation and physical therapy are regarded to have a beneficial effect by improving mobility, strength and fitness, and by preventing or reducing spinal curve abnormalities (Hidding and van der Linden 1995, Tishler et al. 1995, Viitanen et al. 1992, Viitanen et al. 1995d). For many years the Rehabilitation Institute of the Finnish Rheumatism Association has used the inpatient programme for SpA patients described in Table 1 (Viitanen and Heikkilä 2001).

Table 1. Intensive inpatient physiotherapy and weekly exercise programme for spondyloarthritis patients: duration per session and weekly frequency as mean, range and median (Viitanen and Heikkilä 2001).

Physiotherapy/exercise	Mean	Median	Range	Duration (min)
Pain-relieving local managements	3.8	3	0-8	10-25
Water pool (29-30°C)	5.1	6	2-6	15-25
Group gymnastic/exercise, keep-fit club	7.1	9	2-12	25-30
Individual gymnastics/exercise	1.7	2	0-3	25-30
Individual physiotherapy in suspension	1.5	2	1-5	25-30
Stretching or mobilization	0.2	0	0-2	20-30
Massage	1.8	1	0-3	20-30

A programme of supervised physiotherapy in groups consisting of hydrotherapy, exercises and sporting activities twice weekly for three hours per session improved thoracolumbar mobility and fitness (Hidding et al. 1993). Patients may do exercises in hospital or in outpatient clinics, supervised in a group or on an individualised home exercise programme. Cochrane's review (Dagfinrud and Hagen 2002) summarised the scientific evidence available on the effectiveness of physiotherapy interventions in the management of AS: there was a tendency toward positive effects of physiotherapy but sufficient evidence is not yet available to justify recommendations.

There are now core sets for different settings making it possible to demonstrate the efficacy of therapeutic interventions (van der Heijde et al. 1999a). Both the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) may be elevated in AS, although active disease may occur in the absence of elevated levels of acute-phase reactants and neither of these two is superior for assessing disease activity (Dougados et

al.1999, Spoorenberg et al. 1999b). The OMERACT (van der Heijde et al. 1999b) group recommended that ESR as an acute-phase measure should be used whenever possible in cross-sectional studies.

1.6. Outcome

Several endpoints may be researched for measuring the outcome of AS. Work disability is an important outcome measure. After a mean disease duration of 16.5 years, approximately half of one hundred patients with adult-onset primary AS were working full-time. Incapacity for work was associated with female sex, low level of education, uveitis, complete ossification of spine and coexistence of non-rheumatic diseases (Gran and Skomsvoll 1997). Earlier in Finland working disability was found about in one third of AS patients (Lehtinen 1981). In general, the natural course of AS may cause the patients to suffer from stiffness and pain, and the statement “AS never burns out” (Kennedy et al. 1993) may still be true. Mortality can also be used as a rough outcome measure of AS. In a series of Finnish patients the overall mortality was 1.5 times that expected (Lehtinen 1993), and in a population-based study by Myllykangas-Luosujärvi et al. (1998) the lifespan of the subjects with AS was shortened by 6–8 years compared to the Finnish population.

When addressing the outcome of SpA, it is important to provide results separately for the various diseases studied, because AS, ReA, and PsA may show great differences with respect to disease course and final outcome. Overall, the prediction of outcome in early SpA appears to be difficult, and it is difficult to classify a large number of patients into one of the SpA subsets. In a retrospective study, Amor et al. (1994) were able to identify a number of features associated with poor outcome. Psoriasis predicted a poor short-term outcome in patients with recent-onset SpA (Stafford et al. 2001). Leirisalo-Repo et al. (2000) found that patients with ReA had an increased risk of developing chronic rheumatic disease (31% of patients), for which the risk factors were uroarthritis, recurrent infections, recurrent arthritis and HLA-B27; and work disability occurred in 19% of those patients during the 20-year follow-up.

2 Radiology

The radiographic features of enthesitis include enthesal bone insertion osteopenia, bone cortex irregularity at insertion, erosion, enthesal soft tissue calcifications and new bone formation at the enthesis (Watt 1997). Periostitis not related to a defined insertion is also a feature of SpA. In the later phase of the disease typical findings are calcifications of ligaments and annulus fibrosus leading to the development of syndesmophytes, arthritis in the costovertebral and apophyseal joints, and changes in the body of the vertebrae including sclerosis of corners and squaring (Bywaters 1979, Fassbender 1979, Francois 1982, Simikin et al. 1988, Pascual et al. 1992).

If plain film radiography remains uncertain, magnetic resonance imaging or computer tomography may be used (Battafarano et al. 1993). Scintigraphy is very sensitive but non-specific and only of limited value (Blum et al. 1996). Magnetic resonance imaging makes it possible identify sacroilitis earlier than with plain radiography (Oostveen et al. 1999). van der Linden and van der Heijde (2000) still recommend the use of conventional radiography as a first means of investigation, and if it makes a sure diagnosis, no new imaging techniques, such as magnetic resonance imaging and computer tomography, are needed. The application of new methods to AS is under development and so far no quantitative scoring methods are available. The International Assessment in AS Working Group (van der Heijde et al. 1999a) has recommended as instruments in spinal radiography domain anteroposterior plus lateral lumbar and lateral cervical spine and pelvic radiography (sacroiliac and hips).

Radiological evidence of sacroiliac joint damage has been the cornerstone for both clinical and differential diagnoses of AS over several years according to the (modified) New York criteria (van der Linden et al. 1984). The ESSG proposed that criteria for SpA should place less emphasis on radiological change (Dougados et al. 1991). Pelvic radiography reveals the presence of sacroilitis while the degree of asymmetry/symmetry may help in differentiating primary AS or enteropathic disease from psoriatic or post-reactive spondylitis (Edmunds et al. 1991). The presence of vertebral squaring and syndesmophytes with or without fusion illustrates the extent of the disease process. AS is predominantly an axial disease affecting the spine and sacroiliac joints, but large axial joints (hips and shoulders) and peripheral joints may also be affected. Scoring systems for peripheral joints could be adapted from those developed for RA.

A specific scoring system for the spine and sacroiliac joints should be used, and three scoring methods have been described. First Dale and Vinje (1985) developed a grading system involving six stages (with grade IIA unilateral and IIB bilateral) of arthritis from grade 0 = normal joints to grade V = extensive bony ankylosis in the sacroiliac joints (Table 2a) and a scheme applicable for quantitative registration of the radiographic findings of the spine (Table 2b) in AS.

Table 2a. Radiographic grading of sacroilitis in Bechterew's syndrome (Dale 1980).

<i>Grade 0</i>	Normal condition.
<i>Grade I</i>	Suspicious changes.
<i>Grade II</i>	Definite early changes. Pseudo-widening of the joint space and/or localized areas with erosions. Sclerosis of the bone usually on both sides of the joint space. Blurring of joint margins often present.
<i>II A</i>	Unilateral changes.
<i>II B</i>	Bilateral changes.
<i>Grade III</i>	Severe destructive changes. The erosions and often pseudo-widening at least in one joint are more marked than in grade II. The arthritic changes are always bilateral. Small bony bridges may be present.
<i>Grade IV</i>	Regressive changes. Bilateral arthritic changes as described under grade III, but in addition signs of narrowing of the joint spaces with more even margins, often with bony bridges in one or both sacroiliac joints. Some regression of the sclerosis in the neighbourhood of the joints.
<i>Grade V</i>	Terminal changes. Marked signs of bony ankylosis in both sacroiliac joints. Regression of the sclerosis in the neighbourhood of the joints.

Sclerotic anterior borders of vertebrae and/or straightened anterior surface of vertebrae can be seen and sclerotic anterior borders of vertebrae are an earlier finding than syndesmophyte formation.

Except for ankylosis of the apophyseal joints and ossified interspinous ligament most frequently found in the lower lumbar region in patients with duration of disease more than 20 years, all abnormalities of the spine were most common at the dorsolumbar junction. Vinje et al. (1985) presented associations among radiographic findings of the dorsolumbar spine, peripheral joints, tendon insertions and the pubic symphysis. Ankylosis of sacroiliac joints, ankylosis of apophyseal joints, bridging syndesmophytes, ossified interspinous ligament, block vertebrae, arthritis of the pubic symphysis and new bone formation of the ischium were strongly mutually associated. They probably belong to the same subgroup of

the disease and were negatively associated with distal peripheral arthritis. Mixed osteophytes, parasyndesmophytes or shining corners (anterior spondylitis) showed associations. A late stage of sacroilitis was associated with distal peripheral arthritis, but negatively associated with signs of ankylosing processes of the dorsolumbar spine.

Table 2b. Changes of the spine in Bechterew's syndrome, radiographic evaluation (Dale and Vinje 1985). Ankylosing spondylitis (AS).

<i>(1=none, 2=one without bridging, 3=two or more without bridging,</i>	<i>Score in spine:</i>
<i>4=one bony bridge, 5=two or more bony bridges):</i>	
Syndesmophytes laterally	
Syndesmophytes anteriorly	
Parasyndesmophytes laterally	
Parasyndesmophytes anteriorly	
Mixed osteophytes laterally	
Mixed osteophytes anteriorly	
Ossification of interspinous ligament	
Ossification of anterior longitudinal ligament	
<i>(1=no, 2=yes):</i>	
Unilateral ossification	
Extensive asymmetric ossification	
Osteochondrosis	
<i>(from 1=none to 4=four or more vertebrae/three or more joints/three or more loci):</i>	
Partial block vertebrae following spondylitis anterior	
Arthritis apophyseal joints without ankylosis	
Arthritis apophyseal joints with ankylosis	
Sclerotic anterior borders of vertebrae	
Straightened anterior surfaces of vertebrae	
<i>(1=none, 2=suspicious, 3=definite):</i>	
Spondylodiscitis	
Calcification of discs	
Reduced disc spaces occurring with other radiographic indications of AS in the area	
Reduced disc spaces occurring without other radiographic indications of AS in the area	
<i>(1=no, 2=minimal, 3=moderate, 4= marked):</i>	
Spondylosis	
Scoliosis	
Kyphosis	

The second scoring system was the Stoke Ankylosing Spondylitis Spinal Score published by Taylor et al. (1991), and further validated by Aaverns et al. (1996). The third method published was that by Kennedy et al. (1995), which has been modified and called the Bath Ankylosing Spondylitis Radiology Index (BASRI) (Calin et al. 1999a).

No method showed significant changes over a follow-up period of one year in a considerable number of patients (Spoorenberg et al. 1999c).

3 Spinal mobility measurements

Limitation of spinal movements is an early feature of AS and its importance as a clinical sign is emphasised by its inclusion in the New York diagnostic criteria (Bennet and Burch 1968). Numerous physical measurements have consequently become widely used since the original assessments defined by Moll and Wright (1971). Frequently these measurements are not standardised or assessed for reliability, validity, or sensitivity to change (Pile et al. 1991).

The impact of age and gender in general. A meta-analysis of normative cervical motion showed that ROM decreased as age increased, women exhibiting greater ROM values than men (Chen et al. 1999). The results in a study of healthy volunteers indicated that little difference exists between genders for total lumbar sagittal ROM, which declined as age increased (Sullivan et al. 1994). In a large adult population of 3020 people it was shown that spinal ROM was affected by many individual factors like age, sex and height (Batti'e et al. 1987). A decrease in the range of lumbar spine movements was observed when testing early in the morning general young adults (Russel et al. 1992), and warming-up may influence on reliability of measurements in AS (Roberts et al. 1988).

The mobility measurements of spine, hip and shoulder are listed:

The thoracolumbar spine:

- Schober test (Schober 1937) and Modified Schober test (Macrae and Wright 1969)
- Schober sacral 1 test (Pearcy 1985, Viitanen et al. 1995d)
- Thoracolumbar whole flexion (Tautenhahn 1969, Greene and Hechman 1994, Viitanen et al. 1995d)
- Thoracolumbar rotation measured with an instrument (Viitanen 1993)
- Thoracolumbar rotation measured with a tape (Pavelka 1970, Viitanen et al. 1999)
- Thoracolumbar lateral flexion (finger-thigh test) (Domjan et al. 1990)
- Thoracolumbar lateral flexion (xiphisternum-iliac crest distance) (Moll et al. 1972)

The cervical spine:

- Cervical rotation measured with an inclinometer (O'Driscoll et al. 1978, Viitanen et al. 1995d)
- Cervical rotation measured with a tape (Viitanen et al. 1998)

- Cervical lateral flexion measured with an inclinometer (O'Driscoll et al. 1978, Viitanen et al. 1998)
- Cervical lateral flexion measured with a tape (Viitanen et al. 1998)
- Cervical forward flexion (O'Driscoll et al. 1978, Viitanen et al. 1998)
- Cervical extension (O'Driscoll et al. 1978, Viitanen et al. 1998)
- Chin-to-chest distance (Treiber 1967, Viitanen et al. 1995d)

Others:

- Occiput-to-wall distance (Taylor et al. 1991, Viitanen et al. 1995d, Ward and Kuzis 1999)
- Tragus-to-wall distance (Tomlinson et al. 1986, Viitanen et al. 1998)
- Chest expansion (Moll and Wright 1972, Viitanen et al. 1995d)
- Finger-to-floor distance (Kippers and Parker 1987, Viitanen et al. 1995d)
- Intermalleolar distance (Calin 1985, Jenkinson et al. 1994)
- Internal hip rotation and shoulder abduction and flexion (Greene and Hechman 1994).

Assessment methods. Mobility measurements must be reproducible, rapid and simple enough to be collected by routine examination at each follow-up in addition to the assessment of the grade of progression of the disease (Dougados et al. 1998). The most commonly used assessment methods for ROM are a tape method for distance assessment of two points (Frost et al. 1982) and a goniometer for joint (Boone et al. 1978) or cervical (Kadir et al. 1981) movement as grades. The use of an inclinometer for measuring of spinal movement was described by Loeb (1967). The modification of the Myrin inclinometer (Mellin G 1986b) combines gravitation and compass, which can be interfered with magnetic environment; a Crom inclinometer can be used to remove this influence. Viitanen (1993) used the thoracolumbar rotameter with needle indicator for the assessment of thoracolumbar rotation.

Assessment of the stiffness of dorsolumbar joints.

- The most popular measurements are the Schober test (Schober 1937) extending from the fifth lumbar spinous process to 10 cm above and the modified Schober test (Macrae and Wright 1969) extending from a line connecting the Dimple of Venus to 10cm above and 5 cm below. That chosen by WHO/ILAR is performed as follows: With the patient standing erect, make a mark on the back in the midpoint on the imaginary line joining the posterior superior iliac spines. Make another mark 10 cm above the first. Ask the patient to maximally bend forward, keeping the knees fully extended. With the spine in fullest flexion, measure the distance between the two marks. The normal distance is now greater than 15 cm due to stretching of the skin overlying the mobile lumbar spine. Because there is a marked range of motion between the fifth lumbar and the first sacral vertebrae (Percy 1985), the Schober sacral 1 test from the first sacral spinous process to 10 cm above is used in the Rehabilitation Institute of the Finnish Rheumatism Association (Viitanen 1996). The

normal increase after maximal forward flexion in Schober tests is 5 cm or more. The Schober tests assess only mobility in flexion of the lower lumbar region (Dougados et al. 1998).

- The Stibor test (Tautenhahn 1969, Greene and Hechman 1994), the measurement of the whole spine from the first sacral to the seventh cervical vertebra, allows us to evaluate all the segments and to direct the exercises to the site of earlier decreased mobility. The normal increase after maximal forward flexion is 10 cm.
- The finger-to-floor distance gives additional information on subjective mobility, especially hip mobility and tightness of the posterior leg muscles and ligaments. The reliability of the test is good (Kippers and Parker 1987, Viitanen et al. 1995b).
- Lateral bending of the thoracolumbar spine (Moll et al. 1972, Mellin G 1986a, Domjan et al. 1990, van Linthoudt and Francois 1991) may be one of the first reductions in ROMs (Miller et al. 1984), because the first radiographic changes occur in the junction area of the thoracic and lumbar spine.
- The thoracolumbar rotation can be measured with a tape (Pavelka 1970, Viitanen et al. 1999) or with an instrument (Mellin 1987, Viitanen 1993). The normal values vary and the radiological total rotation has been measured to be 77 degrees (Dvorac et al. 1991), but the impact of age on the values is minimal (Russell et al. 1993).

Assessment of the stiffness of cervical joints. The overall range of cervical mobility can be easily obtained by linear measurements using a tape measure. Lateral flexion, and forward flexion and extension are evaluated by the chin-to-sternum distances (jaws closed), and rotations by the chin-to-acromion distances expressed in centimetres. Instruments i.e. a goniometer and an inclinometer can also be used. These cervical mobility assessments have been evaluated in many publications (Alund and Larsson 1990, Pile et al. 1991, Viitanen et al. 1998). Age affects the normal values (total cervical rotation in adults of 20 years is 150 and of 70 years 110 degrees) (O'Driscoll and Tomenson 1982).

Assessment of the stiffness of costovertebral and peripheral joints. Chest expansion is the only measurement of the thoracic cage. The difference between maximal inspiration and expiration is measured with a tape placed circumferentially around the chest wall, the patient in a standing position. The measurements should be taken at both the fourth intercostal space and the level of the xyphoid process to direct the exercises towards either the upper or the lower ribs (Moll and Wright 1972). In peripheral joint assessment (Greene and Hechman 1994), special attention was paid to hip mobility, even without defined arthritis, because mobility can be restricted by tightness of muscles and ligaments.

Abnormal posture. Abnormal posture of the neck tends to forward transfer of the head as a result of increased lower cervical spine flexion and upper cervical spine extension to maintain the gaze in a horizontal plane. This posture can be assessed by tape measurements (Tomlinson et al. 1986, Viitanen et al. 1998). The occiput-to-wall distance measured with a tape represents the degree of forward position of the head. The distance nape of the neck-to-wall represents the degree of flexed position of the lower cervical spine but is less reproducible than the occiput-to-wall distance. The tragus-to-wall distance is measured with a tape between the ear lobe (tragus) and wall. Gradual increase in the dorsal curve may be aesthetically unpleasant, but in case of major kyphosis can also lead to severe disability by restricting the vertical field of vision. The loss of lumbar curve associated with pelvic retroversion generally precedes dorsal kyphosis. The result is a gradual soft forward position of the centre of gravity, which facilitates the spread of dorsal kyphosis. The back surface curvature measurement has poor reliability and poor correlation with radiological segment measures (Stokes et al. 1987).

Compact sets. Although lumbar spinal flexion, extension and lateral bending together with chest expansion are the mobility criteria for AS, knowledge of their clinimetric properties (Pearcy 1985, Pearcy 1986, Wright 1991) is still insufficient. The spinal mobility restrictions are the outcome measures most commonly used in AS (Bellamy et al. 1991, Laurent et al. 1991, Rigby and Silman 1991, Wright 1991, Calin 1994, Viitanen and Suni 1995) and are also of prognostic value (Amor et al. 1994). There are some recommendations for a compact set of the most reasonable measurements in mobility and posture assessment in AS. The Bath Ankylosing Spondylitis Metrology Index (BASMI) is quick, reproducible and sensitive to change across disease spectrum (Jenkinson et al. 1994). It includes the five most accurately axial status reflecting measurements: modified Schober test, lumbar spine lateral side flexion, intermalleolar distance, tragus-to-wall distance and cervical rotation. Viitanen (1996) combined three clinimetric properties (validity, reliability and sensitivity to change) of measurements, and the finger-to-floor distance, the Schober sacral 1 test and the thoracolumbar rotation scored best. The specific instruments for spinal mobility accepted by WHO/ILAR are the modified Schober, the chest expansion and the occiput-to-wall distance (van der Heijde et al. 1999a).

Correlation with radiology. To assess the validity of different clinimetric properties, a correlation with progressive radiological changes is a good indicator of

permanent disease changes (Bellamy et al. 1991, Viitanen et al. 1995c). The Stoke Ankylosing Spondylitis Spinal Score correlated closely with clinical measures, including modified Schober and occiput-to-wall distance (Averns et al. 1996). The BASMI correlated positively with the total radiology score, while the individual BASMI scores correlated positively with their radiology scores. BASMI and radiology did not relate well to each other as BASMI takes account of normal physical limitation and soft tissue involvement (Kennedy et al. 1995). A correlation between mobility restrictions and radiological changes according to the Dale and Vinje system in AS was seen between radiological sacroiliac joint and lumbar spine progression and eight ROM measurements (Shober test, thoracolumbar flexion, thoracolumbar rotation, finger-to-floor distance, chest expansion, occiput-to-wall distance, chin-to-chest distance and cervical rotation) (Viitanen et al. 1995c). Taylor et al. (1991) observed that occiput-to-wall distance, finger-to-floor distance and spinal flexion correlated positively with both lumbar spine scores and computed tomographic sacroiliac ankylosing score.

4 Functional indices

While physical function may be observed and/or tested by physicians or health care professionals, patients with AS have been found to be valid reporters of their signs and symptoms (Dougados et al. 1988, Dougados et al. 1990, Bakker et al. 1993, Calin et al. 1994, Hidding et al. 1994). The most widely used and accepted self-administered questionnaires in AS are the BASFI (Calin et al. 1994) and the DFI (Dougados et al. 1988). The International Assessments in AS Working Group has recommended instruments for core sets for end-points to be used in research projects in AS (van der Heijde et al. 1999a). The OMERACT IV (van der Heijde et al. 1999b) filter concluded that in the domain of function both the BASFI and the DFI can be used in clinical trials.

There are also other functional indices: the HAQ-S (Daltroy et al. 1990) and a Dutch index (Creemers et al. 1994). In addition, a self-administered instrument defined as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (Garrett et al. 1994), focusing on fatigue, axial pain, peripheral joint involvement, enthesopathy, and morning stiffness, is a valid and appropriate composite to define disease activity in AS. As a simple sum of its components, this instrument has excellent content validity (Calin

et al. 1999c). The Bath group also developed the Bath Ankylosing Spondylitis patient Global score (BAS-G) (Jones et al. 1996).

The BASFI, DFI, HAQ-S and the additional indices are described in detail in Appendix 3a.

A comparison of the functional indices BASFI and DFI was carried out in a systematic literature review (Ruof and Sucki 1999). According to this BASFI was shorter, differentiated patients with mild functional disability better and used more sensitive item scaling. The use of visual analogue scales (VAS)s in BASFI allowed for more change than Likert response scales with only 3 categories. Now DFI with 5 Likert scales has been used in a comparative study of BASFI and DFI; and both BASFI and DFI correlated equally well with disease activity and damage (Spoorenberg et al. 1999a). The mean scores for BASFI were 2.5 (range 0–10) and DFI 8.5 (range 0–35).

BASFI appears to be more responsive than the DFI and the HAQ-S in detecting both improvement and deterioration of functional performance (Ruof et al. 1999a). While BASFI is superior to the DFI in physical therapy trials, it needs to be shown whether BASFI also works in NSAID and DMARD trials as well or even better than the DFI, which has been shown to perform well in these settings. No rule regarding the handling of missing data is provided except in DFI assigning the average of the remaining items to the missing values if no more than three items were missing.

Some questionnaires have been reported to be feasible in AS and FM patients (Bakker et al. 1994, Bakker et al. 1995). The spondylitis functional indices (BASFI, DFI and HAQ-S) have not been evaluated in FM patients, who differ from patients with AS or RA in reporting continuous pain and higher levels of fatigue and pain intensity than AS and RA patients (Mengshoel and Forre 1993).

More research is needed to better define the minimum required methodological steps in the translation and adaptation of cross-cultural health related quality of life measurements (Ferraz MB 1997). Both the BASDAI and the BASFI translations into Swedish were found to be reliable and valid (Waldner et al. 1999, Cronstedt et al. 1999). The French version of BASDAI evinced good clinimetric properties in patients with various forms of SpA (Claudepierre et al. 1997). The transculturally adapted German version of BASFI and DFI has been valid, reliable and internally consistent (Ruof et al. 1999b).

5 Sensitivity to change of spinal mobility and functional indices

In core sets for physical therapy there are specific instruments for spinal mobility (the modified Schober, the chest expansion and the occiput-to-wall distance) and for function (BASFI or DFI) in AS (van der Heijde et al. 1999a).

Sensitivity to change of different spinal movement measures in response to physical therapy has been analysed in some studies:

- The BASMI was sensitive to change after a three-week inpatient course of intensive physiotherapy and exercise (Jenkinson et al. 1994).
- All eight cervical and thoracolumbar ROMs were significantly improved after a four-week inpatient physiotherapy and exercise and disease duration did not influence treatment results (Viitanen et al. 1995d).
- The benefit of intensive two-week inpatient physiotherapy was detected in disease activity, functional ability, global well-being and metrology (Band et al. 1997).
- Factors which correlated significantly with global health after group physical therapy, were improvements in chest expansion, fitness, HAQ-S and reduction of stiffness (Hidding and van der Linden 1995).
- For the Cochrane review (Dagfinrud and Hagen 2002) concerning the scientific evidence of the efficacy of the physiotherapeutic interventions for AS only three randomised controlled trials were available. Two studies compared group physiotherapy with an individualised home exercise programme (Helliwell et al. 1996, Hidding et al. 1993) and the third compared an individually supervised exercise and education programme with no intervention at all (Kraag et al. 1990). Spinal mobility outcomes were measured by finger-to-floor distance, the modified Schober test, chest expansion and cervical rotation. After the group or supervised interventions finger-to-floor distance and cervical rotation improved, but not chest expansion or modified Schober test.

Sensitivity to change of the functional indices in response of physical therapy has also been analysed:

- In comparison of BASFI and DFI in the setting of physical therapy there was some advantage in favour of BASFI (Ruof and Stucki 1999). BASFI values revealed a significant improvement in function (20%) while a less impressive response in DFI (6%) over the three-week period of inpatient treatment was observed (Calin et al. 1994).
- BASDAI showed a 16% improvement during the three-week intensive inpatient physiotherapy (Garret et al. 1994).
- In the Cochrane review (Dagfinrud and Hagen 2002) functional ability was not measured with BASFI nor DFI.

- Hidding et al. (1993) found no significant differences in HAQ-S between supervised group exercise and home exercise during the study period of nine months.
- The Health Assessment Questionnaire (HAQ) (Fries et al. 1980) was not an appropriate means of detecting changes in physical impairments due to short-term exercise therapy (van den Ende et al. 1997).

During the follow-up period of two years Ward and Kuzis (1999) showed that changes in HAQ-S and unmodified HAQ were more closely related to changes in pain and stiffness than were changes in the DFI. Both HAQ-S and unmodified HAQ were also more sensitive to change than the DFI. Ward and Kuzis (1999) concluded that HAQ-S showed greater construct validity and sensitivity to change than the DFI but performed similarly to unmodified HAQ.

The question may arise whether spinal movements are associated with the patient's functional ability in AS. Dalayan et al. (1999) showed that disability strongly correlated with spinal mobility measures. In self-administered questionnaires functional scores correlated well with cervical movements, finger-to-floor distance and chest expansion (Abbot et al. 1994). BASFI significantly correlated with Schober's test, finger-to-floor distance and occiput-to-wall distance, but the DFI only with finger-to-floor distance and occiput-to-wall distance (Ruof et al. 1999b). The correlation between mobility and functional ability was not always clear: females had greater disease activity and functional impairments than males, despite better values according to metrology (Taylor et al. 1998).

Aims of the study

The purpose of the present study was to find the most suitable compact set of spinal mobility measurements and the most suitable functional indices to use for patients with SpAs in clinical and scientific work. The specific aims of the present study were:

1. To evaluate the lumbar, thoracic and cervical spinal mobility measurements by comparing their reliability and validity with radiological correlation (I).
2. To identify the spinal mobility measurements most useful for short-term trials by assessing sensitivity to change after inpatient rehabilitation based on intensive physiotherapy and exercise (II).
3. To evaluate Finnish versions of functional indices BASFI and DFI and to validate them with disease activity, spinal mobility and radiology (III).
4. To examine how improvement in spinal mobility correlates with changes in functional indices (IV).
5. To assess long-term functional changes over three years using the functional indices for comparison (V).
6. To compare the functional ability of patients with SpA and FM using the functional indices (VI).

Patients and methods

1 Patients and rehabilitation

All patients from every part from Finland with AS (diagnosis based on the modified New York criteria, van der Linden et al. 1984) and other SpAs (diagnosis based on the ESSG criteria, Dougados et al. 1991) with spinal involvement and FM patients (diagnosis based on the American College of Rheumatology criteria, Wolfe et al. 1990) in these studies attended a three-week inpatient course on the Rehabilitation Institute of Finnish Rheumatism Association in Kangasala. The diagnostic criteria of the diseases are given in Appendix 1. The regional physicians of the Finnish Social Insurance Institution selected the patients for the courses according to the comprehensive medical certificate written by the attending physicians, mostly specialists in rheumatology. The patients had to be in need of rehabilitation to maintain their work or functional ability. The laboratory tests including ESR, haemoglobin (Hb) and CRP were done in their health-care units before the course, and their general health condition had to be in a stable phase to be able to exercise.

1.1 Patients

The randomisation of this prospective study was done in such a way that consecutive patients were collected. The inclusions and exclusions of the patients in Studies II–VI are presented in the Figure 1. The demographic data of the patients in Studies I–VI are shown in Tables 3a and 3b.

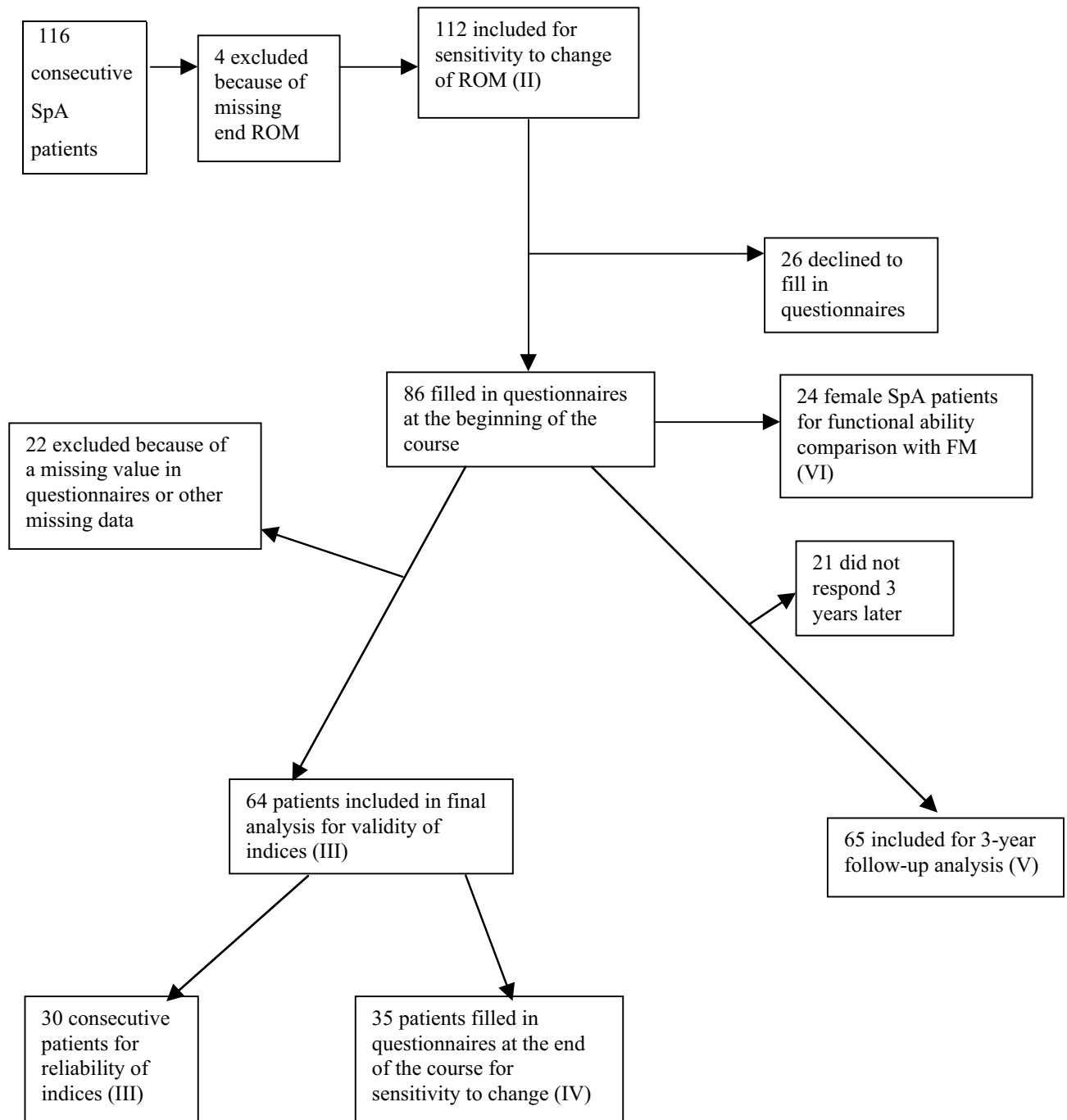


Figure 1. Schematic figure of the exclusion and inclusion of the spondyloarthropathy (SpA) patients in Studies II to VI.

Table 3a. The demographic data of the spondyloarthropathy (SpA) patients in Studies II–VI (the samples were initially derived from the same patient sample in Study II) given as mean and standard deviation (SD); at the beginning of the study. M (male), F (female), ESR (erythrocyte sedimentation rate).

Study	II		III	IV	V	VI
Number	112		64	35	65	24
M:F ratio	74:38		45:19	27:8	44:21	0:24
Gender	Male	Female	Both	Both	Both	Female
Number	74	38	64	35	65	24
Age in years = yrs	47 (9)	48 (11)	46 (10)	45 (10)	49 (11)	49 (13)
Symptom duration,yrs	23 (10)	19 (11)	21 (10)	19 (10)	23 (11)	20 (13)
Duration from diagnosis,yrs	13 (10)	9 (10)	12 (9)	11 (9)	12 (9)	8 (8)
ESR, mm/h	21 (20)	17 (16)	20 (17)	17 (18)	21 (18)	20 (17)

Table 3b. Demographic data of the ankylosing spondylitis (AS) patients in Study I and of the fibromyalgia (FM) patients in Study VI given as mean and standard deviation (SD); at the beginning of the study. M (male), F (female), ESR (erythrocyte sedimentation rate).

Study	I	VI
Diagnosis	AS	FM
Number	52	70
M:F ratio	52:0	0:70
Gender	Male	Female
Age, years (yrs)	45 (11)	47 (8)
Symptom duration, yrs	20 (9)	10 (8)
Duration from diagnosis, yrs	11 (9)	3 (2)
ESR, mm/h	22 (19)	10 (5)

Study I to assess a compact set of spinal mobility measurements included 52 consecutive male patients with idiopathic AS.

Study II to assess the sensitivity to change of mobility tests consisted first of 116 consecutive patients with defined SpA, but four patients were excluded for lack of end measurements having abandoned the course in one and acute infection in three others. From a total of 112 patients (74 male and 38 female) 102 patients fulfilled the modified New York criteria for AS (actually three were juvenile and two possibly undifferentiated SpA), but 15 of them initially had ReA. Psoriatic SpA was found in five patients and enteroarthritis (due to Crohn's disease or colitis ulcerosa) in five patients.

Study III to evaluate Finnish versions of different functional indices was based on 64 patients with SpA out of the former 112 consecutive patients. Eighty-six of these patients filled in the questionnaires but 22 were excluded because of missing values of items in questionnaires or because of other insufficient or incomplete data. The final series thus comprised 64 patients (45 male and 19 female). Most of them had idiopathic AS, nine had initially ReA, three had PsA and two enteroarthritis due to either ulcerative colitis or Crohn's disease. There were no marked differences between included and excluded data. For the reliability analysis of the indices 30 consecutive patients were included.

Study IV to correlate changes in spinal mobility and functional ability consisted of those 35 consecutive SpA patients (27 male and 8 female) from the former third sample who also filled in the questionnaires at the end of the course in addition to the beginning without missing values in items.

Study V for three-year follow-up included 65 patients (44 male and 21 female) of those 86 patients who filled in the questionnaires before the inpatient course. These 65 patients responded to the re-questionnaires three years later by post. Three years later eight patients could not be reached due to unknown new address and 13 did not respond despite being twice invited to do so. The clinical data of those 21 non-responding patients did not differ markedly from those of the study patients at entry, but it is not known what the situation was three years later. Most study patients i.e. 58 suffered from AS with four initially ReA, four enteroarthritis due to colitis ulcerosa or Crohn's disease, one PsA, one juvenile AS and one undifferentiated SpA.

Study VI to compare functional impairment in SpA and FM consisted of 24 female SpA patients from the original sample of 86 patients with both genders who filled in the questionnaires and of 70 female FM patients from the original sample of 76 female FM patients without any inflammatory rheumatic disease. Two of the 26 female SpA patients were excluded, one because of missing items in the HAQ-S questionnaire and one AS patient because of simultaneous FM. Six of the FM patients were excluded by reason of more than one missing item in some questionnaire (five patients in DFI and one patient in BASFI). The exact diagnoses with spinal involvement of the SpA patients were: 17 idiopathic AS, one juvenile AS, three ReA, two enteroarthritis due to colitis ulcerosa, and one undifferentiated SpA.

1.2 Rehabilitation

The inpatient rehabilitation programme was addressed physical, psychological and social aspects. The multidisciplinary group of professionals included physicians (specialists in rheumatology or physical therapy and rehabilitation), physiotherapists, psychologists, social-workers, occupational therapists, nurses, a diet therapist and a foot therapist.

The physiotherapy and exercise programme has been largely unchanged in Kangasala for many years, and has been described previously in detail (Viitanen et al. 1995d). The weekly programme for SpAs includes (frequencies per week as median and duration per one time as minutes in parenthesis): pain relieving local management including local heat, cold and electric treatment modalities (3 times, median and one time duration 10–25 minutes), warm waterpool (6 x 15–25 minutes), group gymnastics/exercise, keep-fit club (9 x 25–30 minutes), individual gymnastic/exercise (2 x 25–30 minutes), individual physiotherapy in suspension (2 x 25–30 minutes), stretching or mobilisation (mean 0.2 x 20–30 minutes) and massage (1 x 20–30 minutes).

The patients also performed self-motivated exercises including walking out in the forests and on the lake shore, swimming in the pool and in the lake, skiing in winter, bicycling in summer etc. and many kinds of individual exercises and not exactly recorded.

Patients got education in several aspects of their diseases, treatment and health in general. They listened to lectures about diseases and drugs, self-management, pain, food, exercise, foot therapy, social benefits and psychological aspects of rehabilitation. They discussed in groups and privately with nurses, a psychologist, a social worker and a diet therapist. They could share thoughts with each other in groups and take part in a social programme including theatre or music. Although the rehabilitation programme included so many things, it was based on intensive physiotherapy and exercise.

The patients were evaluated as a matter of routine by the rheumatologist at the beginning and at the end of the course. During the course patients might have local glucocorticoid injections when needed and obligatory changes in their DMARD or NSAID medications by physicians. Concerning these aspects, among the 86 patients who filled in the questionnaires one patient (1.2%) had begun sulphasalazine two weeks before the course and one patient (1.2%) changed NSAID due to side effects. From the

excluded series two patients began sulphasalazine. Many patients took NSAIDs only when needed and mostly they continued that habit during the course. Some patients could decrease their NSAIDs intake. Thus in total the drug treatment changes were few.

2 Methods

2.1 Radiology

Radiographic records from the health facilities or hospitals in which the patients were treated were used or, if these were not available, recent radiographs were taken for scoring. The detailed radiological assessment was evaluated by the specialist in radiology. (The author did not personally analyse the radiographs.)

The radiological grading based on the method of Dale and Vinje (1985) was used for the sacroiliac joints (Table 2a) and lumbar spine (Table 2b) (Studies I–III), and in addition principally the same assessment method was used for the thoracic and cervical spine in detail (Study I).

Initially the grading of sacroiliac joints involved six stages, but some of them could be combined, thereby reducing the number of stages. It should be noted that the number of grading was from 0 = no changes to 4 = most severe changes in Study I, and from 0 = no changes to 5 most severe changes in Studies II and III.

The sum scores were computed by adding together the sacroiliac plus three spinal area (lumbar, thoracic and cervical) radiological scores. Altogether 23 detailed changes were scored to find out which of them were associated with mobility restrictions due to AS (Study I).

2.2 Mobility measurements

The methods for the mobility measurements are described in Appendix 2 (in Study I measurements numbers 1–17; in Study II measurements numbers 2, 3, 5, 6, 8, 10, 12, 17–21; in Study III measurements numbers 2, 8, 17; in Study IV measurements numbers 2, 3, 5, 6, 8, 10, 17, 21).

In Study I, the evaluation of the whole set, i.e. all 17 ROMs, took 18–19 minutes. Repeated tests (within 72 hours of entry) were carried out without warming-up twice on successive days at the same time (11 a.m. \pm 2 hours – the time interval for each individual patient remained within 1 hour) by the same tester, the personal physiotherapist, for intratester reliability and by another observer, a control physiotherapist (five of the most experienced physiotherapists participated in many standardisation meetings) for intertester reliability assessments. In Studies II–IV the 13 measurements were recorded on average for 2 hours around noon to allow for resolution of morning stiffness. The measurement methods selected here are clinically easy and simple tools, taking 10–11 minutes to implement. The sensitivity to change of measurements in Studies II and IV was assessed as short-term change after a three-week inpatient course.

The validity of the first 17 mobility measurements in Study I was tested by comparing two different modes of assessment – one with an instrument, mostly inclinometer, and the other with a tape, with the exception of thoracolumbar lateral flexion and chest expansion measured only with a tape – with detailed radiological changes in the sacroiliac joints and lumbar, thoracic and cervical spine.

In Study II the validity of mobility tests was shown by computing the correlation between radiological changes in the sacroiliac joints and lumbar spine.

Originally total ROM i.e. the sum of right and left sides in thoracolumbar rotation with the Pavelka method (mm), cervical rotation with an inclinometer ($^{\circ}$) and cervical lateral flexion with an inclinometer ($^{\circ}$) was used but it should be noted that in Studies II and IV the mean of left and right sides was used, for which there was no special reason. The mean of left and right sides of the thoracolumbar lateral flexion was used.

2.3 Functional indices

The functional indices were BASFI, DFI, HAQ-S and the disease activity index BASDAI in addition to VASs for pain, stiffness and patient global assessment. All the indices are based on self-administered questionnaires in which total scores are calculated each by their own rules as explained in Appendix 3a. Although originally the range in BASDAI is 0–10 as in Studies III and V, exceptionally the range was 0–100 in

Studies IV and VI. The range in VASs for pain, stiffness and patient global assessment was originally 0–10 as in Study V and as an exception it was 0–100 in Study IV.

The self-administered questionnaires are in Appendix 3b.

Study III:

The translation of the indices was made in three steps. First, they were translated from English to Finnish by the author (Heikkilä S, specialist in rheumatology). Then a native English-speaking professional linguist translated them from English to Finnish. The translations were similar in content, although some words or word orders were different. Two rheumatologists then discussed the translations and finalised them. Later this professional linguist produced a backtranslation from Finnish back to English, and the result was acceptable in relation to the original English version.

The Finnish versions of the self-administered questionnaires were filled in by the patients making a mark on a scale on the first day of the inpatient course and immediately returning them to their nurse. For reliability assessment a cohort of 30 consecutive patients also filled in the questionnaires on the second day.

To assess the validity of the functional indices BASFI and DFI these were compared with ESR, BASDAI, spinal movement measures (Schober sacral 1 test, chest expansion and occiput-to-wall distance) and radiological changes in the sacroiliac joints and lumbar spine.

Studies IV, V and VI:

For sensitivity to change analysis (Study IV) 35 consecutive patients filled in the questionnaires at the end of the inpatient course. For long-term follow-up (Study V) the patients filled in the same questionnaires three years later by post, where they also answered the dichotomously assessed questions about their state of health and events occurring in their lives as well as an open question regarding their opinion of things having an impact on their functional ability during the follow-up period. For comparing functional impairment of SpA and FM (Study VI) female patients of both groups filled in self-administered questionnaires: BASFI, DFI, HAQ-S, and BASDAI.

Missing values. For the reliability (Study III), validity (Study III) and short-term sensitivity to change (Study IV) analyses no missing values in the items of functional indices were allowed; if there was even one, the patient was excluded. In other studies

(Studies V and VI) the missing values were corrected by the mean value (in BASFI, HAQ-S and BASDAI) and by the mode value (in DFI) of the remaining items.

3 Statistical analysis

Statistical analyses were performed with SPSS (8.0) and SamplePower (version 1.0) software.

Study I: The results were given as means, standard deviations (SD), ranges from minimum to maximum. The correlation between spinal measurements and detailed radiological changes were expressed as non-parametric Spearman's correlation coefficients for the evaluation of validity of each test. Radiological sum scores were average scores calculated from the data on each individual mean score of four radiological areas. The reliability of the mobility measurements indices was given as intraclass correlation coefficients (ICC)s of intertester and intratester.

Study II: The results were given as means, SD, 95% confidence interval (CI), and effect size (ES), i.e. mean change in a test after an intensive course divided by SD of the mean at the onset. Non-parametric Spearman correlation coefficients were used between changes in the mobility tests and other variables to assess the cardinal clinimetric properties of these tests. The statistical power of all measurements was over 95% ($\alpha = 0.05$).

Study III: The data was given as medians, minimum-maximum, means and SD. The coefficient of internal consistency of indices was given as Cronbach's alpha. Reliability was calculated in ICCs. The correlation between BASFI and DFI was given as Spearman's correlation coefficient (r , 95% CI). Spearman's correlation coefficients (r) and age-adjusted values (r') were used between functional indices and other variables to assess the cardinal clinimetric properties of the indices for validity evaluation.

Study IV: The results were given as means \pm SD, ranges, 95% CI, and ES. Wilcoxon's signed rank test and paired t-test were used for statistical evaluation of the change after the inpatient course. Relationships between variables were assessed by non-parametric Spearman rank order correlation.

Study V: The results were given as means, SD and 95% CI. The statistical analyses were performed using the paired t-test and non-parametric Wilcoxon's signed

rank test for paired groups for statistical evaluation of the change after three-year follow-up. The alpha-level was 0.05 in all tests.

Study VI: The demographic data were given as means, SD and range. Normality assumptions were verified, and the medians with interquartile ranges (IQR) of variables were given. The significance of the median differences of variables between SpA and FM were calculated by non-parametric Mann-Whitney U test with Monte Carlo significance and 95% CI.

Results

1 Radiology

Studies I–III:

These results are only briefly described in this dissertation, taking the view that it is restricted to the clinically important aspects. The distribution of radiographic changes varied from initial or no changes to the most severe changes in all those three studies (I–III) where radiological evaluations were used. More than half of the patients had severe changes (grades 3–4) in lumbar and thoracic spine compared to cervical spine, where changes were mostly milder (grades 0–2). The radiological changes were more severe in men than in women, but only slightly worse in those patients who were included in the sample of functional indices (III) compared to the original sample (II).

2 Spinal mobility measurements

2.1 Reliability

Study I:

The ICC showed highly significant reproducibility in the intra- and interobserver assessments of the 17 standardised measurements (measurements numbers 1–17 in Appendix 2). The ICC for intertester assessment varied from 0.84 (thoracolumbar rotation measured with an instrument) to 0.98 (thoracolumbar lateral flexion as finger-thigh test and the cervical rotation measured with an inclinometer). The ICC for intratester reliability was commonly better and varied from 0.87 (thoracolumbar rotation measured with an instrument) to 0.98 (thoracolumbar lateral flexion as finger-thigh test and the cervical rotation measured with a tape). The greatest difference in ICC between intertester and intratester was in chest expansion, where ICC for intertester assessment was 0.85 and for intratester 0.95.

2.2 Correlation with radiology

The correlation between ROM and radiology can be used for the evaluation, whose ROM reflects the radiographic progression. It is noteworthy that the correlation was negative if ROM decreased with increasing radiological changes, and positive, if ROM increased with increasing radiological changes. Mostly the correlation was negative with the exception of finger-to-floor, chin-to-chest, occiput-to-wall and tragus-to-wall and distances. In this dissertation and in the original publications only the absolute values of correlation without positive or negative signs were used.

Study I:

Among the 17 mobility measurements (measurements numbers 1–17 in Appendix 2) the significant correlations of the mobility measurements with the radiographic changes in the sacroiliac joints and different parts of spine were the following.

The radiographic changes in the sacroiliac joints correlated significantly with the following mobility measurements:

- modified Schober test
- thoracolumbar flexion
- thoracolumbar rotation measured with a tape
- thoracolumbar lateral flexion measured as finger-thigh test
- both cervical lateral flexions

The radiographic changes in thoracolumbar and cervical spine correlated significantly with the following mobility measurements:

- both Schober tests
- both thoracolumbar lateral flexions
- thoracolumbar flexion and thoracolumbar rotation measured with a tape
- occiput-to-wall distance, tragus-to-wall distance and cervical extension measured with an inclinometer

The radiographic changes in cervical spine only correlated with the following cervical mobility measurements:

- both cervical lateral flexions
- both cervical rotations
- cervical flexion measured with an inclinometer

Other measurements, i.e. thoracolumbar rotation measured with an instrument, chin-to-chest distance and chest expansion, showed only weak or no correlation with the

detailed radiological changes. The only measurement having no correlation with the sum score was cervical flexion measured with an inclinometer.

Various ROMs correlated highly or moderately significantly with the following detailed radiological changes in the spine: syndesmophytes, changes in the apophyseal joints, straightened anterior surfaces of vertebrae, calcification of discs and ossifications of the anterior long and posterior interspinal ligaments. Other detailed radiological changes in the spine, like mixed osteophytes or unilateral asymmetric ossifications, did not correlate with limitations in mobility. In general calcifications of the ligaments, i.e. syndesmophytes and anterior and interspinal ligaments, showed the most marked correlation with restrictions in mobility.

Study II:

The radiological sacroiliac and lumbar changes correlated with all mobility tests (measurements numbers 2, 3, 5, 6, 8, 10, 12, 17–21 in Appendix 2) highly significantly, the lowest correlations being in internal hip rotation and shoulder abduction, and the highest in the Schober sacral 1 test.

2.3 Correlation with disease duration and age.

Study II:

All 13 mobility measurements (measurements numbers 2, 3, 5, 6, 8, 10, 12, 17–21 in Appendix 2) showed significant correlations with disease duration from initial symptoms, Spearman's rho ranging from internal hip rotation ($r = 0.22$; $p < 0.05$) and shoulder abduction ($r = 0.27$; $p < 0.001$) to the occiput-to-wall distance ($r = 0.49$; $p < 0.001$).

Thoracolumbar rotation measured with a tape ($r = 0.15$) and internal hip rotation ($r = 0.04$) did not correlate markedly with age, while all other measurements did, i.e., Spearman's rho ranged from 0.23 in finger-to-floor distance to 0.46 in intermalleolar distance. Age affected the results, especially those for intermalleolar distance, thoracolumbar lateral flexion as finger-thigh test, occiput-to-wall distance, cervical lateral flexion measured with an inclinometer and cervical rotation measured with an inclinometer.

2.4 Sensitivity to change

Studies II and IV:

In Study II 13 mobility measurements (measurements numbers 2, 3, 5, 6, 8, 10, 12, 17–21 in Appendix 2) were performed before and after a three-week inpatient course. All measurements improved, and it was notable that the change was marked with a minus sign in finger-to-floor distance and occiput-to-wall distance indicating that decrease in these distances means improvement. A positive value for ES corresponded to improvement for any of the ROM measures in this study. (In general, an ES of 0.2–0.5 is small, 0.5–0.8 is moderate, and ≥ 0.8 is considered to be a substantial effect.) The ES varied from 0.16 (occiput-to-wall distance) to 0.43 (finger-to-floor distance). The most significant improvement was seen in the following spinal measurements: finger-to-floor distance (ES = 0.43), thoracolumbar rotation measured with a tape (ES = 0.40), chest expansion (ES = 0.39), and thoracolumbar lateral flexion as finger-thigh test (ES = 0.32), in that order. Hip and shoulder ROMs also improved markedly (ES = 0.29–0.40), while in the Schober sacral 1, thoracolumbar flexion and occiput-to-wall distance no marked effect was observed (ES = 0.16–0.18). The spinal ROMs in samples II and IV were comparable as shown in Table 4.

Table 4. The means with standard deviation (SD) at entry and effect sizes (ES) of the mobility measurements in Studies II and IV shown for comparison between the two samples.

	Mean (SD)		ES	
	II	IV	II	IV
Schober sacral 1, mm	32 (17)	32 (18)	0.18	0.17
Thoracolumbar:				
– Flexion, mm	62 (30)	58 (31)	0.17	0.15
– Rotation (with a tape), mm	22 (15)	20 (19)	0.40	0.30
– Lateral flexion (finger-thigh), mm	101 (65)	101 (52)	0.32	0.26
Finger-to-floor distance, mm	174 (157)	118 (154)	0.43	0.61
Chest expansion, mm	36 (18)	47 (19)	0.39	0.47
Occiput-to-wall distance, mm	55 (70)	45 (76)	0.16	0.15
Cervical rotation, degrees	46 (20)	51 (20)	0.30	0.37

It can therefore be seen that the values of the original sample (II) and the smaller sample derived from it (IV) for correlation analysis with functional indices did not markedly differ.

3 Finnish versions of the functional indices

Study III:

There were no special problems in filling in the questionnaires, except question 4 in the DFI asking ‘Can you get into a bathtub?’. (There were some individual questions with missing answers here and there: altogether among those 86 patients who filled in questionnaires, missing values were found in 10%, 10%, 2% and 1% of answers concerning the DFI, HAQ-S, BASFI and BASDAI questionnaires, respectively.)

3.1 Reliability

The ICC showed good reproducibility 0.99 in BASFI, 0.98 in the DFI and 0.97 in BASDAI. The coefficient of internal consistency (Cronbach’s alpha) for both BASFI and DFI was 0.94 and that for BASDAI 0.88.

3.2 Validity

BASFI correlated markedly with radiological scores for the lumbar spine (Spearman’s rho = 0.48) and sacroiliac joints (Spearman’s rho = 0.36), and the DFI only with the lumbar spine (r = 0.32). The correlation of the spinal mobility measurements, Shober sacral 1, chest expansion and occiput-to-wall distance was significant with both functional indices. The direction of correlation was relevant: the higher score in the functional indices correlated with lower spinal mobility i.e. r is negative. Again the correlation of occiput-to-wall distance was of inverse significance, because in this case a small value meant better condition in a patient’s ROM. The correlation of the functional indices with BASDAI was highly significant, Spearman’s rho = 0.74 for BASFI and Spearman’s rho = 0.69 for the DFI. Only the DFI correlated with age, and

age-adjusted correlation between the mobility measurements showed a slightly more marked effect of age on the DFI than on BASFI. The functional indices correlated neither with ESR nor with disease duration.

3.3 Sensitivity to change

Study IV:

BASFI and HAQ-S, but not the DFI, proved to be sensitive enough to detect significant improvement ($p < 0.05$) after three-week rehabilitation. The mean changes in VAS values for stiffness and pain, BAS-G and BASDAI showed highly significant improvements.

4 Correlation of changes in mobility and function

Study IV:

Thoracolumbar rotation measured with a tape and finger-to-floor distance were the only measurements where changes correlated significantly with changes in functional indices and pain. Changes in BASDAI and pain correlated with changes in thoracolumbar rotation measured with a tape. Changes in patient's global assessment and stiffness VAS did not correlate with any mobility improvement. Thus thoracolumbar rotation measured with a tape and finger-to-floor distance would seem to be the most recommendable clinical measurements for short-term trials since they also reflect changes in function, also thoracolumbar rotation measured with a tape in disease activity.

5 Functional changes during three-year follow-up

Study V:

Functional deterioration was significant in BASFI and the DFI over three years, while changes in HAQ-S were minimal and not significant. BASFI deteriorated more than the DFI. Assessments on BASDAI, BAS-G and stiffness-VAS, showed the presence of

significant deterioration. Fifty out of the 65 patients reported many individual changes in their lives and health situation during the three-year follow-up period. Many factors occurring during the three-year period may have influenced the results of the indices.

6 Comparison of functional indices between spondyloarthritis and fibromyalgia

Study VI:

Self-evaluated functional capacity was only slightly poorer among SpA than among FM patients. The difference was not even statistically significant in BASFI, but was within the limits of significance in the DFI and HAQ-S. BASDAI was poorer among FM patients, and the difference was statistically significant. The functional differences between SpA and FM increased concomitantly with higher score values for functional decline. BASDAI showed higher activity levels in FM than in SpA throughout.

Discussion

Now it is possible to use internationally recommended instruments in the Rehabilitation Institute of the Finnish Rheumatism Association and in rehabilitation courses in general for Finnish SpA patients with spinal involvement. It was reasonable to expand the target group from solely idiopathic AS, because in practice the rehabilitation programme is suitable for all rheumatic axial diseases. I agree with Dougados (1995) that we need to be more problem-oriented and less disease-oriented.

1 Spinal mobility measurements

The spinal measurements used here (Studies I-II) included more measure assessments, a total of 21 (Appendix 2), than in general. Limitation of spinal movement is an important feature of AS (Bennet and Burch 1968) and different sets of measurements have been recommended. Pile et al. (1991) considered that suitable measurements for the continuing assessment of patients with AS would be modified Schober index as a measure of lumbar spinal flexion, cervical seven to iliac crest line distraction as a measure of flexion of the thoracic and upper lumbar spine, fingertip-to-floor distance as a measure of lateral flexion of the thoracolumbar spine, cervical rotation and cervical lateral flexion measured with a goniometer. They considered these to be the minimum number necessary to measure spinal function. BASMI from the Bath group (Jenkinson et al. 1994) included modified Schober test, intermalleolar distance, lumbar lateral flexion measured by fingertip-to-floor distance, cervical rotation and tragus-to-wall distance. The WHO/ILAR recommendations included only modified Schober test, chest expansion and occiput-to-wall distance (van der Heijde et al. 1999a).

In the present dissertation age correlated with all spinal movement measurements except thoracolumbar rotation, and all mobility measurements correlated with disease duration: increase in age and disease duration caused deteriorated mobility (Study II). This is in accordance with a previous study (Viitanen et al. 1995a), where thoracolumbar rotation had the best age-adjusted correlation with disease duration. Many individual factors like age and sex affected spinal ROM in a large adult population of over three thousand people (Batti's et al. 1987) and total lumbar sagittal

ROM declined as age increased (Sullivan et al. 1994). The impact of gender was not investigated here.

In general the validity of measurements when compared to radiological changes (Study I) was good and this is in accordance with the other compact set of BASMI, which was also valid (Kennedy et al. 1995). In the study by Viitanen et al. (1995c) all tested mobility measurements (Schober sacral 1 test, thoracolumbar flexion, thoracolumbar rotation, finger-to-floor distance, chest expansion, occiput-to-wall distance, cervical rotation and chin-to-chest distance) also correlated with radiological changes in sacroiliac joints and lumbar spine. The value of validation of movement measurements might be reduced when restricted to sacroiliac joints and lumbar spine. There were more spinal areas for radiographic correlation in Study I, where measurements other than cervical flexion correlated with the sum score of radiological changes in the sacroiliac joints and lumbar, thoracic and cervical spine. However, there were some variations in correlation between measurements and individual radiological findings of different spinal areas.

The validation of ROM rating against radiological findings entails difficulties. Is it desirable to validate a single measurement only with the corresponding area of spine where this actual movement occurs? AS mainly affects the thoracolumbar spine as shown in Study I. The lumbar spine permits considerable lateral bending in the upper and middle portions, while flexion-extension is greatest in the lumbosacral motion segment. Thus, is it correct to validate these movements only with the radiographic findings of the exactly restricted spine area? Perhaps it is not practical and the sum score mentioned in Study I might be one solution to the problem. The interference effect of muscle tension on ROM reduces the value of validation, but this could be diminished by correlating radiological changes with ROM values after an intensive rehabilitation course.

The intra- and intertester reliability of measurements was good in all measurements in Study I. Partly this reflected the competence of the physiotherapists. The reliability of finger-to-floor distance was not tested in the present study, but previous tests done in the same institute showed it to be excellent, the intra-observer ICC being 0.97 and the inter-observer ICC being 0.98 (Viitanen et al. 1995d). The other only tests elsewhere analysed were intermalleolar distance (Jenkinson et al. 1994) and internal hip rotation and shoulder abduction and flexion (Greene and Hechman 1994). It is notable that reliability of chest expansion was also good in this study having been

poor in previous studies (Pile et al. 1991, Viitanen et al. 1995b). Excellent reliability is a good basis for studies of sensitivity to change due to rehabilitation.

One limitation in this study of the spinal movements was the lack of a control group. The literature contains other spinal diseases with reduction of mobility. Facet joint osteoarthritis affected spinal motion, and axial rotational motion was most affected by disc degeneration (Fujiwara et al. 2000). Diffuse idiopathic skeletal hyperostosis patients had a greater reduction in neck rotation and in thoracic and lumbar movements than healthy controls (Mata et al. 1997). Moreover, the patients with low back pain had restricted measures of spinal mobility (Thomas et al. 1998), and they had smaller ranges of movement than those without low back pain (Barrett et al. 1999).

2 Functional indices

The International Assessments in AS Working Group has developed and WHO/ILAR has accepted BASFI and the DFI for the assessment of function in AS. This allows comparison of the results of clinical SpA trials internationally. The validity should be tested in several countries to be sure that language or cultural differences do not interfere with the results. This has been done in several European countries including Sweden for Scandinavia (Cronstedt et al. 1999, Waldner et al. 1999). Now it has also been performed in Finland in Study III of the dissertation.

It was easy throughout for patients to answer the questions, except for the DFI question ‘Can you get into a bathtub?’. The explanation might be that in Finland bathtubs are by no means common. There were no publications addressing how to react to the missing values. In some studies it was mentioned how, according to the authors, the mean value of other scores was used to replace the missing value if no more than two or three item values were missing in the DFI (Ruof and Stucki 1999, Spoorenberg et al. 1999a). There was no rule regarding the handling of missing data in BASFI (Ruof and Stucki 1999). No corrections were used in the validation study, and patients with even one missing value in any questionnaire were excluded. This led to smaller sample of included patients.

Single missing values were found here and there (Study V): more often in the DFI (10% of patients) than in BASFI (2% of patients) the frequency being comparable with the others, 15% and 4% respectively (Spoorenberg et al. 1999a). The only typical missing value was question four in the DFI. This reduces the value of the DFI in

Finland, but in future explicit rules for treating missing values may emerge (Ruof and Stucki 1999). The DFI also has problems in the Likert scale, because it allows the patient to make the mark between scale points and it has to be remembered how one has reacted to these marks. The original DFI contained 3-point Likert scale and it was used in the present study, but nowadays authors have used the 5-point Likert scale, which allows more alternatives thereby improving the sensitivity to change.

The mean BASFI score here in Study III (3.7) was only slightly higher than the outpatients' mean score (3.6) and clearly lower than the hospital patients' mean score (5.1) in the study by Calin et al. (1994). The mean BASFI score has been higher in hospital patients than in outpatients. The series consisted of inpatients on rehabilitation courses, but the subjects did not need to be hospitalised. Functional difficulties at work or at home were a condition for admission to the course. The mean BASDAI score in the present Study III was 4.2, whereas in the French version of BASDAI tested among inpatients and outpatients, their mean score was 4.8 (Claudepierre et al. 1997). The median BASFI score was 3.6 and median BASDAI 4.4 in a study on the Swedish versions of these indices (Cronstedt et al. 1999, Waldner et al. 1999).

BASFI and DFI results were easily reproducible and showed good concurrence in Study III, as previously documented (Spoorenberg et al. 1999a). There were no problems for patients to produce the same values in questionnaires on consecutive days. Thus the test-retest ICCs were excellent and the coefficients of internal consistency were also good. This is a valuable basis for sensitivity analysis.

Validation is a difficult task, and it will always be a challenge when analysing functional ability. What are the measures against which functional indices are to be rated? The assessment of specificity is problematic in the functional indices, and that aspect was not investigated. These indices are not meant to be diagnostic instruments. Many diseases, even other than rheumatic, may lead to similar declines in functional ability. But now in this connection one naturally considers how well functional ability correlated with other findings of the SpA disease spectrum. The correlation with movement measurements is a good target in this rheumatic disease, because limitations in ROM are those of the principal long-standing findings. The other target is the correlation between permanent changes, i.e. radiographic findings, which are generally seen first and mostly in the sacroiliac joints and lumbar spine. Here in Study III these parts of radiographic changes were used. On the other hand, focusing solely on these areas may reduce the value of validation.

Although cultural and language validation was the main purpose of the validation process as the present task producing good results showed, as earlier mentioned, other aspects were also considered. Both functional indices correlated with the spinal movement measures and radiographic findings and BASDAI. This concurred with other more extensive studies (Spoorenberg et al. 1999a), where BASFI and the DFI correlated equally well with disease activity and damage. The functional indices did not correlate with ESR, whose value is limited in clinical AS trials (Ruof and Stucki 1999). BASFI and the DFI were both reliable and valid among Finnish patients with SpA (Study III), but BASFI is more usable: it includes fewer questions, it is easier and simpler.

In Study III, BASDAI's ICC was good and correlated well with the functional indices BASFI and the DFI. As a simple sum of its components, BASDAI has excellent content validity (Calin et al. 1999c).

Patients with FM seemed to experience functional impairment as patients with SpA, but the results of Study VI were based on self-administered instruments, reflecting the symptoms of the patients. There are reports that the discrepancy between self-report questionnaires and observed functional ability is a most striking feature in FM (Hidding et al. 1994). The aim of this study, however, was to test the self-administered indices.

3 Correlation of functional ability and spinal mobility

Study III showed the correlation between mobility (Shober sacral 1 test, chest expansion and occiput-to-wall distance) and functional ability (BASFI and the DFI). Evaluation has also been done by Ruof et al. (1999b): the BASFI was significantly correlated with Schober test, finger-to-floor distance and occiput-to-wall distance, but the DFI only with finger-to-floor distance and occiput-to-wall distance. The values of functional indices and spinal mobility measurements have been compiled in Table 5 and their correlation evaluated in Finland (Study III), in the Netherlands (Spoorenberg et al. 1999a) and in USA (Ward and Kuzis 1999) for purposes of comparison.

Table 5. Functional indices and spinal mobility measurements and their correlation in Finland (Study III), the Netherlands (Spoorenberg et al. 1999a) and in USA (Ward and Kuzis 1999). FI (functional index), BASFI (the Bath Ankylosing Spondylitis Functional Index), BASDAI (the Bath Ankylosing Spondylitis Disease Activity Index), DFI (the Dougados Functional Index), ROM (range of motion).

	Finland Median (range) in FI, Mean (range) in ROM	Netherlands Median (range)	USA Median (IQR)
BASFI (0–10)	3.1 (0.2–9.2)	2.5 (0–10)	
DFI (0–40)	9.0 (0–26)	8.5 (0–35)	11 (4–17)
BASDAI (0–10)	4.3 (0.6–8.4)		3.6 (0–9.4)
Occiput-to-wall distance, cm	6.0 (0–36)		3.6 (0–10.2)
Chest expansion, cm	3.3 (0–7)		2.3 (1.3–3.7)
Schober, cm	3.0 (0–7)		3.0 (1.5–4.1)
Correlation between FI and ROM as Spearman's rho (r):			
BASFI/DFI	0.85	0.89	
BASDAI/BASFI	0.74	0.59	
BASDAI/DFI	0.69	0.57	
DFI/Occiput-to-wall	0.36		0.14
DFI/Chest expansion	–0.26		–0.27
DFI/Schober	–0.49		–0.13

4 Sensitivity to change due to rehabilitation

The instruments for assessing sensitivity to change must be very reliable to ensure true changes in measures. The reliability of the mobility measurements (Study I) and the functional indices (Study III) used here was sufficient. In Studies II and IV sensitivity to change is evaluated by response to the three-week inpatient course of intensive physiotherapy and exercise. The core set for physical therapy includes specific instruments recommended by the AS Working Group: in spinal mobility modified Schober test, chest expansion and occiput-to-wall distance and in function BASFI or DFI indices (van der Heijde et al. 1999a).

4.1 Sensitivity to change of spinal mobility measurements

In Study II all mobility measurements improved as a response to a three-week inpatient course of intensive physiotherapy and exercise. This concurs with the study by Viitanen

et al. (1995d), where all thoracolumbar and cervical ROMs used improved significantly after a three- or four-week inpatient course and disease duration did not influence treatment outcome. BASMI was sensitive to change in response to a three-week inpatient course of physiotherapy and exercise (Jenkinson et al. 1994). The Cochrane review (Dagfinrud and Hagen 2002) showed a significant improvement in finger-to-floor distance and cervical rotation, but not in modified Schober test or chest expansion comparing between group physiotherapy and home exercise or between individual supervised exercise and no intervention. However, their treatment periods were much longer than in the present study; only one study compared a three-week inpatient programme with a six-week outpatient programme, and in that study cervical rotation improved significantly in the inpatient group, but not modified Schober test nor chest expansion (Helliwell et al. 1996).

To some extent there are variations in the ESs of different ROMs in response to treatment. In Study II the most significant improvement was seen in finger-to-floor distance, chest expansion, thoracolumbar rotation measured with a tape and thoracolumbar lateral flexion as finger-thigh test, the results of which compare well with the study by Viitanen et al. (1995b), where thoracolumbar rotation measured with an instrument, finger-to-floor distance and chest expansion were the most sensitive measurements after an inpatient course. These concur with international findings, where finger-to-floor distance and chest expansion have been sensitive in addition to changes in cervical rotation (O'Driscoll et al. 1978, Tomlison et al. 1986, Roberts et al. 1989), but thoracolumbar rotation was not included in the endpoint measurements. The sensitivity of the Schober test was not good (ES only around 0.2) in any of these studies, and the ES values of chest expansion and occiput-to-wall distance fluctuated. Even though finger-to-floor distance is affected by tight muscles and tendons, it is suitable in short-term trials because the improvement in values correlates with improvement in function.

Spinal mobility measurements have also improved during intense physical exercise in other conditions. Lateral bending and rotation of spine improved highly significantly and flexion significantly during a rehabilitation outpatient course in chronic back pain patients (Hupli and Pylkkönen 1998). Spinal rotation and erector spinae flexibility improved significantly with intensive training in subjects with low back pain, but the gains achieved gains in spinal and muscle flexibility may not be able to be maintained without continued exercise (Kuukkanen and Malkia 2000). On the

other hand, only one 10-minute sports stretch resulted in a significant elongation of the hamstrings (Halbertsma et al. 1996).

4.2 Sensitivity to change of functional indices

BASFI was sensitive enough to detect significant improvement during the rehabilitation course in Study IV. The DFI was not sensitive. This concurs with the previous findings by Calin et al. (1994) and Ruof and Stucki (1999), where in the setting of physical therapy there was also some advantage in favour of BASFI. The DFI with 5-point Likert scale acts differently from 3-point Likert scale DFI in the assessment of sensitivity to change. The effects of a two to three week inpatient rehabilitation course on functional indices in Finland (Study IV), England (Calin et al. 1994, Garrett et al. 1994) and Sweden (Cronstedt et al. 1999, Waldner et al. 1999) have been compiled for purposes of comparison in Table 6.

Table 6. Effects of a short-term inpatient rehabilitation course on functional indices in Finland (Study IV), England (Calin et al. 1994, Garrett et al. 1994) and Sweden (Cronstedt et al. 1999, Waldner et al. 1999). SD (standard deviation), BASFI (the Bath Ankylosing Functional Index), DFI (the Dougados Functional Index), BASDAI (the Bath Ankylosing Spondylitis Disease Aactivity Index).

	At entry			Mean change		
	Finland Mean/SD	England Mean/SD	Sweden Median/range	Finland	England	Sweden
BASFI (0–10)	3.9 (2.7)	4.8 (2.0)	3.1 (0–8.1)	–0.50*	–1.07*	–1.1***
DFI (0–40)	11.2 (7.6)	12.4 (5.7)		–0.31	–0.32	
BASDAI (0–10)	4.53 (2.35)	4.31	4.4	–1.4***	–0.87**	–1.9***
- (range)	(0.8–8.4)	(0.5–10)	(0.5–7.7)			

* p<0.05, ** p<0.01, *** p<0.001

The question may arise as to whether the indices improve without treatment. The solution for this is that the study must be a controlled trial. There was also a control group for sensitivity analysis consisting of 18 consecutive SpA patients on a waiting list for the rehabilitation inpatient course. The control group filled in the questionnaires at home without any inpatient rehabilitation treatment about three months before the inpatient course. They filled in the questionnaires at time zero and immediately mailed them to the institute; and three weeks after that without inpatient rehabilitation and again mailed them to the institute. The values of the control group have been published elsewhere (Viitanen and Heikkilä 2001). The values of these questionnaires in the control group at home without treatment did not change significantly.

4.3 Sensitivity to change of both, functional ability and spinal mobility and other variables

Study IV the changes in functional capacity were slighter when compared with mobility after the rehabilitation course. The correlation between changes in mobility and function was also poor in Study IV; the only correlations were in changes between BASFI and finger-to floor distance as well as between the DFI and finger-to-floor distance and thoracolumbar rotation measured with a tape, but DFI did not change significantly during the inpatient course. It remains obscure how the poor correlation between the changes in spinal mobility and functional ability can be explained. The functional indices BASFI and the DFI had a better discriminant validity than mobility measurements (chest expansion, finger-to-floor distance, occiput-to-wall distance and the Schober test) in AS between placebo and NSAID (Calin et al. 1999b).

HAQ-S improved significantly during the course as did BASFI. This is surprising, because HAQ has not been appropriate of detecting changes due to short-term exercise therapy (van den Ende et al. 1997). Here the unmodified HAQ was not analysed, even though it would be possible, because HAQ-S includes only two additional subscales of the questions.

In the core set for physical therapy the domains in addition to the previously mentioned function and spinal mobility are pain, patient's global assessment and stiffness (van der Heijde et al. 1999a). The recommended instruments for spinal pain due to AS to include VAS at night and VAS without time restraints on average last

week. The instrument for stiffness is specified by VAS duration of morning stiffness of spine and for patient's global assessment by VAS on average during the last week. In the present study the VAS assessments were not so exactly specified.

All these pain, stiffness and patient's global assessment VASs improved significantly during the inpatient course (Study IV). Trials were also found to assess the effect of rehabilitation on pain, function and global assessment in other conditions, AS excluded. A three-week multidisciplinary intensive treatment programme could reduce pension expenditures, sick leave days, health care contacts and pain in patients with chronic low back pain (Bendix et al. 1996). The Cochrane review (Guzman et al. 2002) provided evidence that intensive multidisciplinary bio-psycho-social rehabilitation with a functional restoration approach alleviated pain and improved function in patients with chronic low back pain, but only few trials reported effects on global assessments.

4.4 The role of rehabilitation

Though the inpatient course was based on intensive physiotherapy and exercise, many other things also happened during the rehabilitation course. The influence of psychosocial factors will always be present, because the rehabilitation is aimed at many-sided effects. According to Dougados et al. (1998) the education of the patient is one part of the therapy of SpA, and this was included in the programme. The recreation during free-time and cessation of the work had a great impact, too. It is better to speak about the effect of the rehabilitation, even though the course was based on intensive physiotherapy and exercise.

Analysing the effect of rehabilitation alone is problematic in inflammatory active rheumatic diseases demanding medical interventions. During the rehabilitation course only few changes in medication were needed. There is no simple answer whether patients with local glucocorticoid injections should be included or excluded. If they were excluded, it might lead to selection bias of too mild cases. Most of patients took NSAIDs only when needed and many patients were able to reduce their intake during the course. In the present study no specific joint count was used. In core sets for DMARD and clinical record keeping, the number of swollen joints (44 joint count) (Scott et al. 1994) was recommended as a domain of peripheral joints and entheses as instruments for AS but currently no preferable instrument was available for entheses

(van der Heijde et al. 1999a). Perhaps in the future better drug treatment options may lead to milder case analyses and better chances to keep the inflammation stable without the interfering impact of pharmacological interventions on rehabilitation.

5 Functional long-term changes

One purpose of the study (Study V) was to assess the long-term functional changes of SpA patients. The clinimetric properties of the eligible indices and measurements should be evaluated in various situations, so that optimal tools can be selected for all purposes. During the follow-up of three years functional capacity deteriorated. BASFI and DFI deteriorated significantly but HAQ-S did not change significantly during this three-year period. This finding was in contrast to Ward and Kuzis (1999), who showed that HAQ-S was more sensitive to change over a period of two years than the DFI. Anyway, the natural course of the functional capacity of patients with SpA appears to be one of impairment, when evaluated using these indices. The results of the indices were so compatible that the functional deterioration is reliable.

Many events occurred during the three-year follow-up that might affect the functional capacity of patients. It is very difficult to isolate any effect of rehabilitation in a long-term follow-up study, since so many confounding factors may affect the follow-up population over several years.

Significant deterioration of the values of functional indices indicated that the functional capacity of patients with SpA tends to deteriorate with time despite use of conventional treatment. The deterioration still presents a challenge to the health care system. How this trend can be delayed, is an important question, and the inpatient course may be one answer to this problem, because the improvements occurred during the course. How long this positive effect lasts, is the aim of future studies.

6 Recommendations, weaknesses and subjects for further study

The recommendations for rehabilitation courses is to use BASFI for functional ability assessment, and finger-to-floor distance, thoracolumbar rotation measured with a tape, chest expansion, thoracolumbar lateral flexion as finger-thigh test and cervical rotation

measured with an inclinometer for a compact set of spinal mobility assessments. If only a few mobility measurements are taken, it is worth including the international recommendations, i.e. Schober test, chest expansion and occiput-to-wall distance, but also thoracolumbar rotation measured with a tape. The selection of the recommendations also depends on the purpose of the measurements.

Weaknesses and arguments. There are many weaknesses in this dissertation. The methodology is inconsistent to some degree in the various studies, but this has no essential influence on the main results or conclusions. The lack of a control group was an obvious limitation in drawing conclusions about the effect of the rehabilitation. Actually it was not the aim to show scientific evidence of the effectiveness of the rehabilitation but only to analyse the instruments, their validity, reliability and sensitivity to change, for purposes of future research. The spinal mobility measurements were not analysed in other conditions, but it was known in the literature that similar reductions in mobility may occur in any diseases affecting the spinal movement units regardless of the etiology of the disease. These mobility measurements were suitable for monitoring SpA patients. In the follow-up study there were no objective references for the measurement of functional ability based only on the self-administered questionnaires. Nevertheless it was documented in literature that patients with AS have been found to be valid reporters of their signs and symptoms as first mentioned in the literature review of the functional indices. The Swedish versions of the indices have not been evaluated here.

Subjects for further investigations arising from the present study may be the following. The use of a 5-point Likert scale of DFI instead of this 3-point Likert scale might be advisable, because more alternatives improve the sensitivity to change. The change of the functional indices over a period of six months after the inpatient course is of interest in evaluating the lasting effect of rehabilitation, and in combination with objective outcome instruments such as work ability and sick leaves. One task could be to compare inpatient and outpatient courses. Perhaps some of these instruments now available will be used in future in Finland.

Summary and conclusions

The aim of the present study was to find the most suitable compact set of the best spinal mobility measurements and the most suitable functional indices for everyday use in rehabilitation courses for patients with SpA. The functional indices for validating for Finnish patients were those recommended by the International Assessments in AS Working Group and accepted by ILAR/WHO, i.e. BASFI and DFI.

The most sensitive spinal mobility measurements in response to a three-week inpatient course were finger-to-floor distance, thoracolumbar rotation measured with a tape, chest expansion, thoracolumbar lateral flexion as finger-thigh test, and cervical rotation measured with an inclinometer in that order. All these tests correlated with radiological changes in the sacroiliac joints or spine as well as with disease duration. The intra- and intertester reliability of tests was sufficient.

The questionnaires of the functional indices BASFI and DFI were translated into Finnish, filled in by the Finnish SpA patients and validated by comparing them with disease activity, spinal mobility and radiology. The functional indices BASFI and DFI were valid and reliable. BASFI was sensitive enough to improve during the inpatient course but the DFI was not. The correlation in changes between spinal mobility and functional ability was low, the best correlation with functional improvement was observed in the changes in finger-to-floor distance and thoracolumbar rotation measured with a tape. BASFI was also sensitive over a three-year follow-up declining more than the DFI, which also deteriorated significantly. The natural course of SpAs showing a tendency for declining functional ability over time is a challenge for treatment, not forgetting the documented positive effect of rehabilitation.

The conclusions for patients with SpA are:

1. The best compact set of spinal mobility tests for the assessment of sensitivity to change in response to short-term inpatient rehabilitation course includes: finger-to-floor distance, thoracolumbar rotation measured with a tape, chest expansion, thoracolumbar lateral flexion measured with a tape as finger-thigh test and cervical rotation measured with an inclinometer, but included the additional internationally recommended Schober test and occiput-to-wall distance.
2. Both internationally recommended functional indices, BASFI and DFI, have been translated into Finnish and validated and can be used in Finland.

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Appendix

APPENDIX 1: THE TABLES OF THE DIAGNOSTIC CRITERIA OF AS, SPA AND FM.

Table A. The modified New York criteria for ankylosing spondylitis (AS) (van der Linden et al. 1984).

A. Diagnosis

1. Clinical criteria:
 - a) Low back pain and stiffness for more than 3 months which improves with exercise, but is not relieved by rest.
 - b) Limitation of motion of lumbar spine in both the sagittal and frontal planes.
 - c) Limitation of chest expansion relative to normal values corrected for age and sex.
2. Radiological criterion:
Sacroilitis grade ≥ 2 bilaterally or sacroilitis grade 3-4 unilaterally

B. Grading

1. Defining AS if the radiological criterion is associated with at least one clinical criterion.
2. Probable AS if:
 - a) three clinical criteria are present.
 - b) The radiological criterion is present without any signs or symptoms satisfying the clinical criteria (other causes of sacroilitis should be considered).

Table B. Amor criteria for spondyloarthropathy (SpA) (Amor et al. 1990).

<i>Parameter</i>	<i>Scoring</i>
A. Clinical symptoms or past history of	
1. Lumbar or dorsal pain at night or morning stiffness of lumbar or dorsal pain	1
2. Asymmetrical oligoarthritis	2
3. Buttock pain	1
or, if alternate buttock pain	2
4. Sausage-like toe or digit	2
5. Heel pain or other well-defined enthesopathic pain	2
6. Iritis	2
7. Non-gonococcal urethritis or cervicitis within 1 month before the onset of arthritis	1
8. Acute diarrhoea within 1 month before onset of arthritis	1
9. Psoriasis, balanitis or inflammatory bowel disease (Ulcerative colitis or Crohn's disease)	2
B. Radiological findings	
10. Sacroilitis (bilateral grade 2 or unilateral grade 3)	2
C. Genetic background	
11. Presence of HLA-B27 and /or family history of ankylosing spondylitis, reactive arthritis, uveitis, psoriasis or inflammatory bowel disease	2
D. Response to treatment	
12. Clear-cut improvement within 48 h after nonsteroidal anti-inflammatory drug intake or rapid relapse of the pain after their discontinuation	2

A patient is considered as suffering from spondyloarthropathy if the sum is ≥ 6 .

Table C. The European Spondylarthropathy Study Group (ESSG) criteria for spondyloarthropathy (SpA) (Dougados et al. 1991).

Inflammatory spinal pain or synovitis

- asymmetrical or
- predominantly in the lower limbs

and one or more of the following:

- alternate buttock pain
- sacroilitis
- enthesiopathy
- positive family history
- psoriasis
- inflammatory bowel disease
- urethritis or cervicitis or acute diarrhoea within 1 month before arthritis

Table D. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia (FM) (Wolfe et al. 1990).

1. History of widespread pain.

Definition: Pain is considered widespread when all the following are present: pain in the left side of the body, pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present.

2. Pain in 11 of 18 tender sites on digital palpation.

Definition: Pain, on digital palpation, must be present in at least 11 of the following 18 tender point sites:

- Occiput: bilateral, at the suboccipital muscle insertions.
- Low cervical: bilateral, at the anterior aspects of the intertransverse spaces at C5-7.
- Trapezius: bilateral, at the midpoint of the upper border.
- Supraspinatus: bilateral, at origins, above the scapula spine near the medial border.
- Second rib: bilateral, at the second costochondral junctions, just lateral to the junctions on upper surfaces.
- Lateral epicondyle: bilateral, 2cm distal to the epicondyles.
- Gluteal: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle.
- Greater trochanter: bilateral, posterior to the trochanteric prominence.
- Knee: bilateral, at the medial fat pad proximal to the joint line.

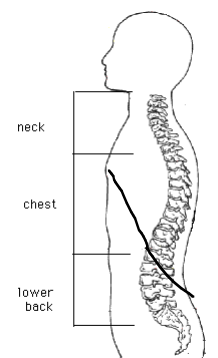
Digital palpation should be performed with an approximation force of 4 kg. For a tender point to be considered 'positive', the subject must state that the palpation was painful. 'Tender' is not to be considered painful.

For purposes of classification, patients will be said to have FM if both criteria are satisfied. Widespread pain must have been present for at least three months. The presence of a second clinical disorder does not exclude the diagnosis of FM.

APPENDIX 2: THE MOBILITY MEASUREMENTS

1. *Modified Schober test.* Increase in the distance between two skin marks 10 cm above and 5 cm below the connecting line between “the Dimples of Venus” after maximal forward bending, measured with a tape.
2. *Schober sacral 1 test.* Increase in the distance between two skin marks on the spinous process of the first sacral vertebra and 10 cm above after maximal forward bending, measured with a tape.
3. *Thoracolumbar flexion.* Increase in the distance between skin marks on the spinous processes of the first sacral and seventh cervical vertebrae measured with a tape in maximal forward bending.
4. *Thoracolumbar rotation (using an instrument).* With the subject sitting on a stool, a 43 cm long stiff needle indicator is firmly attached to the patient’s chest (the xiphisternum) with a belt, and the stool so positioned that the needle indicator points to zero on a semicircular degree scale in front of the patient. The height of the scale is adjusted so that the needle indicator is horizontal. The diagonal of the scale passes through the patient approximately in front of the spine. The examiner fixes the pelvis of the patient with his/her hands during the examination. The patient is asked to rotate the trunk maximally, to left and to right. Maximal rotations on both sides are recorded from the scale. Measured with a rotameter (Viitanen 1993).
5. *Thoracolumbar rotation (the Pavelka method).* Increase in distance between the spinous process of the first sacral vertebra and the head of the xiphisternum in maximal trunk rotation to both sides (right and left) measured with a tape during inspiration.
6. *Thoracolumbar lateral flexion (finger-thigh test).* Distance between two skin marks, recorded at the level of the fingertips on the legs, first standing straight with buttocks and back to wall and then after maximal lateral bending of the trunk to right and left, measured with a tape.
7. *Xiphisternum-iliac crest distance/lateral bending.* Decrease in distance between a horizontal line drawn from the xiphisternum to the lateral rib cage and the iliac crest in maximal lateral trunk bending, measured with a tape.
8. *Occiput-to-wall distance.* Distance between the occiput and a wall measured with a tape while the patient stands heels and back against a wall and tries to get the occiput against the wall with the chin horizontal.
9. *Tragus-to-wall distance.* As above, measured with a tape between the tragus (ear lobe) and a wall.
10. *Cervical rotation.* Total range of rotation of the cervical spine from maximal leftwards to maximal rightwards rotation, measured with an inclinometer.
11. *Chin-coronoideus clavicle distance (cervical rotation measured with a tape).* Decrease in distance between the chin and the coronoideus process of the clavicle in maximal cervical rotation to both sides without cervical flexion, measured with a tape.
12. *Cervical lateral flexion.* Maximal lateral bending of the head without rotation, measured with an inclinometer.
13. *Tragus-coronoideus clavicle distance/cervical lateral flexion.* Decrease in distance between the tragus and the coronoideus process of the clavicle in maximal lateral bending of the head to the left and right, measured with a tape.
14. *Cervical forward flexion.* Maximal cervical forward flexion, measured with an inclinometer in the sitting position.
15. *Cervical extension.* Maximal cervical extension, measured with an inclinometer in the sitting position.
16. *Chin-to-chest distance.* Distance between the chin and the jugulum in maximal flexion of the cervical spine, measured with a tape.
17. *Chest expansion.* Difference in the chest circumference at maximal inspiration and expiration at the level of the fourth intercostal space, measured with a tape.
18. *Intermalleolar distance.* Measured with a tape between the medial malleoli when the supine patient separates the legs maximally with the knees straight (when possible) and the feet pointing straight up.
19. *Internal hip rotation.* Measure supine, legs at 90 degrees in hip and knee joint, and internal rotation in the hip joint recorded as lower leg rotation angle with a goniometer.
20. *Shoulder abduction and flexion.* Measured standing with a goniometer.
21. *Finger-to-floor distance.* Distance between fingertips and floor measured with a tape at maximal flexion of spine and pelvis while the knees are kept in extension.

Illustration of the Pavelka method measured with a tape (~).



APPENDIX 3a: FUNCTIONAL AND OTHER INDICES

Bath ankylosing spondylitis functional index (BASFI). The BASFI comprises of eight items on daily activities and two on assessing the patient's ability to cope with everyday life. Each item is answered on a 10 cm horizontal VAS. The mean of the 10 scales gives the total score between 0 and 10, higher scores indicating more severe impairment.

Dougados functional index (DFI). The DFI consists of 20 items assessing patient's ability to perform distinct daily activities. The questionnaire provides three answer categories to the question 'Can you': 0 (yes, with no difficulty), 1 (yes, but with difficulty), and 2 (no). The total score ranges 0-40.

Health assessment questionnaire for spondyloarthropathies (HAQ-S). The HAQ-S is modified from HAQ, incremented by two subscales, the first with three and the other with two questions. The total score ranges 0-3.0.

Bath ankylosing spondylitis disease activity index (BASDAI). The BASDAI consists of six questions on disease activity, including fatigue, back pain, joint pain, local tenderness, and quality and quantity of morning stiffness evaluated by VAS (10 cm line). Each VAS is scored from 0 to 10. The mean of the two scores relating to morning stiffness is taken. Thus each symptom is given equal weighting. The resulting 0-50 score for the overall index is converted to a 0-10 scale to give the final score.

Bath ankylosing spondylitis patient global score (BAS-G). The BAS-G or the patient global assessment is VAS (10 cm line) for global influence of disease experienced by patients. The score range is from 0 to 10.

Pain-VAS and stiffness-VAS are VAS (10cm line) for pain and stiffness respectively. The total score range is 0-10.

The Dougados Functional Index (DFI):

Please check the one response which best describes your usual abilities.

Questions:	Answers:		
	Yes, with No Difficulty	Yes, but with Difficulty	No
Can you			
1. Put on your shoes	_____	_____	_____
2. Pull on trousers	_____	_____	_____
3. Pull on a pullover	_____	_____	_____
4. Get into a bathtub	_____	_____	_____
5. Remain standing 10 min	_____	_____	_____
6. Climb 1 flight of stairs	_____	_____	_____
7. Run	_____	_____	_____
8. Sit down	_____	_____	_____
9. Get up from a chair	_____	_____	_____
10. Get into a car	_____	_____	_____
11. Bend over to pick up an object	_____	_____	_____
12. Crouch	_____	_____	_____
13. Lie down	_____	_____	_____
14. Turn in bed	_____	_____	_____
15. Get out of bed	_____	_____	_____
16. Sleep on your back	_____	_____	_____
17. Sleep on your stomach	_____	_____	_____
18. Do your job or housework	_____	_____	_____
19. Cough or sneeze	_____	_____	_____
20. Breathe deep	_____	_____	_____

The Health Assessment Questionnaire for Spondyloarthropathies (HAQ-S):

Please check the one response which best describes your usual abilities over the past week.

Are you able to:

	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To Do
1.-dress yourself, including tying shoelaces and doing buttons?	___	___	___	___
-shampoo your hair	___	___	___	___
2.-stand up from an armless straight chair?	___	___	___	___
-get in and out of bed?	___	___	___	___
3.-cut your meat?	___	___	___	___
-lift a full cup or glass to your mouth?	___	___	___	___
-open a new milk carton?	___	___	___	___
4.-walk outdoors on flat ground?	___	___	___	___
-climb up five steps?	___	___	___	___
5.-wash and dry your entire body?	___	___	___	___
-take a tub bath?	___	___	___	___
-get on and off the toilet?	___	___	___	___
6.-reach and get down a 5 pound object, such as a bag sugar, from just above your head?	___	___	___	___
-bend down to pick up clothing from the floor?	___	___	___	___
7.-open car doors?	___	___	___	___
-open jars which have been previously opened?	___	___	___	___
-turn faucets on and off?	___	___	___	___
8.-run errands and shop?	___	___	___	___
-get in and out of a car?	___	___	___	___
-do chores such as vacuuming or yardwork?	___	___	___	___
9.-carry heavy packages such as grocery bags?	___	___	___	___
-sit for long periods of time, such as at work?	___	___	___	___
-work at a flat topped table or desk?	___	___	___	___
Driving a car (Check here ___ if you DO NOT have a driver's license or a car):				
10.-look in the rear view mirror?	___	___	___	___
-turn your head to drive in reverse?	___	___	___	___

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI):

PLEASE PLACE A MARK ON EACH LINE BELOW TO INDICATE YOUR ANSWER TO EACH QUESTION RELATING TO THE PAST WEEK.

1. How would you describe the overall level of fatigue/tiredness have experienced?)
NONE VERY SEVERE
=====
 2. How would you describe the overall level of AS neck, back or hip pain you have had?
NONE VERY SEVERE
=====
 3. How would describe the overall level of pain/swelling in joints other than neck, back or hips you have had?
NONE VERY SEVERE
=====
 4. How would you describe the overall level of discomfort you have had from any areas tender to touch or pressure?
NONE VERY SEVERE
=====
 5. How would you describe the overall level morning stiffness you have had from the time you wake up?
NONE VERY SEVERE
=====
 6. How long does your morning stiffness last from the time you wake up?
=====
- 0 hrs 1/2 1 1 1/2 2 or more hrs

The Bath Ankylosing Spondylitis Patient Global Score (BAS-G):

Please place a vertical mark on the scale below to indicate the effect your disease has had on your well-being over the last week.

NONE VERY SEVERE
=====

Stiffness-VAS:

Please place a vertical mark on the scale below to indicate the stiffness level of your disease over the last week.

NONE VERY SEVERE
=====

Pain-VAS:

Please place a vertical mark on the scale below to indicate the pain level of your disease over the last week.

NONE VERY SEVERE
=====

Original publications