Shoulder function and activity limitations in patients with early rheumatoid arthritis

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"Att tro på de saker du kan se och röra vid är ingen tro alls, men att tro på det osedda är en triumf och en välsignelse"

Abraham Lincoln (1809-1865)

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ABSTRACT

Patients with rheumatoid arthritis (RA) have impaired physical function which can lead to difficulties with daily activities. Despite improved pharmacological treatment, patients with early RA report difficulties with activities involving the shoulder. There is limited knowledge of the shoulder function and activity limitations related to the shoulder, arm and hand among patients with early RA.

The overall aim of this thesis was to investigate shoulder function and activity limitations related to the shoulder, arm and hand, and the relationship between shoulder function, activity limitations and work ability in patients with early RA. A methodological study evaluated the reliability and validity for the Disability of the Shoulder, Arm and Hand (DASH) questionnaire which assess activity limitations related to the shoulder, arm and hand. A controlled cross-sectional study and a cross-sectional study investigated shoulder function and activity limitations related to the shoulder, arm and hand and the relationship between shoulder function, activity limitations and work ability in patients with early RA. A randomized-controlled study evaluted moderately intensive pool exercise for patients with RA.

Main findings**.** DASH was found to possess satisfactory reliability and validity to assess activity limitations in patients with early RA. The shoulder function was found to be impaired, in particular the shoulder muscle strength which was 65% of the muscle strength in the reference group.The majority of the patients reported some activity limitations related to the shoulder,arm and hand when compared with the reference group. Impaired work ability is common among patients with early RA and associated with impaired shoulder function, mechanical exposure and activity limitations related to the shoulder, arm and hand. Moderately intensive pool exercise improved muscle function in the upper and lower extremites, active range of motion of the shoulder, activity limitations and well-being in patients with RA, while the aerobic capacity did not improve. Long-term follow-up showed also improved physical and mental quality of life.

Conclusion. Screening and monitoring of shoulder function from disease onset is warranted as the shoulder function is impaired, in particular the shoulder muscle strength. The majority of the patients with early RA report activity limitations related to the shoulder, arm and hand. DASH can be used to monitor the progress of the upper extremity function and activity limitations in patients with RA. Work ability in early RA is associated with shoulder function, mechanical exposure and activity limitations related to the shoulder, arm and hand. Moderately intensive pool exercise can be recommended for improvement of physical function, activity limitations and quality of life for patients with RA.

Keywords: arthritis rheumatoid, activities of daily living, outcome assessment, shoulder, muscle strength, hydrotherapy, exercise, physical fitness, workload

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SAMMANFATTNING PÅ SVENSKA

Patienter med reumatoid artrit (RA) har nedsatt fysisk funktion vilket leder till svårigheter med dagliga aktiviteter. Trots förbättrad farmakologisk behandling rapporterar patienter med tidig RA svårigheter med aktiviteter som involverar skuldran som att bära tungt och arbeta med armarna ovan axelhöjd. Det finns begränsat med kunskap om skulderfunktionen och aktivitetsbegränsningar relaterade till skuldra, arm och hand vid tidig RA samt hur dessa påverkar patientens förmåga till arbete.

Det övergripande syftet med avhandlingen var att undersöka skulderfunktionen och aktivitetsbegränsningar relaterade till skuldra, arm och hand hos patienter med tidig RA. Delstudie I är en metodstudie där syftet var att undersöka validitet och reliabilitet för frågeformuläret Disability of the Shoulder, Arm and Hand (DASH) som bedömmer aktivitetsbegränsningar relaterade till skuldra, arm och hand. Delstudie II är en kontrollerad tvärsnittstudie där syftet var att undersöka skulderfunktionen och eventuella aktivitetsbegränsningar relaterade till skuldra, arm och hand hos patienter med tidig RA jämfört med ålders- och könsmatchade friska personer. Delstudie III är en tvärsnittstudie där syftet var att undersöka samvariationen mellan arbetsförmåga och skulderfunktion, mekanisk arbetsbelastning och aktivitetsbegränsningar relaterade till skuldra, arm och hand. Delstudie IV är en kontrollerad randomiserad träningsstudie där effekterna av medelintensiv bassängträning utvärderades utifrån kondition, muskelfunktion, ledrörlighet, livskvalitet och aktivitetsbegränsningar.

Resultat. Avhandlingen visar att DASH har acceptabel validet och reliabilitet för bedömning av aktivitetsbegränsningar relaterade till skuldra, arm och hand hos patienter med tidig RA. Skulderfunktionen var nedsatt hos patienterna jämfört med ålders- och könsmatchade friska individer. Skulderstyrkan hos patienterna var 65 % av styrkan hos friska ålders- och könsmatchade referenspersoner. Även hos patienter som inte själva rapporterade axelsymtom var muskelstyrkan nedsatt till 73%. Arbetsförmåga mätt i antalet arbetstimmar per vecka korrelerade med skulderfunktion, mekanisk arbetsbelastning och aktivitetsbegränsningar i skuldra, arm och hand. Bassängträning två gånger per vecka under 12 veckor gav förbättrad muskelfunktion i övre och nedre extremiteterna, ökad axelrörlighet, mindre aktivitetsbegränsningar samt ett ökat välbefinnande hos träningsgruppen jämfört med kontrollgruppen. Långtidsuppföljningen visade även på förbättringar av både fysisk och mental livskvalité för träningsgruppen.

Slutsats. Screening och regelbunden uppföljning av skulderfunktionen, framförallt muskelstyrkan bör initieras redan från sjukdomsdebut eftersom huvuddelen av alla patienter med tidig RA uppvisar nedsatt skulderfunktion. DASH är ett användbart instrument för screening och uppföljning av funktion och aktivitetsbegränsningar i skuldra, arm och hand. Nedsatt arbetsförmåga vid tidig RA har ett samband med nedsatt skulderfunktion och ökad fysisk arbetsbelastning. Bassängträning kan förbättra muskelfunktion, minska aktivitetsbegränsningar samt ge ökad livskvalitet hos patienter med RA. Studier bör initieras för att ytterligare belysa skulderfunktionen och effekten av fysioterapi vid tidig RA.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Bilberg A, Bremell T, Mannerkorpi K. Disability of the Shoulder, Arm and Hand questionnaire in Swedish patients with rheumatoid arthritis: A validity study. *Journal of Rehabilitation Medicine 2012; 44: 7-11*

II. Bilberg A, Bremell T, Balogh I, Mannerkorpi K. Shoulder function is impaired in early rheumatoid arthritis- a controlled study. *Submitted*

III. Bilberg A, Bremell T, Balogh I, Mannerkorpi K. Work status in patients with early rheumatoid arthritis; emphasis on mechanical exposure and shoulder function. *Scandinavian Journal of Rheumatology* 2013, nov 03 [Epub ahead of print]

IV. Bilberg A, Ahlmén M, Mannerkorpi K. Moderately intensive exercise in a temperate pool for patients with rheumatoid arthritis: a randomized controlled stud*y. Rheumatology 2005; 44: 502-508*

CONTENTS

ABBREVIATIONS

ACR	American College of Rheumatology
Anti-CCP	Anti-cyclic Citrullinated Peptides antibodies
Anti TNF	Anti Tumor Necrosus Factor (therapy)
EULAR	European League Against Rheumatism
DAS28	Disease Activity Score 28 joints
DASH	Disability of the Arms, Shoulder and Hand questionnaire
DMARD	Disease Modifying Anti Rheumatic Drug
ESR	Erythrocyte Sedimentation Rate
HAQ	Health Assessment Questionnaire
ICF	International Classification of Functioning, Disability and Health
LTPAI	Leisure Time Physical Activity Index
MEI	Mechanical Exposure Index
NSAID	Non-Steroidal Anti-Inflammatory Drug
PROM	Patient Report Outcome Measure
RA	Rheumatoid Arthritis
RCT	Randomized Controlled Trial
RF	Rheumatoid Factor
ROM	Range Of Motion

SBU	Statens Beredning för medicinsk Utvärdering, Swedish Council on Health Technology Assessment
SF-36	Short Form-36

DEFINITIONS IN SHORT

Aerobic capacity	All bodily movement produced by skeletal muscles that result in energy expenditure. Including sports and non sport activities (Caspersen et al., 1985)
Aerobic exercise	Any activity that uses large muscle groups, can be maintained continuously, and is rhythmic in nature (ACSM 2010)
Activity limitations	A difficulty encountered by an individual in executing a task or action (WHO, 2001)
Borg RPE	Borg´s Rating of Perceived Exertion (Borg, 1982)
Exercise	A planned, structured and repetitive bodily movement done to improve or maintain one or more components of physical fitness (Caspersen, et al., 1985)
Flexibility	The range of motion available at a joint (Caspersen, et al., 1985)
Moderate-intensity level	Physical activity equivalent to 13-14 on the BORG´s RPE scale (Borg, 1982)
Muscle endurance	The ability of muscle groups to exert external force for many repetitions of successive exertions (Caspersen, et al., 1985)
Muscle strength	The amount of external force that a muscle can exert (Caspersen, et al., 1985)
Physical activity	Any bodily movement produced by skeletal muscles that result in energy expenditure (Caspersen, et al., 1985)
Physical function	The capacity of an individual to carry out the physical activities of daily living (Garber et al., 2011)

Rheumatoid Arthritis	According to the 1987 revised ACR criteria for RA(Arnett et al., 1988)
RA, early	Rheumatoid Arthritis according to the 1987 revised ACR criteria, with a disease duration ≤3 years
RA, established	Rheumatoid Arthritis according to the 1987 revised ACR criteria with a disease duration > 3 years
Reliability	Repeatability and stability of a measurement and the random variability associated with it (Fayers, 2000)
Shoulder function	Shoulder-arm movement, activity-induced shoulder pain and shoulder muscle strength
Validity	The degree to which an instrument measures the concept it is supposed to measure (Fayers, 2000)
Work ability	Number of work hours per week

1 INTRODUCTION

Patients with rheumatoid arthritis (RA) have impaired physical function which leads to difficulties in daily activities. During the past decades better and more aggressive pharmacological treatments have resulted in a dramatic decline in disease activity for most of the patients, especially those with recent onset (Goekoop-Ruiterman et al., 2008). However, patients report problems with more demanding activities such as carrying loads or working with the arms above the shoulder level. From a clinical perspective, shoulder function is affected from the onset of disease. However, little is known about shoulder function in early RA and its association with activity limitations in the upper extremities. Moreover, the role of shoulder function for work ability in early RA has not been studied.

1.1 Rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic, autoimmune disease characterized by symmetric inflammation of peripheral joints, often resulting in progressive destruction of articular- and peri-articular structures, with or without generalized manifestations (Dirven et al., 2012; Lee et al., 2001). The etiology is not clear but there is a general opinion that RA is a multifactorial disease where genetic and environmental factors contribute to onset and course of disease (Alamanos et al., 2005). Prevalence rates of RA in Northern Europe and North America are somewhere between 0.5 to 1.1% of the adult population (Alamanos et al., 2006). In Sweden, the prevalence rate ranges between 0.5 to 0.7% (Englund et al., 2010; Neovius et al., 2011b; Simonsson et al., 1999), with an annual incidence rate of approximately 24 cases per 100 000 inhabitants (Soderlin et al., 2002). The disease onset occurs throughout the adult lifespan peaking during the 55-60 years of age (Alamanos, et al., 2005).

The disease causes joint inflammation of the synovial and the teno synovial structures predominately in hands, fingers and feets, but larger peripheral joints can also be involved. The joint inflammation will lead to pain, reduced range of motion (ROM) and reduced muscle strength (Eurenius et al., 2005). The disease can vary from mild to severe often with a fluctuating course, with periods of increased disease activity as well as calmer periods of remissions with the risk of slow deterioration (Lindqvist et al., 2002). Fatigue is another problem often reported by patients (van Hoogmoed et al., 2010). Patients with RA have an increased risk of cardiovascular diseases (Turesson et al., 2008) and mortality (Gabriel et al., 2003). There is

predominance of women, sex ratio 3:1, where women tend to suffer more of the consequences of the disease than men (Bjork et al., 2006; Hallert et al., 2003; Odegard et al., 2005; Thyberg, Hass, et al., 2005). Consequently, the disease causes functional losses and activity limitations as well as reduced health related to quality of life which cause a great number of problems in daily living and sometime impaired work ability (Scott et al., 2005).

1.1.1 ACR criteria

Classification criteria for RA according to the revised 1987 ACR criteria

1. Morningstiffness for at least 1 hour
2. Arthritis of 3 or more joint areas
3. Arthritis of hand joints
4. Symmetric arthritis
5. Rheumatoid nodules
6. Serum Rheumatic Factor
7. Radiographic changes

Figure 1. American College of Rheumatology (ACR) criteria. To fulfill the diagnosis of RA, at least four out of seven criteria must be met. Also, criteria one through four must have been present for at least six weeks

The ACR criteria were designed to indentify patients with established RA (Arnett, et al., 1988). New classification criteria for RA were established in 2010 to distinguish patients at risk for developing persistent erosive and/ or inflammatory disease from those with undifferentiated inflammatory arthritis (Aletaha et al., 2010), although those criteria are not used in this thesis.

1.1.2 Early rheumatoid arthritis

The time definition of early RA is controversial. However, a time limit set has been suggested for "*Very Early Rheumatoid Arthritis*" between ≥3 weeks to ≤ 3 months while the time limit for "*Early Rheumatoid Arthritis*" has been found to vary between two to three years (Zeidler, 2012). The disease duration used in this thesis for early RA was defined as ≥6 months to 3 years and the classification criteria for defining RA were the revised 1987 American College of Rheumatology (ACR) criteria (Arnett, et al., 1988).

1.2 Shoulder function

The shoulder consists of three joints; the glenohumeral, the acromioclavicular and the sternoclavicular articulation. The rotatorcuff; i.e. supraspinatus, infraspinatus, teres minor and the subscapularis musculature keep the humerus in place towards the glenoidale and contribute to movement and, stabilization of the glenohumeral joint. Also the deltoid, lattisimus dorsi and teres major contribute to the stabilization and movement (Hawkes et al., 2012; Saha, 1971). Shoulder function is important for individuals´ daily activities as the shoulder guides the hand to a correct position to perform a physical action. The balance between the anatomical structures of the shoulder can be disturbed and the joint is a location of injuries and degenerative problems.

1.2.1 Shoulder symptoms in the general population

Shoulder pain is the third most common site of musculoskeletal pain in the general community (Urwin et al., 1998). In a Swedish survey of chronic musculoskeletal pain among the adult population, the shoulder-upper arm was found to be the second most reported region of chronic pain with a prevalence of 10.5% for women and 8.5% for men (Bergman et al., 2001). The annual incidence rate of painful shoulders in the general population of Sweden is somewhere between 0.9 and 1.6% (Allander, 1974; Tekavec et al., 2012). The annual consultation prevalence for shoulder pain diagnosis in Sweden is somewhat higher for women 103/10 000 compared to men 98/ 10 000 (Tekavec, et al., 2012). Chronic shoulder pain is associated with age, workload, work situation, trauma, athletic injures, psychosocial stress and reduced health (Badcock et al., 2002; Huisstede et al., 2008; Ostor et al., 2005).

1.2.2 Shoulder function in RA

Shoulder symptoms are common in patients with established RA. Inflammation of the shoulder joint may appear in the glenohumeral, the acromioclavicular and in the sternoclavicular joints (Lehtinen et al., 1999, 2000). In addition to changes in the cartilage and bone, periarticular structures and soft tissues of the shoulder can be affected (Stegbauer et al., 2008; van de Sande et al., 2008). Common clinical symptoms of impaired shoulder function in patients with RA are reduced range of motion (ROM), activity-induced pain, reduced muscle strength and activity limitations (Bostrom et al., 1995; Slungaard et al., 2012). Increased shoulder pain has been found to correlate more strongly with the severity of the disease and less to the duration of the disease in patients with RA (van de Sande, et al., 2008). Traditionally, shoulder joint involvement is associated with patients with established RA, and to older patients, ≥60 years of age at RA onset (van Schaardenburg, 1995). However, there is limited knowledge of how shoulder function is affected in early disease course. A previous study of shoulder function in early RA reported reduced shoulder-arm movements in 30% of patients compared to healthy age matched controls (Olofsson et al., 2003).

1.3 International Classification of Functioning, Disability and Health

The World Health Organisation´s International Classification of Functioning, Disability and Health (ICF frame work) is designed to record and organise a wide range of information about functioning and health (WHO, 2001). The structure of the ICF offers the possibility of measuring health status at several levels: impairment, activity limitations and participation restriction and provides a model for how the different component and factors interact (Figure 1). The ICF organizes information in two parts. One part deals with functioning and disability while the other covers contextual factors. Functioning and disability is related to the body component including *body functions* and *body structures,* as well as with *activities and participation* comprises all aspects of functioning from both the individual and societal perspectives. The ICF also includes contextual factors of importance for the indiviual´s condition including *personal* and *environmental factors*. Environmental factors and personal factors are thought to influence functioning and disability.

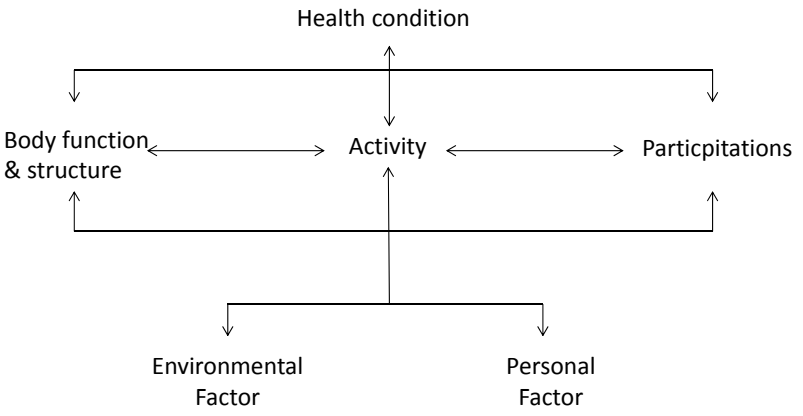

Figure 2. Interaction between the different components in ICF. International classification of functioning, disability and health. Geneva: WHO;2001.

1.3.1 Activity limitations in RA

According to ICF activity limitation is defined as a difficulty encountered by an individual in executing a task or action (WHO, 2001). Activity limitations in RA have been widely investigated and general activity limitations have been found to correlate with disease activity (Courvoisier et al., 2008), pain (Sarzi-Puttini et al., 2002), muscle strength (Thyberg, Skogh, et al., 2005) and depression (Sharpe et al., 2001). The relationship between general activity limitations and radiographic joint destruction in RA has been investigated in several studies (Breedveld et al., 2005; Clarke et al., 2001; Plant et al., 2005), and the relationship tends to become stronger with disease duration. General activity limitations and joint damage are strongly correlated in patients with established RA while the association has been found to be low in studies of early RA patients (Breedveld, et al., 2005; Clarke, et al., 2001; Plant, et al., 2005).

1.3.2 Assessment of activity limitations

Patient reported outcome measures (PROM) are recommended together with more traditional outcome measures when evaluating patients´ health, function, symptoms and quality of life in RA. PROM´s provide additional information from a patient perspective, and is an effective and simple method of collecting important data in routine clinical care as well as in research (ACR, 2002; Combe et al., 2007; Pincus et al., 2003).

General activity limitations in daily life in RA are commonly assessed by the disease-specific self-administered Stanford Health Assessment Questionnaire Disability index (HAQ) (Fries et al., 1980). HAQ includes items of fine movements of the upper extremities and activities of the lower extremities, as well as activities including both the upper and lower extremities. HAQ is suggested to cover the component of activity and participation according to the International Classification of Functioning, Disability and Health (ICF) core set (Stucki et al., 2004).

Another PROM to assess activity limitations is the region-specific outcome measurement Disability of the Shoulder Arm and Hand (DASH) questionnaire. The questionnaire was originally developed to assess disability and symptoms in patients with different musculo-skeletal disorders in the upper extremities (Hudak et al., 1996). DASH has been found to be among the best self-reported questionnaire for assessing disability related to the upper extremities due to its clinimetric properties (Bot et al., 2004). The items in the questionnare have been suggested to cover impairment, activity limitations and participation restrictions according to ICF (Dixon et al., 2008). However, the majority of the DASH items are related to activity limitations. The Swedish version of DASH has been validated for patients with upper extremity orthopedic musculoskeletal disorders but not for patients with RA (Atroshi et al., 2000). We found it important to test the reliability and validity of the DASH for use in Swedish patients with RA.

1.4 Work ability

There is no common definition of work ability as the concept is complex and multidimensional. Work ability can be summarized as the individual´s ability in relation to work requirements, where a person´s work ability is dependent on physical, psychological and social work requirements (Ilmarinen, 2009). In a recent systematic review article, work ability and work disability was defined as “a relational concept resulting from the interaction of multiple dimensions that influence each other through different levels” (Lederer et al., 2013). In this thesis we have applied a more narrow definition of work ability i.e. according to the number of work hours per week.

Impaired work ability has been suggested to be due to an imbalance between work requirements and the individual´s functional ability, capacity and working techniques (Toomingas, 2011). Twenty nine percent of all work related disability payments due to musculo-skeletal disorders in Sweden were found to be related to shoulder-arm disorders (Nygren et al., 1995).

According to a report from the Swedish Council on Health Technology Assessment (SBU, 2012) there is strong evidence that work-related disorders of the neck and shoulder region are related to heavy physical work load. Also static work and highly repetitive movements are related to symptoms in the neck and shoulder region (SBU, 2012). Moreover, work-related mechanical exposure, i.e. work above shoulder level and highly repetitive and static work has also been found to be associated with shoulder symptoms in the general population (Larsson et al., 2007).

1.4.1 Work ability in RA

Work disability, defined as the inability to work, usually occurs soon after disease onset and seems to prevail during the disease course in RA (Eberhardt et al., 2007; Zirkzee et al., 2008). Two to three years after disease onset approximately 20%-40% of RA patients have permanent work disability (Bjork et al., 2009; Hallert, et al., 2003). Although the prevalence of work disability has decreased over recent years (Hallert et al., 2012), patients with RA experience more work disability than the general population (Barrett et al., 2000; Neovius et al., 2011a). Strong predictors of work disability in RA are physically demanding work, low degree of education, older age, and general activity limitations (Barrett, et al., 2000; Bjork, et al., 2009; Eberhardt, et al., 2007).

1.5 Treatment

The treatment goal for patients with early RA is to achieve clinical remission (ACR, 2002; Combe, et al., 2007). If clinical remission is not possible the goal is to control disease activity, alleviate pain, maintain function for activities of daily living and work, and maximize quality of life (Combe, et al., 2007).

1.5.1 Pharmacological treatment

As joint erosions occur early in RA, often during the first two years treatment with Disease Modifying Anti Rheumatic Drugs (DMARD) should be initiated as early as possible (Combe, et al., 2007). NSAID´s and glucocorticoids are additional treatments. If the results are not sufficient more selective immunomodulatory drugs such as anti TNF treatment or other biologics can be considered.

1.5.2 Non-pharmacological treatment

Multidiciplinary teams are recommended for patients with early RA and usually include a nurse, an occupational therapist, a physiotherapist, a

rheumatologist, and a social worker. Moreover, psychologists and dieticians are sometimes included in the team. The different healthcare professionals with their medical, functional and psychosocial perspective contributes to improve and/ or maintain general health, functional ability and work ability for the patient.

1.6 Physical activity and physical function in RA

Physical activity is defined as "any bodily movement produced by skeletal muscles that result in energy expenditure" (Caspersen, et al., 1985), and includes all activities of daily living. A subcategory of physical activity is exercise which is defined as "a planned, structured and repetitive bodily movement done to improve or maintain one or more components of physical fitness" (Caspersen, et al., 1985).

Physical function is defined as "the capacity of an individual to carry out the physical activities of daily living" (Garber et al 2011) and reflects motor function and control, physical fitness, and habitual physical activities.

Patients with RA are less physically active than healthy subjects (Eurenius, et al., 2005). A large international multicenter study reported that only 13.8% of patients with RA were physically active on an exercise level equal to suggested health recommendations. The majority of patients reported that they were physically inactive (Sokka et al., 2008). A systematic review-article of leisure time activity level in RA concluded that patients spend more time on low-intensity and moderate-intensity levels and less on a vigorous-intensity level in terms of physical activity per week (Munsterman et al., 2012).

It has been suggested that patients with RA will benefit from an overall increase in physical activity and exercise intensity level, to improve cardiovascular and muscle function (ACR, 2002; Cairns et al., 2009; Combe, et al., 2007; Stenstrom et al., 2003), mainly in accordance with the recommendation for the general population (Garber, et al., 2011; Nelson et al., 2007). Nevertheless, patients are less physically active (Eurenius, et al., 2005) and have reduced physical function compared to the general population. The aerobic capacity is reduced (Chang et al., 2009; C. Ekdahl et al., 1992; Hakkinen et al., 1995) as well as the muscle strength which has been reported to be reduced by 25% in patients with established RA (C. Ekdahl, et al., 1992), and by 15-30% in early RA (Eurenius, et al., 2005; Hakkinen, et al., 1995).

1.7 Physiotherapy in RA

The main aim of physiotherapy is to promote health. The physiotherapist should regard the patients as a physical, mental, social and existential whole (Broberg et al., 2009). "The nature of physiotherapy is to "provide service to individuals and populations to develop, maintain and to restore maximum movement and functional ability throughout the lifespan". This includes "providing services in circumstances where movement and function are threatened by ageing, injury, disease or environmental factors". Functional movement is central to what it means to be healthy" (WCPT, 2007).

The main goal of physiotherapy in rheumatology is to reduce pain and restore or maintain optimal functioning (Fransen, 2004). Promotion of physical exercise and physical activities as methods of managing pain and improvement of physical function is within the physiotherapists' assignments. Dynamic exercise on a moderate intensity level has been found to be effective with respect to increasing aerobic capacity and muscle strength in patients with RA, without a detrimental effect on disease activity and pain (Cairns, et al., 2009; Hurkmans et al., 2009; Stenstrom, et al., 2003).

1.8 Pool exercise

Pool exercise in warm water is highly valued for patients with RA. The warm water and buoyancy faciliate exercise. The reduced load on the joint together with the warmth facilitates joint movements with reduced activity-induced pain. The hydrostatic pressure in water immersion is suggested to reduce edema, which may have positive effects on the swollen joints and faciliate joint movements. The viscosity of the water provides resistance in the exercises and the desired exercise effect can easily be adjusted by the speed of the movement (Becker, 2009).

Evaluations of the effects of pool exercise program in RA are scarce (Cochrane Verhagen 2008). Only few randomized controlled trials (RCT) have evaluated the effect of exercise in warm water for patients with RA. An RCT study comparing pool exercise and land exercise found similar improvements for joint movement, pain, health status and number of tender joints. However, patients allocated to pool exercise had the greatest reduction in number of tender joints (Hall et al., 1996). Another study, that compared warm water exercise with similar land exercise program found no difference in physical assessments, self-reported quality of life or general activity limitations. However, a significant difference for self-rated overall effect of treatment in favour of the pool exercise group was found (Eversden et al., 2007).

1.9 Validity and reliability

Validation of an instrument is the process of determining whether the instrument measures what it is intended to measure, and if it is useful for its intended purpose (Fayers, 2000).

Reliability and repeatability concerns the random variability associated with measurements (Fayers, 2000).

There are several ways to evaluate the validity and reliability of an instrument. In this thesis the concurrent, convergent and face validity was analysed as well as test-retest reliability over time for the DASH, for use in patients with early RA.

Criterion validity considers whether the scale has associations with external criteria such as other established instruments (Fayers, 2000) and can be divided into concurrent validity and predictive validity. Concurrent validity means agreement with the true value, a "gold standard". As a "gold standard" is not usually available a more common approach involves comparing new questionnaires against a well-established instrument and determining the level of agreement between a new instrument and a previously used instrument (Fayers, 2000).

Construct validity examines the theoretical relationship of the instrument (to other measures) (Fayers, 2000). The two aspects of construct validity are convergent validity and discriminant validity. Convergent validity evaluates if the dimension correlates with other dimensions that it should be related to it (Fayers, 2000).

Face validity refers to if an instrument covers the intended topics clearly and unambiguously. Face validity can be judged by experts, health professionals and patients (Fayers, 2000). It is considered to be the weakest form of validity and concerns judgements about items of an instrument after it is constructed (Fayers, 2000).

Reliability is used as a term to describe aspects of repeatability and stability of measurements (Fayers, 2000). The stability of an instrument means the extent to which similar results are obtained on two separate administrations. The test-retest reliability is used to evaluate an instrument´s stability over time (Fayers, 2000).

2 AIMS

The overall aim of this thesis was to investigate shoulder function and activity limitations related to the shoulder, arm and hand, and the relationship between shoulder function, activity limitations and work ability in patients with early RA. An additional aim was to evaluate moderately intensive pool exercise for patients with RA.

2.1.1 Specific aim

Specific aims of the studies included in this thesis were:

Study I
To investigate concurrent, convergent and face validity of the Disability of the Arm, Shoulder and Hand (DASH) questionnaire and the DASH´s stability over time for patients with early RA in Sweden.

Study II
To investigate the shoulder function in patients with early RA compared to healthy age-matched subjects. An additional aim was to investigate activity limitations related to the shoulder, arm and hand in patients with early RA compared to healthy age-matched subjects.

Study III
To investigate work ability and its associations with shoulder function, work-related mechanical exposure and activity limitations related to the shoulder, arm and hand in patients with early RA.

Study IV
To investigate whether moderately intensive pool exercise for 12 weeks, two times a week, can improve aerobic capacity, physical function of the upper and lower extremities and quality of life in patients with RA.

3 METHODS AND MATERIALS

The present thesis comprised four studies. The methods used are briefly described in Table 1.

Table 1. Research design overview

Study	**I**	**II**	III	IV
Study design	Methodological study	Descriptive controlled cross-sectional study	Descriptive cross-sectional study	Randomized controlled trial
Setting	Sahlgrenska University Hospital Gothenburg,	Sahlgrenska University Hospital Skövde Hospital Uddevalla Hospital	Sahlgrenska University Hospital Skövde Hospital Uddevalla Hospital	Sahlgrenska University Hospital Gothenburg
Participants	Validity n=67 Reliability n=26	Patient n=103 Reference n=103	n=135	Exercise n=20 Controll n=23
Data collection	DAS28 HAQ DASH Shoulder-arm movement Activity-induced shoulder pain Grippit	DAS28 HAQ DASH Shoulder-arm movement Activity-induced shoulder pain Isobex Grippit Physical workload LTPAI	DAS28 HAQ DASH Shoulder-arm movement Activity-induced shoulder pain Isobex Grippit Physical workload MEI	DAS28 HAQ AIMS2 Shoulder-arm movement Shoulder muscle endurance Chair test Grippit IMF Ergometric submaximum test SF36
Analysis	Non-parametric statistical analysis	Non-parametric statistical analysis	Non-parametric statistical analysis	Non-parametric statistical analysis

3.1 Subjects

Table 2. Characteristics of the patients in studies I-IV. Data are presented as mean (SD) or median (min-max), and number of patients n (%)

variables	Study I Validity	Study I Reliability	Study II	Study III	Study IV Exercise group	Study IV Control group
Patients, n	67	26	103	135	20	23
Gender, female, n (%)	52 (78)	20 (77)	103 (100)	103 (76)	17 (85)	21 (91)
Age,year	47 (9.9)	44 (10.9)	47 (10.0)	48 (9.6)	49 (8.7)	46 (11.7)
Disease duration, months	21 (7.6)	51 (33.5)	20.3 (8.5)	21 (9.6)	31 (15.8)	35 (17.1)
DAS28, 0-10	3.0 (1.10)	n.a.	3.8 (1.4)	3.7 (1.37)	4.1 (1.5)	4.0 (1.3)
RF positive, n(%)	47 (69)	n.a.	81 (79)	104 (77)	n.a.	n.a.
Anti-CCP positive, n(%)	n.a.	n.a.	75 (76)	98 (78)	n.a.	n.a.
Erosions, n(%)	n.a.	n.a.	39 (38)	52 (40)	n.a.	n.a.
HAQ, 0-3	0.5 (0.51)	n.a	0.6 (0.55)	0.6 (0.58)	0.9(0.5)	0.7(0.5)
DMARD´s, n(%)	67 (94)	n.a.	91 (89)	119 (89)	18(75)	20(87)
Anti TNF-therapy, n(%)	n.a.	n.a.	14 (14)	21 (16)	n.a.	n.a.

DAS28, Disease Activity Score in 28 joints,; RF positive, Rheumatoid Factor positive; Anti-CCP positive, Anti-cyclic Citrullinated Peptides antibodies positive; DMARD, Health Assessment Questionnaire; Disease Modifying Anti Rheumatic Drug; HAQ, Health Assessment Questionnaire; Anti TNF-therapy, Anti Tumor Necrosus Factor-therapy, n.a.=non applicable

Study I

A total of 67 patients (52 women and 15 men) with early RA were recruited from the Rheumatology Clinic at Sahlgrenska University Hospital to the validity study. Another 30 patients from the same clinic were recruited to the test-retest study, see Tables I and II for recruitment and characteristics.

Inclusion criteria for the validity study: Patients with RA, fulfilling the 1987 American College of Rheumatology (ACR) criteria, (Arnett, et al., 1988) with a duration of RA ranging from six months to three years, aged 20-60 years and possessing the ability to read and speak Swedish.

Inclusion criteria for the test-retest study: The inclusion criteria were the same as for the validity study except for the disease duration comprising six months to ten years and absence of corticoid-steroidal injections during the present week, in order to avoid changes in health status that could interfere with the test-retest reliability results.

Exclusion criteria for the validity and test-retest study: Patients with other severe somatic, chronic or psychiatric diseases.

Study II

Study II includes women with early RA and a reference group of healthy age-matched women, see Tables I and II for recruitment and characteristics.

A total of 103 women with early RA were recruited from three rheumatology units in the Västra Götaland region of Sweden.

Inclusion criteria for the patient group: Women with RA, fulfilling the 1987 American College of Rheumatology (ACR) criteria (Arnett, et al., 1988), with a duration of RA ranging from six months to three years, aged 20-60 years and possessing the ability to read and speak Swedish.

A total of 103 age-matched (±1 year), healthy women were recruited from Gothenburg as a reference group.

Inclusion criteria for the reference group: Self-reported healthy women, aged 20-60 years and possessing the ability to read and speak Swedish.

Exclusion criteria for the patient and reference groups: Severe and or chronic somatic or psychiatric disease, shoulder arthroplasty, any unhealed fracture of the upper extremities or on-going adhesive capsulitis. An additional exclusion criterion for the reference group was rheumatoid arthritis.

Study III

A total of 135 patients with early RA were recruited from three rheumatology units in the Västra Götaland region of Sweden, see Table I and II for recruitment and characteristics.

Inclusion criteria: Patients with RA, fulfilling the 1987 American College of Rheumatology (ACR) criteria (Arnett, et al., 1988) with a disease duration ranging from six months to three years, aged 20-60 years, and possessing the ability to read and speak Swedish.

Exclusion criteria: Patients with other severe and chronic somatic or psychiatric diseases were excluded.

Study IV

A total of 47 patients with RA were recruited from the Rheumatology Clinic at Sahlgrenska University Hospital to a randomized controlled training study.

Inclusion criteria: Patients with RA, fulfilling the 1987 American College of Rheumatology (ACR) criteria (Arnett, et al., 1988) with a disease duration ranging from one to five years, functional class I-III according to Steinbrocker (Steinbrocker et al., 1949), stable medication for the past three months, aged 20-65 years, and possessing the ability to read and speak Swedish.

Exclusion criteria: Other severe diseases or functional limitations that would make pool exercise impossible.

3.2 Ethics

Ethical approval was granted for all four studies in the present thesis by the Regional Ethical Review Board in Gothenburg, Sweden. Written informed consent was obtained from all patients in studies I-III. Written and verbal information was given to all the patients in study IV but no informed consent was required at the time when the study was conducted.

3.3 Assessments

Physical functions

ISOBEX 3.0 dynamometer (Cursor AG, Bern, Switzerland) was used to assess isometric muscle strength of the shoulder abductor muscles in kilograms. The patient was placed in a seated position and the tested arm in lateral elevation of 90° and in the scapular plane (i.e. 30° of horizontal flexion anterior to coronal plane). A strap from the dynamometer, attached to the floor, was placed proximal to the wrist. The patient was instructed to elevate the arm from the original position as much as possible for five seconds. The best performance out of three was recorded (Klintberg et al., 2010).

Shoulder muscle endurance was assessed as the maximum time a person was able to hold his/her arm at a 90° lateral elevation of the shoulder with a 1 kg cuff attached proximal to the wrist. The instrument has shown acceptable reliability for patients with fibromyalgia (Mannerkorpi et al., 1999).

The Grippit (AB Detektor Gothenburg, Sweden), (U. Nordenskiöld, 1990) a digital electronic dynamometer was used to assess hand-grip force in Newtons. The patient was instructed to squeeze the hand around a device as hard as possible for ten seconds. The mean grip force and peak grip force were used for assessment and the best performance out of three was recorded. The Grippit has acceptable reliability for RA patients (U. M. Nordenskiöld et al., 1993).

The chair test was used to assess the muscle function for the lower extremities by counting the maximum number of times the patient was able to stand up from a chair during one minute. The patient was asked to hold the arms across the chest and keep the feet on the floor the whole time. The test has acceptable reliability for patients with Fibromyalgia (Mannerkorpi, et al., 1999).

The Index of Muscle Function (IMF) was used to assess the physical function of the lower extremities. IMF comprises 11 tests of muscle strength, balance, coordination and endurance. The IMF ranges from 0 to 40 where the highest score represent serious impairment of physical function. The test shows acceptable validity and reliability for patients with RA (C Ekdahl et al., 1999).

The Shoulder-Arm Function Impairment Index was used to assess active shoulder-arm movement (Bostrom et al., 1991). The instrument measures five common shoulder movements; hand-raising, hand-to-opposite-shoulder, hand-behind-back, hand-to-neck and hand-to-seat where the score ranges from 1 to 6. The total Shoulder Impairment score is 5 to 30, for each shoulder where a score of 30 represents full ability. The instrument was constructed for patients with RA and the validity and the intra and inter-rater reliability have been proven to be satisfactory (Bostrom, et al., 1991).

Active hand to neck and hand to back was recorded to assess functional arm movements rated on a scale ranging from 0 to 4, where a score of 4 represent the most decreased function. The test has acceptable reliability for patients with Fibromyalgia (Mannerkorpi, et al., 1999).

Shoulder range of motion was assessed by a universal full-circle goniometer (Gajdosik et al., 1987) to record active forward and lateral elevation of the shoulder.

A ergometric bicycle test was used to assess aerobic capacity by estimate the means of a submaximum test according to *Åstrand´s* principle (Astrand, 1960).

Self-administered questionnaires

The Disability of the Arm, Shoulder and Hand questionnaire (Atroshi, et al., 2000; Hudak, et al., 1996) was used to assess activity limitations related to the shoulder, arm and hand. It consists of a 30-item disability/ symptom scale concerning the patients health status during the preceding week. Twenty-one items reflect the degree of difficulty in performing various physical activities due to arm, shoulder or hand symptoms, five items on the severity of each of the symptoms of pain, activity-induced pain, tingling, weakness and stiffness, and four on the effect on social activities, work and sleep and psychological impact, see appendix 1. The items range from 1 to 5 (unable to perform activity or very severe symptom). The scores for the disability/ symptom scale are used to calculate a total score ranging from 0 to 100 (severe disability) and is called the DASH score. The calculation of the DASH score see appendix 2. The questionnaire also includes two optional scales concerning the ability to perform sports and or play a musical instrument and a work module. However, the optional scales are not included in the 30- item DASH score and therefore not included in this thesis. The mean DASH score for norm values for a general U.S. population aged 19 to 75+ is 10 (SD 15), (Hunsaker et al., 2002).

The Health Assessment Questionnaire (HAQ) (C. Ekdahl et al., 1988; Fries, et al., 1980) was used to assess general activity limitations. It is a RA disease-specific instrument that measures eight aspects of activity limitations during the previous week ranging from 0 to 3 (severe difficulties) The instrument possesses satisfactory reliability and validity and sensitivity to change in long-term studies for patients with RA. Three HAQ-items were selected to represent a more specific shoulder-arm-hand function; washing-the-hair, wash-and-drying-oneself and reaching in study I.

The Short Form-36 (SF36) (Sullivan et al., 1995; Ware et al., 1992) was used to assess quality of health. The 36 items generic multidimensional instrument comprises eight dimensions of health, these being physical function, physical role limitations, bodily pain, general health perceptions, vitality, social functioning, emotional role limitations and mental health. The eight subscores give an index for a physical component and a mental component. The total score ranges from 0 to 100 where a score of 100 represent the best health.

T*he Arthritis Impact Measurement Scale (AIMS 2)* (Archenholtz et al., 1995; Meenan et al., 1992) was used to assess health status. The instrument comprises 12 subscales ranging from 0 to 10. The physical dimension, including the subscales of mobility, physical activity, dexterity, household activity, activities of daily living and pain was applied.

The Leisure Time Physical Activity Index (LTPAI) (Mannerkorpi et al., 2005) was used to assess the amount of physical activity during a typical week . The physical activities are divided into light, moderate and vigorious. The total score is the sum of hours for the activities.

The Mechanical Exposure Index (MEI) (Balogh et al., 2001) was used to assess work-related mechanical exposure of the shoulder and neck region. It consists of 11 questions with scores ranging from 0 to 3, and reflects the subject´s perception of their degree of physical strain during work, awkward work posture, static load or high muscular strain during precise movements. The total MEI score ranges from 11 to 33, where a score ≥ 16 reflects high mechanical exposure(Ostergren et al., 2005).

Work and education

Education was categorised according to ≤ 9 years, 10 to 12 years and > 12 years of education, respectively.

For work status, patients were categorized into one of three categories: 0% of the working week spent working; working part-time <80 % of the working week spent working; and ≥80% of the working week spent working.

Physical work load was assessed by type of work categorized using a standard classification system (Larsson et al., 2005). The categories were "heavy material handling", "heavy repetitive", "medium-heavy load", "light repetitive", and "administration/ computer work".

Pain and exertion rate

Borg´s symptom scale (Borg, 1982) was used to record activity-induced shoulder pain during active shoulder-arm movement. The symptom scale ranges from 0 to 10, with a total sum score of 0 to 50 for each shoulder.

Borg´s scale for rating perceived exertion (RPE) (Borg, 1982) was used to record exertion during pool exercise. The Borg´s RPE scale ranged from 6 to 20.

Disease activity

The Disease Activity Score (DAS28) (Prevoo et al., 1995) was used to assess the disease activity and is based on a calculation of the erythrocyte sedimentation rate (ESR, mm/h), number of swollen and tender joints (28-joint index), and self-reported general health perception scored on a visual analog scale (0-100, 0= totally fine). The DAS28 is scored from 0 to 10 with scores <3.2 indicating low and >5 high disease activity, with moderate activity in between.

The Rheumatoid-Factor and Anti-CCP are serological markers assessed at the Sahlgrenska University Hospital laboratories.

Disease progression

Standard radiological examination of the hands, wrists and feet were performed. Patients with at least one erosion were classified as erosive i.e. had a more severe disease

3.4 Procedures

Information on demographic data and disease variables was obtained in interviews and from patient records in all four studies of the thesis.

Study I

Patients were provided with two self-administered questionnaires: the DASH questionnaire and the HAQ. Assessment of shoulder-arm movements, activity-induced shoulder pain, hand-grip force, and the number of swollen and tender joints was made by two physiotherapists specialized in rheumatology. A blood sample was collected to estimate the ESR and Rheumatoid Factor.

Patients in the reliability study were asked to complete the DASH questionnaire on two occasions, two days apart, to be able to investigate the test-retest reliability of the Swedish version of the DASH. Three patients did not complete and return the questionnaire on the second occasion and one patient did not complete the questionnaire properly. The final number of patients participating in the reliability study was 26.

Evaluation of the validity and test-retest reliability of the DASH

The concurrent validity was assessed by studying the association between the Swedish version of the DASH and the HAQ. As the HAQ assesses general activity limitations, including items of the upper extremities, we expected to observe a high correlation ($r_s > 0.75$) between the DASH and the HAQ-index.

The convergent validity was assessed by studying the associations between the Swedish version of DASH and outcome measures assessing different health aspects assumed to be related to activity limitations in the upper extremities. We expected to find moderate associations ($r_s \geq 0.50$) between the DASH and measures of active shoulder-arm movement, activity-induced shoulder pain, hand-grip force and disease activity as the measures do not assess completely the same dimensions.

Face validity was assessed by asking the patients to answer questions about the DASH. The aim was to find out if the questionnaire appeared to measure the shoulder-arm problem for patients with RA and if there were any redundant questions in the instrument. Two questions were graded on a 4 point numeric-scale, ranging from agree totally to do not agree at all, two questions were answered by Yes or No and two questions were open-ended. The questions were: The questions in the DASH score reflect your shoulder-arm problems. The questions were easy to understand. Did the questionnaire contain any redundant questions. Do you have any shoulder, arm and hand symptoms. How long did it take to fill in the questionnaire. Are there any other questions related to the shoulder, arm and hand that you find important and that the DASH questionnaire excluded.

The test-retest reliability was studied for the total score of the DASH. The patients were asked to fill in the questionnaire on two occasions, separated by two days.

Study II

Examinations and administrations of the questionnaires were carried out by four experienced physiotherapists. Examination and assessment of the shoulder function i.e. active shoulder-arm movement, activity-induced shoulder pain, isometric shoulder muscle strength and hand-grip force were conducted. Examinations of the patients´ joints for assessment of tender and swollen joints were conducted under the supervision of an experienced rheumatologist. A blood sample was collected to estimate the erythrocyte sedimentation rate (ESR), Rheumatoid Factor and anti-CCP titers. Examinations and assessments of the reference group for the shoulder function, hand-grip force and administrations of the questionnaires were carried out by two experienced physiotherapists

Study III

For the examinations and administrations of the questionnaires see procedure for the patient group in study II.

Study IV

A physiotherapist blinded to group membership during the whole study conducted the examinations. The primary outcomes where aerobic capacity assessed by an ergometer bicycle test and the physical component of the SF-36. The secondary outcome measures; these were the shoulder muscle endurance test and the chair test. Functional tests assessing limitations in the

upper and lower extremities, self-administered generic and disease specific instruments assessing quality of life, and general activity limitations were also included as exploratory outcome measurements, see Table 1. Patients in the exercise group were tested at baseline, after the intervention period (3 months) and at follow-up after a period of 6 months from baseline. Patients in the control group were tested at baseline and after the intervention period (3 months). Patients were randomly assigned to the exercise group or the control group using optimal allocation with a computer program for a minimization procedure to balance for the background variables of age, disease duration, DAS 28 and aerobic capacity. A blood sample was collected to estimate the erythrocyte sedimentation rate (ESR) and Rheumatoid Factor.

All patients were asked to maintain the type and dosage of pre-entry medications and not to start any other treatment as far, as was ethically possible during the study period.

Intervention group. Patients allocated to the exercise group participated twice a week for a period of 12 weeks in warm water pool exercise, supervised of a physiotherapist. The sessions were 45 minutes long and included exercises for aerobic endurance, and muscle function, flexibility, coordination and relaxation. The intensity of the aerobic part of the program was designed to achieve and maintain a target heart rate of 70% of the maximum heart rate for the patients. The first exercise group started in August 2000 and the last group had completed the program by the end of April 2002. See appendix 3, for details on the exercise program.

Control group. Patients allocated to the control group were asked to maintain their daily physical activities as before entering the study during the whole control period. They were asked not to start any resistance training or pool exercise during the study period of three months.

3.5 Statistical analyses

An overview of the statistical tests used in the thesis is given in Table 3. All the tests were two tailed and conducted at the 5% significant level.

Table 3. An overview of the statistical methods used in the studies.

Statistical methods	I	II	III	IV
Descriptive statistics				
Mean (SD), Median (min-max), Number and percent	X	X	X	X
Intra-individual standard deviation	X			
Differences within groups				
Wilcoxon´s signed rank test	X	X	X	
Differences between 2 groups				
Chi_2-test	X	X	X	
Mann-Whitney U-test	X	X	X	
Mantel Haenszel $Chi-_2$ test	X	X	X	
Fisher´s exact test				X
Fishers non-parametric permutation test				X
Associations				
Spearman´s correlation coefficient (r_s)	X	X	X	
Intraclass Correlation coefficient	X			
Stepwise multiple logistic regression analysis			X	

Descriptive data are presented for continuous variables as mean, standard deviations (SD), median and range, and data for categorical variables as number and percentage.

Spearman's correlation coefficient was used in studies I-III for correlation analyses. The following classification was used to interpret the correlation values: 0–0.25 indicates little or no relationship, 0.25–0.50 indicates a fair degree of relationship, 0.50–0.75 a moderate to good relationship, and a correlation above 0.75 indicates a very good to excellent relationship (Colton, 1974).

Intra Class Correlation (ICC) and Intra-individual standard deviation (SD). The test-retest reliability of the DASH was calculated in Study I using the Intra Class Correlation coefficient (ICC 2.1) with 95% confidence interval (Shrout et al., 1979) as well as the mean, SD, and range of the differences between the readings (Test2-Test1), and the intra-individual SD (Bland et al., 1996). Wilcoxon's signed rank test was chosen to analyze systematic differences in the variables between the two tests. The following classification was used to interpret the ICC values in study I: An ICC of 0.90 is recommended for assessment of individual protocols, while 0.70 is acceptable for group comparison (McHorney et al., 1995).

Between-group comparisons. For comparison between two groups in studies I-III the Mann-Whitney U-test was used for continuous variables and Mantel-Haenszel Chi-square test for ordered categorical variables. Fisher´s exact test was used for comparison between two groups for dichotomous variables in study I-IV. For comparison between the training group and the control group in study IV, regarding both continuous and ordered categorical baseline variables and change in outcome variables Fisher's non-parametric permutation test was used. In study II the difference in means between the patient group and the reference group with 95% confidence interval was calculated.

Within-group comparisons. The Wilcoxon signed rank test was used to study differences within-groups in study II. Fisher's non-parametric permutation test for matched pairs was used for comparisons of changes within-groups over time in study IV.

Stepwise multiple logistic regression analysis. In order to find independent predictors for full-time work all significant variables from the correlation analysis were entered into a stepwise multiple logistic regression analysis. The AUC-values, the area under the Receiver Operating Characteristic (ROC) curve were calculated in study III. For description of goodness of explanatory factors (Hanley et al., 1982) and are presented with 95% confidence interval 0.7≤AUC-values <0.8 indicates that the explanatory variables are acceptable, 0.8≤AUC-values <0.9 indicates that they are excellent and AUC-value ≥0.9 indicates that they are outstanding (Hosmer et al., 2000). Adjusted p-values and adjusted odds ratio (OR) with 95% confidence interval are presented for multivariable models.

Upper limit of expected number of false significances. To control for Typ 1 errors, the upper limit of expected number of false significances for all the outcome variables were calculated in Study IV by the following formula: (number of tests-number of significant tests on the significant level alfa) x alfa / (1-alfa) (Eklund et al., 1965).

4 SUMMARY OF RESULTS

For group characteristics see Table II.

4.1 Study I

Disability of the Shoulder, Arm and Hand (DASH) questionnaire in Swedish patients with rheumatoid arthritis: A validity study.

Validity

All patients (n=67) completed the DASH, while 2 HAQ-protocols could not be calculated due to missing values. The mean HAQ-index was 0.5 (SD 0.51), ranging from 0 to 2.1, while the mean DASH score was 22 (SD 18.0), ranging from 0 to 77.

Concurrent validity. The associations between the DASH score and the HAQ-index was found to be very good to excellent (r_s 0.80, $p<0.001$).

Convergent validity. The association between the DASH score and shoulder function was found to be moderate to good; active range of motion (r_s=-0.50, $p<0.001$) for the right arm, and activity induced pain (r_s=0.66, $p<0.001$) for the right shoulder-arm. The association between the DASH and hand-grip force (r_s= -0.59, $p<0.001$) for the right hand, and the disease activity score (DAS28) (r_s=0.63, $p<0.001$) was found to be moderate to good. Moreover, the DASH score showed moderate to good association with shoulder-specific activities in HAQ, where these were the HAQ-washing-the-hair (r_s =0.55, $p<0.001$), the HAQ-washing-and-drying-oneself (r_s=0.61, $p<0.001$) and the HAQ-reaching (r_s=0.72, $p<0.001$).

Face-validity. Out of 26 patients, 20 reported current symptoms in the shoulder, arm and hand. The majority, (96%) of the patients found the DASH to reflect fully or in general their shoulder-arm-hand problems and found the DASH easy to understand. Seventy-nine percent found the items relevant. However, question number 21, about sexual activities, was found by two patients to be too private and one patient raised a question about car driving and the ability to change gears.

Test-retest reliability

A total of 26 protocols were included in the analyses of the test-retest reliability of the DASH questionnaire.

The ICC (2.1) was 0.99 (95 % CI, 0.98-0.99) for the DASH score, indicating excellent agreement. The mean difference for the DASH score was -0.15 (SD 4.05), ranging from -9 to 12. The intra-individual SD was 2.78. The total score of the DASH for the first and second times was 32 (SD 30.06) and 32 (SD 30.76), respectively. No systemic differences were found for the protocols completed on the two occasions (p=0.652).

4.2 Study II

Shoulder function is impaired in early rheumatoid arthritis, a controlled cross-sectional study

In the patient group, 72.8% worked as compared to 97.1% in the reference group, and the mean working hours per week was significantly ($p<0.0001$) lower in the patient group than in the reference group.
There was no significant difference with regard to physical work load between the patient and the reference groups. The mean time for leisure time physical activity during the previous week in the patient group was significantly lower ($p=0.003$) than in the reference group.
At the time of the assessment, 53.4% of the patients and 20.4% in the reference group reported shoulder symptoms (mostly pain). Thirty-three (32.0%) patients had unilateral symptoms and 22 (21.4%) bilateral symptoms. In the reference group, unilateral shoulder symptoms were found to be more common than bilateral symptoms.

Shoulder function

Ninety percent of the patients and 98.1% of the healthy subjects in the reference group reported right hand dominance. No significant differences between the dominant and non-dominant arm for shoulder strength were found in the RA group, mean difference 0.11 (SD 0.82), ($p=0.091$) kg or in the reference group 0.03 (SD 0.84) ($p=0.56$) kg. Hence, only the dominant arm is presented in the result section.

Patients showed significantly ($p<0.0001$) impaired shoulder function with regard to isometric shoulder muscle strength, shoulder-arm movement, lateral shoulder elevation and shoulder pain compared to the reference group for the

dominant arm. The shoulder muscle strength in the patient group was approximately 65% of the strength in the reference group.

Activity limitations of the shoulder, arm and hand

Activity limitations related to the shoulder, arm and hand (DASH) were significantly higher ($p<0.0001$) in the patient group than in the reference group. DASH was significantly higher ($p<0.05$) for the patients in all age-groups compared with the reference group when the groups were divided into ten-year intervals, see figure 1.

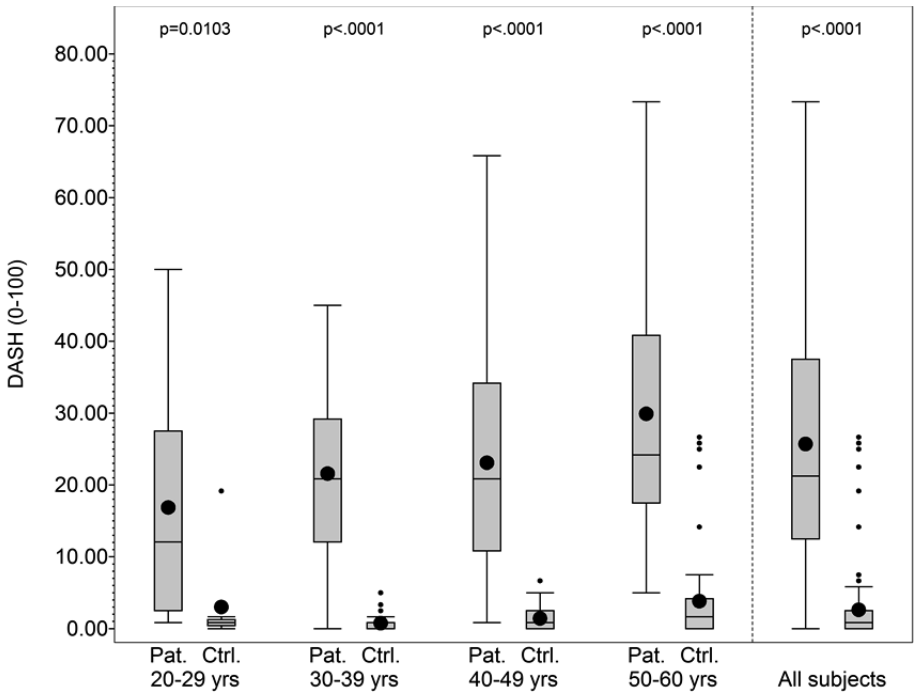

Figure 1. DASH score by age-group for the patient and reference group, and for the total study population

Associations

The associations between the shoulder muscle strength of the dominant arm and shoulder pain (r_s=-0.48, p<0.001), hand-grip force (r_s=0.51, p<0.001), DAS28 (r_s=-0.34, p=0.001), and DASH (r_s=-0.45, p<0.001) were all found to be significant.

Group comparisons

Patients who reported shoulder symptoms (n=54) showed significantly (p<0.01) more impaired shoulder function with regard to shoulder muscle strength, shoulder-arm movement, lateral shoulder elevation and shoulder pain for the symptomatic shoulder than healthy subjects who reported shoulder symptoms (n=21).

Patients reporting no shoulder symptoms (n=49) also showed significantly (p<0.0001) impaired shoulder function with regard to shoulder muscle strength, shoulder-arm movement, lateral shoulder elevation and shoulder pain for the dominant arm when compared with healthy subjects reporting no shoulder symptoms (n=82). The shoulder muscle strength in patients reporting no shoulder pain was approximately 73% of the strength observed for healthy subjects reporting no shoulder symptoms.

4.3 Study III.

Work status in early Rheumatoid Arthritis; emphasis on shoulder function and mechanical exposure

The mean working hours per week was 25.2 (SD 16.4) hours for the study population. Sixty-six patients were working full time and 33 not at all. Thirty-two percent of the patients had an education level of nine years or less, 36.8% between 10 and 12 years of school education, while 30.8% had an education level of more than 12 years. Three percent of the patients had work with that entailed “heavy material handling”, 1.5% patients had “heavy repetitive”, 35.1% patients had “medium-heavy load”, 14.9% patients had “light repetitive”, and 45.5% patients had “administration/ computer work”. The mean value for MEI was 17.7 (SD 4.50).

Work hours and associated factors

Assessments related to work (MEI and physical workload), and shoulder function (shoulder-arm movement, activity-induced shoulder pain, shoulder muscle strength), hand-grip force, activity limitations (DASH and HAQ), and disease activity (DAS28) were significantly ($p<0.01$) associated with work hours, see Table 4. The correlations between work hours and education level, and between work hours and age were found to be non significant, see Table 4.

Table 4. Correlations between work hours and associated factors (n=135). Values are given as Spearman´s correlation coefficients (r_s) and p-value.

Variables	Total Work hours r_s	p-value
MEI (11-33)	-0.34	<0.001
Physical work load	0.26	0.0036
DAS28 (0-10)	-0.43	<0.001
Shoulder-arm movement (5-30)	0.34	<0.001
Activity-induced shoulder pain (0-50)	-0.45	<0.001
Isometric shoulder muscle strength kg,	0.25	0.0032
Hand-grip force, N	0.45	<0.001
DASH (0-100)	-0.61	<0.001
HAQ (0-3)	-0.52	<0.001
Age, years	-0.06	0.508
Education level	0.16	0.0731

Correlation is significant at the $p< 0.05$ level (2-tailed).

All nine variables that correlated significantly with work hours were entered into a stepwise multiple regression analysis in order to find the best explanatory model for full-time work. DASH was found to be the only significant ($p<0.001$) variable to independently explain full-time work, Odds Ratio (OR) = 0.40, (95% CI:0.29-0.55) per ten increments, AUC-statistic = 0.81, (95% CI:0.74-0.89). When DASH was removed from the stepwise analysis HAQ (adjusted $p<0.001$), adjusted OR=0.23, (95% CI:0.09-0.55), MEI ($p=0.018$) OR=0.54, (95% CI:0.33-0.90) per five increments and hand-grip force ($p=0.006$), OR=1.30, (95% CI:1.08-1.57) per 50 Newtons were included as independent predictors into the model (AUC 0.805, (95%CI:0.73-0.88)

A between group analysis for women was conducted to compare work status according to non-working, part-time work and full-time work. The between-group analyses were not conducted for men due to the small sample size. Non-working women reported significantly higher MEI scores ($p= 0.002$) and DASH scores ($p< 0.001$) compared with women working full-time. Shoulder function was significantly impaired among non-working women compared with women working full-time: activity-induced shoulder pain ($p<0.001$), active shoulder-arm movement ($p=0.001$) and shoulder strength ($p=0.002$). Non-working women had significantly lower hand-grip force ($p<0.001$), and significantly lower education level ($p= 0.008$) than women working full-time. Furthermore, non-working women were significantly older ($p=0.023$) and had significantly higher DAS28 scores ($p< 0.001$) than women working full-time. There were similar findings for non-working women compared with women working part-time.

4.4 Study IV.

Moderately intensive exercise in a temperate pool for patients with rheumatoid arthritis: a randomized controlled study

There were no significant baseline differences between the exercise group and the control group in terms of age, disease duration, disease-specific measures, such as DAS 28, and the total HAQ score. Nor were there any significant baseline differences between the two groups with regard to the functional tests or the self-administered questionnaires. Moreover, no significant differences between the groups in medication or injections occurred during the study period. No significant differences were found in medication or injection for the exercise group during the period of six months at follow-up.

Between-group differences

No significant changes were found for the primary outcome measures of ; aerobic capacity and the physical component of the SF-36. The two secondary outcome measures; the chair test (P=0.005), and the shoulder muscle endurance test of the left and the right arm (P<0.001) increased significantly in the exercise group compared with the control group. The maximum and mean hand-grip force of the left hand (P<0.001), the IMF score (P=0.006), the active lateral shoulder elevation for the left (P=0.009) and right (P=0.047) arms, and the active forward elevation of the left arm (P=0.03) increased significantly in the exercise group compared with the control group, see Tables 5 and 6.
Type 1 error. A total of 29 statistical between-group analyses were conducted, and the upper level of number of false significances was 0.94, which indicates that one of the 11 significances found might be false

Within-group differences

At the posttest for the exercise group, the following scores on the SF-36 improved: SF-36 physical function (P=0.0001), bodily pain (P=0.003), vitality (P=0.004) and the physical component (P=0.01). The chair test (P=0.008), the AIMS2 physical dimension (P=0.007) and the HAQ score (P=0.04) also improved. The lateral elevation of the left arm (P=0.04), the shoulder muscle endurance of the right and left arms (P<0.001), maximum hand-grip force of the left side (P<0.001) and IMF score (P=0.007) also improved, see Table 5 to 6.
At the posttest examinations for the control group the maximum (P=0.04) and mean hand-grip force (P=0.03) in the left hand were found to have decreased, while the SF-36 bodily pain (P=0.03) had improved, see Table 5 and 6.

Type 1 error. A total of 29 statistical within-group analyses for the exercise group were conducted, and the upper level of number of false significances was 0.94, which indicates that one of the 12 significances found might be false for the within-group analyses for the exercise group.

Type 1 error. A total of 29 statistical within-group analyses for the control group were conducted, and the upper level of number of false significances was 1,26 which indicates that one or two of the 3 significances found might be false

Table 5. Instruments assessing health at baseline and the post-test in the exercise group and control group

	Exercise group (n=20)			Control group (n=23)			
	Baseline Mean(SD)	**Post-test Mean(SD)**	**Diff. Mean(SD)**	**Basline Mean(SD)**	**Post-test Mean(SD)**	**Diff Mean(SD)**	**Differences between the groups p-value**
SF-36							
Physical functioning	56.0(20.9)	64.7(20.0)	9.5(10.6)***	60.7(18.8)	64.9(21.4)	4.2(11.8)	N.S.
Role Physical	20.2(40.9)	39.5(37.6)	17.1(44.1)	48.9(41.6)	48.9(38.0)	0.0(40.6)	N.S.
Bodily pain	40.7(21.0)	50.8(23.4)	10.7(15.0)**	45.9(22.3)	50.9(21.0)	5.0(10.0)*	N.S.
Social functioning	68.1(29.1)	73.7(22.4)	6.6(21.8)	72.3(23.2)	71.2(21.1)	-1.1(18.4)	N.S.
Mental health	68.4(23.5)	72.4(15.9)	5.5(19.5)	76.9(18.6)	72.7(16.9)	-3.3(19.9)	N.S.
Role emotional	48.3(43.9)	69.6(36.1)	10.5(45.9)	60.9(46.7)	69.6(36.1)	8.7(36.5)	N.S.
Vitality	41.5(23.9)	51.8(22.6)	12.1(17.6)**	51.8(22.1)	49.1(17.6)	-1.6(18.8)	0.021
General Health	46.0(26.3)	49.8(19.3)	6.3(17.8)	59.8(19.6)	59.3(16.1)	-0.5(16.0)	N.S.
Physical component	33.0(9.6)	37.1(10.5)	4.8(7.1)**	37.1(8.9)	38.3(9.6)	1.5(7.5)	N.S.
Mental component	43.1(13.7)	45.1(11.5)	2.8(11.8)	47.6(12.5)	46.2(10.8)	-0.6(12.6)	N.S.
AIMS2							
Physical	2.6(1.5)	2.1(1.4)	-0.6(1.0)**	2.2(1.3)	2.1(1.2)	-0.2(0.7)	N.S.
HAQ	0.9(0.5)	0.7(0.5)	-0.2(0.3)*	0.7(0.5)	0.8(0.6)	0.0(0.2)	0.045

Mean and S.D. for the ratings and the differences within and between the groups are given. *p<0.05; **p<0.01; ***p<0.001.

Table 6. Functional tests at baseline and at post-test in the exercise group and control group

	Exercise group (n=20)			Control group (n=23)			
	Baseline Mean (SD)	Post-test Mean (SD)	Diff. Mean (SD)	Baseline Mean (SD)	Post-test Mean (SD)	Diff. Mean (SD)	Differences between the groups p-value
VO2 ml/ (kg x min)	34.0 (10.9)	33.8 (10.0)	-0.26 (5.4)	34.2 (6.7)	32.4 (7.3)	-1.8 (5.0)	N.S.
Forward shoulder elevation°							
Right	156.0 (29.8)	165.0 (6.3)	9.0 (28.8)	161.5 (25.4)	158.9 (27.2)	-2.6 (15.1)	N.S.
Left	156.8 (28.7)	166.0 (19.6)	9.3 (23.7)	166.1 (19.0)	161.5 (19.8)	-4.6 (15.6)	0.027
Lateral shoulder elevation°							
Right	148.8 (34.7)	160.5 (35.9)	11.8 (35.4)	159.1 (31.0)	154.4 (30.4)	-4.8 (14.8)	0.047
Left	142.8 (38.8)	158.5 (38.2)	15.8 (31.1)*	160.9 (28.6)	155.0 (31.9)	5.9 (21.7)	0.009
Hand to neck (0-4)							
Right	0.3 (0.5)	0.4 (0.8)	0.0 (0.7)	0.2 (0.5)	0.3 (0.7)	0.1 (0.4)	N.S.
Left	0.2 (0.4)	0.2 (0.4)	-0.10 (0.45)	0.3 (0.8)	0.2 (0.5)	-0.09 (0.7)	N.S.
Hand to scapula (0-4)							
Right	0.6 (0.9)	0.2 (0.6)	-0.4 (0.8)	0.4 (0.9)	0.4 (0.9)	-0.04 (0.4)	N.S.
Left	0.6 (0.7)	0.3 (0.7)	-0.3 (0.6)	0.2 (0.5)	0.1 (0.5)	-0.1 (0.3)	N.S.
Shoulder endurance (sec)							
Right	59.8 (54.1)	90.3 (52.2)	30.5 (26.0)**	70.9 (40.0)	58.2 (35.4)	-12.7 (31.4)	<0.001
Left	54.8 (51.6)	80.5 (54.6)	25.8 (23.6)	65.4 (34-3)	59.8 (32.4)	-5.7 (27.3)	<0.001
IMF score	5.4 (7.3)	2.2 (3.6)	-3.2 (5.2)**	2.3 (2.8)	2.2 (3.5)	0.3 (2.6)	0.006
Chair test	20.6 (6.6)	23.7 (7.0)	3.2 (4.5)**	24.3 (6.4)	23.7 (6.2)	-0.7 (3.6)	0.005
Hand-grip force, max (N)							
Right	179.0 (115.2)	181.1 (91.0)	2.1 (48.4)	178.7 (109.6)	180.7 (103.3)	2.0 (36.0)	N.S.
Left	152.4 (106.7)	182.8 (116.7)	30.3 (34.5)***	188.5 (105.3)	172.6 (88.4)	-15.9 (34.6)*	<0.001
Hand-grip force, mean (N)							
Right	140.5 (96.5)	139.0 (72.7)	-1.6 (41.9)	145.1 (89.8)	142.0 (86.7)	-3.1 (30.3)	N.S.
Left	114.3 (89.4)	142.9 (100.4)	28.6 (33.5)***	153.6 (87.3)	137.6 (70.2)	-15.9 (32.8)*	<0.001

Mean and S.D. for the ratings and the differences within and between the groups are given. *p<0.05; **p<0.01; ***p<0.001

Six-month follow-up

The aerobic capacity did not change, while the SF-36 physical component improved significantly ($p<0.01$) compared with baseline values. The secondary outcome measures, the chair test and the shoulder muscle endurance test, also displayed significant improvements ($p<0.05$) at follow-up. Furthermore, 13 of the physical function tests had improved significantly ($P<0.05$) at follow-up, (forward and lateral shoulder elevation for both arms, hand to neck and hand to scapula for the right arm, the mean hand-grip force for both hands and the max hand-grip force for the left hand). Seven of the eight subscales of the SF-36 showed significant improvements ($P<0.05$) (physical functioning, role physical, bodily pain, social functioning, mental health, role emotional, vitality and the mental component). In addition, both the AIMS2 physical dimension and the HAQ score displayed significant improvements ($p<0.05$). No significant deterioration was found for any variables at the completion of the intervention.

Type 1 error. A total of 29 statistical within-group analyses for the exercise group were conducted, and the upper level of number of false significances was 0.26 which indicates that one of the 24 significances found might be false for the within-group analyses for the exercise group.

5 DISCUSSION

5.1 General discussion

The thesis shows that shoulder function, especially shoulder muscle strength, is reduced in patients with early RA. Impaired shoulder function was also seen among patients reporting no shoulder symptoms. Our results imply the importance of regular screening of the shoulder function from disease onset. The "new" instrument, DASH, evaluated in study I appears to cover activity limitations related to the shoulder, arm and hand in patients with early RA. The questionnaire can be recommended to monitor the progress of upper extremity function and activity limitations in RA populations as it was found to possess satisfactory validity and reliability. Work ability was found to be associated with shoulder function, activity limitations in the shoulder, arm and hand and mechanical exposure related to the neck and shoulder region. Moderately intensive pool exercise can be recommended for improving muscle function of the upper and lower extremities, shoulder movements, activity limitations and quality of life in patients with RA.

The patient characteristics in study I,II and III are similar to early RA cohorts in other studies (Hallert, et al., 2003; Rantalaiho et al., 2011) with regard to serological patterns (positive rheumatoid factors and anti-CCP), erosions, gender distribution and progress. The findings in this thesis are therefore applicable to other patients with early RA. Characteristics of the patients in study IV differ slightly from the other studies as two different inclusion criteria were set in this thesis. The inclusion criteria in studies I,II and III for disease duration was between six months and three years, while the inclusion criteria for disease duration in study IV was between one and five years. However, no large difference with regard to disease duration is apparent between the different populations [21(SD 9.6), vs. 31(SD15.8) months]. The results in study IV seem therefore also to be applicable for patients with early RA.

Shoulder function and activity limitations related to the shoulder, arm and hand

Despite improvements in pharmacological treatment, patients report problems with activities involving the shoulder. It has been argued that shoulder involvement is a late symptom in RA (van Schaardenburg, 1995). However, few controlled studies have investigated the shoulder function in the early disease course of patients with RA (Olofsson, et al., 2003). Our results indicate that the shoulder function is impaired already early in disease.

Especially the shoulder muscle strength was found to be reduced, both in patients reporting shoulder symptoms and in patients reporting no shoulder symptoms. The shoulder muscle strength in the total patient group was approximately 65% of the shoulder muscle strength observed in the reference group, while the muscle strength was reduced to 73% in patients reporting no shoulder symptoms. The reduced shoulder muscle strength is also in agreement with a general reduction of muscle strength in early RA as shown in reduced hand-grip force (Eurenius, et al., 2005; Hakkinen, et al., 1995) and reduced muscle strength (Hakkinen, et al., 1995) and muscle function (Eurenius, et al., 2005) in the lower extremities.

Although shoulder movement was found to be significantly reduced in the patient group as compared with the reference group, the majority of the patients seem to have sufficient shoulder movement for daily activities. A previous study reported reduced shoulder-arm movement in 30% of patients with early RA compared to a reference group of healthy subjects (Olofsson, et al., 2003). The better shoulder-arm movement among our patients might have been due to better pharmacological treatment and a female and younger study population.

The impaired shoulder function in patients reporting no shoulder symptoms indicate that patients are not aware of the limitation. A possible explaination might be that patients tend to compensate the lack of function with adjacent joints or using the contralateral arm instead. Thus, this indicate the importance of initiating screening of shoulder function at the time of disease onset in all patients, not just in those reporting shoulder symptoms.

The majority of the patients reported some degree of activity limitations when assessed with DASH compared to the reference group (study II). Moreover, DASH scored significantly higher for patients in all age-classes (20-60 years) when compared with the reference group. The moderate association found in the patient group between DASH and shoulder muscle strength (study II) and the moderate associations found between DASH and active-shoulder movement, activity-induced shoulder pain, and hand-grip force (study I) imply that self-reported activity limitations among patients with early RA are related to shoulder function.

To summarise, our results imply the importance of regular screening of the shoulder function from disease onset, especially as impairment in the shoulder seems to be underreported in early RA. Physiotherapists should monitor shoulder function from disease onset and special attention to the shoulder muscle strength is warranted as reduced muscle strength might contribute to activity limitations and difficulties in daily activities.

Evaluating DASH

DASH possesses acceptable convergent, concurrent and face validity for use in patients with early RA. Our results are in line with a previous study validating the DASH for a German RA population (Raven et al., 2008). The authors in that study found similar correlation between DASH and HAQ as in our study, which supports the concurrent validity for the DASH in the RA population. Moreover, *Raven et al.* found similar or slightly lower correlations between DASH and DAS28, and pain, and hand-grip force compared with our results, which further supports the convergent validity in the RA population. However, compared to our study population, the patients in *Raven et als.* study were older and had a longer disease duration.In addition, all of the patients in that study reported shoulder complaints, as compared with ours, where approximately 50% of the patients reported shoulder symptoms. In total, this indicates that DASH is a feasible instrument for assessing activity limitations in patients with RA regardless of disease duration, age or the severity of shoulder symptoms.

The test-retest reliability was also found to be good as the ICC showed satisfactory stability for the DASH score, indicating that DASH can be used to monitor groups of patients, as well as individual patients (McHorney, et al., 1995). The interval between the two tests for the test-retest reliability was two to five days. To minimize recall bias some authors recommend a one to two week period between the tests, while others use a shorter period of two to three days between the tests in order to avoid possible changes in health status. Since the health status of RA patients can change rapidly, a shorter period of time between the tests was found to be more appropriate for this study. However, the patients' possible recall of previous answers can be considered a methodological limitation of the study. Other studies have found similar ICC values (ICC=0.96-0.97) for test-retest reliability in DASH (Beaton et al., 2001; Raven, et al., 2008) which indicates that the test-retest reliability in our study is inline with theirs.

Our study population found the DASH easy to fill in and it took less than ten minutes to complete the questionnaire. A shorter form of the questionnaire the Quick DASH has been developed (Beaton et al., 2005) and culturally adapted for patients with orthopedic disorders of the upper extremities in Sweden (Gummesson et al., 2006). However, the Quick DASH was not applied in this thesis and needs to be further investigated before considering its use in RA.

To summarise, the Swedish version of DASH appears to possess satisfactory concurrent, convergent and face validity in patients with RA when compared

with other measures assessing activity limitations, shoulder function, muscle strength of the upper extremity and disease activity. The DASH was also found to have satisfactory test-retest reliability, indicating that the instrument can be used to monitor the progress of the upper extremity function. The DASH appears to cover activity limitations related to the shoulder, arm and hand in patients with RA and can be recommended for use in RA populations.

Work ability and associations

In study III, almost half (48.9%) of the study population worked full-time while 26.7% worked part-time and 24.4% not at all. Since there is a risk for patients with RA, who are unable to work early in disease, to remain sick-listed in the long term (Eberhardt, et al., 2007), one quarter of the study population might be at risk of permanent work disability.

Working conditions in Sweden have changed during the past decades, which have led to decreased heavy manual work and increased sedentary work. In study III the majority of the women working full-time had administrative work, while half of the part-time working and non-working women had a current or previous medium-heavy type of work. However, a biomechanical load on the shoulder leading to work-related symptoms seems to be present. Fifty-six percent of the patients found their work to be a physical challenge for the neck and shoulder region assessed with MEI. Since a high MEI score, above 16, has been found to predict neck and shoulder symptoms among working adults (Ostergren, et al., 2005) our results indicate that more than half of the study participants might be at risk of developing shoulder and neck symptoms if they continue to do the same type of work. It is plausible that patients with early RA may be at risk of high work-related mechanical exposure related to the shoulder-neck region. One contributing factor to the high MEI may be the impaired shoulder function among the patients.
The association between work hours and shoulder function indicates that shoulder function is an important factor for work ability in early RA. Moreover, the reduced shoulder muscle strength and higher shoulder pain found among the non-working women, compared with those working full-time, suggests that shoulder pain and muscle strength contribute to impaired work ability.
The majority of the patients in study III reported a DASH score above 10, which indicates some activity limitations related to the shoulder, arm and hand (DASH), compared with norm values (Hunsaker, et al., 2002). The correlation between work hours and DASH, supported by the multiple regression analysis, indicates that DASH is an important instrument, providing information about work ability in early RA.

To summarise, the associations found between work ability, shoulder function, and mechanical exposure related to the shoulder-neck region, and activity limitations related to the shoulder, arm and hand brings additional knowledge about why patients with early RA have impaired work ability.

Pool exercise

Our RCT comparing a pool exercise intervention with normal daily activities could not identify any significant improvement in aerobic capacity and the physical component of self-rated quality of life (SF-36), which were defined as the primary outcomes when designing the study.

However, muscle function of the lower extremities and shoulder muscle endurance of the upper extremities defined as the secondary outcome variables, improved significantly for the exercise group compared with the control group. Also shoulder movement, hand-grip force, activity limitations and well-being showed a significant improvement for the exercise group when compared to the control group. All the improvements remained at the time of follow-up for the exercise group.

Pool exercise in patients with RA is poorly investigated. At the time that we designed and conducted our study, only a few RCT had investigated the effects of a pool exercise intervention for patients with RA (Hall, et al., 1996; Rintala et al., 1996). Today, the number of RCT studies is still limited. There are findings showing that short-term pool exercise (12 weeks) can improve physical function (Hurkmans, et al., 2009) and patients' perceptions of well-being (Eversden, et al., 2007). An RCT combining pool exercise and walking exercise found a 20% increase in aerobic capacity in patients with RA (Minor et al., 1989). However, as the aerobic intervention included two programs, it is impossible to determine the effect of pool exercise from that study.

We found no evidence of an improvement of the aerobic capacity in our short term RCT. The aerobic part of the exercise program was designed to achieve and maintain a target heart rate of 70% of the maximum heart rate, which is considered to improve aerobic capacity (PO Åstrand, 1986) . We measured the heart rate on two sessions to ensure the exercise level; this might have been too infrequent to control the intensity level in the exercise group. Moreover, our study populations had rather good aerobic capacity at baseline when compared with suggested norm data (Astrand, 1960). Patients might have needed a higher intensity level to improve their aerobic capacity. A systematic review article of the effects of dynamic exercise in RA concluded that more benefit was seen in studies with high intensity exercise compared with low intensity (Cairns, et al., 2009). The conclusions of *Cairns et al*. are

supported by another systematic review article of the same topic, where the authors concluded that an intensity level of moderate to hard, performed three times weekly for a duration of 30-60 minutes for improving the aerobic capacity, is recommended (Stenstrom, et al., 2003). This implies that the intensity, duration and the frequency of our exercise program might have been too low to improve the aerobic capacity in the exercise group. Finally, a type two-error can not be excluded in this study as the study population was rather small.

To summarise, moderately intensive pool exercise appears to be an appropriate exercise intervention for improvement of muscle function, joint movements, activity limitations and quality of life. However, pool exercise with this intensity can not be recommended as a mode of exercise to improve aerobic capacity. It is still important to improve aerobic capacity among patients with RA, but other methods of exercise should be recommended.

5.2 Clinical implications

Our results indicate that the shoulder function is impaired already early in disease. Especially the shoulder muscle strength was found to be reduced, both in patients reporting shoulder symptoms as well as in patients reporting no shoulder symtoms. The shoulder muscle strength in the total patient group was approximately 65% of the shoulder muscle strength observed in the reference group, while the muscle strength was reduced to 73% in patients reporting no shoulder symptoms. Screening and monitoring of shoulder function, especially shoulder muscle strength are warranted as impairment of the shoulder function seems to be underreported in patients with early RA.

Activity limitations related to the shoulder, arm and hand are common in patients with early RA. The majority of the study population reported some activity limitations related to the shoulder, arm and hand compared to the reference group of age and gender-matched healthy subjects. DASH appear to cover activity limitations related to the shoulder, arm and hand in patients with early RA, and can be used to monitor the progress of upper extremity function as it was found to possess satisfactory validity and reliability

Work ability assessed as the number of working hours per week was found to correlate with shoulder function, mechanical exposure and activity limitations related to the shoulder, arm and hand. DASH was also found to be the only significant variable to explain the ability to work full-time in patients with early RA.

Moderately intensive pool exercise twice a week for 12 weeks is recommended to improve physical function, activity limitations and quality of life in patients with RA.

6 CONCLUSION

The following conclusions are based on the present studies investigating shoulder function and activity limitations related to the shoulder, arm and hand and the relationship between shoulder function, activity limitations and work ability in patients with early RA and moderately intensive pool exercise for patients with RA.

Patients with RA have impaired shoulder function already at early stages of the disease. Moreover, patients reporting no shoulder symptoms displayed impaired shoulder function.

Isometric shoulder muscle strength in patients with early RA was approximately 65% of the shoulder muscle strength observed in healthy age-matched subjects.

DASH appear to cover activity limitations related to the shoulder, arm and hand in patients with early RA, and can be used to monitor the progress of the upper extremity function and activity limitations.

Work ability is reduced in patients with early RA and is associated with impaired shoulder function, mechanical exposure and activity limitations related to the shoulder, arm and hand.

Moderately intensive pool exercise twice a week for 12 weeks can be recommended for improvement of physical function in the upper- and lower extremities, activity limitations and quality of life.

7 FUTURE PERSPECTIVES

In future studies it would be interesting to develop and evaluate physiotherapeutic interventions for patients with impaired shoulder function in RA. An important question is how to identify individuals with impaired shoulder function in need of more active physiotherapeutical interventions compared with those who manage on their own. An interventional study applying different physiotherapeutic techniques may lead to an establishment of appropriate therapies to master shoulder dysfunction in patients with RA. A longitudinal follow-up of patients with newly onset RA with regard to shoulder function is warranted. Such a study would give an opportunity to identify the patients at high risk of shoulder dysfunction.

Moreover, a close follow-up of activity limitations in the upper extremities may bring knowledge of which parameters that predict future limitations. For use in intervention studies of RA, the DASH questionnaire´s sensitivity to change need to be investigated.

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APPENDIX

Appendix I

Disability of the Shoulder, arm and Hand (DASH) frågeformulär

Hälsoenkät (arm/axel/hand)

Denna enkät berör Dina symtom och Din förmåga att utföra vissa aktiviteter. Svara på **varje fråga,** baserat på hur Du har mått **den senaste veckan,** genom att kryssa för ett svarsalternativ för varje fråga.

Om det är någon aktivitet Du inte har utfört den senaste veckan får Du kryssa för det svar som Du bedömer **stämmer bäst** om Du hade utfört aktiviteten. Det har ingen betydelse vilken arm eller hand Du använder för att utföra aktiviteten. Svara baserat på din förmåga oavsett hur Du utför uppgiften.

	Ingen svårighet	Viss svårighet	Måttlig svårighet	Stor svårighet	Omöjligt att göra
1. Öppna en ny burk, eller hårt sittande lock					
2. Skriva					
3. Vrida om en nyckel					
4. Förbereda en måltid					
5. Öppna en tung dörr					
6. Lägga upp något på en hylla över Ditt huvud					
7. Utföra tunga hushållssysslor (tex tvätta golv och väggar, putsa fönster, hänga tvätt					
8. Trädgårdsarbete					
9. Bädda sängen					
10. Bära matkassar					
11. Bära tunga saker (över fem kilo)					
12. Byta en glödlampa ovanför Ditt huvud					
13. tvätta eller föna håret					

14. Tvätta Din rygg					
15. Ta på en tröja					
16. Använda en kniv för att skära upp maten					
17. Fritidsaktiviteter som tar upp viss kraft eller stöt genom arm, axel eller hand(tex spela golf, använda hammare, spela tennis, skytte, bowling)					
19. Fritidsaktiviteter där Du rör på armen fritt (tex spela badminton, simma, gympa)					
20. Färdas från plats till en annan					
21. Sexuella aktiviteter					

22. Under de **senaste sju dagarna**, i vilken utsträckning har Dina armar-, axel eller handproblem stört Ditt vanliga umgänge med anhöriga, vänner, grannar eller andra?

Inte alls Lite Måttligt Mycket Väldigt mycket

23. Under de sensta sju dagarna, i vilken utsträckning har Dina arm-, axel- eller handproblem stört Ditt vanliga arbete eller dagliga aktiviteter?

Inte alls Lite Måttligt mycket Väldigt mycket

DASH svensk version Gummesson, Atrosh

Ange svårighetsgraden på Dina symptom de **senaste sju dagarna**:

	Ingen	Lätt	Måttlig	Svår	Mycket svår
24. Värk/ smärta i arm, axel eller hand					
25. Värk/smärta I arm, axel eller hand i samband med aktivitet					
26. Stickningar (sockerdrickskänsla) i arm, axel eller hand					
27. Svaghet i arm, axel eller hand					
28. Stelhet i arm, axel eller hand					

29. Har Du haft svårt att sova, under de senaste sju dagarna, på grund av värk/smärta I arm, axel eller hand?

Inte alls Viss svårighet Måttlig svårighet Stor svårighet Mycket stor svårighet

30. Jag känner mig mindre kapabel, har sämre självförtroende eller känner mig mindre behövd på grund av mina arm-, axel- eller handproblem

Instämmer absolut inte Instämmer inte Vet inte Instämmer Instämmer absolut

DASH svensk version Gummesson, Atrosh

APPENDIX II

Poängberäkning (scoring) av the Disability of the Arm, Shoulder and Hand (DASH)

Funktionshinder/symptom (frågor 1-30)

Svarsalternativen för varje fråga poängsätts från 1(inget funktionshinder/ symptom) till 5 (svårast funktionshinder/ symptom)

$$\text{DASH score} = \left(\frac{\text{summa poäng för alla frågor}}{30}\right) \cdot \frac{1}{1,2}$$

- Om upp till 3 frågor är obesvarade, skall dessa ersättas med medelvärdet av svaren på övriga frågor. Tex. om en person lämnat 2 frågor obesvarade, och svarat på var och en av de övriga 28 frågor med "3" poäng, ersätts de 2 saknade svaren med "3".
- Om fler än 3 frågor är obesvarade, går det inte att beräkna DASH-score.

Alternativ poängberäkning (ger samma resultat som metoden ovan)

- Åtminståne 27 av de 30 frågorna måste vara besvarade.
- Summera poängen och dividera med antalet frågor som besvarats. Subtrahera med 1 och multiplicera med 25.

$$\text{DASH score} = \left[\left(\frac{\text{summa av n svar}}{n}\right) - 1\right] \times 25$$

DASH svensk version Gummesson, Atroshi

APPENDIX III

Summary of the pool exercise program

Pool exercise was designed for patients with RA with a clinical perspective but with a scientific approach. Each session lasted 45 minutes in temperate (34°C) water. The exercises were accompanied by music, which gave a standardized pace.

The aim was to improve different components of physical function with a specific aim on aerobic capacity, quality of life and muscle endurance in the upper and lower extremities.

At the start of each exercise group, the physiotherapist demonstrated all the movements at a slow and smooth pace, emphasizing that everyone should adjust the exercise individually with respect to their physical impairments and eventual presence of pain. When the participants had learned the movements and performed them correctly, the pace was increased. Individual instructions were given whenever needed. "Aqua" gloves to increase the turbulence in the water and a floating device to sit on was used during different parts of the program. Patients was instructed to exercise on an intensity level corresponding to (13-14) on the Borg perceived exertion scale.

Warming up. Walking and jogging forwards, backwards and to the side with increasing speed during paddling with arms in water to increase the heart phase.

Three programme sets of co-ordination, flexibility and muscle endurance and muscle strengthening exercises. Reciprocal shoulder-arm elevation forward and backwards, and to the side with "aqua" gloves. Reciprocal internal and external rotation of the shoulder-arm with "aqua gloves, elbows positioned in 90°, with upper arms held by the sides of the thorax. Pendulum exercises with leg straight in different directions and in different paces. Reciprocal boxing with arm up and down, forward and to the sides with "aqua" gloves, combined with leg movements. Additional sets of combined arm and leg movements.

Three programme sets of aerobic exercises. Jogging and walking combined with arm movements. Sitting on the floating device while bicycling with legs and paddling with arms.

Stretching exercises for the larger muscle groups.

Relaxation. Performed either standing and leaning against the wall or in supine position floating in water. Floating devises such as air filled tires or neck collars where provided.