Exercise and Functional Performance in Middle-aged Patients with Knee Osteoarthritis

Thorstensson, Carina

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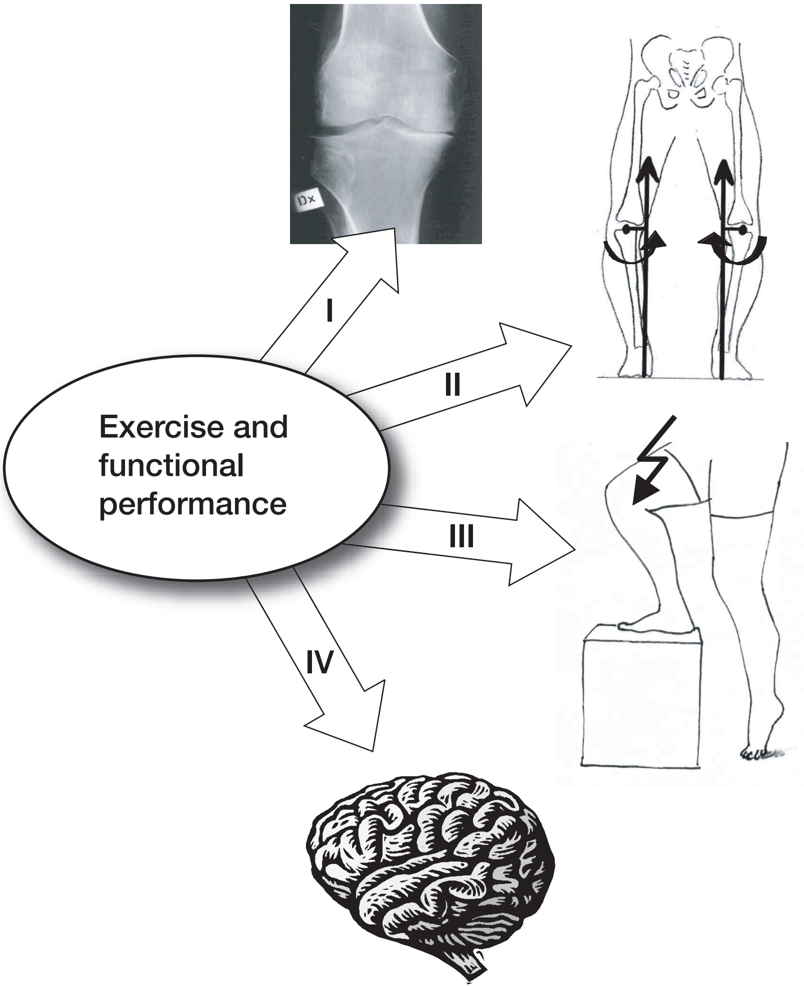
Contents

This thesis

This thesis comprises four studies with different perspectives of exercise and functional performance in knee osteoarthritis. Paper I studied the relationship between functional performance and development of radiographic knee osteoarthritis. Paper II explored the effect of exercise on joint load. Paper III examined the effect of exercise on pain and self estimated function, while paper IV focused on the patients' conceptions of exercise as treatment.



List of papers

I. Thorstensson CA, Petersson IF, Jacobsson LT, Boegard TL, Roos EM. Reduced functional performance in the lower extremity predicted radiographic knee osteoarthritis five years later. Annals of the Rheumatic Diseases 2004; 63: 402-407.

II. Thorstensson CA, Henriksson M, von Porat A, Sjödahl C, Roos EM. The effect of exercise on knee adduction moment during one-leg rises in patients with early knee osteoarthritis. In manuscript

III. Thorstensson CA, Roos EM, Petersson IF, Ekdahl C. Six-week high intensity exercise program for middle-aged patients with knee osteoarthritis – a prospective, randomized, and controlled study. Submitted.

IV. Thorstensson CA, Roos EM, Petersson IF, Arvidsson B. How do middle-aged patients conceive exercise as a form of treatment for knee osteoarthritis? Disability and Rehabilitation, in press.

Some additional data, not previously presented, have been included in the results and discussion sections of this thesis.

Thesis at a glance

Paper I – Is reduced functional performance a risk factor for development of knee osteoarthritis?

Patients: 148 persons with chronic knee pain.

Methods: Prospective design, 5-year follow-up, tests of functional performance, radiographs.

Conclusions: Reduced functional performance increased the risk of incident knee osteoarthritis five years later, also when controlled for age, sex, BMI and pain.

Characteristics of the 94 subjects without radiographic OA at baseline

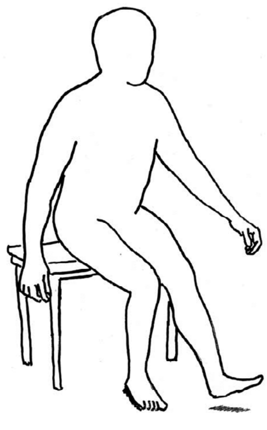
	Incident OA (n=41)	No OA (n=53)	OR (95% CI)
Age, median (range)	48 (35–54)	44 (35–54)	1.58 (0.69–3.60)
Sex (women/men)	18/23	21/32	0.84 (0.37–1.92)
Body Mass Index, median (range)	25.2 (19.3–37)	25.4 (18.3–34)	0.96 (0.42–2.20)
Pain VAS 0-100, median (range)	3 (0–51)	0 (0–84)	1.33 (0.52–3.44)
Maximum number of one-leg rises, median (range)	17 (0–99)	25 (1–229)	2.55 (1.08–6.02)

Paper II – Is it possible to reduce knee adduction moment by exercise, and to estimate knee adduction moment with maximum number of one-leg rises?

Patients: 13 patients from paper I.

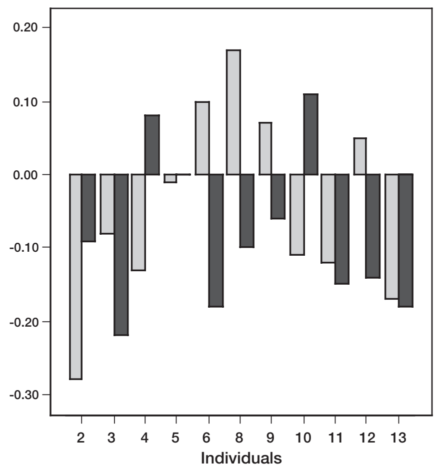
Methods: Uncontrolled, prospective design, exercise intervention, 8 week follow-up, 3-dimensional movement analysis, maximum number of one-leg rises.

Conclusions: Peak adduction moment could be reduced by exercise. Higher adduction moment was related to reduced maximum number of one-leg rise.



Test of maximum number of one-leg rises

Mean change in adduction moment during one-leg rise

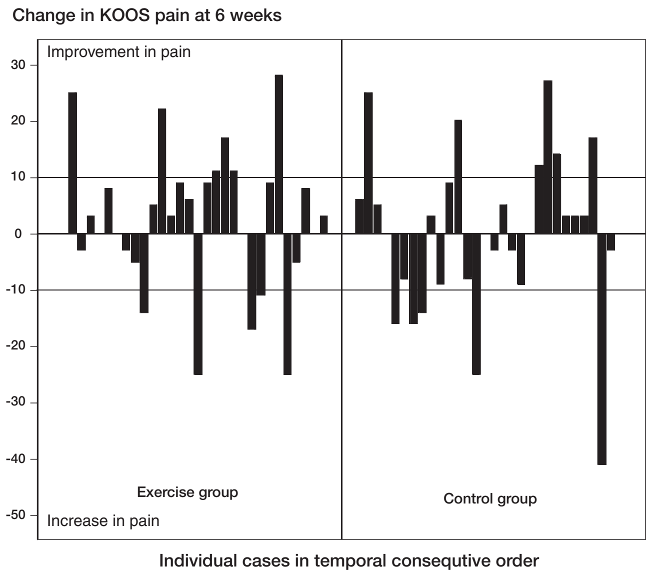


Paper III – Does intensive exercise reduce pain and improve function in middle-aged patients with moderate to severe knee osteoarthritis?

Patients: 61 patients with knee pain and significant radiographic osteoarthritis.

Methods: RCT, 6 week exercise intervention vs. non-intervention, 6 months follow-up, KOOS and SF-36.

Conclusions: No improvements were seen in pain or function. Despite this, quality of life improved after 6 weeks of intensive exercise, and was maintained at 6 months. We found no significant predictor of the large variations in the inter-individual responses in pain and function.

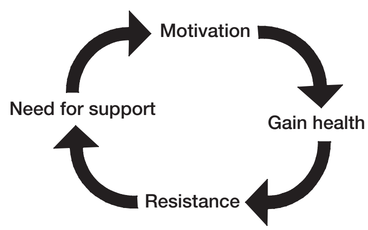


Paper IV – How do middle-aged patients with moderate to severe knee osteoarthritis conceive exercise as treatment?

Patients: 16 patients from exercise group in paper III.

Methods: Qualitative design, interviews.

Conclusions: The degree of motivation to exercise varied. The patients were aware of health benefits from exercise, but felt doubts about exercise as treatment, even when they had benefited from an exercise programme. Continuous support was considered necessary to comply with exercise.



Description of contributions

Paper I

Study design: Carina Thorstensson, Ewa Roos, Ingemar Petersson, Lennart Jacobsson
Data collection: Carina Thorstensson, Ingemar Petersson, Torsten Boegård
Data analysis: Carina Thorstensson
Manuscript writing: Carina Thorstensson
Manuscript revision: Ewa Roos, Lennart Jacobsson, Torsten Boegård, Ingemar Petersson

Paper II

Study design: Carina Thorstensson, Ewa Roos
Data collection: Carina Thorstensson, Catharina Sjödahl, Anette von Porat
Data analysis: Carina Thorstensson, Marketta Henriksson
Manuscript writing: Carina Thorstensson
Manuscript revision: Ewa Roos, Marketta Henriksson, Anette von Porat, Catharina Sjödahl

Paper III

Study design: Carina Thorstensson, Ewa Roos, Ingemar Petersson, Charlotte Ekdahl
Data collection: Carina Thorstensson
Data analysis: Carina Thorstensson
Manuscript writing: Carina Thorstensson, Ewa Roos
Manuscript revision: Charlotte Ekdahl, Ewa Roos, Ingemar Petersson

Paper IV

Study design: Carina Thorstensson, Barbro Arvidsson, Ewa Roos, Ingemar Petersson
Data collection: Carina Thorstensson
Data analysis: Carina Thorstensson, Barbro Arvidsson
Manuscript writing: Carina Thorstensson
Manuscript revision: Barbro Arvidsson, Ewa Roos, Ingemar Petersson

Definitions and abbreviations

ACR American College of Rheumatology
BMI body mass index
IASP International Association for the Study of Pain
KOOS Knee injury and Osteoarthritis Outcome Score
MRI magnetic resonance imaging
OA osteoarthritis
OARSI Osteoarthritis Research Society International
RCT randomized controlled trial
SF-36 Short-Form 36-item Health Survey
VAS visual analogue scale
WHO World Health Organisation
WOMAC Western Ontario and McMaster Osteoarthritis Index

Definitions used in this thesis:

Adduction moment – in this thesis I refer to external adduction moment (ground reaction force x perpendicular distance from ground reaction force to the axis of knee ab- adduction movement), i.e. the angular force acting on the medial compartment of the knee, compressing the joint surfaces of tibia and femur. The external adduction moment corresponds to an equally sized internal abduction moment, produced by the active and passive soft tissues, preventing the knee from lateral gapping.

Coordination – activating the right muscles with right force at the right time.

Exercise – "a subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate objective the improvement or maintenance of physical fitness" (Caspersen et al. 1985).

Functional performance – muscle function in physical activities.

HKA – hip-knee-ankle angle. Radiographic assessment of alignment, defined as the lateral angle between the lines from the centre of the tibial spines to the centre of the femoral head and the talus respectively. An angle of more than 180° denotes a varus alignment (Odenbring et al. 1993).

Kellgren and Lawrence – radiographic osteoarthritis classification system, based on joint space narrowing and osteophytes (Kellgren and Lawrence 1957):
grade 0 – normal radiographs,
grade 1 – minute osteophytes, doubtful significance,
grade 2 – definite osteophytes,
grade 3 – joint space narrowing,
grade 4 – joint space greatly impaired, sclerosis of subchondral bone .

Knee osteoarthritis – in this thesis; radiographic features of osteoarthritis of the tibiofemoral joint, with or without knee symptoms.

Kinetics – movements including forces and moments.

Kinematics – movements including spatiotemporal parameters, excluding forces and moments.

Laxity – insufficient tension in the passive soft tissues, causing displacement or mediolateral rotation of the tibia in relation to the femur.

Middle-aged – in this thesis; individuals aged between 35 and 65 years.

Muscle function – a combination of strength, endurance and coordination.

Physical activity – "any bodily movement produced by skeletal muscles that result in energy expenditure" (Caspersen et al. 1985).

1 RM – one repetition maximum, the highest weight possible to lift once, but not twice.

Introduction

Knee osteoarthritis – diagnosis

According to the World Health Organisation, osteoarthritis is one of the ten most disabling diseases in adults over thirty years (WHO). Knee osteoarthritis is common and presents with insidious onset, unclear prognosis and large consequences for the individual as well as for the society. Currently there is no cure for osteoarthritis. Treatments focus primarily on relieving symptoms and preventing progress (Altman et al. 2000; Jordan et al. 2003; Läkemedelsverket 2004).

Knee osteoarthritis can be conceptualized in different ways; 1) as a biochemical process, characterized by disequilibrium between cartilage synthesis and degradation (Andriacchi et al. 2004; Lohmander et al. 2003); 2) as radiographic or MR detected features typical of knee osteoarthritis (Ahlback 1968; Altman et al. 1995; Boegard et al. 1998; Kellgren and Lawrence 1957); or 3) as a disease causing pain and disability to the patient (Dieppe et al. 2000; Felson et al. 2000a; McAlindon et al. 1993; Peat et al. 2001) (Figure 1). The choice between these concepts depends on the context in which they are used. The American College of Rheumatology have developed a set of criteria to clinically verify the osteoarthritis diagnosis; age > 38, presence of knee pain, morning stiffness and joint crepitus (Altman et al. 1986). The 'classic' diagnosis of osteoarthritis is based on the contemporary presence of radiographic features and symptoms (Lohmander 2002).

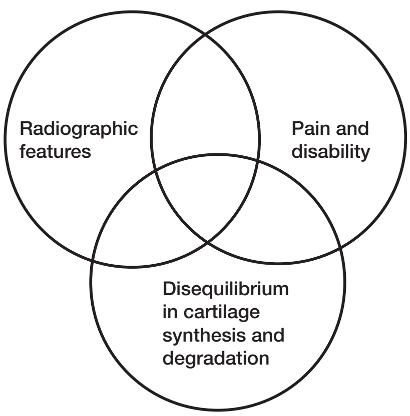


Figure 1. Osteoarthritis can be conceptualized in different ways; as radiographic features, pain and disability or as disequilibrium in cartilage synthesis and degradation.

The natural course of osteoarthritis is not well explored in longitudinal studies. A study evaluating the radiographic progression of knee osteoarthritis after 11 years found that about 30% deteriorated, but 10% improved (Spector et al. 1992). Another study, exploring the natural course of pain severity and disability after 8 years revealed that about 60% of the patients with knee osteoarthritis deteriorated, however 20% perceived less severe pain and overall condition (Dieppe et al. 2000).

Radiographic changes in knee osteoarthritis

Knee osteoarthritis affects body structure components through cartilage degradation, bone remodelling and soft tissue weakness (Brandt et al. 1998). Structural changes in knee osteoarthritis are usually verified through radiographic imaging, and there are several classification systems to grade osteoarthritis severity. The most commonly used classification was described by Kellgren and Lawrence in 1957 (Kellgren and Lawrence 1957). The severity of radiographic changes is graded from 1 to 4, where grade 1 corresponds to doubtful osteophytes and 4 is classified as severe radiographic changes, with impact on bone formation, joint space width and subchondral bone thickness (Table 6, see page 19). The most common cut-off used to define knee osteoarthritis is Kellgren and Lawrence grade 2, i.e. definite osteophytes. However, less significant osteophytes, grade 1, have been found to correlate with cartilage changes detected with magnetic resonance imaging (MRI) (Boegard et al. 1998), and seem to predict radiographic progression of knee osteoarthritis (Hart and Spector 2003). The Ahlbäck classification system (Ahlback 1968) incorporates joint space width and bone attrition. The atlas of Osteoarthritis Research Society International (OARSI) scores the joint space width and osteophytes separately (Altman et al. 1995).

Radiographic changes develop slowly (Gandy et al. 2002), and only a minority of patients with knee osteoarthritis will ever develop a severe stage requiring knee surgery (Peat et al. 2001). The prognostic factors are not clear, but it has been suggested that overweight (Dougados et al. 1992; Schouten et al. 1992), local joint load (Miyazaki et al. 2002) and knee malalignment (Sharma et al. 2001) are associated with progression of radiographic changes.

Radiographic knee osteoarthritis in the middle-aged

The prevalence of osteoarthritis varies between studies, depending on the population studied and the criteria used to define knee osteoarthritis. The presence of osteoarthritis is strongly related to age. From the age of 55 years and older the prevalence of radiographic knee osteoarthritis ranges from 4 to 45 %, with higher percentages present in older ages (Davis et al. 1991a; Felson et al. 1987; Hernborg and Nilsson 1973; Stauffer et al. 1977; van Saase et al. 1989) However, knee osteoarthritis is not only a disease of the elderly. A cross sectional study of a community based sample with knee pain did not show increased joint space narrowing in older age-groups (Lanyon et al.). A population based survey of people aged 35–54, with chronic knee pain without major knee trauma, showed a prevalence of radiographic features corresponding to knee osteoarthritis of 1.5% (Petersson et al. 1997). Injury to the meniscus or anterior cruciate ligament is related to an increased risk of knee osteoarthritis 10–15 years later (Roos et al. 1995), and studies involving patients 12–14 years after anterior cruciate ligament injury reveal a prevalence of radiographic and symptomatic knee osteoarthritis exceeding 40% in a population younger than 40 years (Lohmander et al. 2004; Von Porat et al. 2004). In meniscectomized patients with a mean age of 54, 43% had radiographic changes 16 years after meniscectomy (Englund et al. 2003).

Pain and function in knee osteoarthritis

The most common complaint of patients with knee osteoarthritis is pain, continuous or during weight bearing activities. Pain is the reason why patients with osteoarthritis seek medical care. Osteoarthritis pain can increase or decrease without relationship to radiographic changes (Dieppe et al. 1997). The cartilage has no pain receptors. Pain in osteoarthritis may arise in synovium, joint capsule, bone, periosteum or soft tissues like muscle, tendons and ligaments (Brandt et al. 1998; Creamer 2000). Normally these structures are relatively insensitive. It has been suggested in osteoarthritis that certain mediators possibly arising from bone or synovium, increase the sensitivity of joint nociceptors, thus enabling mechanical stimuli to be perceived as local pain (Kidd 1998). The increased frequency of input from peripheral nociceptors contributes to an increased sensitivity of the central nervous system, therefore the mechanical input from normal activities of daily living can trigger pain in wider areas or as referred pain (Kidd 1998). Pain is subjective and individually interpreted, and defined by the International Association for the Study of Pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"(IASP). Pain intensity can fluctuate, but over the years most patients with osteoarthritis experience increased pain. In the Bristol OA500 study 69/111 (62%) of patients with knee osteoarthritis reported worsening in pain over 8 years, while 22 (20%) reported improvement (Dieppe et al. 2000).

Perceived pain and reduced muscle function contribute to limitations in activities related to mobility and transfer in daily living, for example walking, stair climbing or rising from a chair (Davis et al. 1991a; Dieppe et al. 2000; Hurley et al. 1997; McAlindon et al. 1993). More generalized knee pain is associated with worse physical function than medial knee pain alone (Creamer et al. 1998). Knee osteoarthritis is further related to several aspects of physical function, such as increased knee joint laxity (Sharma et al. 1999b), stiffness (Altman et al. 1986), reduced range of motion (Al-Zahrani and Bakheit 2002), altered joint load (Sharma et al. 1998), and reduced muscle function (Hurley et al. 1997). Psychological factors are also affected in knee osteoarthritis (Dieppe et al. 2000; Keysor et al. 1998).

Discrepancy between radiographic changes and symptoms/function

The relationship between radiographic changes and pain is weak. A longitudinal study, including patients aged 24–88 years referred to a rheumatology clinic with symptomatic knee osteoarthritis, found no significant association between change in pain and change of radiographic features, neither for improvement nor worsening (Dieppe et al. 1997). In a population based study including subjects aged 25–74, less than 50% of those with radiographic changes corresponding to mild to severe radiographic knee osteoarthritis reported symptoms, and among the subjects reporting knee pain, radiographic features of knee osteoarthritis were found in less than 20% (Hannan et al. 2000). The relationship between pain and radiographic features becomes stronger with increased disease severity (Cooper et al. 2000; Felson et al. 1987).

Some of the discrepancy between radiographic changes and knee symptoms might be explained by psychological factors. Anxiety and depression are strong predictors of pain (Creamer et al. 1999; Salaffi et al. 1991; Summers et al. 1988). The disability associated with knee osteoarthritis is more related to pain, strength, age, and obesity than to radiographic features (Creamer et al. 2000; McAlindon et al. 1993). However, individuals with both pain and radiographic changes seem to have a worse disability score (Williams et al. 2004). Elderly patients with arthritis are usually less physically active than younger patients (Fontaine et al. 2004), and inactivity is also associated with increased disability (Steultjens et al. 2002). Effective coping strategies among patients with self-reported osteoarthritis and osteoporosis have been suggested to mediate the relationship between activity limitations and perceived disability (Wang et al. 2004).

Non-modifiable and modifiable risk factors

The risk factors for development of incident knee osteoarthritis and progression of established knee osteoarthritis may be different, and the inter relationship between these factors is not clear (Andriacchi et al. 2004; Cooper et al. 2000) (Table 1).

Non-modifiable risk factors for development of incident knee osteoarthritis include genetic factors (Spector et al. 1996), older age (Felson et al. 1987; Hart et al. 1999; Hernborg and Nilsson 1973; van Saase et al. 1989), and female sex (Felson et al. 1987; Manninen et al. 1996). There seems to be an inverse relationship between osteoporosis and osteoarthritis, indicating that high bone mineral density might contribute to osteoarthritis development (Dieppe et al. 1993; Hart et al. 1994; Radin and Rose 1986). The inverse relationship has only been studied in cross-sectional studies, including patients with established osteoarthritis, and is thus still a matter of debate (Dequeker et al. 2003).

Table 1. Risk factors associated with incident radiographic knee osteoarthritis, i.e. osteophytes and radiographic progression, i.e. joint space narrowing. The interrelationship between risk factors and the fact that different atlases and cut-offs have been used to classify knee osteoarthritis has not been taken into account.

Risk factor	Osteophytes	JSN
Age (Felson et al. 1987; Hart et al. 1999; Hernborg and Nilsson 1973; van Saase et al. 1989)	•	
Sex (Felson et al. 1987; Manninen et al. 1996)	•	
Genetic influence (Spector et al. 1996)	•	
Bone mineral density (Dieppe et al. 1993; Hart et al. 1999; Radin and Rose 1986)	•	•
Obesity (Felson et al. 1988; Felson et al. 1997; Hart et al. 1999; Manninen et al. 1996; Sandmark et al. 1999)	•	•
Joint injury (Gelber et al. 2000; Lohmander et al. 2004; Roos et al. 1995; Von Porat et al. 2004)	•	
Muscle weakness (Slemenda et al. 1998)	•	
High impact joint load (Miyazaki et al. 2002; Radin et al. 1991)	•	•
Biomechanical factors (Cicuttini et al. 2004; Felson et al. 2004; Miyazaki et al. 2002; Sharma et al. 2003; Sharma et al. 2001)		•

Genetic factors are important determinants of osteoarthritis in the hand and knee, and a study on female twins estimated the genetic influence of osteoarthritis development to be between 35-65% (Spector et al. 1996). The influence of age on osteoarthritis development could be related to degeneration of cartilage, increasing the vulnerability to biomechanical risk factors.

At ages below 50 years the prevalence of knee osteoarthritis is somewhat higher in men, however as age progresses the prevalence becomes more common in women (Davis et al. 1991a; Felson 1988; Felson et al. 2000a; Felson et al. 1987). The increased rate of knee osteoarthritis among men at younger ages could be related to a higher physical activity level, and thereby an increased frequency of activity related injuries.

Modifiable risk factors include obesity (Felson et al. 1988; Felson et al. 1997; Hart et al. 1999; Manninen et al. 1996; Sandmark et al. 1999), injury to the menisci or cruciate ligament (Gelber et al. 2000; Lohmander et al. 2004; Roos et al. 1995; Von Porat et al. 2004), and factors related to heavy joint load at work or leisure (Coggon et al. 2000; McAlindon et al. 1999; Sandmark et al. 2000). Recently, reduced muscle function has been suggested as a risk factor of knee osteoarthritis development in women (Slemenda et al. 1998). Moderate weight loss has been suggested to reduce the risk of developing incident knee osteoarthritis in women (Felson et al. 1992). The effects from injury prevention programmes, reduced joint load or increased muscle function on development of knee osteoarthritis are not documented.

The role of muscle weakness in knee osteoarthritis could be related to biomechanical factors. During gait a weaker quadriceps muscle is related to higher knee joint load in healthy women (Mikesky et al. 2000). It is suggested that muscle weakness could cause a shift in the mechanical axis, moving joint load to areas not capable of coping with the increased compression, causing a local over-load (Andriacchi et al. 2004). Experimental models have demonstrated that repetitive impulsive joint load could cause 'micro traumas' in the cartilage, and increase the sclerosis of the underlying bone, leading to an increase in shear stress of cartilage (Radin et al. 1991a; Radin and Rose 1986).

It has been suggested that biomechanical factors, such as knee malalignment contribute to radiographic progression of knee osteoarthritis (Cicuttini et al. 2004; Felson et al. 2004; Miyazaki et al. 2002; Sharma et al. 2001). Strong quadriceps muscles may contribute to the risk of radiographic progression in mal-aligned knees through increased compressive forces in the medial joint compartment (Sharma et al. 2003b). Exercise may have the potential to normalize the mechanical axis, and reduce the impulsive joint load. The impact of exercise on joint load needs to be confirmed in longitudinal studies.

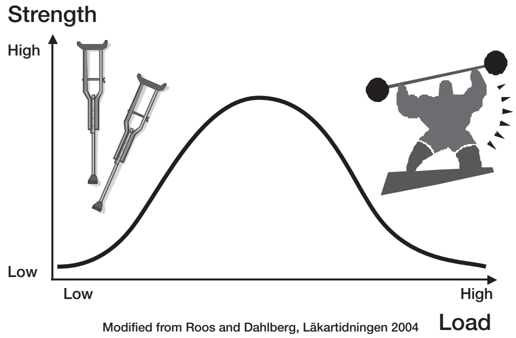


Figure 2. Schematic view of the relationship between load and strength in biological tissues.

Joint cartilage is dependent on dynamic joint load to get nutrition. Under-use of the knee joint could disturb the equilibrium of cartilage repair and degradation (Carter et al. 2004) (Figure 2). Animal models have demonstrated a regress of cartilage when limbs are immobilized (Brandt 2003; Jortikka et al. 1997), while moderate exercise reduced structural lesions and too extensive exercise seemed to abolish the positive effects in experimentally induced osteoarthritis (Galois et al. 2004). Healthy cartilage may recover with resumed activity, but osteoarthritis affected cartilage may not (Brandt 2003). In hamsters, daily exercise seems to improve the quality of cartilage (Otterness et al. 1998). These findings are not yet proved to be valid in humans. However, it has been suggested that increased physical activity is related to improvement in knee cartilage structure in patients at risk of osteoarthritis development (Dahlberg and Roos 2003), confirming the previously found effects from moderate physical activity in dogs (Kiviranta et al. 1988).

Joint load in knee osteoarthritis

Patients with knee osteoarthritis walk with reduced stance phase (Schipplein and Andriacchi 1991), shorter stride length, slower walking speed (Al-Zahrani and Bakheit 2002; Stauffer et al. 1977), and greater medial-to-lateral forces (knee adduction moment) during gait compared to knee-healthy subjects (Baliunas et al. 2002; Schipplein and Andriacchi 1991). Severe radiographic knee osteoarthritis is associated with higher peak adduction moment during gait (Sharma et al. 1998). Young individuals, with previous episodes of knee pain, and therefore assumed to be predisposed to knee osteoarthritis development, have increased impulsive joint-load during heel-strike compared to age-matched subjects without a history of knee pain (Radin et al. 1991b). This cross-sectional study suggested that increased joint load during gait might precede osteoarthritis development. However, the association has not been established in prospective longitudinal studies. Patients with symptomatic knee osteoarthritis seem to walk 'carefully', since pain reduction has been associated with an increased joint load during gait (Hurwitz et al. 1999; Hurwitz et al. 2000; Schnitzer et al. 1993; Shrader et al. 2004). It has been suggested that patients adapt their movement pattern to reduce the knee adduction moment (Andriacchi 1994; Kaufman et al. 2001; Mundermann et al. 2004; Stauffer et al. 1977). The effects of these strategies on pain, function or disease progression however have not been confirmed in longitudinal studies.

Knee adduction moment

About 70% of the medial-to-lateral forces during gait act on the medial tibiofemoral compartment, causing an external knee adduction moment (Schipplein and Andriacchi 1991). During weight-bearing activities, like gait or stair climbing, the adduction moment compresses the medial compartment of the knee, and causes a lateral "gapping", which is prevented by active and passive soft tissues (Schipplein and Andriacchi 1991)(Figure 3). The size of the knee adduction moment is determined by the ground reaction force, acting through the foot and medial to the knee joint, and the perpendicular distance from ground reaction force to the axis of the knee joint ab- and adduction movement (Andriacchi 1994).

The shape of the bone ends and articular surfaces in the knee does not provide a stable position in itself. Thus stability of the knee is totally dependent on ligaments and muscle function, producing an internal abduction moment of equal size as the external moment acting on the knee (Andriacchi 1994; Jackson et al. 2004). Passive soft tissues can only act as stabilizers and produce a force when they are stretched. Knee joint laxity, caused by lax ligaments, is more common in patients with knee osteoarthritis than in healthy knees (Sharma et al. 1999b), increasing the risk of lateral joint opening and transferring of the entire joint load to the medial compartment (Schipplein and Andriacchi 1991). The external knee adduction moment is used as an approximate measurement of the net internal load acting on the medial knee joint compartment (Andriacchi 1994). The internal moment is determined by multiple muscles and ligaments acting simultaneously in multi-dimensional directions. Invasive measurement techniques are required to assess the specific internal moments which is not easily applicable in humans.

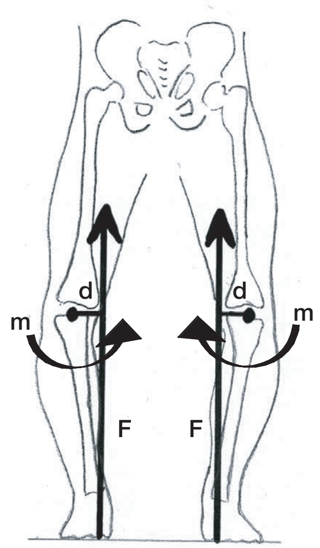


Figure 3. The external knee adduction moment (m) is a rotating force, trying to adduct the medial compartment of the knee. The magnitude of the adduction moment is determined by the magnitude of the ground reaction force (F) and the perpendicular distance (d) from the ground reaction force to the axis of knee movements in the frontal plane.

Treatment guidelines

Guidelines suggest a combination of pharmacological and non-pharmacological interventions as optimal treatment of mild to moderate knee osteoarthritis (Altman et al. 2000; Felson et al. 2000b; Jordan et al. 2003; Läkemedelsverket 2004) (Figure

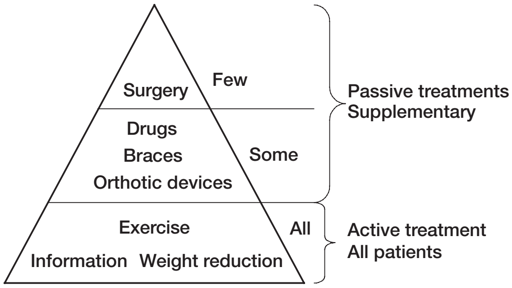


Figure 4. Treatment guidelines for knee osteoarthritis. Active treatments should be recommended to all patients. Passive treatments should be considered as supplementary treatments. Modified from www.mpa.se

4). Information, exercise and weight reduction can be regarded as active treatments, requiring participation from the patient and/or processing and transforming new knowledge into behavioural changes or change in attitude. Active treatments are advantageous since they are non-invasive, the side effects are small compared to pharmacological treatments (Jordan et al. 2003), and patients are less dependent on accessibility to health professionals. Severe disease, requiring surgical interventions, will only occur in a small proportion of all patients with osteoarthritis, and an English study estimated that about 10 % of all patients with knee pain will ever be considered for knee osteoarthritis surgery (Peat et al. 2001).

Exercise as osteoarthritis treatment

Exercise is the most cost-effective treatment achievable for knee osteoarthritis, according to an Australian study evaluating the cost-benefit relationship for different osteoarthritis treatments (Segal et al. 2004). Treatment utility was determined by time lived in particular health states, described in previous studies of osteoarthritis. Exercise had the lowest costs, about 5000$ per quality-adjusted life-year, compared to total knee replacement, which also is a cost-effective treatment (10 000$ per quality-adjusted life-year). Exercise is as effective as pharmacological treatment in pain relief (Fransen et al. 2003; Jordan et al. 2003; Pendleton et al. 2000), and is recommended as one of the most important parts of knee osteoarthritis treatment in American, European, and Swedish guidelines (Altman et al. 2000; Jordan et al. 2003; Läkemedelsverket 2004). Both aerobic and strengthening exercises have positive effects on pain and function (Ettinger et al. 1997). A randomized controlled trial comparing high and low intensity ergometer cycling for 10 weeks showed improvement in gait-speed, chair-rising and pain in both groups (Mangione et al. 1999). A study comparing the effect of dynamic strengthening exercises with static strengthening exercises on pain and time to ascend and descend a flight of stairs showed similar positive results in both groups compared to the control group (Topp et al. 2002). This latter finding is in contrast to findings from dynamic versus static exercises in patients with rheumatoid arthritis, where dynamic strengthening exercises had greater benefits (Ekdahl et al. 1990).

The optimal dose or type of exercise in knee osteoarthritis is yet to be determined (Brosseau et al. 2003; Fransen et al. 2003; O'Reilly and Doherty 2001). At least 30 minutes of accumulated moderate physical activity on most days of the week is recommended to prevent obesity and development of inactivity related diseases, such as cardiovascular disease, diabetes and colon cancer (Pate et al. 1995; WHO 2003). In the absence of specific exercise guidelines for knee osteoarthritis, these general recommendations should be implemented in patients with mild to moderate knee osteoarthritis as well.

Patients who are physically active have better self-efficacy for exercise than inactive patients (Hopman-Rock and Westhoff 2000; Rejeski et al. 1998). Self-efficacy also improves the likelihood of compliance with exercise and thus maintained physical function (Gecht et al. 1996; Sharma et al. 2003a). Besides self-efficacy, positive effects of exercise have been shown on depressive symptoms, anxiety and health related quality of life (Fransen et al. 2001; Minor et al. 1989).

Moderate exercise do not contribute to overload

Moderate exercise is not associated with risk of osteoarthritis development or progression (Conaghan 2002; Hannan et al. 1993; Hootman et al. 2003; Sutton et al. 2001). A recent review of the clinical literature showed that there has been a shift in the view upon exercise in knee osteoarthritis, from exercise as additive 'wear and tear' to exercise as a means of osteoarthritis treatment (Shrier 2004). The risk of osteoarthritis due to exercise is

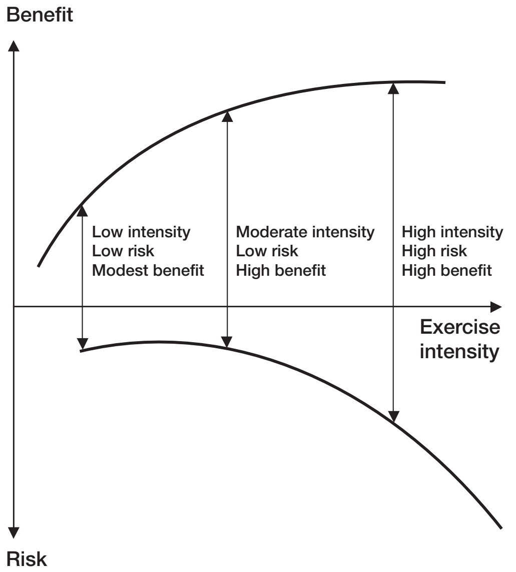


Figure 5. The relationship between risk and benefit in exercise. The benefits from exercise exceed the risks during low to moderate exercise intensity. At high intensity exercise the risk increases rapidly. Modified from (Powell and Paffenbarger 1985).

related to repetitive high joint load activities and the risk of knee injury (Conaghan 2002; Lohmander et al. 2004; Roos et al. 1995; Roos et al. 1998c; Von Porat et al. 2004). The risk-benefit relationship in exercise is non-linear. With higher levels of activity the risks increase dramatically while the benefits stay the same (Figure 5) (Powell and Paffenbarger 1985).

Barriers to exercise as treatment

Perceived barriers to exercise are common in the general population. It has been estimated that 25–30% of the adult men and 10–15% of the adult women in Sweden are not physically active at all (www.fysisktaktiv.nu, accessed March 24, 2005). Of all Swedish adults, 44% are physically active at least two times per weeks (www.scb.se, accessed March 24, 2005). Patients with osteoarthritis should be offered information about the possible benefits of exercise and weight reduction on pain and function, as well as interventions targeting physical functioning and overweight (Jordan et al. 2003). Of the US adults with arthritis 40% meet the recommendations of regular physical activity (Fontaine et al. 2004; Keefe et al. 2000). Physical therapists have specific knowledge about exercise at different stages of disability, but physiotherapy is underused, and only 10% of patients with osteoarthritis have ever been to a physical therapist or tried to loose weight (Fontaine et al. 2004; Hsieh and Dominick 2003; Jordan et al. 2004). This could be related to contrasting perspectives of doctor and patient, influencing the agreement in treatment planning (Carr and Donovan 1998; Donovan 1991). Longitudinal studies report a decrease in compliance to exercise over time (Ettinger et al. 1997; Sullivan et al. 1998). In exercise as well as in any intervention, compliance is a prerequisite for optimal treatment effect (Carr 2001; Ettinger et al. 1997; Kettunen and Kujala 2004; Thomas et al. 2002; van Baar et al. 2001). Non-compliance is usually based on rational and logical decisions, based on the patient's knowledge and convictions (Campbell et al. 2001; Donovan 1991). Another barrier to exercise as osteoarthritis treatment is that osteoarthritis often has been thought of as a result of "wear and tear", an irreversible end-stage not possible to influence (Campbell et al. 2001; Okma-Keulen and Hopman-Rock 2001).

Aims of the study

General

The overall purpose of this thesis was to explore the impact of exercise and functional performance on development and treatment of knee osteoarthritis in the middle-aged.

Specific

- To determine whether, in a population-based cohort of middle-aged subjects with chronic knee pain at baseline, reduced functional performance in the lower extremity predicted development of radiographic knee osteoarthritis five years later.

- To study the effect of exercise on knee adduction moment during one-leg rise and gait in middle-aged patients with mild knee osteoarthritis.

- To study the relationship between knee adduction moment during one-leg rise and the maximum number of one-leg rises in middle-aged patients with mild knee osteoarthritis.

- To study the effects of a short-term, high-intensity exercise program in middle-aged subjects with symptomatic and moderate to severe radiographic knee osteoarthritis on self-reported pain, function and quality of life.

- To describe conceptions, as registered by a semi-structured interview, of exercise as treatment among sixteen middle-aged patients with moderate to severe knee osteoarthritis.

Subjects and methods

Subjects

209 patients from two different cohorts were included in the studies (Figure 6). They were all younger than 65 years at inclusion and 44% were women. Patient characteristics are shown in Table 2. The two populations differed according to severity of radiographic features and symptoms (Table 3 and Table 6).

The Spenshult cohort (paper I and II)

Patients from a population based cohort, with chronic knee pain at inclusion, were included in paper I and II (Petersson et al. 1997). Two thousand people aged between 35–54 (963 women and 1 037 men) were randomly selected from a district in the south-west of Sweden. This mixed urban and rural population, received a postal questionnaire in 1990 concerning prevalence of chronic knee pain. Chronic knee pain was defined as “pain in either of your knees on most days during the last three months”. One thousand eight hundred and fifty-three persons (93%) answered the questionnaire, of whom 279 (15%) persons reported chronic knee pain.

Those who had chronic knee pain were offered radiographic and clinical examination (Petersson et al. 1997) and 204 agreed to participate. One hundred and fifty two subjects were available for follow-up five years later. As the aim was to determine risk factors for development of radiographic features, four patients with radiographic regression in one knee and radiographic progression in the other knee at follow-up were excluded. Thus 148 subjects constituted the cohort for paper I. Fifty four patients had radiographic changes corresponding to Kellgren & Lawrence grade I or more (minor osteophytes), and 94 patients had no radiographic features of osteoarthritis.

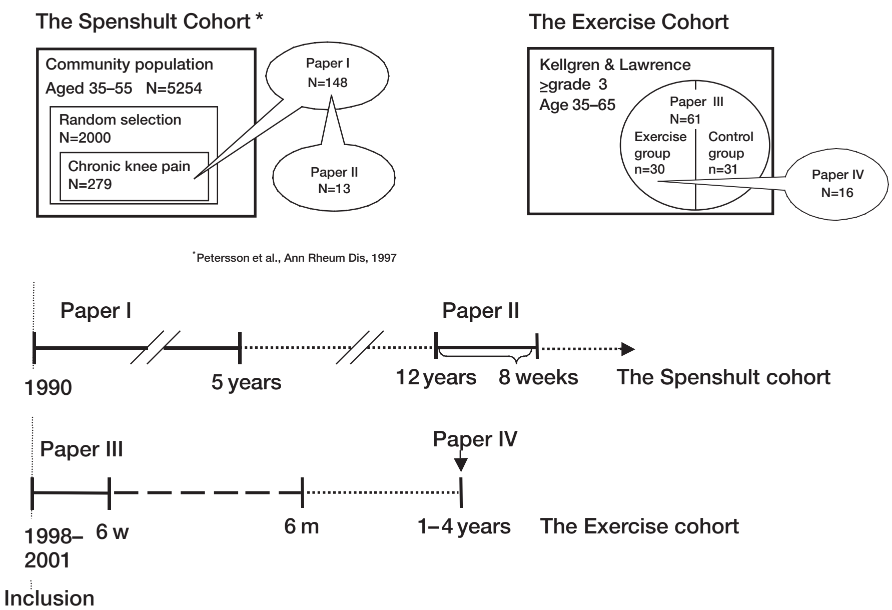


Figure 6. Description of study populations and the time disposal for recruitment and interventions in paper I–IV. For paper I and II patients were recruited from the Spenshult cohort. For paper III and IV patients were recruited from the Exercise cohort.

Table 2. Patient characteristics of the 209 patients included in paper I–IV. Pain is derived from the KOOS pain subscale (Roos et al. 1998) , 0–100, worst to best scale.

Cohort	Paper	N	K&L grade	Age mean (range)	Sex % women	BMI mean (range)	KOOS pain score
Spenshult cohort	I, II	148	0–3	53.1 (35–54)	42%	25.8 (18.3–37.5)	97
Exercise cohort	III, IV	61	3–4	56.1 (36–64)	51%	29.5 (22.5–49.7)	61

Table 3. Clinical criteria of knee osteoarthritis in the Spenshult cohort and Exercise cohort according to ACR (Altman et al. 1986). Values are number (%)

	The Spenshult cohort		The Exercise cohort	
	Paper I N=148	Paper II N=13	Paper III N=61	Paper IV N=16
Knee pain on most days last month	148 (100)	4 (31)	53 (87)	12 (75)
Morning stiffness	45 (30)	2 (15)	53 (87)	16 (100)
Grinding	78 (53)	8 (62)	56 (92)	14 (88)
Age > 38	128 (86)	13 (100)	60 (98)	16 (100)
OA according to ACR criteria	24 (16)	1 (8)	45 (74)	12 (75)

In paper II, patients from the same cohort with radiographic signs of knee osteoarthritis, corresponding to Kellgren & Lawrence grade I (minor osteophytes) in 1995, and aged < 65 years at inclusion in 2003 were included. Forty patients fulfilled the inclusion criteria, and were contacted by telephone. Patients with dysfunction in the back or lower extremity (n=10), inflammatory joint disease (n=3), previous knee injury (n=2), chronic widespread pain (n=4) or depressive symptoms (n=1) were excluded. Seven patients declined to participate due to lack of time, leaving 13 eligible patients.

The Exercise cohort (paper III and IV)

The second cohort was recruited at the department of radiography at the Halmstad County Hospital in the south-west of Sweden. Radiologists and orthopedic surgeons as well as general practitioners within the catchments area of this hospital, were informed about the study (paper III) and were asked to list patients with radiographic knee osteoarthritis on a "patients eligible for research" list. Between October 1998 and October 2001 121 patients, referred by their general practitioner to radiographic examination because of knee pain, were listed. Ninety-seven fulfilled the inclusion criteria: age range 35–65, diagnosis of radiographic osteoarthritis of Kellgren and Lawrence grade III or more, i.e. definite osteophytes and joint space narrowing, and living in the defined geographic area. Twenty-eight patients declined participation for various reasons, the most common reason being lack of time and interest. To ensure only those patients with symptoms due to knee osteoarthritis and who were eligible for exercise intervention were included, the following exclusion criteria were applied: inflammatory joint disease, medical record of anterior cruciate ligament injury, symptomatic meniscal injury, hip symptoms more aggravating than the knee symptoms, about to have knee replacement surgery within 6 months, and co-morbidities not allowing exercise. Four patients were wrongly randomized, and thus 61/97 patients were included in paper III. In paper IV, 16 patients, aged 39–64, randomized to exercise intervention in paper III, were interviewed. They were strategically chosen so as to obtain a variation in variables that might influence their conceptions of exercise as a form of treatment. In this study different ages, genders, levels of education, occupations, previous exercise habits, disease durations, and different outcomes of the exercise trial with regard to pain were considered as factors of importance to conceptions of exercise as treatment (Table 4).

Table 4. Subjects in paper IV were purposively chosen from the exercise group in paper III, to obtain a variation of variables that could affect their conceptions of exercise.

Variable/Categories	
Age range	39–64
Male/female (number)	10/6
Highest level of education (number)	
University	2
Continuation of the 9-year compulsory school	4
Compulsory school	10
Joint load in occupation (number)	
High	7
Low	8
Retired	1
Previous experience from exercise (number)	
Regularly exercised	10
Never exercised regularly	6
Pain duration (years)	0.25–30
Change in pain from exercise intervention (number)	
Improved	8
No change	2
Worsened	6

Figure 7. Patients were told to align the knee over the toes during knee bending activities.

Interventions

Supervised group exercises, performed at stations, and with an intensity of ≥ 60% of maximum heart rate were used in both interventions (paper II and III). Exercises comprised postural control and lower extremity strength and endurance. Intensity was individually adjusted, and patients were encouraged to exercise at their most vigorous intensity possible, without losing quality in performance or severely exacerbating pain. Pain during exercise was not regarded an obstacle if the patient perceived it as “acceptable” and no increased symptoms persisted after 24 hours (Thomee 1997). If pain exceeded this level, exercise intensity was reduced occasionally, until the “acceptable” level was found. Intensity was gradually and individually increased. The aim of the exercise intervention was to increase muscle function and functional performance in the lower extremity. The effects on maximum number of one-leg rises and knee adduction moment was assessed in paper II. In paper III, the main outcome was self-estimated pain, function and quality of life.

After discussion with a panel of clinically experienced physical therapists, the exercises in paper II were chosen to fit younger patients with knee osteoarthritis. After warming up the program consisted of rebounder exercises, sit-ups, pulley exercises, step-ups, sit-to-stand, hip-abduction, and hip-extension. Exercises were conducted for eight weeks, twice a week at four stations, with three exercises per station, performed 3 × 15 times or 3 × 60 seconds (rebounder). Patients were told to align the knee over the toes throughout all exercises by using the hip external or internal rotators (Figure 7). Slide-board and soft-balls were used to challenge the postural control. Intensity was increased by using longer lever arms, dumbbells, bar-bells or medicine balls. A prerequisite to increase intensity was that exercises could be performed with full muscle control, i.e. constant speed and knee aligned with the toes.

Exercises in paper III followed the concept of a previously described study comprising patients with rheumatoid arthritis, with 6 weeks of one hour sessions twice a week (Ekdahl et al. 1990). Intensity was modified to fit patients with less physical impairment, by increased lever arms or performance on one leg instead of two. Types of exercises were similar to paper II, but with less demanding starting-positions and less frequent use of external weights. Exercises were carried out at three stations, with two to four exercises per station. 15 repetitions were performed before changing to next task.

Table 5. Outcome measures used in papers I–IV.

	Paper I	Paper II	Paper III	Paper IV
Knee radiographs	•	•	•	
HKA		•		
One-leg rise	•	•		
KOOS		•	•	•
SF-36		•	•	
Interviews				•
Gait analysis		•		

Outcomes

Radiographic examination (paper I, II and III)

A summary of outcomes used in paper I–IV is shown in Table 5.

In paper I, posteroanterior radiographs of both tibiofemoral joints were obtained at baseline, with straight legs in weight-bearing position and with the weight equally distributed on both legs. The medial aspects of the feet were aimed to be parallel to each other. The central x-ray beam was horizontal and aimed at the level of the centre of the popliteal fossa and the right and left knees were reproduced by the same exposure.

Five years later, in 1995–1996 (paper I and II), posteroanterior radiographs of both tibiofemoral joints were obtained in weight bearing under fluoroscopic control. The patients stood with almost the entire weight on the examined leg, with the knee flexed 30–50°, and with the patella and the big toe touching the table of the fluoroscopy unit. The medial aspect of the foot was parallel to the central X-ray beam and the beam was adjusted to be tangential to the anterior and posterior aspect of the medial tibial condyle.

All radiographs were read by an experienced radiologist. The intra-observer agreement for rereading the radiographs from baseline has been evaluated previously, showing high agreement (κ 0.88) (Petersson et al. 1997). The inter- and intra-observer agreement for minimum joint space and osteophytes in the semi-flexed position used in 1995-96 ranged from κ 0.72-0.98 (Boegard et al. 1998; Boegard et al. 1997).

Radiographic features were classified using the Kellgren and Lawrence index (Kellgren and Lawrence 1957) (paper I, II and III, Table 6). We defined Kellgren and Lawrence grade one as prevalent osteoarthritis (paper I and II) (Boegard et al. 1998; Hart and Spector 2003). A change of one grade or more according to Kellgren and Lawrence was defined as progression (paper I) (Hart and Spector 2003; Spector et al. 1992).

The hip-knee-ankle (HKA) angle was assessed in a standing anteroposterior radiograph of the lower limb (paper II). The patient was barefoot and stood with equal weight on both legs and with 15° of knee flexion. The X-ray beam was centred on the knee at a distance of 2.2 m. The frontal projection was perpendicular to a lateral view of the knee, which was achieved by superimposing the dorsal aspects of the femoral condyles. The landmarks used were the centre of the femoral head, the centre of the tibial spines, and the centre of the talus. The HKA angle was defined as the lateral angle between the lines from the centre of the tibial spines to the centre of the femoral head and the talus respectively (Figure 8). An angle of more than 180° denotes a varus alignment (Odenbring et al. 1993). All radiographs were read by the same experienced radiologist.

Table 6. Definition of Kellgren and Lawrence grade (Kellgren and Lawrence 1957) and number of patients within each category in paper I–IV.

K&L grade	Radiographic feature	Paper I N=148	Paper II N=13	Paper III N=61	Paper IV N=16
0	Normal radiographs	94	1	–	–
1	Minute osteophytes, doubtful significance	36	3	–	–
2	Definite osteophyte, unimpaired joint space	9	8	–	–
3	Moderate diminuition of joint space	9	1	42	9
4	Joint space greatly impaired, sclerosis of subchondral bone	–	–	19	7

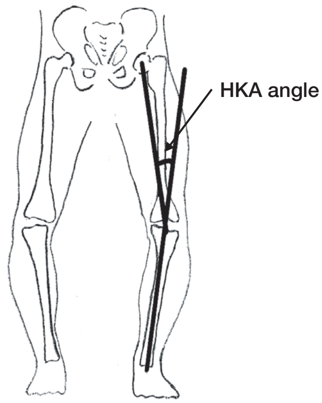


Figure 8. HKA-angle is assessed using the line from the centre of the talus to the centre of the tibial spines, and form the centre of the tibial spines to the centre of the femoral head.

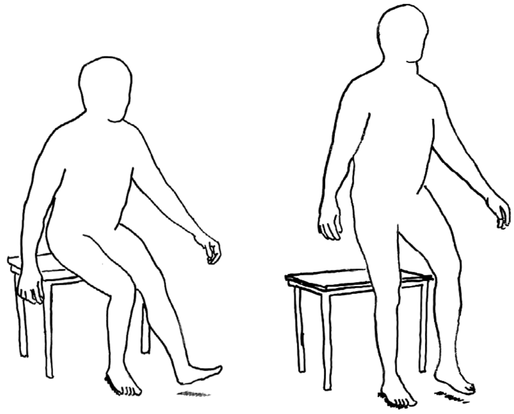


Figure 9. The one-leg rise test. The maximum number of one-leg rises from a stool is counted.

Tests of functional performance

The maximum number of one-leg rises from a stool (48 cm) was assessed (paper I and II). Patients were allowed to try out the best foot-stool-position before the trial, by rising up and sitting down a couple of times. They were asked to perform as many one-leg rises as possible, with arms hanging along the body, and without putting the other foot on the floor (Figure 9). The test should be performed with full muscle control, i.e. the sitting down phase should be performed with constant speed and the rising up phase without adding any arm or trunk movement. The foot position was not to be changed during the test, and body-weight had to be kept on the supporting leg and foot during the entire sitting-down phase. The numbers of adequately performed rises were counted. To avoid influence of aerobic capacity on test performance, a pause was held before the testing second leg. The length of the pause was decided by the patient.

Time spent walking 300 m indoor was assessed (paper I). Patients were told to walk as fast as they could without running, 150 m and pass a line on the floor, before turning around and walking back. Another line on the floor marked start and stop. Patients were told to keep up the speed past the stop-line. Time was measured in minutes and seconds using an analogue stopwatch.

Timed standing on one leg with simultaneous, rapid repeated neck rotations, with eyes open and arms hanging along the body was assessed (paper I). One attempt was allowed before the time was measured using an analogue stopwatch. When the lifted foot touched the floor, when support was needed, or after 30 seconds, which was considered "normal", the test was interrupted.

To assure the *effectiveness of the exercise interventions* used in paper II and III, five tests of functional performance and ergometer cycling were used.

1. Åstrand's bicycle-ergometer test (Paper II, III) (Åstrand and Saltin 1961).
2. Rising on one leg, from sitting on lowest possible height (Paper III) (Ostenberg et al. 1998; Roos et al. 2001).
3. One-leg hop (paper II, III) (Ostenberg et al. 1998; Tegner et al. 1986).
4. Lateral step-up (paper II, III) (Ross 1997).
5. One-leg semi squatting; maximum number during 30 seconds (paper III) (Roos et al. 2001).
6. Heel-raises on one leg; maximum number during 20 seconds (paper III) (Kaikkonen et al. 1994; Roos et al. 2001).

Self-reported measures of pain, function, quality of life, and health status

The Knee injury and Osteoarthritis Outcome Score (KOOS) (paper II, III and IV) is a disease-specific self-administered questionnaire with 42 questions in five subscales; pain, other symptoms, activities of daily living (ADL), function in sport and recreation (sport/rec) and quality of life (QOL), and takes about 10 minutes to complete (Roos et al. 1998a; Roos et al. 1998b). The KOOS is scored from 0

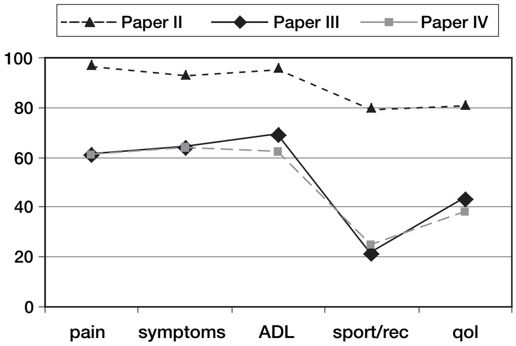


Figure 10. KOOS profiles for the Spenshult cohort (paper II) and the Exercise cohort (paper III and IV) at inclusion. The KOOS is a disease specific questionnaire with five subscales; pain, other symptoms, functioning in daily living (ADL), functioning in sport and recreation (sport/rec), and quality of life (qol) (0-100, worst to best score) (Roos et al. 1998a; Roos et al. 1998b).

to 100, separately for each subscale, 0 indicating extreme problems and 100 indicating no problems. The mean KOOS scores in the Spenshult cohort and the Exercise cohort at inclusion are shown in Figure 10. A change of 10 points or more is considered a clinically significant change (Roos and Lohmander 2003). If 50% or more of the answers within the KOOS subscale quality of life and 2 of the 4 additional scales were answered with at least a one-step decrease from the best response, patients were categorized as having symptomatic knee osteoarthritis (paper II)(Englund et al. 2004). This cut-off was chosen to identify individuals likely to seek medical care. The questionnaire and scoring manual can be found at www.koos.nu. The Western Ontario and McMaster Osteoarthritis Index (WOMAC) (Bellamy et al. 1988) is included in the KOOS, and WOMAC scores can also be calculated.

The Short Form-36 item (SF-36) (paper III) is a generic, widely used measure of general health status, which comprises eight subscales: Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health (Ware and Sherbourne 1992). The SF-36 is self-explanatory and takes about 10 minutes to complete. The SF-36 is scored from 0 to 100, 0 indicating extreme problems and 100 indicating no problems. To avoid significant results by chance (type 1 error), the Physical Component Summary scale (PCS) and the Mental Component Summary scale (MCS) were calculated from the eight subscales (Ware and Kosinski 2004). These scores are normalized with mean of 50 and standard deviation of 10, using U.S. general population norms from 1998. A score above 50 indicate health above average, while a score below 50 indicate health below average (Ware and Kosinski 2004).

Figure 11. Special markers were placed at anatomical landmarks, according to the biomechanical model described by Kadaba (Kadaba et al. 1990) and Davis (Davis et al. 1991).

Gait analysis (paper II)

Vicon 612 (OMG, Oxford, UK) was used to assess kinetics and kinematics of the knee joint (paper II). This is a system consisting of six 100 Hz cameras with infrared strobes, one AMTI force-plate (Advanced Mechanical Technology, Inc., USA), one data-station and one PC, where the information was gathered and processed in Plug-In Gait software.

Special markers, reflecting the infrared light from the cameras, were attached by a physical therapist with specific knowledge and experience within the area of motion analysis, over standardised landmarks (anterior superior iliac spine, lower lateral third of the thigh, lateral epicondyle of femur, lower lateral third of the calf, lateral malleolus of fibula and over the second metatarsal head, on

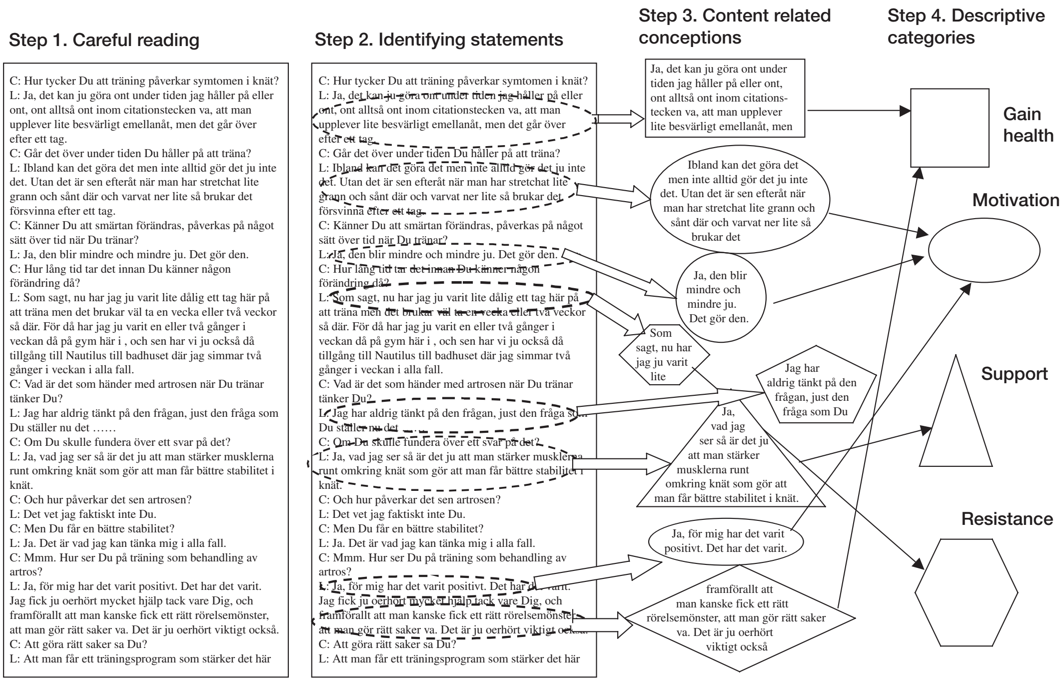


Figure 12. Illustration of the 4 step analysis process in phenomenography. Example is authentic (Swedish), and only to be considered as an illustration of the process.

the posterior calcaneus at the same distance from ground level as the forefoot marker and one marker between the posterior superior iliac spines (Figure 11) according to the biomechanical model of Kadaba et al. (1990) and Davis et al. (1991b).

Anatomical measures of anterior superior iliac spine distance, femur epicondyle width, ankle width and leg length were obtained in a standardized way, by the same physical therapist, and height and body weight were registered.

The peak knee adduction moment during one-leg rise and gait was used as the main outcome. Knee adduction moment was computed by Vicon software, and approximates the product of the ground reaction force, acting through the foot and medial to the knee joint, and the perpendicular distance from the ground reaction force to the axis of the knee joint ab- and adduction movement (Andriacchi 1994).

Phenomenographic approach (paper IV)

Phenomenography is one out of several qualitative methods. It is an explorative approach, developed in educational research and first described by Marton (Marton 1981), and the method has been used in nursing and health care research (Barnard et al. 1999; Sjostrom and Dahlgren 2002). This research approach is usually based on interviews or observations, and aims at identifying and describing different ways of experiencing phenomena in the world that surrounds us. In phenomenography, it is not the reality or how something really is that is interesting, but how different people experience a phenomenon (Marton 1981).

Procedure: A strategically chosen sample of patients from the exercise intervention in paper III was interviewed. The interviews were performed in a conversational style, audio-taped and verbatim transcribed. Six open-ended questions served as a guide of the conversation. These questions were constructed in consultation with a researcher with broad experience from phenomenography, and aimed at catching the conceptions of exercise as treatment of knee osteoarthritis. The questions were;

- What does exercise mean to you?
- What does osteoarthritis of the knee mean to you?

- How does exercise affect you?
- How does exercise affect osteoarthritis of the knee?
- How do you conceive the importance of exercise as a form of treatment?
- How has your conception of exercise changed over time?

Each interview lasted between 20 and 90 minutes, and was conducted at a place preferred by the patient.

Data analysis The transcribed interviews were analysed in four steps (Figure 12) (Dahlgren and Fallsberg 1991). In step one, the transcribed interviews were carefully read while listening to the tape recording, in order to correct errors in the transcript and to become familiar with the material. The next step was to identify the statements, which corresponded to the aim of the study. Thereafter the statements were assigned to content-related categories; conceptions. In this phase the number of conceptions was large. In the fourth step similarities and differences between conceptions were observed, and conceptions that had the same theme were grouped together and further assigned to a more general category; a descriptive category. A revision of the conceptions decided upon in a previous step was necessary on a few occasions in order to continue. The fourth step continued until descriptive categories emerged, which were different in content and meaning, and corresponded to the context. The final descriptive categories were illustrated with carefully selected quotations from the interview statements.

Statistics

Due to rather small study samples (paper I, II, III) data were analyzed using nonparametric tests. P-values of less than or equal to 0.05 were considered to be statistically significant, and all tests were two-tailed. To compare groups, Mann-Whitney U-test was used (paper I, II and III). Spearman's test was used to determine correlations (paper I and II). Friedman's test was used for repeated measures analysis of variance (paper III). Wilcoxon signed rank test was performed to study paired analysis of variance (paper II and III). Logistic regression was used to determine the odds ratio (95% confidence interval) of progression of radiographic features (paper I). Analyses were performed using SPSS for Windows.

Results

Functional performance and risk of incident knee osteoarthritis (Paper I)

Incident osteoarthritis developed after five years in 41/94 subjects (44%) without radiographic features of osteoarthritis at baseline. The test of maximum number of one-leg rises from sitting significantly predicted development of incident knee osteoarthritis five years later (median 17 vs. 25 times, OR 2.6, 95% CI 1.1–6.0). Age, sex, body mass index and baseline pain did not predict incident radiographic osteoarthritis. The number of subjects did not allow for multiple regression analyses, however, the impact of fewer one-leg rises on the development of incident osteoarthritis at follow-up remained significant even when controlling for age, sex, body mass index and baseline pain one by one. The number of adequately performed one-leg rises was not significantly associated with baseline pain.

A cut-off between 20 and 24 one-leg rises could best discriminate between no radiographic changes and incident knee osteoarthritis (Figure 13) (data not shown in paper I).

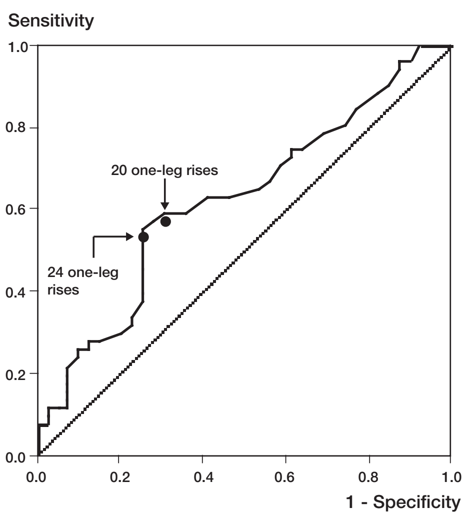


Figure 13. Receiver operating characteristic (ROC) curve. Result of maximum number of one-leg rises to determine incident radiographic knee osteoarthritis five years later among subjects with knee pain.

Progression in radiographic status was seen in 29/54 subjects (54%) with radiographic features of osteoarthritis at baseline. None of the variables analysed could explain the radiographic progression, although those who progressed tended to have higher body mass index, perform fewer one-leg rises, and manage a shorter time standing on one leg.

Regression with regard to radiographic features was seen in 11/54 patients at follow-up. A comparison of characteristics between them and the remaining cohort showed that they had a lower body mass index (23.4 vs. 25.5 kg/m^2, p=0.05).

The effect from exercise on knee joint load (paper II)

Results are presented as mean (SD), if nothing else is stated.

Change in peak adduction moment during one-leg rise

The individual peak adduction moment at baseline ranged from 0.41 to 0.86 for the index knee, and for the opposite knee from 0.37 to 0.79 Nm/kg.

For the index knee ('the worst knee') peak adduction moment during one-leg rise was reduced from 0.57 (0.14) Nm/kg to 0.51 (0.13) Nm/kg (p=0.04, Figure 14). For the opposite knee there was no significant change in peak adduction moment from baseline to follow-up. No significant changes were seen for the index knee or the opposite knee in peak adduction moment during gait. In most cases, the exercise-induced changes in knee adduction moment were larger during one-leg rises than during gait (Figure 14).

Relationship between peak adduction moment and maximum number of one-leg rises

Higher peak adduction moment was correlated to reduced functional performance, measured as

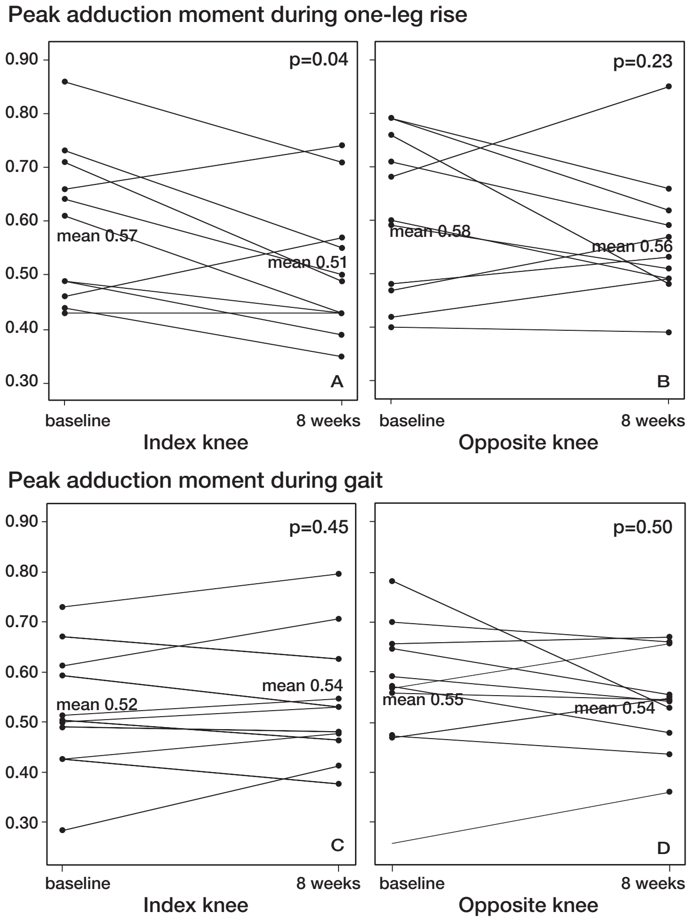


Figure 14. Change over time in peak adduction moment during one-leg rise (A and B) and during gait (C and D) in index and opposite knees.

maximum number of one-leg rises. The correlation for the index knee was r_s = -0.35 at baseline and -0.65 at the 8 week follow up (p=0.24 and 0.03 respectively). For the opposite knee the correlation was r_s = -0.47 at baseline and 0.13 at follow-up. To determine the number of one-leg rises best predicting a higher than median peak adduction moment, a ROC curve was calculated (Figure 15). For the 26 knees included at baseline, 23 to 29 one-leg rises best separated a higher than median from a lower than median peak adduction moment.

The effect from exercise on pain and function (paper III)

There were no significant differences in pain, self-estimated function or quality of life between the exercise group and the control group. *In the exercise group*, significant improvement was seen in the KOOS subscale Quality of Life at the six week follow up (45 vs. 40, p=0.04, Figure 16). This improvement persisted at six months (46 vs. 40, p=0.05). The individual changes over time ranged from clinically significant improvement to clinically significant deterioration in all KOOS subscales in both the exercise and control groups.

Significant improvement compared to baseline was found in the exercise group at six weeks with regard to the SF-36 Physical Component Summary scale (PCS) (45.7 vs. 42.5, p=0.02). This improvement persisted over time. Within the control group no significant improvement was found.

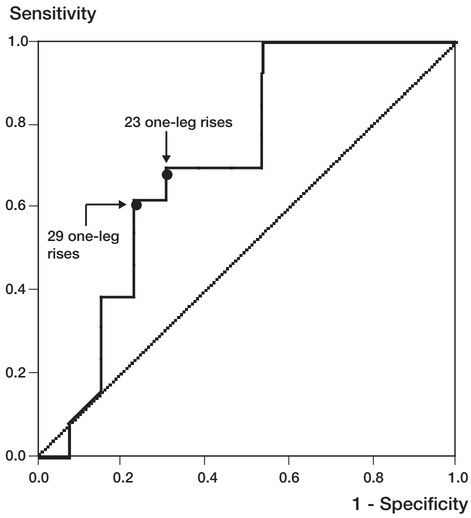


Figure 15. Receiver operating characteristic (ROC) curve. Result of maximum number of one-leg rises to determine a higher than median (0.56 Nm/kg) peak adduction moment among subjects with mild to moderate knee osteoarthritis.

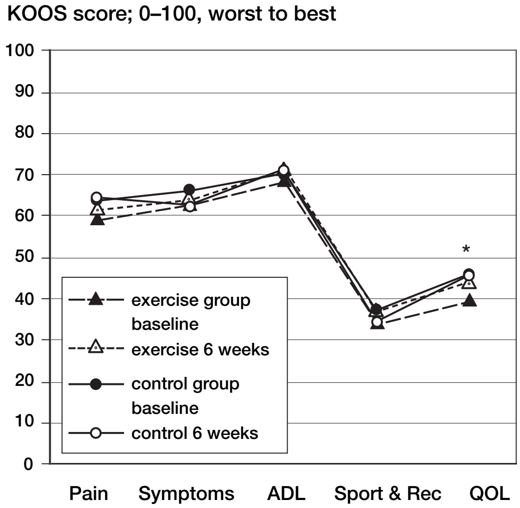


Figure 16. KOOS scores at baseline and 6 weeks follow up in the exercise and control group. No changes were seen for pain and function after exercise intervention. A significant change from baseline was seen in quality of life in the exercise group *p=0.04.

According to the tests of functional performance, the exercise program improved aerobic capacity and endurance in the lower extremity; The number of knee bendings and lateral step ups in 30 seconds increased from baseline to 6 weeks, and the results persisted over time ($p<0.05$).

Patients' experiences from exercise as osteoarthritis treatment (paper IV)

Four descriptive categories emerged from the analysis of the transcribed interviews: To gain health, to become motivated, to experience the need for support, and to experience resistance. These four descriptive categories together included 13 conceptions (paper IV).

Conceptions were labelled as positive, but could hold a range of statements from positive to negative.

Descriptive category – To gain health

This category contained conceptions about experienced or known health related effects of exercise and consisted of five conceptions: to experience coherence, to experience well-being, to be in control, to experience improved physical functioning, and to experience symptom relief.

Patients related their knowledge about osteoarthritis to knowledge and experiences of exercise. They were satisfied and convinced of the effectiveness of exercise for health.

The moments immediately following the exercise sessions were associated with mental and physical relaxation, satisfaction and well being.

Several patients had experienced how exercise could improve their ability to handle their daily situation, and cope with the problems related to knee osteoarthritis. Some were able to regain functional performance or performing daily recreational activities more easily after the exercise intervention. However, the effects of exercise on pain and other symptoms were described within a range from total pain relief to a worsening of symptoms.

Descriptive category – To become motivated

This category contained three conceptions dealing with the informants' desire to exercise: To experience inspiration, to be prepared to persevere, and to experience the need to exercise. Despite pain, the informants talked about exercise with varying degrees of enthusiasm and a sense of duty.

They experienced a wide range in motivation to exercise, from a desire to exercise regularly to having no motivation to exercise at all. Most of them were exercising despite pain and discomfort, because of the known benefits on health related aspects. The definition of exercise needed varied greatly. Some felt that daily living demands movement was enough exercise, while others thought of regularly exercise sessions as important to maintain physical functioning.

Descriptive category – To experience the need for support

This category described conceptions of conditions necessary for wanting to exercise. Three conceptions emerged: To have structure, to receive guidance, and to devote time.

Accessibility was described as a prerequisite for exercise, and exercise should be of high quality, concerning the individual performance as well as the purpose with and type of exercise. All patients expressed a perceived need for moral support, encouragement and instructions on how to exercise. They were worried about doing something wrong and felt need for support to comply with exercise.

Different aspects of time were mentioned as essential for the effectiveness of the exercise. It concerned the most appropriate time point during the disease course to start exercise, and also how to find adequate time to exercise.

Descriptive category – To experience resistance

This category described the reasons for not exercising and comprised two conceptions: To hesitate and to deprecate.

Patients felt doubts about the benefits of exercise. Experiencing pain while exercising made it difficult to decide whether exercise was beneficial or counterproductive. They were worried that exercise could cause harm. Some considered other treatments to be more effective, and thought of exercise as unnecessary.

Conceptions of knee osteoarthritis

Some patients described their view of why they had knee osteoarthritis; hard work (n=2), injury from traffic accident (n=1) and heredity (n=1).

Patients talked about the limited physical performance due to knee osteoarthritis (n=13), avoidance of activities causing pain (n=9), and altered movement pattern (n=5). Osteoarthritis was described as painful by 14/16 patients. Five patients described discouragement from knee osteoarthritis; frustration (n=3), depression (n=3) and fear or anxiety (n=3). (Results not described in paper IV).

General discussion

Main message

Based on the results from the papers included in this thesis, I suggest that sufficient lower extremity muscle function reduces the risk of incident knee osteoarthritis (paper I), and that exercise has the potential to alter joint load (paper II). Exercise should be performed at an early stage of the disease, and preferably during periods of less pain (paper II, III, IV). Some patients with more severe disease benefit from exercise, but the prescription of exercise should be individual, based on patients' preferences and previous experiences (paper III, IV). Continuous support, guidance and encouragement are essential components to avoid anxiety about exercising with knee osteoarthritis (paper IV).

Incidence of osteoarthritis

The incident rate of osteoarthritis after five years, defined as Kellgren and Lawrence grade one or more, in the Spenshult cohort was 44% (paper I). Applying the method used by Hart et al. (Hart et al. 1999) and Cooper et al. (Cooper et al. 2000) the yearly incident rate was 8.8% per year which is high compared to other studies. The comparison of incidence rates between different studies is complicated by several factors, such as different age-groups, previous joint injury, percentage of women, presence of knee pain like in the Spenshult cohort, patellofemoral involvement, and also by the fact that different radiographic atlases and different cut off points for 'no osteoarthritis' and 'incident osteoarthritis' are used (Cicuttini et al. 1996; Cooper et al. 2000; Felson et al. 1997; Gelber et al. 2000; Hart et al. 1999; Spector et al. 1994). The incident rate in a Bristol population, aged 55 years or older, was 3.3% per year (Cooper et al. 2000), and in the Chingford study, which comprised middle-aged women, the incidence rate was 5.8% per year (Hart et al. 1999).

Developing a chronic disease requires larger readjustments in life than losing a job or getting married (Holmes and Rahe 1967; Scully et al. 2000). Feelings of helplessness, fear and isolation found in our study population (paper IV) have been described previously among younger individuals (aged 25–45) with knee osteoarthritis (Keysor et al. 1998). Women in the community with knee pain but without radiographic knee osteoarthritis report higher anxiety scores than women with knee pain and radiographic features of knee osteoarthritis (Creamer et al. 1999). When patients with arthritis discover reduced ability to perform the activities they are used to doing, they feel upset, frustrated and worried (Keysor et al. 1998; Tallon et al. 2000).

Modifiable risk factors

Muscle weakness

Knee osteoarthritis is associated with muscle weakness (Hurley et al. 1997; Lewek et al. 2004; Pap et al. 2004; Toda et al. 2000). Whether the muscle weakness is a cause or consequence of knee osteoarthritis has been a topic for discussion (Hurley 1999; Roos 2005; Shrier 2004).

For assessment of muscular strength isokinetic or isometric muscle forces have most commonly been determined. These apparatuses however, are not readily available in clinical practice. Isokinetic and isometric assessments are laboratory tests, assessing dynamic lower extremity strength for one group of muscles at a time, using constant speed or constant force in open chain movements. In activities of daily living the conditions are more complex. It has been suggested that assessing different aspects of physical function might be more informative about overall functional performance (Hurley et al. 1997). The maximum number of one-leg rise test is such a test and is easily applied in clinical practice, and could be used to screen patients at increased risk of developing knee osteoarthritis.

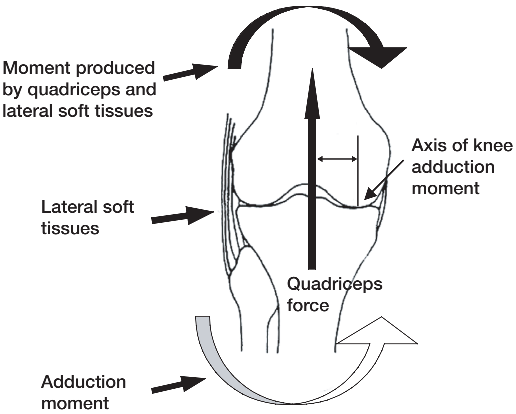


Figure 17. The quadriceps acts lateral to the axis of the adduction moment in a knee with neutral alignment. Together with the passive lateral soft tissues, quadriceps prevent lateral gapping. Modified from (Schipplein and Andriacchi 1991).

We found reduced muscle function to be a risk factor for incident knee osteoarthritis five years later, controlling for known confounding factors like age, gender, body mass index and pain (paper I). These results support the suggestion by Slemenda et al. that reduced quadriceps strength in relation to body weight is a risk factor of knee osteoarthritis in women (Slemenda et al. 1998).

Muscle function can be improved through exercise (Deyle et al. 2000; Ettinger et al. 1997; O'Reilly et al. 1999; Petrella and Bartha 2000; Thomas et al. 2002), and it is possible that the risk of osteoarthritis development thereby could be reduced. In retrospective studies, moderate exercise has been associated with reduced risk of incident osteoarthritis (Sutton et al. 2001) and osteoarthritis requiring joint replacement (Manninen et al. 2001).

Joint load

In a knee with neutral alignment, the lever arm between the quadriceps tendon and the medial joint contact surface – the axis of the adduction moment – is longer than in the varus knee. The quadriceps then acts, lateral to the axis of the adduction moment, as a stabilizer against lateral gapping, together with the passive lateral soft tissues (Figure 17)(Schipplein and Andriacchi 1991). Weak muscles put a greater demand on the passive lateral soft tissues. Insufficient tension of the lateral passive soft tissues contributes to a lateral gapping of the knee joint, and a shift in the local joint load (Andriacchi et al. 2004; Schipplein and Andriacchi 1991).

It seems possible to reduce peak adduction moment with exercise (paper II), indicating the role of the muscles as dynamic stabilisers of the knee joint. Previously, high tibial osteotomy has been shown to reduce the peak adduction moment, by reducing the varus alignment (Prodromos et al. 1985). Valgus braces intended to reduce the adduction moment have been studied with various results (Hewett et al. 1998; Pollo et al. 2002; Self et al. 2000). In future studies it would be interesting to explore the effect on joint load of combined treatments in knee osteoarthritis.

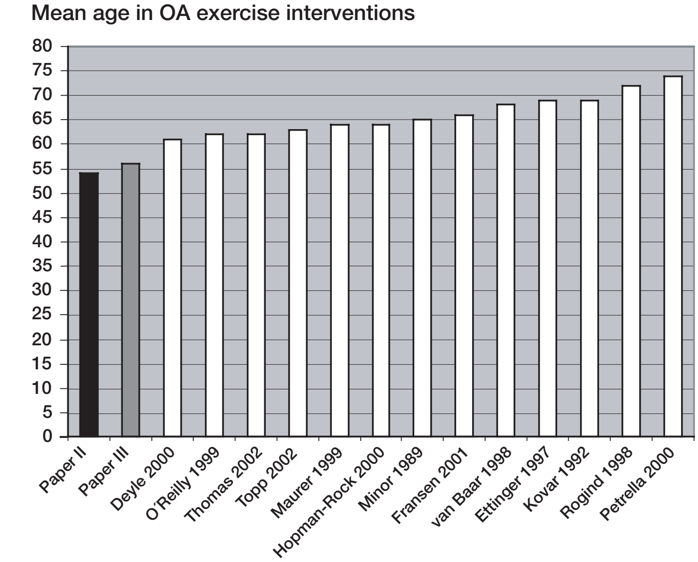
Exercise as osteoarthritis treatment

Effect of exercise

Most studies of the effects of exercise in knee osteoarthritis have included elderly subjects and have higher proportions of women than the populations included in paper II and III (Figure 18).

The mean changes in pain score and self-reported function in paper III were small and not significant (ranging from 2 to 4 points), however, some patients reported more than 10 KOOS points improvement in pain or function, while others reported similar deteriorations. The diverging results in our study are not unique (Fransen et al. 2001; Minor et al. 1989). It is a challenge to health care professionals to determine who will improve from exercise and who will not. Knee joint laxity or malalignment were not assessed in the population included in paper III, thus it is possible that local biomechanical factors contributed to the lack of improvement in pain and self-reported function (Sharma et al. 1999b). Sharma et al. (Sharma et al. 1999a; Sharma et al. 2003a) suggested that muscle strengthening exercise cannot contribute to increased functional performance, unless the dynamic alignment is normalized, and a cross-sectional relationship has been reported between strong quadriceps in knees with static malalignment and increased risk of progression of radiographic changes (Sharma et al. 2003b).

Patients in paper II and the exercise group in paper III were told not to exercise with more



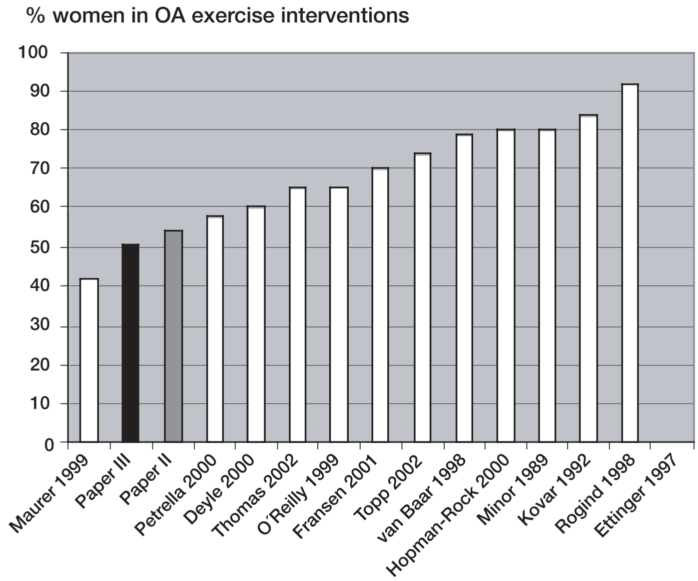


Figure 18. The mean age of subjects, and proportion of women included in paper II and III compared to other exercise interventions in patients with knee osteoarthritis.

than 'acceptable pain', but it might be difficult to decide how much pain is 'acceptable'. There is a risk that they might have had neglected or distracted pain during exercise. Patients have different coping strategies, and neglecting or distracting pain in knee osteoarthritis has been demonstrated to increase pain 6 months later (Steultjens et al. 2001). The study by Steultjens et al. concluded that if patients pretend the pain is not there or is less severe, they might neglect pain as a warning signal of overuse. It has been suggested that pain reduction results in increased knee joint load (Hurwitz et al. 2000), and that the pain in fact might be protective in that it prevents from further joint load on the affected cartilage (Hurwitz et al. 1999).

It is also possible that some of the variation could be related to unknown factors that might interfere with the severity and course of disease. Knowledge about the natural course of osteoarthritis is limited, but indicates that patients with osteoarthritis show great variability over time in self-reported pain and function (Dieppe et al. 2000; Paradowski et al. 2004).

Type of exercise

The exercise intensity in paper II and III was moderate/intensive, and patients exercised at the most vigorous intensity possible, without exacerbating pain. One of the problems with randomized controlled trials using exercise interventions is that the intervention is assumed to be uniform to all patients. No significant difference in effect on group level has been demonstrated between different types of exercise interventions (Brosseau et al. 2003; Ettinger et al. 1997; Fransen et al. 2003; Mangione et al. 1999; O'Reilly et al. 1999; Topp et al. 2002). However, the individual experience may vary between patients, even within the same exercise program (paper IV). This could affect the outcomes, especially self-estimated pain and function.

The intervention length of 6 weeks, used in paper III, was short (Ettinger et al. 1997; Minor et al. 1989; O'Reilly et al. 1999; Petrella and Bartha 2000; van Baar et al. 2001), however we found improvements in aerobic capacity and lower extremity endurance at six weeks which were maintained at 6 months. Hurley and Scott demonstrated positive effects on quadriceps strength, voluntary activation and functional performance after five weeks of exercise, in patients with knee osteoarthritis according to the ACR criteria (Altman et al. 1987), and data from 25 of the 60 (42%) patients who completed the exercise intervention in that study indicated that the results persisted over time (Hurley and Scott 1998).

Compliance with exercise

Patients have doubts about exercising, even when they have perceived benefit from exercise (paper IV). The hesitation can be related to fear of worsening the osteoarthritis or to the uncertainty about how to exercise, but also to more practical problems, like access to gyms, available time or transport to the exercise class (paper IV). Compliance to exercise is probably related to factors other than benefit of exercise (Campbell et al. 2001; Hsieh and Dominick 2003). Lack of time was mentioned as a reason not to exercise in paper IV, and it has been shown to be the most common reason not to exercise among younger and middle-aged women (Anderson 2003).

Another obstacle to compliance with exercise is the discrepancy between treatment recommendations and treatment preferences among patients with knee osteoarthritis (Fontaine et al. 2004; Jordan et al. 2004; Tallon et al. 2000). Results from paper IV showed that some patients prefer passive treatments, like pills or injections, and therefore think of exercise as unnecessary.

Supervised exercises seem to have better compliance, and thus better effects than home exercises (Fransen et al. 2003; Kettunen and Kujala 2004). The exercises in paper II and III were supervised and combined with home exercises. Home exercises combined with initial instructions and supervision have been shown to be more effective than home exercises alone or telephone advice (McCarthy et al. 2004; Thomas et al. 2002). To get the highest possible compliance, patients' preferences should be recognized and wishes about certain conditions should be met, without losing the intention of treatment.

Pain and exercise in knee osteoarthritis

The lack of improvement in pain and function from exercise in patients with moderate to severe knee osteoarthritis in paper III coincides with the theory by Fransen et al. suggesting the effect from exercise being negatively correlated to grade of radiographic changes (Fransen et al. 2001). Interviews with 16/30 patients from the exercise group (paper IV) demonstrated that patients would prefer exercise at an earlier stage of the disease. Exercising at an early stage of the disease is less likely to induce severe pain, since pain becomes more intense and frequent with increasing radiographic severity (Cooper et al. 2000; Felson et al. 1987). Experiencing pain from exercise contributed to difficulties for the patients to determine the degree of benefit or damage related to exercise, and thus caused feelings of anxiety and helplessness (paper IV). Pain also seems to interfere with the possibility to achieve increased functional performance (paper II, III, IV). Thus, it is desirable to initially combine exercise with analgesics or acupuncture.

Motivational factors for exercise

Information, continuous support, encouragement and patience are important to achieve a change in behaviour among patients with osteoarthritis (paper IV). The results from paper IV indicated that the motivation to exercise varied. One factor suggested to interact with motivation to exercise is coping with the disease. Patients with rheumatoid arthritis who thought of the disease as possible to influence and were motivated to exercise were prepared to comply with exercise and physical activities despite the disease, while those who had accepted the disease but thought of it as impossible to influence were less eager to be physically active (Eurenius et al. 2003). It seems as if coping with the disease is of similar importance in knee osteoarthritis (paper IV). Patients who use passive strategies, like rest, to cope with osteoarthritis pain are at higher risk of developing physical disability over time (Steultjens et al. 2001). Patients with mild disease participate more frequently in exercise and have a stronger belief in exercise than patients with moderate to severe knee osteoarthritis (Gecht et al. 1996).

Strengths and limitations

Outcomes

I suggest that muscle function is more appropriately assessed using functional performance tests than isokinetic or isokinetic muscle strength testing. The maximum number of one-leg rises assesses a combination of muscle function, i.e. strength, endurance and proprioception, balance, and motivational factors. Sit to stand is performed several times per day in activities of daily living, and perceived difficulties are described by patients with knee osteoarthritis. The difficulty with rising from sitting is evaluated in WOMAC (Bellamy et al. 1988) and KOOS (Roos et al. 1998a; Roos et al. 1998b), both questionnaires frequently used in patients with knee osteoarthritis. 50/61 (82%) of the patients in the exercise cohort in this thesis described at least some difficulty with the task. This makes the test relevant in this population. The reliability of maximum number of one-leg rises is yet to be determined.

Three-dimensional gait analysis, or analysis of other activities of daily living is widely used to describe kinetics and kinematics in healthy subjects as well as in patients with lower extremity dysfunction (Al-Zahrani and Bakheit 2002; Amin et al. 2004; Chmielewski et al. 2001; Draganich and Kuo 2004; Herzog et al. 1989; Hinman et al. 2002; Kaufman et al. 2001; Mikesky et al. 2000). Three-dimensional motion analysis provides the researcher with rich information about limb position, degrees of motion, speed, frequencies, and external forces across several joints, in the frontal, coronal and sagittal planes simultaneously 100 times per second (100 Hz). Beforehand decisions have to be made about variables of interest. These decisions are guided by previous research and clinical questions. The anatomical landmarks for the reflective markers are clearly defined (Davis et al. 1991b; Kadaba et al. 1990), and correct placement is crucial for the reliability. In the current study we have not assessed the reliability of the procedures, which of course could bias the results. A second source of unreliability was introduced since peak adduction moment was obtained from graphs. To minimize bias the graph reader was blinded to subject, knee, and if data was obtained before or after the intervention. Other concerns are the small number of patients included, and the lack of knowledge about peak adduction moment during tests of functional performance, and the lack of control group. Previous studies comprising 18–19 patients have shown significant differences on gait parameters over time (Schnitzer et al. 1993; Shrader et al. 2004). Our study should be considered as a pilot study within the field, and the clinical importance of the significant changes in paper II should be determined in future studies.

Qualitative research methodology

Life-style, knowledge, and previous experiences are factors that influence people's acting and beliefs. The characteristics and effect of these factors are often not explored within quantitative research. The variation in responses to questions in a questionnaire is often predetermined by fix alternatives, like in a Likkert Scale. In quantitative studies individual answers are grouped together, and useful information might be lost, or the results may indicate ‘no difference’ on group level (paper III). Qualitative studies can contribute to a deeper understanding, by taking the individual responses and perspectives into account. Based on the participants’ conceptions individual differences can be illuminated and provide a deeper perspective on the results (Malterud 2001). Qualitative research is based on data not able to describe or analyze with statistical methods. Paper IV was undertaken to elucidate such a situation, where there were no change at group level but a wide variation in individual outcomes after an exercise intervention (paper III). A recent study has shown that there is a lack of agreement between pain assessed by questionnaires and by interviews (Campbell et al. 2003). In paper IV however, the range of statements obtained by means of interviews concerning symptom relief clearly correlated with the divergent outcome derived from paper III. I found that the patients with moderate to severe knee osteoarthritis were worried about the pain they had felt during exercise. All the informants in paper IV expressed doubts and concerns about exercise as a form of treatment, even though they did believe in general health benefits from exercise, and some of them had experienced pain relief from exercise.

I used phenomenography to analyze the data in paper IV. The method is descriptive and results are presented on group level. The methodological objective was to remain close to empirical data in order to gain a better understanding of how patients with knee osteoarthritis experience exercise as treatment, and since this was the objective, it was considered logical and appropriate to use phenomenograpic approach. The possibility to formulate and test new hypothesis within phenomenography is restricted compared to other qualitative methods, which limits the interpretation of the results into a wider context. The results could however be applied in clinical practice and taken into account in planning of future exercise trials.

Clinical implications

Incorporating the results from paper I and II in clinical practice, would suggest that if a patient with knee pain (and no radiographic features of knee osteoarthritis) perform more than 29 one-leg rises, the risk of having a high peak adduction moment during one-leg rise is low. If the patient performs less than 20 one-leg rises, the risk of developing radiographic knee osteoarthritis is increased (Figures 13 and 15).

Muscle weakness is associated with increased or altered joint loads (Andriacchi et al. 2004; Mikesky et al. 2000). The results from paper II indicated that also reduced functional performance, i.e. fewer one-leg rises, was associated with increased peak adduction moment. In future studies it would be of interest to explore if maximum number of one-leg rises could be used to screen patients for joint load in large scale studies and clinical practice.

Pain during exercise is related to feelings of hesitation about if exercise might cause further harm (paper IV). By initially combining exercise with analgesics, acupuncture or pain coping strategies compliance could be enhanced. The choice of exercise should be based on patient’s preferences and previous experiences. Structured exercises and continuous feed-back and encouragement should be provided.

Conclusions

- Reduced functional performance, assessed by maximum number of one-leg rises, predicted development of incident knee osteoarthritis in middle-aged subjects with knee pain.
- Exercise has the potential to reduce peak adduction moment in mild to moderate knee osteoarthritis.
- Increased peak adduction moment was correlated to a lower number of one-leg rises
- Six weeks of high-intensity supervised group exercise in patients with moderate to severe knee osteoarthritis had no effect on pain and self-reported function, however the quality of life improved.
- Among patients with moderate to severe knee osteoarthritis the individual changes in pain and function after 6 weeks of exercise ranged from clinically significant improvement to clinically significant worsening.
- Middle-aged patients with moderate to severe knee osteoarthritis and knee pain had doubts about exercise as osteoarthritis treatment, despite known and perceived benefits from exercise on health aspects and symptoms related to osteoarthritis.
- Patients with moderate to severe knee osteoarthritis expressed that exercise as treatment for osteoarthritis should be supervised, and that continuous encouragement and support is crucial to compliance.

Summary

Knee osteoarthritis is one of the ten most disabling diseases in adults older than 30. Previous knee injury increases the risk of developing knee osteoarthritis already in middle-age. It can be estimated that approximately 5% in the age group 35-54 have radiographic features of knee osteoarthritis. Of these, 2/3 have a previous knee injury and 1/3 have knee pain without known previous knee injury. Muscle weakness is associated with increased joint loads. Increased or altered joint loads will finally result in osteoarthritis. It is not clear whether muscle weakness is a cause or consequence of osteoarthritis. Exercise reduces pain and improves function in knee osteoarthritis and is recommended as the first line treatment in international guidelines.

In this thesis, I have studied a population based cohort of middle-aged subjects (35–54 years, 42% women) with chronic knee pain at baseline, to evaluate the longitudinal effect of muscle weakness on knee osteoarthritis development, the relationship between muscle function and joint load and the effects of exercise on joint load. I have also studied the effect of exercise on pain and function in another middle-aged cohort (36–65 years, 51% women) with moderate to severe knee osteoarthritis, and explored their conceptions of exercise as treatment.

In the first study, 148 subjects with chronic knee pain underwent radiographic examination and tests of functional performance at baseline. 94 of them had no radiographic signs of knee osteoarthritis. Five years later they had new radiographs taken and 41/94 (44 %) had developed incident knee osteoarthritis. I found that reduced functional performance, assessed by maximum number of one-leg rises from a stool, predicted knee osteoarthritis development. The result was controlled for the previously known risk factors of age, BMI and pain.

In the second study, I used three-dimensional motion analysis to explore the possibility of altering joint load by exercise. The medial compartment joint load (peak adduction moment) during maximum number of one-leg rises was assessed in 13 subjects with early radiographic signs of knee osteoarthritis from the cohort in study one, before and after 8 weeks of exercise. Two subjects were lost to follow up for reasons not related to the knee. The peak adduction moment could be reduced by exercise, and a high maximum number of one-leg rises was associated with lower levels of peak adduction moment.

The third study included 61 subjects with moderate to severe radiographic knee osteoarthritis. They were randomized to 6 weeks of intensive exercise or to a control group. The effects of exercise were assessed using questionnaires. No effects were seen on pain or self estimated function, however, the quality of life improved. The individual response to exercise ranged from clinically significant improvement to clinically significant worsening.

As an attempt to understand this large inter individual response to exercise, I designed the fourth study, where I interviewed 16 of the 30 patients in the exercise group about their conceptions of exercise as treatment. The interviews were analysed using qualitative methodology, and it was revealed that all patients were aware of the general health benefits of exercise, but had doubts about exercise as treatment of osteoarthritis even if they had perceived pain relief and improvement in physical function from the exercise intervention. The pain experienced during exercise caused the patients to believe that exercise was harmful to their knees, and some of them would prefer not to exercise at all. They thought that exercise should be introduced early during the course of the disease, and all of them expressed the need of continuous encouragement and support to adhere to exercise.

From this thesis I conclude that reduced muscle function is a risk factor of knee osteoarthritis development among middle aged subjects with knee pain. Reduced muscle function is associated with increased joint load, which seem to be modifiable by exercise. Initial pain when starting exercise, or occasional pain from exercise, should be treated by combining exercise with pain relief such

as analgesics or acupuncture. Pain contributes to the difficulty patients have determining the degree of benefit or damage related to exercise, and thus causes feelings of anxiety and helplessness (paper IV). Pain also seems to interfere with the possibility of achieving increased functional performance (paper II, III, IV).

Sammanfattning på svenska

Artros i knäleden är en av de tio vanligaste orsakerna till smärta och funktionshinder hos vuxna. Ett av problemen med artros är att det är svårt att diagnosticera vid ett tidigt stadium. Det kan synas som förändringar på röntgen, men ofta inte förrän flera år efter att det utvecklats. Mina studier visar att det finns ett samband mellan muskelfunktion i benen och risken att senare utveckla artros. Jag har också i olika studier undersökt huruvida träning kan minska belastningen på knäleden, vilka effekter träning kan ha på smärta och funktion hos patienter med dokumenterad artros, samt hur patienterna ser på träning som behandling.

Artros är en sjukdom som drabbar hela leden, men där effekterna märks främst på ledbrosk och ben. Ledbrosket blir skört och tunnas ut, det bildas bennabbar på ledytans kanter och benvävnaden under ledbrosket förtätas. Ett tidigt och mycket vanligt symptom vid artros är smärta, som leder till svårigheter att belasta leden. En skada av knäleden ökar risken för artros på lång sikt, men även utan tidigare skada är det ungefär 1.5 % av befolkningen som drabbas. Alltför stor belastning på leden medför ökad risk för artrosutveckling. Svaga lårmuskler är vanligt vid knäartros och det har diskuterats om det är en riskfaktor eller en konsekvens av artros. Träning rekommenderas ofta som behandling och har i studier av äldre personer med knäartros visats kunna minska smärtan och förbättra funktionen.

I min första studie undersöktes muskelfunktion i benen hos ca 150 medelålders personer, som alla hade knäsmärta. Bland annat fick de fick resa sig och sätta sig så många gånger de kunde på ett ben från sittande. Deras knäleder röntgades och ungefär 1/3 hade förändringar som vid artros medan resten var ”knäfriska” enligt röntgen. Fem år senare togs nya röntgenbilder och då hade 44 % av de tidigare ”knäfriska” utvecklat artros. Jag fann att de som hade sämre förmåga att resa sig på ett ben från sittande i större utsträckning hade utvecklat artros, även om hänsyn togs till övervikt, ålder och kön. Det betyder att nedsatt muskelfunktion i benen ökar risken för att utveckla knäartros.

I studie två ville jag undersöka om belastning på knäleden kan påverkas med träning. För att bestämma belastningen under rörelse användes tredimensionell rörelseanalys; försökspersonerna rör sig i ett laboratorium med reflexmarkörer fastsatta på huden över speciella landmärken. Speciella kameror registrerar markörerna och ett avancerat datorprogram beräknar belastningen på knäleden. 13 personer med tidiga tecken på artros fick utföra maximalt antal uppresningar på ett ben i laboratoriet och jag mätte ledbelastningen under uppresning före och efter åtta veckors träning. Belastningen på knäleden minskade efter träning och de som klarade flest antal uppresningar hade lägst ledbelastning. Knäsmärta påverkade inte möjligheten att förändra ledbelastningen, men minskade förmågan att förbättra muskelfunktionen. Studien är mycket liten och resultaten får därför tolkas med stor försiktighet.

Den tredje studien inkluderade drygt 60 personer som alla hade knäsmärta och måttliga till svåra artrosförändringar enligt röntgen. De lottades hälften till 6 veckors intensiv träning och hälften till en kontrollgrupp som levde som vanligt. Jag mätte effekten av träningen med frågeformulär och resultaten visade att träning inte påverkade vare sig smärta eller funktion i träningsgruppen, men att livskvaliteten förbättrades jämfört med kontrollgruppen. Resultatet på individnivå varierade från tydlig förbättring till tydlig försämring.

För att försöka förstå dessa variationer mellan individer genomförde jag i min fjärde studie intervjuer med hälften av de personer som varit med i träningsgruppen. Jag ville undersöka hur de såg på träning som behandling av artros. Resultaten visade att alla var medvetna om de positiva effekter som träning har på hälsan, men tvivlade på om träning var bra för artros även om de själva hade upplevt förbättring av träning. Att det gjorde ont att träna medförde att de kände sig osäkra på om träning kunde skada leden ytterligare och vissa av dem ville helst inte träna överhuvudtaget. Många ansåg att träning bör introduceras tidigt i sjukdomsförloppet och alla uttryckte att det krävs kontinuerligt stöd och uppmuntran för att fortsätta träna.

Baserat på resultaten av studierna drar jag följande slutsatser:

- Nedsatt muskelfunktion medför ökad ledbelastning och är en riskfaktor för att utveckla artros hos medelålders med knäsmärta.
- Träning kan förbättra lårmuskelfunktionen och tycks minska ledbelastningen i knäna och kan således kanske minska risken för såväl utveckling som progress av röntgenverifierad knäledsartros.
- Träning bör introduceras i ett så tidigt skede som möjligt innan smärtan har hunnit bli för svår, för att få bästa effekt på muskelfunktionen och minska oron hos patienterna.
- Träning kan i vissa fall minska smärtan och förbättra funktion även vid måttlig till svår artros, men hänsyn bör tas till individuella önskemål och kontinuerligt stöd och vägledning bör erbjudas under träningen.

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He wakes up the next morning and he has a fresh new world to work with, but he has something else too. He has his yesterday.

From “The five people you meet in heaven” by Mitch Albom