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Riikka Elina Juhakoski

Hip Osteoarthritis; Risk Factors and Effects of Exercise Therapy

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RIIKKA ELINA JUHAKOSKI

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ABSTRACT

The causes of hip osteoarthritis (OA) appear to be heterogeneous with genetic, environmental and lifestyle-related risk factors influencing the development of the disease. Hip OA causes pain and disability, reducing the quality of life, and there is no treatment to prevent or cure it after the onset of development. Therefore, the reduction of pain and improvement in physical function are important outcomes when evaluating the effective treatment strategy for hip OA.

The aim of the study was to identify independent risk factors for developing hip OA in a prospective population-based study with a follow-up period of up to 22 years. An assessment was made of the short-term and long-term effectiveness of exercise-based rehabilitation in reducing pain, maintaining physical function and limiting direct health care costs attributable to hip OA in a two-year randomized controlled trial. A further aim was to identify predictors of pain and disability in hip OA. Objective and subjective physical function were investigated with a battery of physical function tests and questionnaires, including Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and RAND 36-Item Health Survey (RAND-36).

Heavy manual work and musculoskeletal injuries were found to predict the development of hip OA in the 22-year follow-up study. Factors explaining and predicting disability and pain in hip OA are multidimensional and no single factor was found to be more important than any other. Higher educational levels, absence of knee OA and comorbidities, supervised exercise training and habitual physical activity predicted a lower prevalence of pain and a better functional status in patients with hip OA.

Exercise therapy for hip OA had no significant effect on self-reported pain or general physical health, but it slightly improved self-reported physical function in individuals with hip OA. Based on these findings, the clinical importance of exercise therapy remains uncertain and it is unclear whether exercise training translates into true improvement in physical performance or reduced health care costs.

National Library of Medicine Classification: WE 860, WL 704
Medical Subject Headings: Exercise Therapy/economics: Osteoarthritis, Hip; Pain/rehabilitation; Risk factors; Treatment Outcome

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Lonkkanivelrikon riskitekijät ja terapeuttisen harjoittelun vaikutukset lonkkanivelrikkopotilaan toimintakykyyn
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TIIVISTELMÄ

Lonkan nivelrikon syyt ovat moninaisia. Taudin syntyyn vaikuttavat geneettiset sekä ympäristöön ja elintapoihin liittyvät tekijät. Lonkan nivelrikko aiheuttaa kipua ja rajoittaa toimintakykyä eikä sen etenemistä kyetä estämään tai parantamaan enää taudin syntymisen jälkeen. Sen vuoksi, arvioitaessa hoidon vaikuttavuutta, lonkan nivelrikon hyvän hoidon tunnusmerkit tulisi olla elämänlaadun parantaminen lievittämällä kipua ja ylläpitämällä fyysistä toimintakykyä.

Tutkimuksen tavoitteena oli löytää lonkan nivelrikkoa ennustavia tekijöitä 22 vuotta kestäneellä väestötutkimuksella ja arvioida terapeuttisen harjoittelun vaikutuksia kipuun ja toimintakykyyn sekä lonkan nivelrikon aiheuttamiin välittömiin terveydenhuollon kustannuksiin satunnaistetulla kontrolloidulla tutkimuksella. Lisäksi pyrittiin löytämään menetelmiä, joilla kivun lisääntymistä ja toimintakyvyn heikkenemistä olisi mahdollista ennustaa taudin edetessä. Fyysistä toimintakykyä tutkittiin objektiivisin ja subjektiivisin menetelmin toimintakykytesteillä ja kyselyillä kuten Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) ja RAND 36-Item Health Survey (RAND-36) mittareilla.

Väestöpohjaisen 22-vuotisen seurantatutkimuksen perusteella lonkan nivelrikon kehittymistä ennustaviksi tekijöiksi osoittautuivat raskas työn fyysinen kuormitus sekä tuki- ja liikuntaelinten vammat. Lonkan nivelrikossa toimintakykyyn ja kipuun vaikuttavat monet tekijät, joista mikään ei näyttänyt olevan muita tärkeämpi nivelrikon oireiden etenemistä tai toimintakyvyn laskua ennustava tekijä. Korkeampi koulutustaso, polvinivelrikon ja muiden sairauksien puuttuminen, ohjattu terapeuttinen harjoittelu ja säännöllinen liikunta ennustivat vähäisempää kipua ja parempaa toimintakykyä.

Terapeuttinen harjoittelu ei merkittävästi vaikuttanut potilaiden lonkkanivelen kiputuntemuksiin tai fyysiseen terveydentilaan liittyvään elämänlaatuun, mutta potilaiden oman arvion mukaan se saattoi jonkin verran parantaa heidän fyysistä toimintakykyään. Näiden havaintojen perusteella terapeuttisen harjoittelun merkitys on epävarma ja on epäselvää, saadaanko siitä todennettavaa hyötyä tai säästöjä terveydenhoidon välittömissä kustannuksissa lonkkanivelrikkoa sairastavilla potilailla.

Yleinen Suomalainen asiasanasto: riskitekijät; harjoittelu; nivelrikko; lonkka, kipu; toimintakyky.

To my family

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Riikka Juhakoski

List of the original publications

This dissertation is based on the following original publications:

I Juhakoski R, Heliövaara M, Impivaara O, Kröger H, Knekt P, Lauren H, Arokoski JPA. Risk factors for the development of hip osteoarthritis: a population-based prospective study. *Rheumatology (Oxford) 2009; 48 (1): 83-87.*

II Juhakoski R, Tenhonen S, Anttonen T, Kauppinen T, Arokoski JP. Factors affecting self-reported pain and physical function in patients with hip osteoarthritis. *Arch Phys Med Rehabil 2008; 89 (6): 1066-73.*

III Juhakoski R, Tenhonen S, Malmivaara A, Kiviniemi V, Anttonen T, Arokoski JPA. A pragmatic randomized controlled study of the effectiveness and cost consequences of exercise therapy in hip osteoarthritis. *Clin Rehabil 2011; 25 (4): 370-83.*

IV Juhakoski R, Malmivaara A, Lakka TA, Tenhonen S, Hannila M-L, Arokoski JPA. Determinants of pain and functioning in hip osteoarthritis - a two-year prospective study. *Clin Rehabil 2013; 27 (3): 281-7.*

Contents

Abbreviations

ACR	American College of Rheumatology
ANCOVA	Analysis of covariance
BDI	Beck depression inventory
BMI	Body mass index
CI	Confidence interval
GP	General practitioner
HRQOL	Health related quality of life
K-L	Kellgren-Lawrence osteoarthritis grading scale
LS	Life satisfaction scale
MRI	Magnetic resonance imaging
6-MWT	6-minute walk test
10-MWT	10-meter walk test
NSAID	Non-steroidal anti-inflammatory drug
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society International
OR	Odds ratio
RAND-36	RAND 36-Item Health Survey
ROM	Range of motion
SD	Standard deviation
SF-36	The 36-item Short-Form Health Survey
THA	Total hip arthroplasty
TUG	Timed Up & Go test
VAS	Visual analogue scale
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

1 Introduction

Osteoarthritis (OA) is the most common form of joint disease worldwide, with an age-associated increase in both incidence and prevalence (Oliveria et al. 1995). It is therefore one of the most common causes of physical disability in the elderly population (Dawson et al. 2004). OA is characterised by degeneration of articular cartilage, joint space narrowing, pain and disability (O'Reilly and Doherty 2003). It has been estimated that hip OA affects approximately 7%-25% of individuals in the over 55 year group and is more common among males than females (Felson et al. 2000). The social and economic impact of OA is substantial and consequently affects the quality of life at the individual level (Reginster 2002). In 2003 the annual cost of hip joint replacement operations in Finland totaled nearly 70 million € without taking into account post-surgery rehabilitation (Remes et al. 2007). Today in Finland 6% of all disability pension payouts can be attributed to OA. In addition it is estimated that the direct and indirect costs of OA in Finland are nearly 1 billion € per year (Heliövaara and Paavolainen 2008). The number of people with OA disability is expected to double by the year 2020 (Bradley 1991, Elders 2000), thereby further increasing the already substantial economic impact of OA.

It is important to understand potential determinants and modifiable risk factors of hip OA in order to develop efficient prevention strategies for hip OA or the treatment of its consequences both at the individual and population levels. The causes of hip OA appear to be heterogeneous with genetic, environmental and lifestyle-related risk factors influencing the development of the disease (Felson 1998). Ageing is the most consistent risk factor for the development of hip OA in both males and females (Heliövaara et al. 1993b, Tepper and Hochberg 1993, Karlson et al. 2003). Twin studies have found a strong genetic link to hip OA (Lanyon et al. 2000, MacGregor et al. 2000). An individual may have an inherited predisposition to the disease, without any symptoms of OA (Spector and MacGregor 2004) but is only likely to develop it when a biomechanical insult e.g. joint injury occurs (Felson et al. 2000, Lievense et al. 2003). OA can either be a consequence of an abnormal mechanical load on a healthy joint or of a normal mechanical pressure on unhealthy cartilage tissue (Nuki and Salter 2007). Moderate evidence exists for the association of hip OA with obesity (Lievense et al. 2002) or sporting activities (Lievense et al. 2003) or a history of physical load work (Lievense et al. 2001, Jensen 2008) or physical load leisure activities (Vingård et al. 1997). Several studies also advocate that injury is a major risk factor (Heliövaara et al. 1993b, Tepper and Hochberg 1993, Cooper et al. 1998, Lau et al. 2000). However, most of these studies regarding the potential risk factors of hip OA have been cross-sectional (Tepper and Hochberg 1993, Lau et al. 2000) or at their best prospective, with a short follow-up period (Teperi et al 1993, Cooper et al. 1998, Lau et al. 2000).

The natural history of OA is poorly understood and there is no preventive treatment or cure after the onset of development (Brandt et al. 2006). Therefore focus on the consequences of hip OA such as reduction of pain and improvement in physical function and quality of life are important in the evaluation the most effective treatment strategy. According to evidence-based recommendations for the management of OA, exercise is a commonly included as an effective treatment for patients with lower limb OA (Arokoski et al. 2012, Hochberg et al. 2012, Zhang et al. 2008, Zhang et al. 2010). The American College of Rheumatology (ACR) subcommittee on OA guidelines, the Osteoarthritis Research Society International (OARSI) Group and the Consensus of a Multidisciplinary Guideline Development Group (MOVE Consensus) have all concluded that strength training and aerobic exercise can both reduce pain and improve function and health status in patients with hip OA (Hochberg et al. 2012, Zhang et al. 2008, Zhang et al. 2010, Roddy et al. 2005).

However, these recommendations are based on a very low level of scientific evidence and many unanswered questions remain concerning the long-term benefits of treatment, adherence to the exercise programme as well as the overall cost-effectiveness of this approach.

The aim of this doctoral thesis was to identify potential risk factors for hip OA and to evaluate their roles in its etiology in a population-based 22-year follow-up study. Another purpose of the thesis was to assess the short-term and long-term effectiveness of exercise-based rehabilitation in reducing pain, maintaining physical function and limiting direct costs to health care systems attributable to hip OA during a two year randomized controlled trial.

2 Review of the literature

2.1. PATHOGENESIS OF HIP OSTEOARTHRITIS

The hip joint is a synovial joint formed by the articulation of the rounded head of the femur and the cup-like acetabulum of the pelvis. The hip joint is reinforced by five ligaments, of which four are extracapsular and one is intracapsular. The strong but loose fibrosus capsule of the hip joint permits the hip joint to have a large range of motion (ROM) and jet support the weight of the body, arms and head. Both joint surfaces are covered with a strong but lubricated layer called articular hyalinen cartilage. The cartilage is composed of four distinct zones, characterised by chondrocytes and collagen fibers. Chondocytes are responsible for synthesising the cartilage extracellular matrix. The extracellular matrix is composed of collagen (10 to 20%), proteoglycans (10 to 20%) and water (65 to 80%). The viscoelastic behavior of cartilage is dependent on the water binding properties of the matrix protein-polysaccarides (Sharma and Berenbaum 2007).

OA is a condition that represents a pathological imbalance of degenerative and regenerative processes of joint structures. Any consideration of a pathologic process of osteoarthritis begins with articular cartilage, but ultimately the disease affects the whole joint, including cartilage, subchondral bone, synovium and periarticular soft tissues (Brandt et al. 2006, Goldring and Goldring 2007) (Figure 1).

Biochemically OA can be seen as a process where the deterioration of the extracellular matrix starts to predominate over cartilage repair activities (Goldring and Goldring 2007). In early stages of OA both the degenerative and regenerative enzymes of cartilage and associated genes are activated in the chondrocytes. Later on the proteolytic breakdown predominates, when proteolytic enzymes such as proteoglycans, collagens and metalloproteinases (e.g. stromelysin and collagenase) increase and participate in the degradation of them (Lammi et al. 2008). The metalloproteinases are activated by inflammatory cytokines, such as interleukin-1 and tumor necrosis factor-α, nitric oxide and synovial inflammatory transmitters. Adipokine hormones e.g. leptin and adiponectin have been identified as a regulatory factors in inflammation and arthritis (Neumann et al. 2011, Comez et al. 2011). Leptin and adiponectin are found to be synthesized by white adipose tissue. Recent studies show that leptin and adiponectin are possible links between obesity and OA, since these are increased when obesity occurs and these hormones induce the production of matrix matalloproteinases, proinflammatory cytokines and nitric oxide in chondrocytes (Vuolteenaho et al. 2009, Koskinen et al. 2011,). Structurally the decrease of the proteoglycan concentration in cartilage, collagen network disorganisation and softening are signs of cartilage injury and OA (Buckwalter 1995, Arokoski et al. 2000).

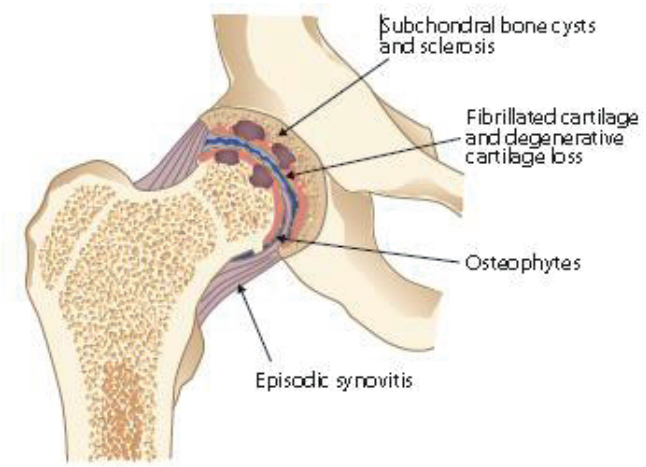


*Figure 1.*The pathophysiological findings involved in hip OA.

OA can either be a consequence of an abnormal mechanical load on a healthy joint or of a normal mechanical pressure on unhealthy cartilage tissue (Nuki and Salter 2007). The highly specific microscopic anatomy and physiology of articular cartilage can be disrupted by small, superficial injuries, even without immediate cartilage loss. Superficial damage will injure chondrocytes, limit their metabolic capacity for repair and lead to decreased proteoglycan concentration, increased hydration and altered fibrillar organisation of collagen. This leads to biochemical consequences which eventually manifests themselves as OA; joint structural changes and pain (Nuki and Salter 2007, Goldring and Goldring 2007).

Structural, biochemical and biomechanical changes in the subchondral bone are a major characteristic of OA (Arokoski et al. 2000). Structural alterations manisfest themselves as osteophyte formation and subchondral sclerosis, which are important in radiological diagnosis. Subchondral bone changes not only occur during the final stage of OA but also at the onset of the disease; possibly even prior to cartilage degradation becoming evident. This early phase bone loss due to extensive remodeling may precede later observed sclerosis. A biochemical and biomechanical mutual interaction between subchondral bone and the overlaying cartilage is nowadays considered attributable to the progressive character of OA (Radin and Rose 1986). On the other hand, osteophytes that are considered to develop early in the disease and are included in the first measurement of Kellgren-Lawrence (K-L) OA grading system may also develop later in the joint degenerative process.

OA is not considered a classic inflammatory arthropathy due to the lack of systemic manifestations of inflammation. However, OA is frequently associated with signs and symptoms of inflammation including joint pain, swelling and stiffness leading to a significant functional impairment and disability (Felson 2006). Synovial inflammation is a factor that is likely to contribute to deregulation of chondrocyte function, leading to an imbalance between the catabolic and anabolic activities of the chondrocyte in remodeling the cartilage extracellular matrix (Loeser et al. 2012).

Hip OA can also lead to changes in periarticular muscles (Liikavainio and Arokoski 2009). The cross sectional area of the pelvic or thigh muscles is significantly lower in the more severely affected hip compared to the hip on the better or healthy side of subjects with hip OA (Arokoski et al. 2002, Rasch et al. 2007, Grimaldi et al. 2009). In hip OA there is a selective atrophy of type II muscle fibers in comparison to healthy subjects (Amaro et al. 2007). Several mechanisms have been proposed as being involved in muscle weakness in OA: firstly the disuse atrophy of muscles due to joint pain; secondly reflex inhibition of

muscles moving the affected joint; thirdly incapacity to fully activate the muscle resulting in decreased force production (Hurley 1999, Mizner et al. 2005).

Despite numerous identified predisposing factors and the involvement of mechanics, the exact pathogenesis is still the subject of debate and research. Specifically, the very early changes are largely unknown because they cannot be studied easily in humans. This is attributable to the changes appearing well in advance of OA diagnosis in clinical practice.

2.2 EPIDEMIOLOGY AND RISK FACTORS OF HIP OSTEOARTHRITIS

2.2.1 Prevalence of hip osteoarthritis

Although OA may affect any joint in the body, it most commonly affects the knee followed closely by the hip (Felson 1990). Radiographic primary hip OA is in approximately 5% to 10% of the adult population (Dagenais et al. 2009). However, due to heterogeneous radiographic methods of diagnosis and divergent criteria, the overall estimates of radiographic primary hip OA vary from 0.9% to 27.0% in different populations (Dagenais et al. 2009).

The prevalence of radiographic hip OA has been best studied in population surveys. The Framingham Study advocates that radiographic hip OA occurs in 3-4 per cent of individuals aged 63 and over (Felson 1988). Symptomatic OA is generally defined as frequent joint pain and structural alterations in radiography. A recently published population based survey, assessing the prevalence of symptomatic and radiographic hip OA in a multiregional sample in France, estimated that hip OA prevalence according to age class ranged from 0.9% to 3.9% for men and 0.7% to 5.1% for women (Guillemin et al. 2011).

According to the Finnish Health 2000 Survey, the age-adjusted prevalence of clinically diagnosed hip OA was 5.7% in males and 4.6% in females (Arokoski et al. 2007). The prevalence was consistently higher in males except in the 75 to 84 year age group where it was the same for both sexes. In men the prevalence of hip OA ranged from 0.5% in the youngest age group to 39.8% in the oldest (those aged 85 years or more) and in women from 0.4% in the youngest to 24.5% in oldest. The age-adjusted prevalence of hip OA showed negative correlation with years of education in both genders. Among the Finnish population the prevalence of hip OA has not been changed during 20 years (Heliövaara et al. 1993a, Arokoski et al. 2007), whereas the prevalence has decreased in middle-age groups (from 45 to 64 years) and increased in the oldest (those aged 85 years or more).

2.2.2 Risk factors

Although the pathogenesis of hip OA remains partly unknown, there are several risk factors that may predispose to OA (Felson 1998). Hip OA is considered a multifactorial disease that involves interplay of several risk factors e.g. age, gender, genetics, dysplasia, mechanical work load, obesity, joint injury or sporting activities. Epidemiological studies indicate that OA of the hip frequently occurs in the absence of OA in other large joints. This suggests that local biomechanical factors are important in its pathogenesis (Cushnaghan and Dieppe 1991, Ecker et al. 2007, Wright et al. 2009). The details of the results from previous epidemiological studies concerning the risk factors for hip OA are presented in Table 1. The most consistent risk factors are considered to be age, genetics, congenital disorders of the hip joint, overweight or obesity, occupational and sporting related overload of the hip joint and joint injuries.

2.2.2.1 Age

The prevalence of hip OA correlates strongly with age and it starts to increase in middle age in both genders (Heliövaara et al. 1993b, Arokoski et al. 2007, Dagenais et al. 2009, Guillemin et al. 2011). Geographic or ethnic differences in prevalence estimates have also

been reported (Yoshimura et al. 1998, Inoue et al. 2000, Nevitt et al. 2002) but discrepant estimates of prevalence mainly result from variable definitions of hip OA.

According to the Finnish Health 2000 Survey, the prevalence of radiographic and clinical hip OA increases with age in both males and females (Arokoski et al. 2007). A clear trend towards increasing prevalence of radiographic hip OA with advancing age from 35 to 85 years was also confirmed in a recent systematic review (Dagenais et al. 2009). The mean increase in the prevalence of radiographic hip OA was 1.2% for each 5-year age group from 35 to 85 years.

2.2.2.2 Gender and hormonal factors

The prevalence of hip OA in females increases after menopause (van Saase et al. 1989, Felson et al. 2000, Guillemin et al. 2011). This observation has contributed to the theory that decreased oestrogen levels play a role in OA pathogenesis (Felson 1988). Some cross-sectional studies have found that oestrogen replacement therapy is associated with lower rates of hip or knee OA (Nevitt et al. 1996, Spector et al. 1997). However, the inverse relationship between oestrogen use and OA has been inconsistent in epidemiological studies (Nevitt et al. 1996, Spector et al. 1997, Sandmark et al. 1999, Jacobsen et al. 2004). Data from the First National Health and Nutrition Survey (NHANES I) in the United States suggest that etiological factors associated with hip OA may differ between males and females and differ between unilateral and bilateral hip OA (Tepper and Hochberg 1993). A recent population-based survey in France confirmed that the prevalence of symptomatic hip OA increases with age in both genders (Guillemin et al. 2011). The age-related prevalence of symptomatic hip OA of radiographic K-L grade ≥ 2 ranged from 0.9% to 3.9% in men and from 0.7% to 5.1% in women.

2.2.2.3 Genetic factors and race

Genetic factors appear to influence the risk of developing primary hip OA. Twin studies have shown a strong contribution of genetic factors in the development of hip OA (Lanyon et al. 2000, MacGregor et al. 2000). Similar to many common complex diseases and disorders, the genetic background of OA has not yet been characterised. The manner in which genes specifically influence the incidence and progression of OA and associated disability is difficult to ascertain from the available data. The genetic background of OA is likely to be polygenic with multiple gene variants each of them having a small effect (Valdes et al. 2011). Different genetic associations are seen in European descent compared with Asian populations. In European descendants three genetic variants have been associated with genome wide significance in large joint OA (Valdes et al. 2008). The variants implicated in OA among Caucasians map to the GDF5 gene and the MCF2L gene. GDF5 is a chondroprotective growth factor and MCF2L is associated with neurotrophin regulated cell motility of neurons and thus potentially affecting nociception (Kerkhof et al. 2010). More specific outcome measures of OA are required to assist with a better understanding of the effects of genetic factors on different stages of joint degradation.

OA varies across racial groups, including differences in prevalence and radiographic features and differences in pain and function (Allen et al. 2010). Regarding the prevalence of OA, prior studies indicate hip and OA is less common among Chinese individuals compared with U.S. Caucasians (Newitt et al. 2002) and that self-reported OA may be less common among Hispanics than Caucasians in the United States (Allen 2010).

2.2.2.4 Congenital disorders

Childhood disorders of the hip joint, such as congenital hip dysplasia, Legg-Calve-Perthes disease or slipped capital femoral epiphyses, are modifiable risk factors, if identified early (Harris 1986, Lane et al. 2000). In adults evidence of hip dysplasia in X-rays is strongly associated with prevalent hip OA (Jacobsen 2004). In the Rotterdam Study (Rejma et al. 2005)

examined males and females of at least 55 years of age with no signs of radiographic OA of the hip at baseline. This study found that acetabular dysplasia was a strong independent determinant of incident radiographic OA of the hip amongst the elderly population. There is also evidence that mild acetabular dysplasia (McWilliams et al. 2010) and femoroacetabular impingement as a consequence of abnormal contact between the acetabular rim and femoral head-neck junction, resulting in damage to the chondral surface and labrum, can lead to the development of OA of the hip (Beck et al. 2005, Ganz et al. 2008).

2.2.2.5 Overweight and obesity

Excessive weight or body mass index (BMI) strongly increases the risk of developing symptomatic and radiographic knee OA (Spector et al. 1994, Cooper et al. 2000). Being overweight adds higher loads on weight-bearing joints and could thereby contribute to the development of hip OA. However, the relation of excessive weight or obesity with hip OA is not as well defined as the association of them with knee OA. Several cross-sectional (Olsen et al. 1994, Flugsrud et al. 2006, Franklin 2009) and cohort studies (Tepper and Hochberg 1993, Flugsrud et al. 2002, Karlson et al. 2003, Järvholm et al. 2005, Liu et al. 2007) have indicated an increased risk of hip OA linked to obesity. A number of others have failed to support the association (Saville and Dickson 1968, Lau et al. 2000). A recent meta-analysis (Jiang et al. 2011) displayed that the risk of hip OA increases with BMI and a dose-response relationship exists. A 5-unit increase in BMI was associated with an 11% increased risk of hip OA. It has been suggested that obesity not only increases the risk of radiographic hip OA but also symptomatic hip OA. In the population-based Mini-Finland Health Survey, BMI was directly proportional to the prevalence of bilateral hip OA. The survey showed that individuals with a BMI > 35 had a 2.8 times higher risk of having bilateral hip OA than those with a BMI < 25, while the association of BMI with the prevalence of unilateral hip OA was much weaker (Heliövaara et al. 1993b).

A population-based prospective cohort study assessed incidences of knee and hip joint replacements due to OA in relation to different body mass measures including body weight, BMI, waist circumference and percentage of body fat (Locmander et al. 2008). BMI was associated with a much higher relative risk than waist circumference or percentage fat. This suggests that being overweight is a particularly important risk factor for developing knee and hip OA. BMI, adipose tissue mass and central adiposity (waist circumference and waist to hip ratio) were directly related to the risk of primary knee and hip joint replacements for OA, whereas waist circumference was directly associated only with the risk of knee replacement (Wang et al. 2009).

2.2.2.6 Occupation

The association between heavy manual work and an increased risk of radiographic hip OA has been demonstrated in several cross-sectional studies amongst males (Tyyppö 1985, Jacobsson et al. 1987, Croft et al. 1992, Olsen et al. 1994, Coggon et al. 1998, Cvijetic et al. 1999, Lau et al. 2000) and females (Vingård et al. 1997, Tyyppö 1985) as well as in prospective studies among males (Vingård 1991, Thelin and Holmberg 2007) and in both sexes (Flugsrud et al. 2002). A number of occupations, such as construction work, coal mining, fire fighting, abattoir work, ballet dancing and farming have been associated with an elevated risk (Andersson 1984, Andersson et al. 1989, Vingård 1991, Croft et al. 1992). Additionally the association of recurrent exposure to manual load handling with radiographic and clinical hip OA was assessed in a Finnish population based cross-sectional study in the Health 2000 Survey (Kaila-Kangas et al. 2011). The research group concluded that employment history involving the manual handling of loads of over 20kg was strongly associated with hip OA in both genders aged 30 to 97. The problem became apparent after approximately 12 years exposure in all age groups except the youngest (from 30 to 39 years). Researchers suggest that one explanation for the result might be that hip OA takes a long

time to develop and that young people do not generally choose to work in physically demanding occupations. Moreover, the study indicated that hip OA is much more common among working-aged males than females. A recently published systematic review also summarised that individuals who had been involved in occupational heavy lifting had a significantly increased risk of hip OA in 12 of 14 studies with different study designs. As many as 13 of the 14 studies displayed a significantly increased risk of hip OA among farmers (Jensen 2008). When completely removing substantial physical labour is an unrealistic goal, minor alterations in ergonomics, training in correct lifting techniques and the use of mechanical handling equipment may reduce occupation related OA risk.

2.2.2.7 Sporting activities

Most studies support the view that regular physical activity does not increase the risk of development or progression of hip OA (Lane et al. 1998). However, elite athletes have been shown to have a 2 to 3 fold higher risk of radiologic OA of the knees and hips (Tveit et al. 2012). This suggests that the duration rather than frequency of training is important (Spector et al. 1996). The results of other studies evaluating the risk of OA among professional athletes indicates that male athletes have higher rates of hospital admission for ankle, knee or hip OA than matched healthy male controls and OA changes commonly manifests itself in athletes over 65 years of age (Kujala et al. 1994).

A recent prospective cohort study concluded that long-distance skiers have a higher risk of subsequent arthroplasty of the knee and hip due to OA than individually matched controls, who were not participating in long-distance ski races during the study period of 10 year (Michaelsson et al. 2011). Moreover, one systematic review concluded that there is moderate evidence for a direct association between sporting activity and hip OA (Lievense et al. 2003), but that the evidence tends to weaken due to the heterogeneity of the study populations and outcome measures. Impact of physical activity on the etiology and prognosis of OA also seems to depend on the type, intensity and components of physical activity (Michaelsson et al. 2011).

2.2.2.8 Joint injury

Joint injuries in sports significantly increase the risk of knee OA (Felson 1990, Roos 2005). A similar trend for hip injuries leading to radiographic hip OA has also been reported in cross-sectional studies (Cooper et al. 1998, Lau et al. 2000). There is only one cohort study showing the direct association between hip traumas and an increased risk of radiographic hip OA (Tepper and Hochberg 1993). In a retrospective analysis of the Mini-Finland Health Survey individuals with a history of traumatic lower-limb injury had a 2.1-fold risk of having unilateral hip OA, diagnosed either clinically or radiographically, and a 1.5-fold risk of having bilateral hip OA (Heliövaara et al. 1993b).

Table 1. Studies on risk factors of hip OA.

Research group, publication year	Subjects	Age	Diagnostics	Risk factors statistically significantly associated with hip OA	Possible risk factors not associated with hip OA
Cross-sectional studies					
Coggon and coworkers 1998	611 subjects (66% women) listed for THA and individually matched controls	45-91 years, mean 70 years	Radiographic (Listed for THA)	Work load (for men) Lifting over 50kg loads over 10 years or longer	Work load (women) Occupational activities other than lifting
Cooper and coworkers 1998	611 subjects (66% women) listed for THA and individually matched controls	45-91 years, mean 70 years	Radiographic (Listed for THA)	Previous hip injury	Heberden's nodes BMI
Croft and coworkers 1992	167 male farmers and 83 controls (office workers)	60-76 years	Radiographic	Work load Farming	No
Cvijetic and coworkers 1999	593 subjects (50% women)	over 45 years, mean 63 years	Radiographic and clinical	Work load 80 % of the time in the standing position (women) Jobs with high physical strain (men)	No
Flugsrud and coworkers 2006	1 200 000 men and women and 1 152 006 individually matched controls attended a screening for tuberculosis	18-67 years	THA	BMI	No
Franklin and coworkers 2009	1 473 subjects (59% women) THA = 927 TKA = 431 THA + TKA = 115	64-93 years, mean 74 years	THA or TKA	BMI (TKA for men and women) BMI (THA for men)	BMI (THA for women)
Heliövaara and coworkers 1993	7 217 men or women	30 years or over	Radiographic and clinical	BMI Work-load	No
Jacobsen and coworkers 2005	3568 subjects (63% women)	20-91 years, mean 61 years	Radiographic	Age Hip dysplasia	BMI Smoking
Jacobsson and coworkers 1987	85 men listed for THA and 267 individually matched controls	mean 73 years	Radiographic (Listed for THA)	Work load Farming Heavy labor Heavy lifting	Injury
Kaila-Kangas and coworkers 2011	6 556 subjects (53% women)	mean 52 years	Clinical	Work load Manual handling of loads over 20 kg	No

Lau and coworkers 2000	796 subjects (75% women) hip (138) and knee (658) OA and 796 individually matched controls	Not informed	Radiographic	Injury Lifting heavy weight Climbing stairs frequently BMI (highest quartile)	Smoking Sport activities
Olsen and coworkers 1994	239 men with THA and 302 individually matched controls	50-70 years	THA	Work load Sport activities Overweight	No
Roach and coworkers 1994	99 men and 233 individually matched	mean 68 years	Radiographic	Work load	No
Tyyppö and coworkers 1985	919 subjects (55% women)	16-86 years, mean 57 years	Radiographic	Work load	Work load
Vingård and coworkers 1997	230 women with THA	50-70 years	THA	Work load	No
Yoshimura and coworkers 2000	114 subjects (90% women) listed for THA	45 years or over, mean 64 years	Radiographic (Listed for THA)	Lifting heavy loads	Obesity
Cohort retrospective studies					
Flugsrud and coworkers 2002	50 034 subjects (50% women) follow-up 9 years	46-67 years, mean 55 years	THA	Work load BMI	Leisure time physical activity
Gelber and coworkers 1999	1180 men median follow-up 36 years hip and knee OA	20-49 years	Radiographic	No	BMI
Spector and coworkers 1996	81 women (ex-elite athletes) hip and knee OA and 977 individually matched controls	40-65 years	Radiographic	Weight-bearing sport activities	No
Vingård and coworkers 1991	250 217 men (83%) Hip or knee OA	Not informed	Hospital care for OA of hip or knee	Heavy physical work load	No
Cohort prospective studies					
Järvholm and coworkers 2005	320 192 men Follow-up 11 years	15-67 years	THA or TKA	BMI Age	No
Karlson and coworkers 2003	121 701 women Follow-up 6 years	30-55 years	THA	Age BMI	Alcohol intake Smoking Leisure time physical activity Postmenopausal hormone use Oral contraceptive use

Lane and coworkers 2000	9 704 women	65 years and over	Radiographic	Dysplasia	No
Liu and coworkers 2007	490 532 women Hip or knee OA Follow-up 2,9 years	50-69 years	THA or TKA	BMI	No
Lohmander and coworkers 2009	27 960 men or women Hip or knee OA Follow-up 11 years	45-73 years, mean 58	THA or TKA	BMI, waist circumference, waist-hip ratio, weight, percentage of body fat	No
Michaelsson and coworkers 2011	53 983 subjects (10% women)	15 years and over, mean 39	THA or TKA	Intensive exercise at a level required to complete multiple and fast long-distance skiing races)	No
Thelin and coworkers 2007	1 220 men (farmers) controls (1) 1130 rural non-farming men controls (2) 1087 urban men	Not informed	Radiographic THA	Occupation Farming	No
Teperi and coworkers 1993	2 358 men and women	55 years and over	Radiographic	Hip trauma Obesity Age	Sex Marital status Race Family income Education
Wang and coworkers 2009	39 023 men or women	27-75 years	THA or TKA	Weight, BMI, fat mass, percentage body fat , waist circumference	WHR

Total hip arthroplasty (THA), Total knee arthroplasty (TKA), Osteoarthritis (OA), Body mass index (BMI), Fat mass (FM).

2.3 SYMPTOMS AND SIGNS OF HIP OSTEOARTHRITIS

2.3.1 Symptoms

The main symptoms of hip OA are pain, stiffness and altered function (van Baar et al. 1998). Pain is the most dominant symptom in hip OA. Initially symptoms are typically aching in nature, related to joint use, and relieved by rest. As OA progresses, pain may become more persistent and occur at rest and at night. Interference with restorative sleep may further aggravate the pain severity trough associated fatigue and lack of well-being. Typically the gradual progression of pain is observed. Several studies have confirmed that the association between radiologic OA and clinical symptoms is contradictory (Arokoski et al. 2004, Summers et al. 1988, Barker et al. 2004, Hall et al. 2006, Szebenyj et al. 2006). Pain, caused by hip OA, correlates strongly with psychological variables such as anxiety and depression (Davis et al. 1992, O'Reilly et al. 1998).

True hip pain is most commonly felt in the groin but can also present in the buttock and often down the anteromedial tight to the knee (Lesher et al. 2008). Nearly half of patients with radiological features of OA have no symptoms and vice versa (Hannan et al. 2000). Since articular cartilage is aneural, early changes do not produce clinical signs unless innervated tissue becomes involved. This is one reason for the late diagnosis of OA.

In comparison with other joints, such as the knee, pain from the hip is difficult to define, for three possible reasons (Birrell et al. 2005): first, the joint is not superficial, so pain arising from structures in and around of the hip joint can be felt across a broader region; second, pain from structures outside the hip, for example the low back, the groin and the urinary and the genital tracks, may also be associated with pain in the hip region; third, it is unclear whether there is a specific topographical area that can usually be distinguished as 'the hip'. In contrast to inflammatory arthritis, with its prolonged morning stiffness and worsened pain in the morning, hip OA pain and stiffness tends to worsen as the day progresses.

The mechanism of pain production in OA remains unclear (Felson 2005, Hochman et al. 2011, Mease et al. 2011). However, the OA process may affect all intracapsular and periarticular tissues of the synovial joint leading to various causes of pain. Pain during the weight bearing is typically felt maximally deep in the anterior groin (femoral nerve), but may be referred over a wide area including the lateral thigh and buttock (sciatic nerve), anterior tight and knee (obturator nerve) and as far down the leg as ankle (O'Reilly and Doherty 2003). Articular cartilage itself is aneural but there is rich sensory innervation in other joint tissues. Raised intraosseus pressure, presumably secondary to venous obstruction, is a suggested major cause of nocturnal pain in large OA joints (Arnoldi et al. 1975). Peripheral and central sensitisations have been suggested as two of the underlying mechanisms of pain in OA (Felson 2005, Arendt-Nielsen et al. 2010). Continuous and intense nociceptive input from the OA-damaged knee joint is assumed to play an important role in pain mechanisms in OA (Felson 2005). Pain in hip OA seems to deteriorate slowly, with limited evidence of worsening after three years of follow-up (van Dijk et al. 2006).

Patients report symptoms that limit their day-to-day activities, such as stair climbing, walking and doing household chores (van Baar et al. 1998). The explanation for disability, functional loss and muscle weakness is not always clear. The symptoms of hip OA diminish the patient's physical activity (Dekker et al. 2009, Veenhof et al. 2012) and quality of life (O'Reilly and Doherty 2003).

The stiffness in hip OA is termed "inactivity stiffness" and contrasts with the prolonged "morning stiffness" of rheumatoid arthritis. Stiffness in hip OA lasts less than 30 minutes and occurs when the patient gets up and bears weight after a prolonged period of immobility (Hooper and Moscowitz 2007).

Among self-reported measurement tools, assessing the level of symptoms caused by hip OA, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (Bellamy et al. 1988) and Lequesne (Lequesne 1991) questionnaires are the most used.

WOMAC is a well-studied instrument with long established reliability and validity, including the use of the subscales separately. It consists of three subscales; pain, stiffness and function. The visual analogue scale (VAS) version allows the patients to estimate the symptoms by marking an X on a 100 mm long line (the beginning of the line = no symptoms, the end of the line = worst possible symptoms). The Lequesne Index is a 10-question survey with 5 questions pertaining to pain or discomfort; one question dealing with maximum distance walked and 4 questions about activities of daily living. The total questionnaire is scored on a 0 to 24 scale. Lower scores indicate that there is less functional impairment.

2.3.2 Clinical findings

The visual observation of gait while the subject walks on a level surface shows an apparent decreased weight bearing on the involved leg, which may already be a signal of hip OA (Hasan and Schuscelt 2010). A patient will often walk with a limp and wadding Trendelenburg gait (a pelvis drop on either side during the stance phase of gait due to muscle weakness of the abductors of the hip) may be evident during the later stages. Additionally anterior groin palpation tenderness, lateral to the femoral pulsation, is possible.

Although hip pain is common in the community, population studies have shown that it has only a weak relationship with hip OA (Lawrence et al. 1989). Restriction of the ROM has been proposed as a useful diagnostic tool (Cibulka and Threlkeld 2004) and hip joint ROM has shown to be a sensitive marker of the radiographic severity of OA (Birrell et al. 2001). The hips of the OA subjects have shown a 13% - 52% restriction of ROM compared to those of healthy subjects (Arokoski et al. 2004). The largest relative differences are in this order: extension; internal rotation; abduction; external rotation; adduction and flexion (Arokoski et al. 2004). Typically this is accompanied by pain with internal rotation of the hip joint. A fixed flexion, external rotation deformity is the most usual end-stage symptom, with compensatory exaggerated lumbar lordosis and pelvic tilt (O´Reilly and Doherty 2003).

Adequate muscle strength seems to be an important factor in maintaining the ability to perform daily living activities in hip and knee OA (Liikavainio and Arokoski 2009). Patients with hip OA have reported a reduction in isometric and isokinetic muscle strength of pelvic and thigh muscles. This manifests itself in significantly lower abduction, adduction, and flexion muscle strength (pelvic and thigh muscles) in comparison with the healthy age matched controls (Arokoski et al. 2002). In this case muscle strength of the OA subjects was 68-87% of that in the controls. Rasch et al. (2007) showed in their studies, that a substantial loss of strength and mass in the affected limb exists compared to the contra lateral (healthy) side in patients with unilateral hip OA. This finding contributed to the reduced ambulatory capacity of OA patients (Rash et al. 2007). Concurrently, Sueta et al. (2007) demonstrated a marked side to side difference with decreased muscle mass, maximal muscle strength, neuromuscular activation and rapid muscle force characteristics on the arthritic side compared to the healthy side in hip OA.

2.3.3 Radiological findings

In clinical practice, frontal, anteroposterior radiograph of the pelvis demonstrates the degree of hip joint OA. Other hip radiograph protocols include the anterior-posterior radiograph centered on one hip and the hip profile of Lauenstein (Adam et al. 2008).

The cardinal radiographic features of OA include the formation of osteophytes on the joint margins or in ligamentous attachments, the narrowing of the joint space associated with sclerosis and cysts of subchondral bone and the altered shape of the head of the femur (Goker et al. 2000, Lequesne et al. 2004). The identification of OA on plain x-rays means that

there is already full thickness cartilage loss and even bone-on-bone contact. These radiographic findings occur relatively late in the course of OA.

There are several classification systems for assessing the severity of hip OA (Rejman et al. 2004). Classically the radiological classification criteria of hip OA in epidemiological studies have relied on the characteristic radiographic changes described by Kellgren and Lawrence in 1958. Based on the results of more recent studies, K-L grade appears to remain a useful OA definition (Kellgren and Lawrence 1957, Reijman et al. 2004). Radiographic K-L grading of the severity of hip OA is based mainly on narrowing of the joint space and bone changes as follows: grade 0 as normal; 1 as possible narrowing of joint space and possible osteophytes; 2 as definite narrowing of joint space and definite osteophytes; 3 as marked narrowing of joint space, definite osteophytes and some deformity of femoral head and 4 as gross loss of joint space, large osteophytes and marked deformity of femoral head.

New physical methods for early diagnosis of OA are under intensive development (Vasara et al. 2005, Hannila et al. 2007, Jurvelin et al. 2008). Magnetic Resonance Imaging (MRI) has emerged as an excellent modality for detection of OA when the plain radiographs indicate no disease or mild disease and the patient's symptoms are out of keeping with the apparent severity of disease (Hall and Tyler 1995). MRI can detect large focal articular cartilage lesions that cannot be detected on plain film (Boegard et al. 1998, Cibere 2006). Articular cartilage lesions of the hip are not accurately diagnosed by standard MRI alone differing from the lesions of the knee. Part of the reason is that the cartilaginous surfaces of the femoral head and acetabulum are not well differentiated. Moreover, the articular cartilage thickness is extremely thin, measuring only 1 to 2 mm in diameter compared to 7 mm in the retropatellar cartilage (Watanabe et al. 2002). However, MRI can be a more accurate diagnostic tool in cartilage pathology as an alternative to arthroscopy. Schmidt et al. (2003) were able to detect chondral abnormalities with fairly accurate sensitivity and specificity. Traction on the hip during MRI could also improve cartilage visualisation (Nakanishi et al. 1999). Special techniques such as a water-excitation 3D double-echo steady-state sequence have also been shown to provide increased conspicuity of cartilage lesions (Knuesel et al. 2004). However, this technique is not routinely used in clinics.

2.3.4 Criteria for diagnosis

The diagnosis of hip OA can be radiographic, clinical or based on a combination of these two (Arokoski et al. 2012). The American College of Rheumatology (ACR), when diagnosing hip OA has preferred the combined radiographic and clinical criteria for use (Arokoski et al. 2012, Altman et al. 1991). According to the ACR the clinical criteria for hip OA consists of pain in the hip joint region within the previous month and radiographic joint changes evident in radiographs (Altman et al. 1991) (Table 2).

Table 2. Combined clinical (history, physical examination, laboratory) and radiographic classification criteria for osteoarthritis of the hip, tradition format of ACR*.

Hip pain
and
At least 2 of the following 3 features
ESR < 20 mm / hour
Radiographic femoral or acetabular osteophytes
Radiographic joint space narrowing (superior, axial, and / or medial)

*This classification method yields a sensitivity of 89% and a specificity of 91%.
ESR = erythrocyte sedimentation rate.

However, many authors have suggested use of a clinical method (not focusing to radiographic changes) to diagnose hip OA in epidemiological studies (Altman 1991, Birrell et al. 2001, Arokoski et al. 2000, Heliövaara et al. 1993a). The studies recommended using clinical variables, such as pain location or duration, hip ROM, age or aggravating movement. Among the different clinical criteria, diminishing hip ROM is the most common component used to indicate the presence of hip joint OA. This is because the hip joint ROM has shown to be a sensitive marker of the radiographic severity of OA (Arokoski et al. 2004).

2.4 TREATMENT OF HIP OSTEOARTHRITIS

There is no cure for hip OA or treatment proven to slow OA progression. The main treatment goal for patients with hip OA, therefore, is considered to be reducing joint pain and physical disability. Treatment of hip OA is a combination of pharmacological, non-pharmacological and surgical modalities (Arokoski et al. 2012, Hochberg et al. 2012, Vignon 2006, Zhang et al. 2008, Zhang et al. 2010) (Figure 2). Physiotherapy and occupational therapy are regarded to be important components of any therapeutic program for OA. These non-pharmacological treatments are as important as drug treatment in hip OA (Arokoski et al. 2012, Hochberg et al. 2012, Vignon 2006, Zhang et al. 2008, Zhang et al. 2010). Pharmaceutical treatment should not be used as the sole treatment of OA (Arokoski et al. 2012, Hochberg et al. 2012, Vignon 2006, Zhang et al. 2008, Zhang et al. 2010). The main indication for hip arthroplasty is pain that cannot be controlled by conservative means.

2.4.1 Conservative treatment

2.4.1.1 Patient education

Patient education and weight loss are generally used as primary therapeutic approaches in the treatment of patients with primary OA (Arokoski et al. 2012, Hochberg et al. 2012, Vignon 2006, Zhang et al. 2008, Zhang et al. 2010). As part of a comprehensive treatment plan, subjects with hip OA need to receive information on the disease. This gives the patient a coping strategy to remain active despite pain and disability. Books, videos, pamphlets and newsletters can be used as educational material. It has also been shown that periodic telephone support interventions by lay personnel promoting self-care for patients with OA is associated with relief of joint pain and improved physical function and the authors concluded that telephone contact is cost-effective intervention in OA (Rene et al. 1992, Weinberg et al. 1993).

2.4.1.2 Weight loss

Body weight has shown to be a risk factor for functional decline in OA of the hip (Dekker et al. 2009). Treatment guidelines (Arokoski et al. 2012, Hochberg et al. 2012, Vignon 2006, Zhang et al. 2008, Zhang et al. 2010) recommend different weight loss programs similar to those used in knee OA to improve joint pain and function. However there are no controlled studies on the effects of weight loss on hip OA symptoms.

Bariatric surgery is currently the only evidence-based approach to marked weight loss in obese individuals (Buchwald et al. 2004). However, there is currently limited literature to evaluate the role of bariatric surgery in hip and knee OA. A recent systematic review demonstrated that bariatric surgery, as part of a comprehensive weight management strategy with subsequent marked weight loss may lead to improved hip and knee pain and function in obese patients with hip or knee OA (Gill et al. 2011). However, this review identifies the need for randomized controlled trials to clarify the role and indicators for supporting treatment by bariatric surgery.

2.4.1.3 Physical therapy

Many physical modalities i.e. different thermal (e.g. cryotherapy, thermotherapy (ultrasound and short wave diathermy) and electromagnetic modalities [e.g. Transcutaeous Electrical Nerve Stimulation (TENS) or laser) have been used for the alleviation of symptoms in knee and hip OA. However, these treatment methods appear to have no benefit for people with hip OA (Arokoski et al. 2012).

2.4.1.4 Occupational therapy

Occupational therapy plays a central role in the management of hip OA patients with functional limitations (Arokoski et al. 2012, Hochberg et al. 2012, Vignon 2006, Zhang et al. 2008, Zhang et al. 2010). The occupational therapist may be able to improve the patient's ability to perform daily activities and to teach them the principles of energy conservation and joint protection (Minor 1999, Hochberg et al. 1995). Environmental modifications and adjustments of workstation furniture at home and in the workplace have been evaluated. Different assistive devices i.e. raised toilet seats, grab rails / wall bars, seat cushions, a riser to adjust seat height and dressing stick appear to be useful in helping patients to cope with routines of daily living.

2.4.1.5 Drug treatment

Paracetamol is shown to be effective in the treatment of hip OA pain (Hochberg et al. 2012, Vignon et al. 2006, Zhang et al. 2008, Zhang et al. 2010, Arokoski et al. 2012). It has also shown to improve pain at rest and to be better tolerated than nonsteroidal anti-inflammatory drugs (NSAIDs) (Bradley 1991). To avoid side-effects the dose of paracetamol > 3g / day should not be exceeded (Zhang et al. 2010). If the efficacy of paracetamol is not adequate, NSAIDs are recommended. NSAIDs (conventional and COX-2 selective) are effective and widely used to reduce pain and to improve function in patients with hip OA (McCormack 2011, Bingham et al. 2011). Due to serious cardiovascular and gastrointestinal side effects of all the NSAIDs, they should be used in the lowest effective dose and their long-term use should be avoided, if possible (Gabriel et al. 1991, Graham et al. 2005). Opioids are conditionally recommended in patients who have had an inadequate response to initial therapy. Opioid analgesics are recommended for patients who are either not willing to undergo or had contraindications for total joint arthroplasty and have failed to respond to medical therapy (Arokoski et al. 2012).

2.4.1.6 Exercise therapy

Current international guidelines for the treatment of hip OA recommend therapeutic exercise, land or water-based, to be included in management strategies (Arokoski et al. 2012, Hochberg et al. 2012, Vignon 2006, Zhang et al. 2008, Zhang et al. 2010). Exercise intervention aims to alleviate the structural and functional impairments that accompany the pathologies, rather than addressing the pathology itself. Currently, there is a lack of data to support the putative benefits of exercise programmes in relieving pain associated with hip OA (van Baar et al. 1999, Pisters et al. 2007, Hernandez-Molina et al. 2008, Fransen et al. 2009, Fransen et al. 2010, McNair et al. 2009, Escalante et al. 2010). Most randomized controlled trials include patients with both knee and hip OA. It is difficult to differentiate between these two entities and often patients with hip OA tend to be a minority in the sample (van Baar et al. 1998, Hopman-Rock and Westhoff 2000, Foley et al. 2003, Hoeksma et al. 2004, Lin et al. 2004, Ravaud et al. 2004, Cochrane et al. 2005, Veenhof et al. 2006, Fransen et al. 2007, Hinman et al. 2007, Pisters et al. 2010). Only two randomized controlled trials published to date restricted recruitment to people with symptomatic hip OA (Tak et al. 2005, Fernandes et al. 2010). Tak et al. demonstrated a favorable and significant short-term effect of exercise on pain in hip OA and Fernandes et al. showed significant improvement in

WOMAC physical function. The details of the results from previous randomized studies on the effects of exercise in hip OA are given in table 3.

Researchers have also stated that there has been a lack of detailed exercise programs specifically for patients with hip OA. Only one therapeutic program (Fernandes et. al. 2010) and one multimodal treatment program, including therapeutic exercises (Bennell et al. 2011), have been published.

A number of studies have compared the cost-effectiveness of pharmacological therapies for OA (Zabinski et al. 2001, Gillette and Tarricone 2003). In contrast to operative treatment of hip OA (total hip replacement), that has shown to be cost-effective (Jenkins et al. 2013), little is known about the cost-effectiveness of non-pharmacological or non-operative treatments, such as exercise, in hip OA.

2.4.2 Surgical treatment

Surgical intervention is required when there is a significant level of pain that limits normal functional activities of daily living such as the ability to walk, stand, negotiate stairs, climb in and out of a car and put on shoes and socks. Surgical options depend on the diagnosis, severity of OA, patient age and activity level, patient occupation, patient medical health and patient expectations (Eskelinen et al. 2010). Surgical options are grouped to five main categories; arthroscopy, arthrodesis, osteotomy, pelvic osteotomy and hip joint arthroplasty (Moscowitz et al. 2007).

Arthroscopy is a less invasive tool to diagnose and treat hip pathology. Its indications include labral tears, capsular laxity, chondral injury and ligament tears avulsion. Less commonly they can include management of osteonecrosis, inflammatory synovial processes, infection and possibly early to mild OA (Kelly et al. 2003).

Osteotomies of the pelvis and / or femoral osteotomies can alter force transmission through the hip joint and thus potentially influence clinical symptoms and the course of the OA process. The underlying diagnoses in which one would consider an osteotomy include young patients with secondary OA from hip dysplasia and residual deformities from childhood conditions such as Perthes disease and slipped capital femoral epiphysis (Millis et al. 1996).

Total hip arthroplasty (THA) is considered to be one of the most beneficial surgical procedures on health-related quality of life that currently performed (Wiklund and Romanus 1991, Laupacis et al. 1993,). It has also shown to be cost-effective (Jenkins et al. 2013). There is no standard care randomized controlled trial for THA in existence. However, there are a large number of head to head comparisons between different types of prosthesis and uncontrolled follow up studies (Fizpatric et al. 1998, Faulkner et al. 1998). A systematic review of 118 uncontrolled follow-up studies identified that the percentage of patients free from pain at the end point ranged 43.2% (95% CI 34% to 49%) to 84.1% (95% CI 46% to 100%) depending upon the type of prosthesis (Fizpatric et al. 1998).

Marked improvements in physical function, social interaction, and over-all health have been demonstrated after THA (Laupacis et al. 1993). Different procedures of pre and postoperative physical therapy and rehabilitation programs have been evaluated to improve the outcome of surgery. There is little evidence to support the use of preoperative education over and above standard care to improve postoperative outcomes in patients undergoing hip replacement surgery, especially with respect to pain, function and length of hospital stay (McDonald et al. 2004). However, perioperative exercise programs are proven to improve functional recovery of subjective stiffness, hip strength and walking speed after THA (Wang et al. 2002, Gilbey et al. 2003). Also a postoperative home program of physical therapy or treadmill training with partial body-weight support is effective in improving hip muscle strength, walking speed and the functional activity (Sashika et al. 1996, Hesse et al. 2003).

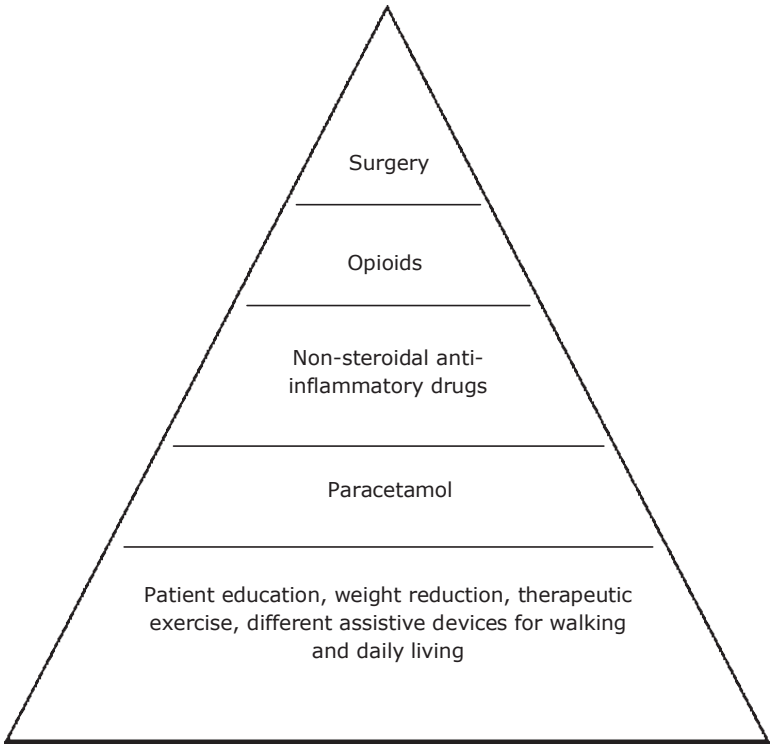


Figure 2. Treatment guidelines for hip OA in Finland. The conservative non-pharmacological interventions should be recommended for all patients. Redrawn with modifications from Arokoski et al. (2012).

Table 3. Randomized controlled trials concerning the effects of exercise in hip osteoarthritis.

Research group, publication year	**Subjects**	**Intervention**	**Follow-up, Outcomes Measures**	**Results**
Van Baar and coworkers 1998	201 men (21%) or women (79%) (mean 68 years) Hip and knee OA	Individual program (12 weeks) G1 = Land-based, 17 x physiotherapy + GP care + education, n = 98 G2 = Control (GP care + education) , n = 102	At 12 weeks: Pain (VAS) Function IRGL Use of NSAID and Paracetamol Observed disability¤	Significant improvement of pain (VAS) and observed disability and decreased use of paracetamol in the exercise group No significant difference of physical function or use of NSAID
Hopman-Rock and coworkers 2000	105 men (17%) or women (83%) (mean 65 years) Hip and knee OA	Glass-based (6 weeks) G1 = Land-based, 6 x education + exercise, n = 56 G2 = Control, n = 49	At 6 weeks: Pain (VAS, IRGL subscale of pain) Mobility IRGL Quality of life (QOL) Objective assessments§	Moderate effect on pain at 6 weeks, no difference between the groups at 6 months
Foley and coworkers 2003	105 men (50%) or women (50%) (mean 71 years) Hip and knee OA	Glass-based (6 weeks) G1 = Aquatic, n = 35 G2 = Land-based, 18 x strengthening, ROM, n = 35 G3 = Control, n = 35	At 6 weeks: Pain (WOMAC) Function (WOMAC, walking speed and distance, quadriceps strength)	No significant difference between the groups in WOMAC pain Significant improvement in gym and aquatic groups for objective function tests
Hoeksma and coworkers 2004	109 men (30%) or women (70%) (mean 72 years) Hip OA only	Land-based (5 weeks) G1 = Land-based, 9 x strengthening G2 = Manual therapy (manipulations and mobilisation of hip joint) 9 x	At 29 weeks: Pain (VAS) Function (HHS, SF-36)	Significant improvement for HHS function in the manual therapy group Significant improvement for VAS pain up to 29 weeks
Lin and coworkers 2004	106 men (13%) or women (87%) (mean 69 years) Hip and knee OA	Community-based aquatic exercise (12 month) G1 = Aquatic exercise programme, n = 66 G2 = Control n = 40	At 12 month: Pain (WOMAC) Function (WOMAC, battery of physical function tests) Stiffness (WOMAC)	Modest improvement (small but significant) in measures of physical function, pain, general mobility and flexibility
Ravaud and coworkers 2004	2 957 men (24%) or women (76%) (mean 66 years) Hip and knee OA	G1 = Standardised tools (ST = assessment of pain and functioning with the WOMAC), n = 220 G2 = Exercise, home-based, non supervised, n = 213 G3 = ST + exercise, n = 213 G4 = Usual care, n = 221	At 24 weeks: Pain (WOMAC, VAS) Function (WOMAC)	No significant difference between the groups in the outcome measures
Tak and coworkers 2005	109 men (32%) or women (68%) (mean 68 years) Hip OA only	Class-based (8 weeks) G1 = Land-based, 8 x strengthening + home program, n = 55 G2 = Control, n = 54	At 8 weeks: Pain (HHS, VAS) Function (GARS)	Significant improvement of HHS pain No significant difference of physical function

Cochrane and coworkers 2005	106 men (12%) or women (88%) hip/knee	G1 = Aquatic (12 months) G2 = Control	At 6 months: Pain (WOMAC) Function (WOMAC)	Significant reduction in pain and improvement in physical function
Veenhof and coworkers 2006	200 men or women (mean 65 years) Hip and knee OA	G1 = Behavioral graded activity (BGA), n = 97 G2 = Usual care (exercise therapy and advice)	At 0, 13, 39 and 65 weeks: Pain (VAS, WOMAC) Function (WOMAC)	Significant reduction in pain and improvement in physical function in both groups, no differences between the groups
Fransen and coworkers 2007	152 men (25%) or women (75%) (mean 70 years) Hip and knee OA	Class-based (12 weeks) G1 = Aquatic, n = 55 G2 = Tai Chi, n = 56 G3 = Control, n = 41	At 12 and 24 weeks: Pain (WOMAC) Function (WOMAC, SF-12 (PCS)) Physical performance tests* Psychological well being (DASS21, SF-12 (MCS))	Significant improvement in WOMAC pain and function in both intervention groups Better improvement in physical performance tests in aquatic therapy group
Hinman and coworkers 2007	71 men (32%) or women (68%) (mean 63 years) Hip and knee OA	G1 = Aquatic exercise (6 weeks, twice a week, individually instructed program) n = 36 G2 = Control (instructed to continue their usual daily activities, no exercise) n = 35	At 6 and 12 weeks: Pain (VAS, WOMAC) Function (WOMAC, muscle strength) Quality of life (AQoL = Assessment of quality of life)	Significant, but small improvement in pain and physical function, strength and quality of life
Fernandes and coworkers 2010	109 men (46%) or women (54%) (mean 58 years) Hip OA only	G1 = Patient education (PE), n = 54 G2 = PE + Land based, 24 supervised exercise (SE), n = 55	At 16 months Pain (WOMAC) Function (WOMAC, SF-36, PASE) Stiffness (WOMAC)	No significant difference for WOMAC pain or stiffness, PASE or SF-36 function Significant improvement for WOMAC physical function in the PE+SE group compared to PE only
Pisters and coworkers 2010	200 men (23%) or women (77%) (mean 65 years) Hip and knee OA	G1 = Behavioral graded activity (BGA) with exercise therapy, 12 week period with a maximum 18 sessions of BGA n= 97 G2 = Usual exercise therapy n = 103	At 3, 9, 15 and 60 months Pain (WOMAC) Function (MACTAR Questionnaire)	No differences between the groups in the long-term

N = Number, F = Female, G = Group, VAS = Visual Analogue Scale (0 – 100), IRGL = Influence of Rheumatic Diseases on General Health and Lifestyle, NSAID = Non-Steroidal Anti-Inflammatory Drug, ROM = Range of Motion, HHS = Harris Hip Score, GARS = Groningen Activity Restriction Scale, SF-12 = The Short-Form From 12 Health Survey-version, PCS = Physical Component Summary, Computed Score of SF-12, DASS21 = Depression, Anxiety and Stress scale, MCS = Mental Component Summary, Computed Score of SF-12, SF-36 = The Short-Form Health Survey, PASE = Physical Activity Score for Elderly.
¤Studying videos of patients' performance in a series of standardised tasks, which included walking, sitting down, bending and reclining.
§Range of motion, muscle strength, 20 m Walking Test, Timed Up and Go test, stair walking and "reaching for toes" in sitting position test.
*Timed 50-foot Walk Test, Stair Climb Test and Timed Up and Go Test.

3 Aims of the study

The first aim of this study was to examine potential risk factors hip OA. The second aim was to study factors associated with self-reported pain and physical function in patients with hip OA and to identify deeper determinants of disability and pain in hip OA. The third aim was to evaluate the effect of exercise training on pain, functional ability and healthcare costs in hip OA.

The detailed goals of the present series of studies can be outlined as follows:

1. To examine potential risk factors for hip OA in a 22-year prospective population-based study (Article I).
2. To determine factors associated with self-reported pain and physical function in patients with hip OA. The potential factors assessed were age, education, depression, life satisfaction, smoking, duration of sports activities, radiologic score of hip OA, body mass index, comorbidites and duration of knee pain were also analysed (Article II).
3. To assess the short-term and long-term effects of strengthening, land-based exercise on hip OA taking into account both impairment (pain, functional limitations) and the financial burden (utilisation of medical and rehabilitation services and drug use) caused by this disease (Article III).
4. To assess factors related to OA in the prediction of pain and physical and mental function in a two year randomized controlled trial among patients with hip OA (Article IV).

4 Methods

4.1 STUDY POPULATION AND STYDY DESING

4.1.1 The prospective population-based study (Article I)

Between 1978 and 1980, a sample of 8000 people, representative of the Finnish population aged 30 years or over, was drawn from the population register and invited to participate in a cross-sectional study on health, the Mini-Finland Health Examination Survey (Aromaa et al. 1989). In brief, 7217 subjects (90 % of the sample) participated in the screening phase of the study, which comprised questionnaires, interviews and standard laboratory tests and clinical examination. The examination, methods and the diagnosis of hip OA have been described in detail elsewhere (Heliövaara et al. 1993a, Aromaa et al. 1989, Mäkelä et al. 1993, Aho K 1989).

The questionnaires were checked and the interviews were performed by specially trained nurses. Information concerning educational level (years), smoking history (never-smoked, ex-smoker, smoker), alcohol intake (expressed as absolute alcohol in grams/week) and level of physical activity (inactive, irregularly active, regularly active) was elicited by means of standard questionnaires. Body height and weight were measured and BMI was calculated by dividing body weight (kg) by body height squared (m^2). The subjects were asked to attend a clinical examination if they had experienced any difficulties in walking due to hip pain during the previous month or if they were found to have difficulty in performing the function tests, for example, when asked to squat or climb stairs. At the clinical examination stages 3-6 months later, specially trained physicians carried out the clinical examinations according to a standardised written protocol.

Between 2000 and 2001, another cross-sectional population study on health in a representative sample of Finnish men and women, the Health 2000 Survey, was conducted (Aromaa et al. 1989) (Figure 3). The Health 2000 Survey was designed to have the same protocol and assessments as the Mini-Finland Health Survey. All participants of the Mini-Finland Health Survey who were alive in 2000 and living in or around any of the five major regional cities were invited for re-examination in conjunction with the Health 2000 Survey. Altogether 1286 former participants were invited and 909 of these participated in the follow-up study. At baseline these subjects were on average 42 years old (SD 8 years, range 30 to 72 years). At follow-up their mean age was 63 years (SD 8 years, range 50 to 94 years). After exclusion of individuals with hip OA at baseline and those who were retired, 840 subjects remained (371 males and 469 females) and constituted the present study population (Figure 3). All participants signed a written consent and the study was approved by the Ethical Committee for Epidemiology and Public Health in the hospital district of Helsinki and Uusimaa, Finland.

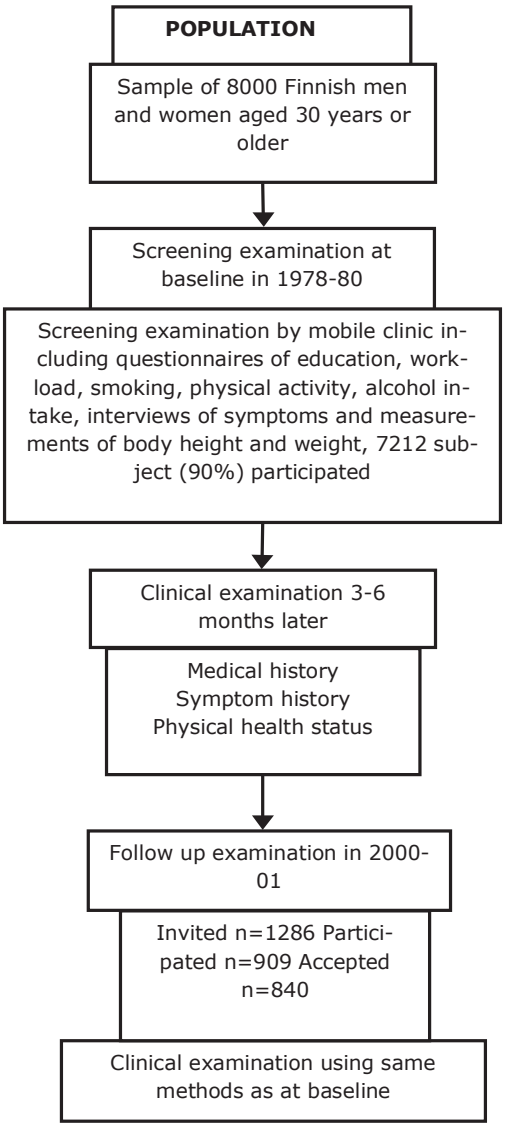


Figure 3. The flow of activities during the Mini-Finland Health Survey and the Health 2000 Survey follow-up examination in 2000-01.

4.1.2 Randomized controlled trial (Articles II, III, IV)

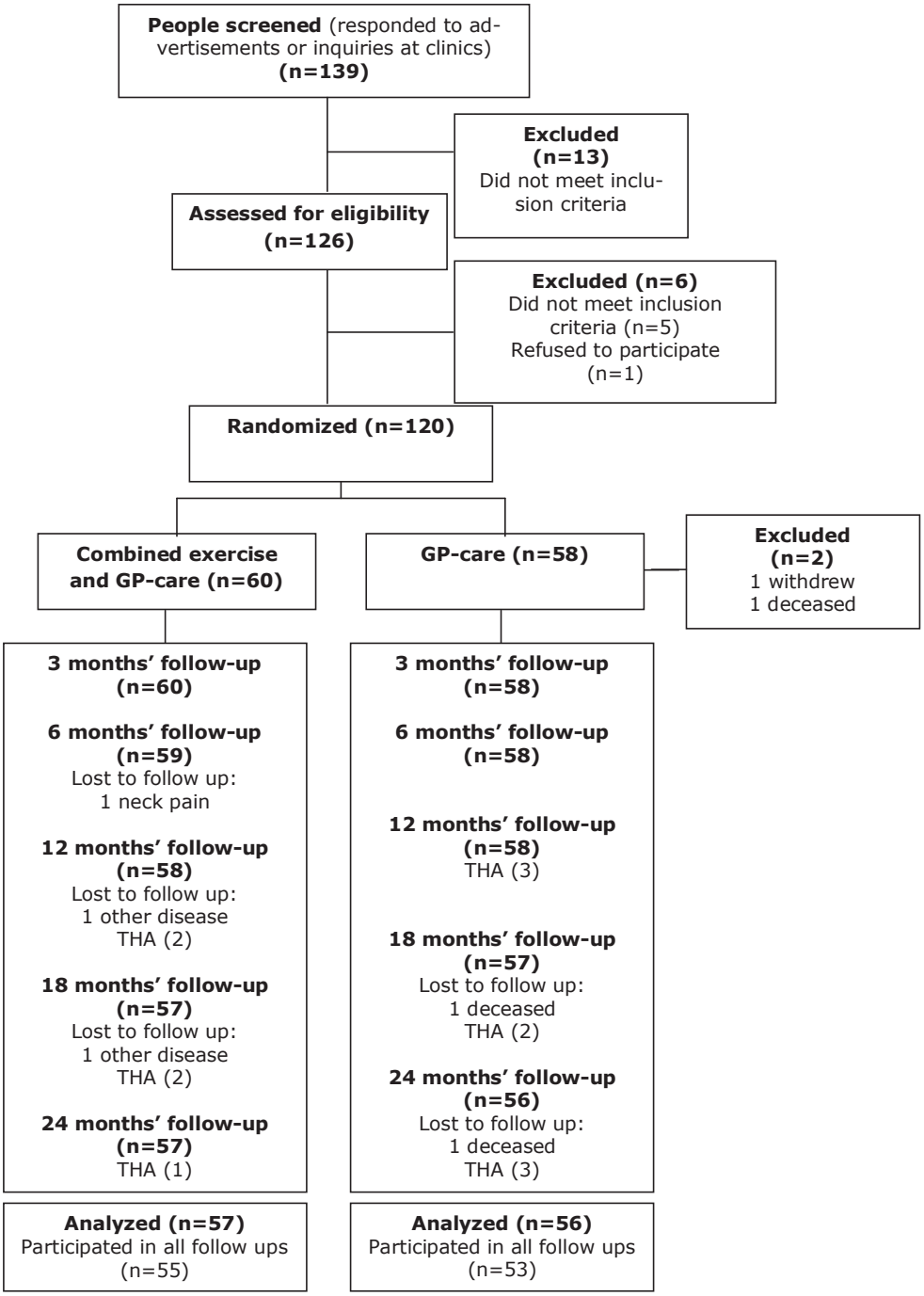
4.1.2.1 Subjects

The subjects for the randomized controlled trial (120 males and females, aged from 55 to 80 years) were recruited from the city of Mikkeli, Finland, and the surrounding area. The recruitment was carried out primarily by an advertisement in a local newspaper (n=113) and to a lesser degree from specialists' clinics (n=2) or general practitioners' clinics (n=5) (Figure 4). The recruitment period took place from August 2005 to February 2006. The subjects were included in the study if they were 50 – 80 years of age and willing to participate in a study lasting for two years and they had unilateral or bilateral hip OA with K-L grade ≥ 1 (X-ray examination less than 3 years old) and pain experienced in the hip region (groin and lateral hip region) within the preceding month as indicated in the clinical criteria of the ACR (Altman et al. 1991). The exclusion criteria were THA, rheumatoid arthritis, cognitive impairment, a major surgical operation within the preceding six months in the lower limb or lower back, an acute or sub-acute lower back pain and cardiovascular or pulmonary disease or other chronic diseases that would prevent full participation in the training program.

Randomization was performed using the stratified block randomization procedure in order to balance subjects for gender and age (Figure 4). The number of strata was four (gender and age groups: 55-67 and 68-80 years) and patients were randomized into three blocks (block size n = 40). Prior to randomization to the combined exercise plus general practitioner group and to general practitioner group, a physician specialising in physical and rehabilitative medicine gave a 1-hour lecture on the basic principles of non-operative treatment of hip OA. The combined exercise and general practitioners care group received 12 supervised 45 minute exercise sessions once a week at baseline and four additional booster sessions at a time point one year later between the 12^{th} and 13^{th} month of follow-up. A primary care physiotherapist supervised exercise sessions consisting of 10 participants at a given time. Once the physiotherapist was certain that the participants had mastered the exercises, a recommendation was made to perform the specific exercises using the same protocol three times per week for two years. The exercise program was developed with common training principals, modified to suit patients of hip OA (Peloquin et al. 1999, Rogind et al. 1998). Each training session consisted of a warm-up session (marching in place and leg raises to the front, back and side) then strengthening and stretching sessions. The intensity of the strengthening exercises was the same for each participant. The subjects were recommended to perform the exercises with maximal effort in order to achieve the highest possible movement velocity. Stretching exercises were done to the point of mild tension and relaxation as the subject held the stretch. The participants in the combined exercise plus general practitioner care group also received normal routine care offered by their own general practitioner including analgesics and physiotherapy.

The participants in the general practitioner care group received standard care [normal routine care offered by their own general practitioner (analgesics and physiotherapy)].

Outcome variables were assessed at study entry and at 3, 6, 12, 18 and 24 month visits. The flowchart of the study is presented in Figure 4. The protocol was approved by Mikkeli Central Hospital Research Ethics Committee. All participants provided a written consent.



GP = general practitioner
THA = total hip arthroplasty

Figure 4. Flowchart of the study.

4.2 ASSESSMENT OF RISK FACTORS AND OUTCOME MEASURES

4.2.1 Assessments in the prospective population-based study (Article I)

4.2.1.1 Assessment of leisure time physical activity

Leisure time physical activity was assessed by one item from a self-administered questionnaire. The subjects were classified into three categories as follows:

1. Little physical exercise: mostly reading, watching television, listening to the radio, going to the cinema or restaurants or doing tasks that do not require much physical exertion.
2. Irregularly physical exercise and/or in connection with some hobbies or as the main pastime or in addition to Group 1: fishing, hunting, gardening, going on family outings fairly regularly or taking some other form of exercise occasionally.
3. Regular physical exercise: as the main pastime or in addition to the Groups 1 and 2: some form of physical exercise regularly or fairly regularly, e.g. running, skiing, cycling, ball games, swimming, gymnastics, weight lifting regardless of whether these were done competitively, as a hobby or to improve physical condition.

4.2.1.2 Assessment of physical workload

Physical workload was assessed by one item from a self-administered questionnaire. The subjects were classified into six categories as follows:

1. Light sedentary work: mainly consisting of sitting at a table, by a machine, etc. and involving only light manual work, e.g. intellectual work, studying, sedentary office work, handling light objects.
2. Other sedentary work: mainly sedentary, but involves occasionally handling fairly heavy objects, e.g. industrial work on a production line.
3. Light work standing or moving: mostly standing work without cumbersome movements or moving from one place to another without carrying heavy burdens, e.g. shop assistant, crane operator, laboratory work, office work or teaching all requiring some mobility.
4. Medium-heavy work involving movement: involves a great deal of mobility and a certain amount of stooping down or carrying light objects, also work involving walking up and down stairs or fairly rapid motion over rather long distances, e.g. light industrial work, forest surveying, messenger work.
5. Heavy manual work: either mostly standing work involving regular lifting of light objects or lifting and carrying heavy objects, drilling, excavating, hammering etc., but with some sitting or standing, e.g. work in heavy engineering or manufacturing, construction work, using or assembling heavy tools, goods or parts, agricultural work using machines.
6. Very heavy manual work: mostly consisting of continuous or fairly continuous heavy movement, often done without interruption for long periods, e.g. carrying furniture, forestry work (felling trees), heavy non-mechanised agricultural work, fishing with heavy tackle, heavy construction work, manual excavation.

4.2.1.3 Assessment of injuries

Injuries sustained since the baseline examination were classified by a physician according to the 8th edition of the International Classification of Diseases on the basis of all available medical history, symptoms and clinical findings during medical examination. Musculoskeletal injuries were taken into account only if they had led to a permanent damage or to any continued impairment or complaint.

4.2.1.4 Assessment of other risk factors

Age (years), sex, education (years), smoking (never smoked, ex-smoker, smoker) and alcohol intake (g/week) were assessed by a self-administered questionnaire. Body height and weight were measured and BMI was calculated by dividing body weight by body height squared (kg/m^2).

4.2.1.5 Diagnosis of hip osteoarthritis

Specially trained physicians undertook the clinical examinations and diagnosed hip OA according to a standardised written protocol (Heliövaara et al. 1993a, Aromaa et al. 1989, Mäkelä et al. 1993). The clinical diagnosis of hip OA was made on the basis of disease histories, symptoms and clinical findings according to standard criteria (Table 4). The physicians were unaware of the potential predictor variables recorded at the baseline. For the present study the definite and probable diagnoses were combined into one diagnostic group. The sensitivity of the screening procedure for hip OA was 100% and a satisfactory agreement (kappa (κ) 0.44) has been found between the clinical and radiological diagnosis of hip OA, used in the Mini-Finland survey (Heliövaara et al. 1993a). The agreement between definite clinical and radiological hip OA diagnosis (K-L grading scale 2 – 4) has been proved to be moderate (Kaila-Kangas et al. 2011). The κ value was 0.66 (95% CI 0.29 to 1.00).

In the Health 2000 Survey there were two physicians in each of the five regional field teams. The quality assurance program comprised four separate days during which the repeatability of the clinical diagnosis of hip OA was tested across the field teams. For this all together 173 volunteers, aged 45-82, were recruited from outside the survey sample. Two physicians always chosen from two separate field teams independently examined each subject. The κ-value for the repeatability was 0.49 (95% CI 0.09 – 0.90) for OA in the left hip (with a prevalence of 2.3% in both the first and second examinations). Similarly, the κ-value was 0.61 (95% CI 0.26 – 0.96) for OA in the right hip (with a prevalence of 2.3% and 2.9% in the two sets of examinations respectively).

Table 4. Diagnostic criteria for hip OA in the clinical examination of the Mini-Finland Health Survey and the Health 2000 Survey.

Hip osteoarthritis	
Definite	Probable
Documented history of previously diagnosed hip osteoarthritis or hip arthroplasty due to osteoarthritis based on convincing findings. OR At least moderate restrictions in extension (limitation over five degrees) or in inner rotation (maximal range less than 20 degrees) or in outer rotation (maximal range less than 30 degrees), especially if combined with tenderness associated with movement. OR Slight restrictions in extension (limitation less than five degrees) or in inner rotation (maximal range 20–30 degrees) or in outer rotation (maximal range 30–40 degrees) or at least moderately restricted abduction-adduction (maximal range less than 50 degrees) AND either of the following: • documented history of previously diagnosed hip osteoarthritis but no grounds for the diagnosis given; • typical symptoms of hip osteoarthritis (stiffness, pain when moving after inactivity, pain during prolonged strain).	Documented history of previous hip arthroplasty but no convincing evidence of diagnosed hipos-teoarthritis. OR Typical symptoms of hip osteoarthritis AND either of the following (even in the absence of clinical findings in the current examination): • history of previously diagnosed hip osteoarthritis without documentation; • documented previous diagnosis of hip osteoarthritis but no grounds for the diagnosis given. OR Clinical findings suggesting hip osteoarthritis (slightly restricted extension or inner or outer rotation or at least moderately restricted abduction-adduction) but no corresponding history.

4.2.2 Assessments in randomized controlled trial (Articles II, III, IV)

4.2.2.1 Assessment of physical activity

Habitual conditioning physical activity was assessed using a leisure time physical activity history developed in the Kuopio Ischaemic Heart Disease Risk Factor (KIHD) Study (Lakka and Salonen 1987). Leisure-time physical activity was assessed from 12-month history modified from Minnesota Leisure Time Physical Activity Questionnaire (Taylor et al. 1978). The checklist included the most common leisure-time physical activities of middle-aged Finnish men and women, selected on the basis of a previous population study in Finland (Mälkiä et al. 1988). For each activity performed, the subjects were asked to record the frequency (number of sessions per month), average duration (hours and minutes per session) and intensity (scored as 0 for recreational activity, 1 for conditioning activity, 2 for brisk conditioning activity and 3 for competitive, strenuous exercise).

The intensity of physical activity was expressed in metabolic units (MET, or metabolic equivalents of oxygen consumption). One metabolic unit corresponds to an energy expenditure of approximately 1 kcal per kilogram of body weight per hour, or an oxygen uptake of 3.5 ml per kilogram per minute.

4.2.2.2 Assessment of depression and life satisfaction

The Beck Depression Inventory (BDI) with scores from 0 to 63 was used to assess possible depression. The cutoff point for clinically significant depression was set at 15 or over, which has been found to have good sensitivity (.835), specificity (.813), positive predictive value (.968) and negative predictive value (.419) in screening major depression (Beck 1961). Life Satisfaction (LS) scale was included to assess mental well-being. For each item participants chose the statement that best described their experience. The sum scores were analysed continuously or dichotomously (the satisfied croup had scores 4-11 and the dissatisfied group had 12-22) (Koivumaa-Honkanen 1998).

4.2.2.3 Assessment of other possible risk factors

Demographic characteristics collected included information on the sex, age, working status, duration of hip symptoms, presence of knee OA and/or knee pain, comorbidites and BMI.

4.2.2.4 Assessment of pain

Self-reported pain was assessed by using the visual analogue scaled format of the WOMAC OA index, designed specifically for people with hip or knee OA (Bellamy 1988). The visual analogue scaled version allows the patients to estimate the symptoms by marking an X on a 100 mm long line (the beginning of the line = no symptoms, the end of the line = worst possible symptoms). Subscale pain consists of 5 questions. The mean score of hip pain was generated by summing the coded responses and then dividing by the number of items.

4.2.2.5 Assessment of physical function

The specific physical function of self-reported diseases was determined by using the subscale of physical function of the WOMAC OA index that consists of 17 questions concerning physical function (Bellamy et al. 1988). The mean score of hip function was generated by summing the coded responses and then dividing by the number of items.

Self-reported generic physical function was determined using the physical function part of the RAND-36 questionnaire. The instrument contains exactly the same questions as the 36-item Short-Form Health Survey (SF-36) (Ware and Sherbourne 1992). The reliability and construct validity of the RAND-36, as a measurement of the health-related quality of life (HRQOL) in the Finnish general population, has been established (Aalto et al. 1999). The RAND-36 survey comprises 8 multi-item dimensions: general health, physical function, mental health, social function, vitality, bodily pain and physical and emotional role function. Each subscale ranges from 0 to 100 with higher scores indicative of a better HRQOL.

The passive hip flexion and the hip internal rotation ROM measurements were determined by using 2-arm goniometry (Arokoski et al. 2004). The passive movement, including stretching, was done until the firm or bony end was reached and/or discomfort limited the motion or compensatory movement occurred.

The objective physical function was measured by using a battery of tests performed in a random order (the six-minute walk test (6-MWT), the 10-meter walk test (10-MWT), the timed up & go test (TUG test), the sock test and the leg extensor power measurement) as follows;

The six-minute walk test, a reliable, valid and safe test, was used to quantify the participant's walking ability (Guyatt et al. 1985). The 6-MWT is measure of both gait speed and function as well as endurance exercise capacity. The score recorded was the total distance travelled (in meters) during 6 minutes.

The 10-meter walk test, a measure of gait velocity, was performed indoors on a 10-meter long track and the time spent to complete the walk, in seconds, was measured (Watson 2002).

The timed up & go test is a performance based measure, which is clinically well established as a measurement of function for knee OA (Podisalo and Richardson 1991).

Participants are asked to stand up from the chair, walk 3 m, turn, walk back and sit down quickly and safely. The time, in seconds, required to complete the test was recorded.

The sock test (Strand and Wie 1999), for evaluating activity limitation in patients with musculoskeletal pain, was used to describe the functional loss caused by hip OA. The patient is asked to sit on a high bench, with both hands, one on each side, grabbing the toes with the fingertips of both hands. The foot must not touch the bench and should be in the air at all times during the test. After testing each leg once, the patient is given a score on the most restricted performance (scores are valued from 0 to 3).

The extensor power of the lower limb was recorded by using the leg extensor power rig (Concept 2, dynamic strength training). The subject was seated in the upright position with arms folded. Comfortable extension of at the knee in conjunction with full depression of the foot pedal determined the seat position. The subject was instructed to depress the foot pedal as hard and as fast as possible. The measure of leg extensor power was expressed as relative power (absolute power divided by body weight (W/kg)). The one-week inter-day inter-tester and intra-tester reproducibility was 0.982 and 0.996, respectively (Robertson et al. 1998).

4.2.2.6 Radiological assessment

The same physician specialising in radiology, analysed the degree of hip OA from antero-posterior radiograph of the hip joint. The mean age of the radiographs was 8.7 ± 10.3 months. The K-L method of classification was used as described in page 14 (Kellgren and Lawrence 1957). The intra-rater reproducibility of K-L grading has been established as being high (.85 – .91) (Sun et al. 1997).

4.2.2.7 Assessment of the use of medication

The use of analgesic (paracetamol and weak opioid (tramadol, codeine)) and NSAIDs for the treatment of hip OA were assessed using patients' reports. The original drug use assessment was based on the following questions: 0 = not using, 1 = using, but less frequently than once a week, 2 = using 1 to 4 times a week, 3 = using 5 to 6 times a week, 4 = using daily (the dose of drugs taken was not evaluated). In the final analysis the drug use categories (drug use in a week) were computed as follows; 0 = not using, 1 = using, but less than daily, 2 = using daily.

4.2.2.8 Assessment of health care costs

The evaluation of direct health care costs was assessed by recording the number of visits to a physician and the number of visits of physiotherapy due to hip OA, when not part of the intervention and the number of total hip replacements. The use of physiotherapy, again not as part of the intervention, was calculated as sum score including either exercise physiotherapy and/or physical therapy modalities (e.g. thermal modalities, transcutaneous electrical nerve stimulation, acupuncture) as follows; 0 = not using, 1= using either exercise physiotherapy or physical therapy modalities, 2 = using both exercise physiotherapy and physical therapy modalities. The questionnaire also included other aspects of physiotherapy e.g. osteopathy, hip traction and also inquired if steroid injections had been administered in the hip region. These accounted for only very few visits and therefore only physiotherapy, including the exercise physiotherapy or physical therapy modalities, were taken into consideration in the analysis.

The direct medical costs (supervised group therapy, doctor visits, use of physiotherapy when not part of the intervention and total hip replacement) were evaluated, but indirect costs, such as absence from work were not estimated. The direct costs were calculated as the mean cost per patient, in Euro, over the 24 month period based on the supervised group exercise therapy costs in the Mikkeli Health Care Center (Ollikainen 2008) and healthcare unit costs (doctor visits, physiotherapy when not part of the intervention and total hip

replacement) in Finland 2006 (Hujanen et al. 2008). The costs of total hip replacement surgery were analysed separately.

4.3 STATISTICAL METHODS

4.3.1 The prospective population-based study (Article I)

Multivariate logistic regression analyses were used to estimate the risk of hip OA according to the baseline risk factors and potential confounding factors. Relative risks were estimated as adjusted odds ratios (ORs) with 95% confidence intervals (CIs). In order to study the effect modification, the first-degree multiplicative interaction terms of workload and injury, one by one, were entered into the logistic regression model. Associations with p-values of less than 0.05 were considered statistically significant. The statistical significance of the interactions was tested against the likelihood ratio test and expressed as exact p-values. All analyses were performed using the SAS System for Windows, version 9.1 (SAS Institute, Inc., Cary, NC).

4.3.2 Randomized controlled trial (Articles II, III, IV)

The differences in baseline characteristics between the groups (combined exercise plus general practitioner care and general practitioner care only) were evaluated using independent samples t-test for continuous variables and Fisher's exact test for categorical variables. Associations with p-values of less than 0.05 were considered statistically significant. The analyses were conducted using SPSS for Windows 17.0.

At baseline Pearson's coefficients for correlation were used for continuous variables and Spearman's coefficients for correlation were used for the ordinally-scaled education variable to study associations between explanatory and outcome variables. Analysis of covariance (ANCOVA) was used to identify independent risk factors for self-reported pain, self-reported disease-specific physical function and self-reported generic physical function by entering all explanatory variables that correlated ($p < 0.01$) with the outcome variables into the ANCOVA models. The RAND-36 general health, mental health, social function, vitality, bodily pain and physical and emotional role function and the WOMAC subscale stiffness were not entered into the models of self-reported mobility measures because of possible co-linearity with pain and physical function. The data are presented as means with standard deviations (SDs) and standard errors or medians with ranges or frequencies and percentages depending on the outcome variables and the types of statistical analysis.

A 20% reduction in the primary outcome (WOMAC pain) in response to the exercise intervention was considered clinically relevant. The SD for WOMAC pain was assumed to be 16.5mm based on previous studies (Tubach et al. 2005). Using these assumptions the appropriate sample size was 120 patients (60 per group) with an alpha equal to 0.05 and power equal to 80% and a 10% loss to follow-up.

Repeated measures analysis of variance was used to examine the differences over time between the combined exercise and general practitioner care group and the general practitioner care group, followed by post hoc comparisons of groups at each time point. The post hoc comparisons were based on the estimated marginal mean. The analyses for the WOMAC, RAND-36 and secondary outcomes, except for the sock test, were adjusted for gender, age at baseline, radiologic K-L score of hip OA, the number of comorbidities, the existence of knee OA or knee pain and the duration of hip symptoms. Due to the somewhat unexpected differences between the study groups in the WOMAC-pain at baseline, the repeated measures analyses of variance for the WOMAC, RAND-36 and secondary outcomes were additionally adjusted for the baseline values of the response variable. Randomly missing data in the longitudinal set-up was imputed using the 'last observation carried forward' principle before the analysis (WOMAC, RAND-36 and secondary outcomes) in order to follow the intention to treat principle. Results related to

the WOMAC, RAND-36 and performance-based outcome score (except for the sock test) are presented as adjusted estimated marginal means, standard errors and 95% CIs.

The analysis of occasions of health services 'usage and health services' direct costs were carried out using the non-parametric Mann-Whitney U-test for continuous variables and the Fisher's exact test for categorical variables. Fisher's exact test was used to investigate whether distributions of categorical drug use variables differed from one another.

To identify the predictors of disability and pain in hip OA, the intervention and control groups were combined in the analyses. The baseline and two-year follow-up data on all 118 participants were analysed together; group randomization was considered as one of the possible predictors for the outcomes. The outcome variables were self-reported disease-specific pain and physical function subscales of the WOMAC and RAND-36 measured at 0, 3, 6, 12, 18 and 24 month follow-up. The possible explanatory variables were age, gender, educational level (secondary school examination; no vs. yes), comorbidities (no vs. yes), prevalent obesity (BMI < 30.0 kg/m^2 vs. BMI ≥ 30.0 kg/m^2), working status (employed; no vs. yes), the radiological grade of hip OA (K-L 1 vs. K-L 2-4) (Kellgren et al. 1963), the duration of hip symptoms (years), knee symptoms (no vs. yes), study group (control group vs. intervention group) and habitual conditioning physical activity (hours per week) that was not part of the exercise intervention. The associations of possible explanatory variables with the outcome variables were assessed by multivariate linear mixed models in which the correlation structure of data due to the multiple measurements per individual could be taken into account.

5 Results

5.1 THE PROSPECTIVE POPULATION-BASED STUDY (ARTICLE I)

5.1.1 Characteristics of subjects

The distributions of age (mean, SD, range) and other characteristics (number, percentage) of the participants at baseline of the Mini-Finland Survey in 1978-80 and at follow-up in 2000-2001 are presented in Table 5. After 22 years of follow-up, hip OA was diagnosed in 17 men (4.9%) and in 24 women (5.1%).

5.1.2 Definition of risk factors

Table 6 shows the odds ratios for having hip OA, adjusted for age and sex and for age, sex and all other covariates. Heavy manual labour was a statistically significant predictor of the development of hip OA even adjusted for all covariates. In addition, individuals who had had a musculoskeletal injury that had led to permanent damage or long-term impairment had a statistically significantly higher risk of developing hip OA than those without such an injury. Education, BMI, smoking, alcohol intake and leisure time physical activity were not associated with the risk of developing hip OA (Table 6). None of these factors modified the associations of heavy labour or major injury with the risk of hip OA (data not shown).

Table 5. Characteristics of the subjects in the prospective population-based study.

Characteristics	**People not invited (%)**		**People invited, but not participated (%)**		**All participants at baseline in 1978-1980 (%)**		**Participants at follow-up in 2000-2001 (%)**	
Age (years)								
Mean	52.9		48.3		51.3		42.5	
SD	14.4		11.4		14.2		9.0	
Range	30-95		30-77		30-95		30-72	
Sex								
Men	2797	(47)	139	(38)	3322	(46)	386	(42)
Women	3142	(53)	230	(62)	3895	(54)	523	(58)
Education (years)								
0-9	4312	(73)	222	(60)	4905	(68)	371	(41)
10-12	1138	(19)	93	(25)	1506	(21)	275	(30)
> 13	489	(8)	54	(15)	806	(11)	263	(29)
Body mass index (kg/m^2)								
<25.0	2590	(44)	172	(47)	3305	(46)	543	(60)
25.0-29.9	2370	(40)	148	(40)	2815	(39)	297	(33)
>30.0	979	(16)	49	(13)	1097	(15)	69	(7)
Physical work load								
not working*	2118	(36)	181	(26)	2273	(32)	60	(7)
light sedentary	735	(12)	86	(23)	1151	(16)	330	(36)
other sedentary	201	(3)	13	(4)	250	(3)	36	(4)
light standing / movements	772	(13)	60	(16)	1031	(14)	199	(22)
fairly light / medium heavy	1010	(17)	76	(21)	1266	(18)	180	(20)
heavy manual	823	(14)	35	(9)	950	(13)	92	(10)
very heavy manual	280	(5)	4	(1)	296	(4)	12	(1)
Smoking								
never smoked	3336	(56)	192	(52)	4009	(55)	481	(53)
ex-smoker	1215	(21)	79	(21)	1505	(21)	211	(23)
smoker	1388	(23)	98	(27)	1703	(24)	217	(24)
Alcohol intake (g/week)								
0	2914	(49)	163	(44)	3296	(45)	219	(24)
1-49	2382	(40)	157	(42)	3080	(43)	541	(60)
50-249	210	(4)	21	(6)	285	(4)	54	(6)
>250	433	(7)	28	(8)	556	(8)	95	(10)
Leisure time physical activity								
little physical exercise	2292	(39)	122	(33)	2636	(37)	222	(24)
irregular physical exercise	2873	(48)	173	(47)	3477	(48)	431	(47)
regular physical exercise	764	(13)	74	(20)	1094	(15)	256	(28)
Injury								
No	5287	(89)	341	(92)	6484	(90)	856	(94)
Yes	652	(11)	28	(8)	733	(10)	53	(6)
Hip OA								
No	5593	(94)	357	(97)	6848	(95)	898	(99)
Yes*	346	(6)	12	(3)	369	(5)	11	(1)

*Excluded from the follow-up analyses.

Table 6. Adjusted ORs for risk factors of hip OA.

Risk factor	**Number of subjects examined**	**Number of OA cases (%)**	**Adjusted for sex and age OR (95 % CI)**	**Adjusted for all covariates OR (95 % CI)**
Age (years)*	840	41		1.4 (1.0-2.0)
Sex				
Men	371 (44)	17 (41)		1.0
Women	469 (56)	24 (59)		1.9 (0.8-4.5)
Education (years)				
0-9	331 (39)	17 (41)	1.0	1.0
10-12	255 (31)	15 (37)	1.3 (0.6-2.8)	1.6 (0.7-3.5)
> 13	254 (30)	9 (22)	0.8 (0.4-1.9)	1.5 (0.5-4.1)
Body mass index				
<25.0	507 (60)	20 (49)	1.0	1.0
25.0-29.9	272 (33)	17 (41)	1.4 (0.7-2.8)	1.3 (0.6-2.8)
>30.0	61 (7)	4 (10)	1.4 (0.4-4.3)	1.1 (0.3-3.6)
Physical work load				
light sedentary	327 (39)	10 (24)	1.0	1.0
other sedentary	36 (4)	1 (2)	0.9 (0.1-7.2)	1.1 (0.1-10.0)
light standing / movements	196 (23)	6 (15)	1.0 (0.3-2.7)	1.2 (0.4-3.4)
fairly light / medium heavy	178 (21)	13 (32)	2.4 (1.0-5.7)	3.1 (1.2-8.0)
heavy manual	91 (11)	11 (27)	4.6 (1.8-11.5)	6.7 (2.3-19.5)
very heavy manual	12 (2)	0		
Smoking				
never smoked	435 (52)	22 (54)	1.0	1.0
ex-smoker	197 (23)	10 (24)	1.0 (0.5-2.4)	1.0 (0.4-2.4)
smoker	208 (25)	9 (22)	1.0 (0.4-2.2)	0.9 (0.4-2.3)
Alcohol intake (g/week)				
0	185 (22)	11 (27)	1.0	1.0
1-49	508 (61)	24 (59)	0.9 (0.4-1.9)	1.1 (0.5-2.4)
50-249	53 (6)	0		
>250	94 (11)	6 (15)	1.5 (0.5-4.7)	2.2 (0.6-7.7)
Leisure time physical activity				
little physical exercise	199 (24)	9 (22)	1.0	1.0
irregular physical exercise	395 (47)	21 (51)	1.1 (0.5-2.4)	1.2 (0.5-2.9)
regular physical exercise	246 (29)	11 (27)	0.9 (0.4-2.3)	1.1 (0.4-2.8)
Injury				
No	793 (94)	34 (83)	1.0	1.0
Yes	47 (6)	7 (17)	3.5 (1.4-8.7)	5.0 (1.9-13.3)

OR = odds ratio, CI = confidence interval.
*Mean 41.8, SD 8.4, range 30-72 (OR per increment by one SD).

5.2 THE RANDOMIZED CONTROLLED TRIAL (ARTICLES II, III, IV)

5.2.1 Characteristics of subjects at baseline

Figure 4 shows the participant flow and reasons for withdrawal and loss to follow-up at different stages of the study. Baseline characteristics of the participants are shown in Table 7 and 8. In general, the patients in the combined exercise and general practitioner care and general practitioner care groups did not differ at baseline, but WOMAC pain was statistically significantly higher in the general practitioner care group than in the combined exercise and general practitioner care group.

Table 7. Baseline characteristic in the randomized controlled trial.

Variables	**Valid percent**
Gender	
Male	30.0
Female	70.0
Working status	
No-longer employed	72.0
Part-time employed	11.0
Employed	16.9
Radiographic grade of hip osteoarthritis	
Kellgren-Lawrence grade 1	41.7
Kellgren-Lawrence grade 2	42.5
Kellgren-Lawrence grade 3	13.3
Kellgren-Lawrence grade 4	2.5
Knee osteoarthritis	33.9
Comorbidities	
No chronic disease	41.5
One chronic disease	44.9
Two or more chronic diseases	13.6
Overweight	
No (body mass index < 25 kg/m²)	19.7
Yes (body mass index ≥ 25 kg / m²)	80.3
Depression	
No depression (Beck depression inventory score <15#)	88.6
Depression (Beck depression inventory score ≥ 15#)	11.4
Life satisfaction	
Satisfied with life (Life Satisfaction scale = 4-11)	79.7
Unsatisfied with life (Life Satisfaction scale = 12-20)	20.3

#Beck depression inventory scores range from 0 to 63.

5.2.2 Factors affecting self-reported pain and disability at baseline (II)

The bivariate correlations of pain, self-reported disease specific physical function and self-reported generic physical function with all independent variables are shown in Table 9. The number of comorbidites and the duration of knee pain and LS explained 22% of self-reported pain. The number of comorbidites, passive hip flexion and the TUG test explained 20% of self-reported disease specific physical function whereas the passive hip flexion, 6-MWT and educational level explained 25% of self-reported generic physical function.

Table 8. Self-reported and physical performance measures at baseline.

Variables	Mean ±SD	Range
Symptoms of hip osteoarthritis		
Pain index from WOMAC* (mm)	25.2 ± 18.0	2-75
Stiffness index from WOMAC* (mm)	35.3 ± 24.4	0-90
Physical function index from WOMAC* (mm)	26.8 ± 19.7	0-83
Components of health related quality of life (HRQOL)		
Physical functioning from RAND-36†	62.3 ± 20.2	15-100
Role physical from RAND-36†	51.3 ± 39.0	0-100
Bodily pain from RAND-36†	57.5 ± 18.3	13-100
General health from RAND-36†	56.1 ± 17.3	5-95
Vitality from RAND-36†	66.0 ± 16.8	10-100
Social functioning from RAND-36†	80.5 ± 18.5	38-100
Role emotional from RAND-36†	67.0 ± 39.3	0-100
Mental health from RAND-36†	78.4± 15.0	36-100
Physical performance tests		
10-meter walk test (time (s))	5.9 ± 1.4	3.5-14.3
6-minute walk test (distance (m))	480.8 ± 85.2	222.0-709.0
Timed up & go test (time (s))	7.0 ± 1.4	4.5-13.3
Leg extensor power test (W/kg)$	1.1 ± 0.3	0.36-2.26
Passive hip flexion (angle (º))¶	97.4 ±16.8	60-130
Passive hip internal rotation (angle (º))¶	28.8 ± 8.2	10-47

*Western Ontario and McMaster Universities OA Index ranges from 0 mm (no symptoms) to 100 mm (maximal symptoms).

†RAND-36 is the Finnish version of the Short-Form Health Survey (SF-36) assessing wellbeing and ranging from 0 (maximal symptoms) to 100 (no symptoms).

$Leg extensor power was measured by Concept 2-dynamometer.

¶Passive hip flexion and internal rotation of more painful hip was measured by goniometry.

Table 9. Pearson's coefficients for correlation between dependent (outcome) and independent (explanatory) variables.

Variables	WOMAC pain#	WOMAC physical function#	RAND-36 physical function†
Kellgren-Lawrence grade of hip OA∞	.027	.016	-.018
Body mass index (kg/m²)	.137	.252**	-.290**
Comorbidites	.369**	.313**	-.220*
Duration of knee pain (years)	.198*	.195*	-.104
Age (years)	.123	.149	-.138
Education (years)	-.276**	-.264**	.291**
Beck depression inventoryμ	.196	.131	-.184
Life satisfaction scale¤	.299**	.204	-.319**
Smoking (years)	-.102	-.097	-.019
Duration of sport activities (years)	.163	.079	.101
Physical performance tests			
Leg extensor power (W/kg)$	-.191*	-.277**	.256**
Passive hip flexion (angle (º))¶	-.261**	-.286**	.239**
Passive hip internal rotation (angle (º))¶	.050	-.010	.090
Sock test°	.134	.243**	-.303**
10-meter walk test (time (s))	.233*	.208*	-.338**
Timed up & go test (time (s))	.251**	.282**	-.344**
6-minute walk test (distance (m))	-.277**	-.286**	.417**

*p < 0.05 **p < 0.01.

#Western Ontario and McMaster Universities OA Index ranges from 0 mm (no symptoms) to 100 mm (maximal symptoms).

†RAND-36 is the Finnish version of the Short-Form Health Survey (SF-36) assessing wellbeing and ranging from 0 (maximal symptoms) to 100 (no symptoms).

∞Kellgren-Lawrence grade (0 - 4).

μBeck depression inventory scores from 0 to 63. Cut-off point for clinically important depression was 15 or over.

¤Life satisfaction scale; 4-11 (satisfied group scores) 12-20 (dissatisfied group scores).

$Leg extensor power was measured by Concept 2-dynamometer.

¶Passive hip flexion and internal rotation of more severe hip was measured by goniometry.

°Sock test scale from 0 to 3; 0 (no difficulties with simulating sock wearing) up to 3 (remarkable difficulties with simulating sock wearing).

5.2.3 Effectiveness of exercise therapy (III)

Adherence to supervised exercise sessions was 86% during the first intervention year that contained 12 supervised sessions during the first three months and 58% during the second intervention year that contained four additional sessions at the 12 month time point. Adherence to the exercise program was commendable during the first year of follow-up with the mean (range) of performed exercise sessions being 2.5 sessions per week during months 0-3, 2.1 sessions per week during months 4-6 and 1.9 sessions per week during months 7-12. A slight decline was observed during the second year of follow-up with the mean being 1.7 sessions per week during months 13-18 and 1.6 during months 19-24.

According to self-reported disease-specific pain (WOMAC), there was no overall statistically significant effect of exercise intervention on self-reported disease-specific pain (Figure 5) at two years and no statistically significant difference between groups was observed at the different time points.

The overall effect of the exercise intervention on self-reported disease-specific function (WOMAC) was statistically significant (p=0.04) (Figure 6). At the 6 and 18 months' time points a statistically significant difference in favor of the combined exercise and general practitioner care group was observed in the self-reported disease-specific function. No differences were detected between the groups in self-reported physical function scale score of RAND-36.

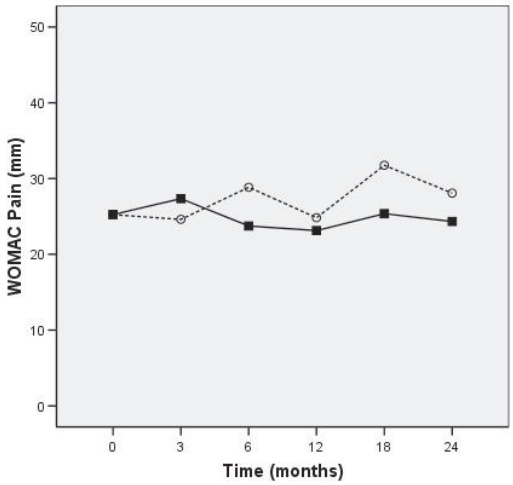


Figure 5. Self-reported disease-specific pain (WOMAC (mean)).

Combined exercise and general practitioner care group ——
General practitioner care group ·····

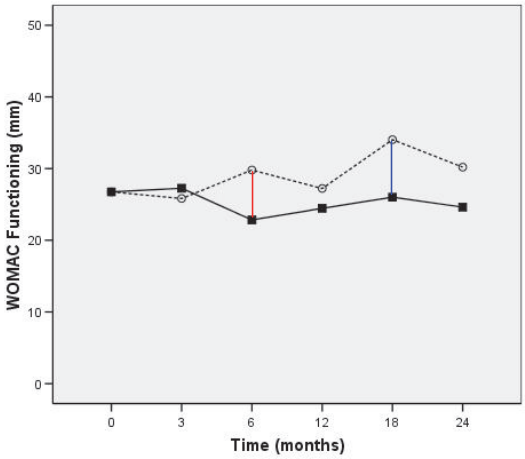


Figure 6. Self-reported disease-specific functioning (WOMAC (mean)).

Combined exercise and general practitioner care group ——
General practitioner care group ·····
p = 0.02 ——, p = 0.04 ——

No statistically significant differences between groups were observed in BMI at the separate time points. Furthermore, there were no significant differences between the groups in measures of physical performance, including the passive internal rotation and flexion of the hip joint, the extensor power of lower limb, in the distance walked in the 6-MWT, in the sock test, 10-MWT and in the TUG tests.

No differences were detected between the groups in the use of paracetamol or weak opioids. At the 12 (p = 0.03) and 18 (p = 0.01) month time points a statistically significant difference in favour of the combined exercise and general practitioner care group was observed in the use of NSAIDs. In the combined exercise and general practitioner care group at the 12 month and 18 month time points 59% (66%) were not using, 31% (25%) were using less than daily and 10% (9%) were using daily NSAIDs. In the general practitioner group at the 12 month (and 18 month) time point 36% (39%) were not using, 55% (50%) were using less than daily and 7% (11%) were using daily NSAIDs.

5.2.4 Cost consequences (III)

Cost consequences of combined exercise and general practitioner care versus general practitioner care alone are shown in Table 10. Neither the number of visits to the doctor nor the mean costs of those visits due to hip OA differed significantly between the groups. The use of physiotherapy due to hip OA was significantly lower in the combined exercise and general practitioner care group compared to the general practitioner care group during the second year of follow-up. In addition, the mean cost of physiotherapy per patient was significantly lower in the combined exercise and general practitioner care group as compared to the general practitioner care group.

5.2.5 Predictors of pain and physical function in two-year follow-up (IV)

Table 11 describes the associations of baseline variables with the outcome variables. Lower disease specific pain and better physical functioning (WOMAC) were predicted by supervised exercise training (p = 0.010, p = 0.004), a higher level of habitual conditioning physical activity (p = 0.048, p = 0.044), a higher educational level (p = 0.004, p = 0.012), the absence of comorbidities (p = 0.042, p = 0.019) and the absence of additional knee OA (p = 0.017, p = 0.021) respectively.

Better general physical function score (RAND-36) was predicted by supervised exercise training ($p = 0.026$), a higher level of habitual conditioning physical activity ($p = 0.012$), a higher educational level ($p = 0.007$) and the absence of additional knee OA ($p = 0.015$).

The following predictors for the RAND-36 physical component summary scores were supervised exercise training ($p = 0.034$), a higher educational level ($p = 0.009$) and the absence of knee OA ($p = 0.043$). Younger age ($p = 0.003$) was associated with better RAND-36 mental component summary scores. Gender, the radiological grade of the hip joint, obesity or being retired predicted none of the outcomes characterising pain or physical functioning in hip OA.

Table 10. Number of the doctor visits (during the first and the second years) and use of physiotherapy services associated with hip OA and total hip arthroplasty surgery and health care system direct costs during the two year follow-up.

		Combined exercise and general practitioner care (n = 55-58)			General practitioner care (n = 51-58)				
Outcome variable (with unit costs (€))°	**Time (mo)**	**Median (range)/ number of patients**	**Mean (SE)**	**Mean (SE) cost per patient (€)°**	**Median (range)/ number of patients**	**Mean (SE)**	**Mean (SE) cost per patient (€)°**	**p≠**	**p (mean cost per patient)°%**
Supervised group-therapy¤ (60.04€)	0-3 12			96.1					
Doctor visits* (81.5€)	0-12 12-24	0 (0 – 4) 0 (0 – 3)	0.5 (0.1) 0.5 (0.1)	77.1 (13.8)	0 (0 -10) 0 (0 – 8)	0.8 (0.2) 1.1 (0.2)	152.0 (28.7)	0.38 0.05	0.07
Physiotherapy§ (91.3€)	0-12 12-24	1 (0 – 6) 0 (0 – 2)	1.3 (0.2) 0.4 (0.1)	157.7 (23.4)	2 (0 – 8) 1 (0 – 5)	2.0 (0.3) 1.3 (0.2)	298.5 (35.0)	0.05 <0.001	0.002
Costs without total hip replacement	0-24			330.9 (30.1)			454.5 (54.7)		0.12
Total hip replacement (8089.6€)	0-12 12-24	2 3		709.6 (305.8)	3 5		1155.7 (433.8)	0.68 0.49	0.51
All costs per patient				1066.3 (331.5)			1406.3 (441.8)		0.13

°An analysis of health care providers direct costs was counted as mean cost per patient (€) from the 0 to 24 month time period based on the supervised group exercise therapy costs in the Mikkeli Health Centre and health care unit costs (visits to the doctor, physiotherapy and total hip replacements) in Finland.
≠Difference in the number of visits to the doctor, sum score of the use of physiotherapy and THA (yes/no) during the first and second year of the follow-up between the groups (Mann-Whitney U-test and Fisher's exact test).
%Difference in the health care providers direct mean cost per patient during two year follow-up between the groups (Mann-Whitney U-test).
¤Exercise, included in intervention (12 group exercise therapy sessions from 0 to 3 months and 4 group exercise therapy sessions from 12 to 13 months).
*Number of visits to a doctor concerning hip OA.
§Sum score of physiotherapy visits including either exercise physiotherapy and/or physical therapy modalities associated with hip OA (not as part of the intervention).

Table 11. Parameter estimates (and their 95 % CIs) from multivariate linear mixed models with the following explanatory variables (one model per dependent variable) i.e. average differences in outcome variables of hip pain and functioning between groups of categorical predictors and average change per single unit of continuous predictors.

Parameter	**WOMAC pain**[a]	**WOMAC function**[a]	**RAND-36 function**[b]	**RAND-36 PCS**[b]	**RAND-36 MCS**[b]
Age (per 10 years)	0.90 (-4.57–6.35)	0.12 (-0.48–0.71)	-0.41 (-1.06–0.23)	-5.10 (-11.00–0.79)	**-8.25**** **(-13.60–-2.91)**[l]**
Gender (male vs. female)	2.36 (-4.02–8.73)	1.62 (-5.31–8.55)	1.62 (-5.92–9.17)	-0.12 (-7.02–6.78)	0.20 (-6.05–6.45)
Education (elementary school vs. secondary school or high school)	**9.61**** **(3.15–16.07)**[c]**	**9.07*** **(2.05–16.09)**[f]**	**-10.59**** **(-18.24–-2.94)**[i]**	**-9.36**** **(-16.35–-2.36)**[k]**	-2.91 (-9.24–3.42)
Comorbidities (no vs. yes)	**-6.30*** **(-12.35–-0.24)**[d]**	**-7.87*** **(-14.45–-1.30)**[g]**	5.77 (-1.40–12.94)	5.10 (-1.46–11.67)	2.16 (-3.77–8.09)
Body mass index (< 30.0 kg/m² vs. ≥ 30.0 kg/m²)	2.51 (-4.27–9.48)	-0.96 (-8.53–6.61)	5.27 (-2.97–13.51)	2.97 (-4.57–10.52)	-1 49 (-8.32–5.33)
Retired vs. employed or part-time employed	0.33 (-7.32–7.98)	3.54 (-4.88–11.79)	-1.18 (-10.25–7.89)	1.46 (-6.83–9.76)	7.48 (-0.01–14.97)
Radiological grade (Kellgren-Lawrence 1 vs. Kellgren-Lawrence 2-4)	1.58 (-4.58–7.75)	0.74 (-5.95–7.43)	0.93 (-6.35–8.22)	0.07 (-6.60–6.74)	0.39 (-5.65–6.43)
Duration of hip symptoms (years)	0.17 (-0.14–0.49)	0.19 (-0.15–0.53)	-0.12 (-0.50–0.25)	-0.18 (-0.52–0.16)	-0.26 (-0.57–0.04)
Knee pain (no vs. yes)	**-7.62*** **(-13.87–-1.36)**	**-8.02*** **(-14.81–-1.23)**	**9.25*** **(1.85–16.65)**	**7.00*** **(0.23–13.77)**	2.09 (-4.03–8.21)
Group (intervention vs. control)	**-10.13*** **(-17.87–-2.39)**	**-11.58**** **(-19.40–-3.77)**	**9.31*** **(1.14–17.47)**	**8.26*** **(0.61–15.91)**	4.86 (-2.60–12.32)
Conditioning physical activity (hours/week)	**-0.48*** **(-0.96–-0.01)**[e]**	**-0.39*** **(-0.84–0.05)**[h]**	**0.56*** **(0.13–1.00)**[j]**	0.42 (-0.01–0.85)	0.42 (-0.03–0.87)

*p < 0.05, **p < 0.001.

[a]Western Ontario and McMaster Universities OA Index (WOMAC (mm)).
[b]The Finnish version of the Short-Form Health Survey (SF-36) subscales for function and Physical Component Summary (PCS) and Mental Component Summary (MCS) scores.
[c]9.61 higher pain score (0 = no symptoms, 100 = maximal symptoms) with lower educational level.
[d]6.30 lower functional impairment with no comorbidities.
[e]0.48 lower pain score in relation to increase of conditioning exercise training for one hour per week.
[f]9.07 higher functional impairment with lower educational level.
[g]7.87 lower functional impairment with no comorbidities.
[h]0.39 lower functional impairment in relation to increase of conditioning exercise training for one hour per week.
[i]10.59 higher functional impairment (0 = maximal symptoms, 100 = no symptoms) with lower educational level.
[j]0.56 lower functional impairment in relation to increase of conditioning exercise training for one hour per week.
[k]9.36 higher functional impairment with lower educational level.
[l]8.25 higher mental impairment in relation to increase of 10 years of age.

6 Discussion

6.1 THE PROSPECTIVE POPULATION-BASED STUDY (ARTICLE I)

6.1.1 Methodological considerations

One of the fortes of this study is its design: it was a population-based, prospective study with a long follow-up period extending up to 22 years. A limitation is that the diagnostic criteria of the ACR were not applied. The explanation for this is that the baseline survey was conducted more than two decades ago when the ACR criteria had not been devised. In the follow-up examination, the original criteria of hip OA used in the Mini-Finland Health Survey were conformed to. Hip OA was diagnosed by specially trained physicians who applied uniform diagnostic criteria that took into account medical histories, symptoms and the physical status of the hip joints assessed according to a standardised clinical procedure. However, it is possible that there was some inconsistency between physicians in the diagnostics of hip OA. Therefore the repeatability of the diagnoses was tested across the field teams in the Health 2000 Survey (follow-up) and repeatability shown to be acceptable. This was as displayed in the previous national health examination survey using similar protocol and the same diagnostic criteria (Heliövaara et al. 1993a). In the current survey, the agreement between definite clinical and radiological diagnoses of hip OA proved to be moderate (Kaila-Kangas et al. 2011). The results of the present study may therefore differ from the observations of previous studies, which have diagnosed hip OA on the basis of radiographic findings.

The two-stage selection from the baseline examination to the invitation and subsequently to the participation in re-examination may have attenuated the risk estimates. At the first stage, factors associated with morbidity, and disability, such as old age, male sex, a lower level of education, a history of very heavy manual labour and all obvious factors that are more common in rural than urban settings, led to a decreased likelihood of re-examination. At the second stage, obesity 22 years earlier was still associated with non-participation. Consequently, the prevalence of major risk factors and the magnitude of the effects of the risk factors may have lowered, whereas any severe bias in the other direction would have barely registered.

6.1.2 Main findings

Physical loading related to heavy manual labour and permanent damage as a consequence of any musculoskeletal injury proved to be independent risk factors for developing hip OA in this population-based study.

Several studies have shown that farmers have a higher risk of developing hip OA than other occupationally active men (Croft et al. 1992, Thelin and Holmberg 2007). Previous studies have also suggested that lifting heavy objects is a significant risk factor for clinical and radiological hip OA (Lievense et al. 2001, Jensen 2008, Kaila-Kangas et al. 2011). A recent review concluded that there is moderate to strong evidence for a relationship between heavy lifting and hip OA (Jensen 2008). However, the role of heavy workload in the pathogenesis of hip OA has not been clarified. A widely accepted theory is that susceptibility to OA may be the result of an interaction between systemic (such as genetics, dietary intake, oestrogen use, and bone density) and biomechanical factors (such as muscle weakness, obesity, heavy workload, and join laxity) (Felson et al. 2000).

OA may occur when activity is excessive or when a lower load acts on a vulnerable joint. Considerable effort has been made over the years to describe the variety of forces that contribute to the joint reaction force of the human hip (Bergman et al 2001, Arokoski et al.

2000). Direct measurements of such forces are very cumbersome and to date are not possible in humans. During slow walking the hip joint is loaded with approximately 3 times body weight just after heel strike, with forces increasing 4 times body weight just before toe-off (Kabada et al. 1989). During running, forces equivalent to 7 to 8 times body weight are transmitted across the hip joint during heel strike and increase to a value slightly higher than that during toe-off (Kabada et al. 1989).

Cartilage damage attributable to trauma can compromise the ability of cartilage to function and survive in the strenuous mechanical environment normally found in load-bearing joints. Joint injury and subsequent joint instability, from loss of ligamental or meniscal support, are known to be significant risk factors for knee OA (Radin et al. 1991). In the Framingham study (Felson 1988) both males and females who had suffered major knee injuries in the past were subsequently prone to develop knee OA. However, major injuries leading to ligamental tears and cartilaginous damage are rare in the hip. Cross-sectional studies (Heliövaara et al. 1993b, Cooper et al. 1998, Lau et al. 2000, Thelin and Holmberg 2007) have inferred that traumatic injuries might also give rise to hip OA. Nonetheless, the findings of the present study were surprising: individuals who had sustained traumatic injuries displayed a fivefold risk of developing hip OA during the follow-up period. A closer inspection of the anatomical distribution of the traumatic injuries indicated that the hip joint was only rarely directly affected in these cases. One possible explanation for this finding might be that the cases were overloaded and under pressure at work and therefore more liable to sustain traumatic injuries in a variety of parts of the body.

The hypothesis of our study was that, within 22 years of follow-up, excess body weight would emerge as a strong independent risk factor for hip OA. However, the association of obesity with increased risk of hip OA was not found. Although epidemiological studies have observed the direct association of obesity with hip OA (Jiang et al. 2011), the results of some studies are inconsistent (Heliövaara et al. 1993b, Hartz et al. 1986, Gelber 2003). It has also been suggested that metabolic or inflammatory factors contribute to the relationship between obesity and OA (Vuolteenaho et al. 2009). Recent research seems to be focused on distinguishing specific phenotypes of OA by different pathogenic pathways (Bijlsma et al. 2011). These may reveal a new perspective and lead to a deeper understanding development of OA helping to find new treatment strategies at an earlier stage. It is hoped that future research will clarify the potential role of systemic and local inflammatory and metabolic factors associated with adipose tissue as contributors to the risk of hip OA.

6.1.3 Clinical implications

Working conditions and workplace ergonomics should be taken into account in order to develop strategies aimed at the prevention of hip OA and its medical, functional and economic consequences. Using a preventative strategy to protect individuals from excessive workloads could probably avoid many cases of hip OA.

6.2 RANDOMIZED CONTROLLED TRIAL (ARTICLES II, III, IV)

6.2.1 Methodological considerations

A particular strength of the present study was the design; a randomized controlled trial. Moreover, patients included had all been diagnosed with hip OA prior to the study and used interventions especially designed for hip OA. The subject groups had hip OA with mild to moderate symptoms, as indicated by relatively low WOMAC scores of pain and physical function, which are commonly seen in patient groups in primary care (Lievense et al. 2007). In addition, patients with hip OA with K-L grade 1 were included although grade 1 is not considered to be a definite indication of OA. This inclusion decision was taken because OA diagnosis is based not only on radiological but also on clinical symptoms as indicated in the clinical criteria of the ACR (Altman et al. 1991). Although the patients scored mild to moderate symptoms on the WOMAC, a total of 13 patients (11%) had to undergo

total hip replacement surgery within the 2-year period. This indicates that the patients included in the trial had noticeable symptoms for which they needed efficient treatment modalities.

Despite the appropriate randomisation and concealment of allocation, an unexpected difference in WOMAC-pain, one of the primary measures of the study, was observed between the groups. Repeated measures ANCOVA was used to analyse the data. Treatment group, measurement time (visit) and their interaction were used as fixed factors in the model. WOMAC-pain at baseline was included in the model as continuous covariate and other adjusting variables as fixed factors or covariates depending on their measurement scale. Repeated measures analyses were used to adjust for the differences in the response variable's baseline values, in order to minimise the risk of bias.

The underlying study principle was that any possible result could be applied in primary health care as well as in specialist clinics. Therefore, the intervention was accomplished as collaboration between the rehabilitation clinic of a central hospital and the primary health care organisation with the participants mainly being recruited from the primary health care. Consequently, the study sample comprises a representative sample of patients with hip OA and not those collected from patients attending orthopedic clinics. This can be considered as a genuine strength of the study. It was also important that the exercise programme could be performed without the requirement for specialist training equipment. For practical reasons the exercise program was generic and not individually tailored for each participant. Greater improvements may have been reached in self-reported function and performance based outcome scores if more individualised and intensive strengthening exercise treatment programmes had been used (Hinman et al. 2007).

The majority of studies evaluating exercise as treatment for patients with OA have encountered difficulties in compliance with treatment by the subjects themselves (Williams et al. 2008, Domino 2005). The low dropout rate is a major strength of this study. The exercise programme was generally well tolerated, resulting in commendable adherence to it especially during the first year. The mean of exercise sessions per week was 2.5 during months 0-3, 2.1 during months 4-6 and 1.9 during months 7-12. A slight decline was assessed during the second year of follow-up with the mean being 1.7 in months 13-18 and 1.6 in months 19-24. These exercise frequencies are below those recommended for the study's rehabilitation programme. For example, research has consistently shown that as many as half of all patients with diagnosed hypertension do not follow their recommended drug regime (Domino 2005, Williams et al. 2008). This issue manifests itself equally with respect to exercise therapy and at worst, can nullify any conclusions about therapeutic efficacy. The duration of the exercise period and the amount of individual exercises performed per session would be sufficient in terms of evaluating the potential effect of exercising (Feigenbaum and Polock 1999, Wernbom et al. 2007).

6.2.2 Main findings

The present randomized controlled trial showed slight benefits of improved self-reported physical function but detected no significant effect on disease-specific pain during a two-year follow-up. However, deeper analyses of the study in the same subjects provides somewhat stronger evidence that exercise therapy can reduce pain and help maintaining physical function in hip OA patients. This is because exercise training generally predicted a lower presence of pain and better functional status in patients with hip OA. The weaker evidence from the randomized controlled trial than from the latter analyses may be attributable to the relatively small study population. The smaller group lowers statistical power to detect statistically significant effects in the intervention study. The more detailed analyses of pain and physical function resulted in an improved outcome in the exercise therapy group. The results emphasise exercise training to be beneficial in the management of hip OA and are aligned with existing recommendations (Roddy et al. 2005, Hochberg et al. 2012).

In this study, there was no significant difference in self-reported pain score between the groups. However, participants in the combined exercise and general practitioner care group used less NSAIDs compared to the general practitioner care group. The use of painkillers may be a more objective indicator of long-term pain than pain symptoms. The difference between the groups was nearly significant at the 6-month time point and statistically significant at the 12 and 18-month time points; the second year of follow-up. These results support the view that exercise has a long-term pain-relieving effect in hip OA.

The minimal difference in WOMAC sub-scores of 0.67 – 0.75 points (scale 0 – 10) in absolute values and 11 – 26% in relative values has been suggested necessary to achieve clinical significance in rehabilitation studies (Angst et al. 2001, Fransen et al. 2008). In this study, the mean difference in WOMAC physical function scores between the groups was 7.5 mm (scale 0-100) at 6 months and 7.9 mm at 18 months, which can be considered relatively small. Tubach et al. (2005) determined the minimal clinically significant improvement of functional impairment in patients with knee and hip OA. They suggested that the statistically significant difference is predominantly a matter of sample size. Whereas a more difficult issue is whether an observed or estimated difference is clinically important. They assessed that the minimal clinically important improvement in absolute (and relative) change of WOMAC function subscale in knee and hip OA was –7.9mm (– 21.1%). In the present study the mean statistically significant difference in the improvement of WOMAC function index between the groups was about 8 mm (i.e. about 24% difference) at 6 and 18 months, the difference could be considered clinically significant.

It was not possible to undertake a comprehensive cost-effectiveness analysis, because only a limited number of direct medical costs and no indirect costs were assessed. Direct medical costs due to supervised group therapy, visits to the doctor, physiotherapy and THA are considered the most important expenses for the cost-effectiveness analysis. In this trial the number of THAs was lower in the combined exercise and general practitioner care group than in the general care group. However, the observed difference may be due to chance because of a small number of subjects who needed THA in the study groups. In general, this study provides only weak evidence for the cost-effectiveness of exercise therapy. This was because it did not include a sufficient number of subjects for comprehensive cost-effectiveness analyses.

It was found that a higher educational level, the absence of comorbidities and additional knee symptoms as well as being in the exercise therapy group predicted lower pain scores and a better function during a two year follow-up. Furthermore cross-sectional analyses at baseline indicated that educational level, life satisfaction, the duration of knee symptoms and the number of comorbidities were associated with self-reported pain and function in hip OA.

Educational level and working status predicted a better outcome in the present longitudinal study, whereas disease-related factors showed no or only a weak association with pain and functional status. A recent study (Schäfer et al. 2010) demonstrated that socioeconomic position (social, educational and occupational factors) had a significant impact on functional outcome and response to hip replacement. The present study is the first to report the association of socioeconomic position with pain and physical function prior to hip replacement among patients with hip OA.

The results of the present study suggest that comorbidities predict a poorer pain and physical function outcome among the hip OA patient during a two-year follow-up. It was also demonstrated that knee pain or knee OA, in addition to hip OA, are significant when determining the factors affecting pain and functional status. This is the first longitudinal study on these associations among patients with hip OA. It has been suggested that comorbidities and cognitive decline also increase limitations in activities in elderly patients with OA (van Dijk et al. 2009). OA is one of the diseases with a high rate of comorbidities (Leite et al. 2011). There is evidence that as high as 68-85% of patients with OA have comorbidities (Tuominen et al. 2007, van Dijk et al. 2009). Conditions that frequently occur alongside

OA are diabetes, hypertension, depression and cardiovascular diseases (Lago et al. 2011) and often comorbidities are related to disability (Marks and Allegrante 2002). Cognitive impairment is frequently observed in the elderly but their prevalence and association with limitations in activities have not been studied in patients with OA.

Leite and co-workers found, in a cross-sectional study, that hip OA patients often have depression, metabolic syndrome and its components, which can worsen pain and physical dysfunction (Leite et al. 2011). Dekker and co-workers indicated that comorbidities are important risk factors for functional decline among patients with hip or knee OA (Dekker et al. 2009). Such results emphasise the requirement for assessing and treating those comorbidities in OA patients.

6.2.3 Clinical implications

A low educational level, life dissatisfaction and comorbidities were important determinants of self-reported pain and physical dysfunction. Factors explaining and predicting disability and pain in hip OA are multidimensional and no single factor was identified as more significant than others.

The present two-year randomized controlled trial shows that exercise therapy may slightly improve self-reported physical function in individuals with hip OA. However, it is unclear whether the improved physical function translates into true improvement in physical performance or reduced health care costs. A higher educational level, absence of knee OA and comorbidities, supervised exercise training and habitual conditioning physical activity predicted a lower existence of pain and a better functional status. The radiographic severity of hip OA was associated with pain and disability in the prospective study.

The results of the present study emphasise the requirement for focusing not only on disease-specific impairment (e.g. radiological severity of hip OA) as well as general support such as preventing the functional decline associated with the disease. This type of global approach to rehabilitation, taking into account individuals background (education) and comorbidities, is important when developing optimal treatment strategies for hip OA. The results of this study provide additional evidence to support the view that clinical decisions cannot be made only by radiographic findings of the hip joint alone; symptoms and physical function, of the patient suffering from hip OA, are also important factors.

7 Conclusions

The principal findings of these studies (Papers I-IV) are:

I
Physical loading related to heavy manual labour and musculoskeletal injuries are independent risk factors for developing hip OA. Working conditions and ergonomics should be taken into account in the prevention of hip OA. (I).

II
Exercise therapy for hip OA had no significant effect on self-reported pain or generic physical health, but it slightly improved self-reported physical function in individuals with hip OA. It is unclear whether the improved self-reported physical function translates into true improvement in physical performance or reduced health care costs (III).

III-IV
Factors explaining and predicting disability and pain in hip OA are multidimensional and no single factor was more significant than any other (II). Higher educational levels, absence of knee OA and comorbidities, supervised exercise training and habitual conditioning physical activity predicted a lower presence of pain and a better functional status in patients with hip OA (IV).

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Riikka Elina Juhakoski

Hip Osteoarthritis; Risk Factors and Effects of Exercise Therapy

The causes of hip osteoarthritis (OA) are heterogeneous with genetic, environmental and lifestyle-related risk factors influencing the development of the disease. Hip OA causes pain and disability and reduces the quality of life. In this thesis, risk factors for hip OA and effects of exercise therapy in hip OA were determined. Heavy manual work and injuries increased the risk of hip OA. Exercise did not effect on pain, but slightly improved function.

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