MUSCLE MASS AND FUNCTION AFTER TOTAL HIP ARTHROPLASTY

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To Märtha and Ingrid
ABSTRACT

Osteoarthritis (OA) of the hip is a common disease among elderly causing pain, joint stiffness and reduced mobility. Outcome studies have shown total hip arthroplasty (THA) to be a successful surgical procedure. Studies of muscle strength and function after THA are more scarce and results vary. It has been suggested that unloading of the OA limb due to pain, results in hip and thigh muscle weakness and atrophy causing an abnormal gait and impaired postural control. Muscle atrophy can be quantified with computerized tomography (CT) by determination of cross-sectional area (CSA) and radiological density (RD; in Hounsfield units: HU). Atrophy will manifest as a reduced CSA and RD, where a lowered RD represents a muscular fatty infiltration. The aim of this thesis was to characterize muscle strength, atrophy, gait and postural stability in patients with unilateral hip OA before and after operation with THA. We hypothesized that muscles would not recover fully after operation.

We have evaluated the reproducibility of a dynamometer assessing maximal isometric voluntary force of hip and knee muscles and an opto-sensor walkway detecting limp. A test-retest design was used. Ten young and thirteen aged healthy volunteers and eleven patients with unilateral hip OA were tested for muscular strength. Twenty-five volunteers underwent gait analysis. Coefficient of variation (CV%) for unilateral strength measurements ranged between 7-12 % and for gait parameters between 4-8 %.

Twenty patients with unilateral OA were assessed preoperatively, 6 months and two years after THA for strength of hip and knee muscles, gait, postural control and clinical scores (HHS, SF-36, EQ-5D). Also, CSA and RD of hip, thigh, calf and back muscles were assessed using CT. Preoperatively, strength in OA relative to the healthy limb was reduced by 9-27 % in all muscles except knee flexors. CSA was reduced by 5-15 %, except for gluteus medius/minimus and ankle plantar flexors and RD was reduced by 3-14 HU. Gait analysis demonstrated a shorter single stance phase (limp) for the OA compared to the healthy limb preoperatively. No significant difference in postural control between healthy and OA limb could be demonstrated.

At the two years follow-up, hip muscles showed a remaining 6 % weakness in OA compared to the healthy limb. Preoperatively and 6 months postoperatively that deficit was 18 % and 12 %, respectively. Among individual muscles the largest deficit (15%) was observed in hip abductors. Knee extensors and calf muscles recovered fully. There was still a reduction in CSA for m. iliopsoas (7.0 %) and hip adductors (8.4 %) and in RD for mm. gluteus maximus (10.1 HU), gluteus medius/minimus (5.6 HU), iliopsoas (3.9 HU) and adductors (2.4 HU). Limp was recovered already at the 6 month follow-up. Bilateral postural stability and all clinical scores improved after operation.

We concluded that our dynamometer system and technique for gait analysis provides reliable measurements. Muscles acting about the hip and knee joints showed substantial loss in strength and mass before operation. Decreased muscle CSA could not fully explain the strength loss. Infiltration with fat in OA limb muscles was substantial and if not adjusted for there is a risk that muscle atrophy is underestimated. Two years after THA there is a persisting hip muscle atrophy and weakness, marked at 6 months. An earlier operation, a less invasive surgical trauma or a more qualified rehabilitation model, targeting hip abductors might speed up muscular recovery.

Key words: Osteoarthrosis, Arthritis, Joint disease, Hip muscle strength, Hip muscle function, Outcome, Elderly, Attenuation, Fatty infiltration, Gait analysis, Balance
LIST OF PUBLICATIONS


IV. Rasch A, Dalén N, Berg HE. Muscle strength, gait and balance in 20 patients with hip osteoarthritis followed 2 years after THA. Submitted for publication.
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INTRODUCTION

Osteoarthritis (OA) is a common disease among elderly (Felson and Zhang 1998) and the prevalence is known to increase with age (Hamerman 1995). The symptoms are pain and joint stiffness due to the destruction of joint cartilage leading to restricted locomotion activity. Unloading of the painful OA limb will result in muscular atrophy and weakness which is one of the earliest signs of hip and knee OA (Hurley 1999). The mechanism for the atrophy prior to operation, or the anticipated postoperative recovery, has not been identified. Both factors precipitated by the painful OA joint, and the indirect effects of limb unloading might trigger muscular adaptation. Since the causes of OA remain unclear there is no way to prevent or slow the progression of the disease. Initial treatments are anti-inflammatory drugs, physiotherapy and weight loss and if that is insufficient the patient will become a candidate for total hip arthroplasty (THA).

Total hip arthroplasty is a successful surgical procedure to relieve pain and discomfort in end-stage hip osteoarthritis. It is one of the most common operations in the developed world and due to an increasing aged population the volume is increasing every year. Sir John Charnley developed the concept of total hip replacement in the early sixties and since then the surgical technique and postoperative rehabilitation have improved and as a consequence the expectations on the outcome have increased as well. The patients not only expect a pain free joint but also a fast return to normal life and a normalization of physical function (Kennedy et al. 2006). Several different surgical approaches are used, including less invasive techniques with the objective to preserve soft tissue integrity and function (Berry et al. 2003) as well as faster rehabilitation and a reduced hospital stay. At the same time, the use of hip resurfacing prosthesis in young active patient groups are growing where muscle fibres are more traumatized and larger surgical incisions are needed. There is a large gap of knowledge about postoperative muscular recovery and function after those operations. Some reports of damages of the gluteal nerves and hip muscles related to different surgical approaches have been published and hip abductor damage has been correlated to limp and pain (Meneghini et al. 2006).

Loss of lower limb muscle strength has been shown to be a predictor for the onset of activity of daily living (ADL) dependence in aged individuals (Rantanen et al. 2002) and several studies have demonstrated the relationship between muscle strength and walking capacity (Manini et al. 2007, Rantanen et al. 1994, Wolfson et al. 1995) and muscle strength and postural stability (Fiatarone et al. 1990). Maintenance of locomotion activity is one of the most important factors influencing physical function in OA patients (Bendall et al. 1989, Vaz et al. 1993) and postural stability is of great importance since an impaired balance and muscular strength are major risk factors for causing falls in elderly (Gehlsen and Whaley 1990, Whipple et al. 1987). It would therefore be of interest to characterize the typical OA patient, and specifically to value the need for perioperative intervention. Thus, data can be used both to design specific rehab training programs, and to evaluate and develop surgical techniques.
A substantial muscular weakness has been observed on the affected side; 30-50% strength loss compared to healthy side (Arokoski et al. 2002, Horstmann et al. 1994, Shih et al. 1994), but comparisons between the changes in muscular force and mass along the limb are still lacking. A basic test of muscular strength in hip patients includes force measurements of hip extension, flexion, abduction and adduction (Markhede and Grimby 1980, Nemeth et al. 1983, Wretenberg and Arborelius 1994). But there are several reasons to also incorporate knee muscle strength. For example, the primary knee flexor muscles (hamstrings) are of major importance also for performing effective hip extension (Markhede and Grimby 1980). Moreover, the adaptation to hip joint disease, including the physical inactivity due to pain upon weight-bearing, probably affects multiple lower limb muscles. Also, for comparisons with the vast scientific database on the adaptation of knee joint muscles, including knee OA (Slemenda et al. 1997), the ability to map out muscular changes along the limb would clearly add scientific value. The majority of earlier studies have evaluated hip abduction strength only, and we found no study with the simultaneous measurement of hip and knee muscle strength in OA patients.

One objective of this study was to measure a complete set of muscle actions around the hip and knee joints, in order to map out muscle function of both lower limbs. Longitudinal data of hip muscle strength after THA is scarce (Bertocci et al. 2004, Horstmann et al. 1994) and postoperative data of muscle atrophy has only been presented for the thigh (Suetta et al. 2004). Because longitudinal information of hip muscle atrophy is still lacking, a second objective was to quantify the loss of contractile muscle mass in the major muscle groups responsible for hip and knee function.

Aged and inactivated muscles are known to have increased fat content (Goodpaster et al. 2001) and therefore the conventional use of muscle volume or cross-sectional area (CSA) to quantify muscle mass might overestimate the actual amount of contractile muscle. An additional loss of contractile muscle can be inferred from the fat infiltration, as indicated by a reduced radiological density (RD) in Hounsfield units (HU) (Goodpaster et al. 2000). We therefore employed computerized tomography (CT) to measure both CSA and radiological density (RD) of each muscle group. Fat infiltration of the supraspinatus muscle after a traumatic shoulder rotator cuff tear has been deemed irreversible (Gladstone et al. 2007), and thus a negative prognostic factor for muscular recovery. Preoperative fat infiltration in hip and thigh muscles has not previously been acknowledged, and its potential for resorption after operation has yet to be proven. Although a few studies have indicated altered muscular composition in response to training (Horber et al. 1985) or inactivity (Berg et al. 1991) (Manini et al. 2007), there are currently no data to tell whether there is a plasticity in muscular fat in response to rehabilitation after THA.

The main purpose of this study was to map out the natural history of muscle mass and strength in the lower limb during the first two years after standard THA. We hypothesized that several muscles along the extremity would not recover fully after postoperative rehabilitation, because of tissue changes due to a chronic preoperative inactivity. A second purpose was to characterize changes in gait and postural control after operation and we hypothesized a postoperative recovery due to a reduced pain. To achieve this purpose, we have developed a dynamometer for hip and knee muscle
strength assessments, which is well tolerated by elderly patients with hip osteoarthritis, and equipment for gait analysis. We also introduced a test protocol for CT measurements where identical anatomical levels within the muscle can be identified that is crucial for accuracy of repeated measurements.
AIMS

The general aim of this study was to evaluate the postoperative long term recovery of muscular morphology and function in lower extremity in patients with unilateral osteoarthritis of the hip. The specific aims were:

I To evaluate a dynamometer for hip and knee muscle strength assessments, which are well tolerated by old sedentary patients with hip osteoarthritis, and to evaluate equipment for gait analysis.

II To quantify preoperative muscular atrophy and strength loss of muscles in lower extremity in patients with unilateral hip OA.

III To quantify postoperative recovery of muscular atrophy in lower extremity in patients with unilateral hip OA operated with THA.

IV To quantify postoperative recovery of muscle strength in lower extremity in patients with unilateral hip OA operated with THA, and to characterize gait and postural stability before and after THA.
PATIENTS

Paper I

Thirteen healthy aged (eight males and five females; 69±8 yrs, 174±8 cm, 78±13 kg) and ten young (five males and five females; 36±6 yrs, 179±10 cm, 73±14 kg) individuals were used to test the reproducibility of the muscle strength measurements. They were recruited from hospital staff (n=13) or from local recreational walking groups (n=10). Accepted subjects had no pain or limitation in hip movement and no previous surgery of the lower extremity.

A group of eleven patients (six males and five females; 69±8 yrs, 173±7 cm, 76±15 kg) with unilateral hip OA were tested to evaluate the test procedure for a group of OA patients. They were recruited from our waiting list for hip arthroplasty and were tested prior to planned surgery.

Twenty-five healthy volunteers (10 males and 15 females; 42±14 yrs, 177±9 cm, 73±14 kg) underwent two sessions of gait evaluation, approximately one week between sessions. Individuals with neurological diseases or lower extremity co-morbidities such as misalignment or osteoarthritis at other joints that could have affected gait were not included.

Paper II-IV

Twenty two patients (4 males and 18 females; 67 (54 to 77) yrs, 168 (157 to 183) cm, 79 (57 to 114) kg) with unilateral hip osteoarthritis planned for total hip replacement were consecutively recruited between January to May 2005, and measured the day before surgery and at 6 months and 2 years after THA. Accepted subjects had no previous surgery of the lower extremity and individuals with neurological and advanced cardiopulmonary diseases or lower extremity co-morbidity were excluded. One patient with a peroperative femur fracture and one patient operated with a lateral approach were excluded from data analysis. Thus, all presented patients were operated with the posterior approach (Moore). At the six months follow-up, there were three drop-outs (one muscular tear just before measurements, one patient emigrated and one patient did not want to attend) and at the 2 years follow-up all 20 patients were measured. One patient had an early postoperative hip dislocation treated with a brace for six weeks. Five patients were not able to perform the preoperative gait analysis and one foot standing and one patient could not perform two foot standing due to pain and the use of crutches. All 20 patients were measured for gait and postural control at six months and two years follow-up.
METHODS

General design

In the first experimental study, we have tested the reliability of a dynamometer especially developed for measurements of muscles acting about the hip and the knee joints (see details below). The individuals were tested on two separate days with an interval of at least one week, where test conditions and test leaders were maintained. Both right and left limbs were measured. In this study we also tested the reliability of an opto-sensor walkway especially developed to detect limp (see details below).

In the second experimental study, a cohort of twenty two patients (4 males and 18 females; 67 (54 to 77) yrs, 168 (157 to 183) cm, 79 (57 to 114) kg) with unilateral hip osteoarthritis planned for total hip replacement were followed for two years after THA. Measurements of muscle strength and morphology in lower extremity, gait, postural stability and clinical scores were collected the day before surgery and at 6 months and 2 years after. In paper two, preoperative data of muscle strength and morphology is presented and in paper three, postoperative data of muscle atrophy and clinical scores are presented. In paper four, we report postoperative data of muscle strength and results from gait and postural control measurements.

All patients except one, which was excluded, were operated with a posterior (Moore) approach. We used two different types of hip prostheses, one cement less porous coated femur stem, Bi-metric (Biomet Inc., Warsaw, IN, USA), and one cemented polished and tapered femur stem , CPT (Zimmer Inc., Warsaw, IN, USA). The acetabular component used in all patients was a cemented highly cross linked polyethylene cup, Muller (Stryker Howmedica Inc., Rutherford, NJ, USA). All patients were allowed weight bearing.

The clinical scores SF-36, Harris hip score (HHS) and Euroqol (EQ-5D) were collected from all patients. Medical history, duration of hip symptoms and the use of pain relief medications were noted. The subjective severity of hip pain was rated before measurements using the visual analog scale (VAS); range 0-10, where zero is no pain and ten is unbearable pain. All patients completed ten sessions of weekly group training postoperatively and there after home exercises were encouraged. At the two years follow-up, training habits varied among individuals with a range from no exercise to several times per week. Body weight after 2 years 80 (60 to 127) kg, indicated no major change in body composition. All patients provided written informed consent before participation.

Muscle strength measurement

_Hip and knee strength dynamometer_: A test device that allows measurement of hip or knee muscular strength was developed. In the seated position, unilateral isometric knee extension or flexion force is measured. Hip extension and flexion as well as abduction or adduction force is measured with the subject in the standing semi-prone position (see photos). Traditional strain-gauges (Burster Gmbh, Germany) are
incorporated in padded sling latches which are fixed around the distal ankle or thigh, respectively. Using four different strain-gauge positions, and the two alternative body positions, a total of twelve different isometric strength measurements can be obtained (see further below descriptions). Calibration of the dynamometer was carried out before or after measurements, using standardized weights. The dynamometer was connected to a data processing system (MuscleLab; Ergotest Technology AS, Norway), where the force curve could be monitored during tests, and accepted measurements stored for later processing.

**Knee strength assessment:** When measuring knee extension or flexion, the patient is seated with a 90-degrees flexion of the hip and knee. The pelvis is stabilized with a strap and the arms crossed over the chest to minimize interference of accessory muscle groups. A second strap stabilizes the thighs to the flat seat. The strain-gauge was attached with the sling around the ankle. Patients were first tested for right knee extension, then flexion, whereafter the procedure was repeated on the left limb. Each test started with a total of five sub-maximal contractions at 70 (x3), 80 and 90 per cent of the perceived voluntary maximum, respectively to warm up and to get familiar with the testing device and procedure. Thereafter two maximal isometric contractions were performed, approximately 3-5 sec each, and separated by at least twenty seconds rest. Similar verbal encouragement was given during all measurements. If force measurements differed more than five per cent, then a third measurement was performed. The force signal was digitized at 200 Hz into the MuscleLab system. From each maximum trial contraction, the peak force value (Newton; N) of a 1.0 sec window average was selected. Mean values of the two best trials were used for comparisons between test sessions (Berg et al. 1997).

**Hip strength assessment:** When measuring hip muscles, the standing subject leaned forward 45 degrees to rest the trunk and pelvis against an abdominal platform support (see photos). The pelvis was stabilized with a strap around the upper gluteus, and the subject kept a firm grip on two handles. While one limb supported the body weight, the other was attached to the dynamometer with the sling latch re-adjusted around the thigh just above the patella. The tested limb was held with semi-flexed knee while the support leg was straight. Patients were tested in the order of right hip extension, flexion, abduction and adduction, whereafter the procedure was repeated on the left limb. Warm up and test procedures were identical to the knee strength assessment.

To clarify that different muscles are acting about different joints, averages were formed for knee extension/flexion (Ktot) and hip extension/flexion/abduction/ adduction (Htot). Also an average of all six measurements (Tot) was formed to be able to detect small changes in force over time. Average knee force (Ktot), hip force (Htot) or total limb force (Tot) were formed by calculating the arithmetic means of individual measurements. To evaluate if a low preoperative muscle function predispose for a slow postoperative recovery patients were divided into two equal size groups; low or high force deficit, according to their preoperative force deficit in OA compared to healthy limb for total hip force (Htot), and differences in force deficit between the two groups were compared using Students t-test at 6 months and 2 years after THA.
Hip strength assessment

Knee strength assessment
Computerized tomography (CT)

Muscle cross-sectional area (CSA; mm²) and radiological density (RD; in Hounsfield units, HU) were assessed in multiple hip, thigh, calf and back muscle groups bilaterally, using trans-axial CT scans (General Electric Spiral scan, GE Medical System, London, UK; 130kV, 200mAs, 1.5 sec scan time). Radiological density values on CT are measured in HU, which are based upon a linear attenuation coefficient scale using water (0 HU) and air (-1000 HU) as the reference (Hounsfield 1973). CT can discern fat and muscle because of their different attenuation characteristics. It is commonly regarded that fat tissue displays attenuation values in the negative range (-190 to -30 HU) and muscle has a positive attenuation (0 to 100). Adipose tissue is indicated by darker areas, muscle is lighter and bone is very bright due to a very high attenuation on CT (Fig 1.).

Scans were obtained after a 30-60 minute bed rest to minimize the influence of postural fluid shifts on muscle CSA (Berg et al. 1993). The radiation dose was minimized by limiting scan volumes via anatomical landmarks on scout images (Fig 1.). Thus, two scans (10 mm slice thickness) of the thigh and two scans of the calf were obtained 20 cm proximal and 12 cm distal to the joint line of the right and left knee, respectively. In order to isolate comparable images (5 mm slice thickness) of the right and left hip muscles at the top of foramen ischiadicum, one 30 mm slab was obtained just proximal to the caput femoris. One slice (10 mm) was obtained through the central part of the third lumbar vertebrae to visualize the erector spinae and m. psoas. Using dedicated software (Osiris 4.0, University Hospital of Geneva, Switzerland) for computerized planimetry, areas of interest of individual muscles or groups were manually circumscribed and automatically computed. CSA and RD for each individual muscle group were determined twice by two independent observers to calculate the intra and inter-observer reproducibility. The average of these measurements was used for comparison between healthy and OA limbs. The gluteal muscle group, as assessed from hip scans comprises musculus gluteus maximus (primary extensor) and gluteus medius et minimus (abductors). In paper II, m. psoas assessed from the lower back scan and m. rectus femoris from the thigh scan were chosen as hip flexors. In paper III, m. iliopsoas was chosen as the hip flexor and assessed from hip scans. Hip adductors were assessed from thigh scans, where m. adductor magnus dominates at this anatomical level. The knee extensor group comprises vastus lateralis, medialis and intermedius. The hamstring group (m. biceps femoris brevis et longus, semimembranosus and semitendinosus) was used as the knee flexors. Ankle plantar flexors comprise m. soleus and m. gastrocnemius and the ankle dorsal flexors comprise m. tibialis anterior, m. extensor digitorium longus and m. extensor hallucis longus. RD of separate muscles was averaged across each CSA.

Goodpaster et al (Goodpaster et al. 2000) conducted repeated CT measurements and demonstrated a variability of less than 1% (CV%) in RD of thigh or calf muscles. We have previously found the variability (CV%) in thigh and calf muscle CSA less than 2%(Berg 1996). We have not found any data on methodological errors of tomographic hip muscle assessment, but since there are no difficulties to circumscribe those large muscle bellies, and the bony landmarks of the pelvis are easily identified, we have no reason to believe that the error in hip muscle measurements would differ. Also, variation (intra-interindividual) of measurements was similar for all sites along the limb.
Fig 1. Anatomical locations of the trans-axial CT images. In scans A-D, arrows point out muscle groups on the healthy left side which were compared to the smaller and less signal intense muscles of the atrophied right OA hip side. The lumbar scan (A) shows the erector spinae muscle group (A1; back extensor). The trans-gluteal scan (B) shows m. iliopsoas (B1; hip flexor) mm. gluteus medius et minimus (B2; hip abductors) and m. glut. maximus (B3; hip extensor). The mid-thigh scan (C) shows the mm. vastii (C1; knee extensors), mm. adductor magnus et longus (C2; hip adductors) and the hamstring muscle compartment (C3; knee flexors). The proximal calf scan (D) shows the ankle dorsal flexors (D1) and the ankle plantar flexors (D2).
Gait analysis

A flat opto-sensor walkway with two separate lanes, instrumented with photocells in order to assess right and left foot contact times was used. This system (IVAR Jump & Speed Analyzer, Estonia) was originally designed for measuring contact and flight times in runners using one lane only; and not discriminating data from right or left feet. We have developed this method further and our custom made version allows the measurement of touch down and lift off of both feet separately when walking on the parallel right and left foot lanes without crossing the midline. The equipment is validated and described in detail elsewhere (Rasch et al. 2005, Viitasalo et al. 1997). Reproducibility (CV%) varied between 4.5-7.4 %. Briefly, one bar containing four light transmitters is placed at the end of each lane. They send infrared light beams which are individually received by four matching photocells mounted in a bar at the start of the walkway. Transmitters and photocells are placed approximately 6 mm above the flat walkway and 50 mm apart, allowing the detection of touch-down and toe-off of right and left foot across two 150 mm wide lanes, respectively. Ground contact times below 0.2 seconds are filtered and thus not registered, in order to block false data input because of shuffling. The above four detected signals are streamed to an electronic box, and later ported and stored on a PC laptop.

Each test session was comprised of three trial runs without the use of shoes. Starting with the right foot, a relaxed walking speed was maintained while not crossing the midline, and at least 10 steps (five gait cycles) were measured. A typical gait cycle consists of four phases. During the first double stance phase, both feet are in contact with the floor. During the second phase, the right foot is lifted (right swing phase) whereby the left foot is in the single support phase. The third phase (another double stance) starts as the right foot touch down. Lastly, the fourth phase; the right single stance phase (equals the left swing phase), starts as the left foot is lifted and ends at touch down. Step frequency (steps/s), single and double stance duration (expressed in sec or as a percentage of the gait cycle), were calculated. Means of each variable were derived from five gait cycles, whereby the first cycle of each run was excluded since many individuals swayed in their first steps.

Postural stability assessment

A force plate (MuscleLab, Langesund, Norway) connected to a laptop with a software, which analyzes lateral and sagittal sway was used. The patients were told to stand as still as possible on the force plate with a gap of 20 centimeter between the feet. Six measurements standing with two limbs on the ground and alternating open and closed eyes were first conducted followed by six measurements standing with one limb on the ground and with eyes opened alternating OA and healthy limb. To facilitate one limb standing in these sedentary patients, the patients were allowed to stabilize with a rod in con-tralateral side hand. The rod was placed 10 cm in front of the lifted foot with the upper arm in contact with the trunk and the elbow in a 90 degree position (see photo). Each test was 30 seconds long followed by 20 seconds of rest. Three tests were conducted for each position and the mean of the two best measurements were used for comparisons. The movement of center of gravity (sway path) was assessed as the
standard deviation of the movement for lateral and sagittal (anterior-posterior) sway. This method has been used by previous investigators of postural stability and have shown moderate to excellent reproducibility (Birmingham 2000, Ekdahl et al. 1989, Goldie et al. 1989).

Postural stability assessment  Gait analysis
Clinical scores

*SF-36*: A non-disease-specific self-reported questionnaire consisting of 36 questions evaluating quality of life (Sullivan et al. 1995). Results are presented as a profile in four physical domains (physical function, role physical, bodily pain, general health) and four mental domains (social function, role emotional, mental health and vitality).

*EuroQoL*: A non-disease-specific self-reported questionnaire consisting of five questions which defines a total of 243 health states (1990). The five questions represent five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. There are three levels of severity: no problems, moderate problems and severe problems. The answers are converted into a number between zero and one, where best possible health state has the value one and death has the value zero.

*Harris Hip Score*: A disease-specific physician-reported questionnaire evaluating pain, function, deformity and range of motion (Harris 1969). Points are apportioned as follows: pain (0-44); function, divided into activity, limp, distance walked and support (0-47); physical examination, divided into deformity (0-4) and range of motion (0-5).
Statistical analysis

**Paper I:** Repeated measures ANOVA was performed on force data from healthy test subjects, and single contrast means comparisons were made for the selected factors. Absolute force divided by bodyweight (N/kg) was used to correct for differences related to age or gender. Comparisons between OA patients (affected limb) and old volunteers (right limb) were performed using Student’s t-test. Average knee force, hip force or total limb force were formed by calculating the arithmetic means of individual measurements. The variance of force data was calculated for each individual across the two consecutive trials, or between means of trials across the two test sessions, respectively. The square root of that group average, in percent of the overall mean, expressed the relative coefficient of variation (CV%). Statistical significance was set at P<0.05.

**Paper II:** Comparisons between arthritic limbs and healthy limbs were performed using paired t-tests. Absolute force divided by bodyweight (N/kg) was used to correct the differences related to subject size. Average knee force, hip force or total limb force were formed by calculating the arithmetic means of individual measurements. Statistical significance was set at P<0.05, or for repeated tests P<0.01.

**Paper III and IV:** Statistical analysis was performed using the paired t-test or ANOVA for single measures, setting the significance level at p<0.05. For repeated measures, a two-factor ANOVA (limb x time) was used, with a lower significance level at p<0.03, where an error rate for multiple comparisons of simple main effects was calculated partitioning the family of the main factors and the interaction term (0.05 x 3 = 0.15) and dividing by 5 planned comparisons (Kirk 1995, p 389). For the repeated Student’s t-tests the p-value of <0.025 for significance was chosen.
Ethical considerations

The included studies were all conducted in conformity with the Helsinki Declaration and separate protocols were approved by the local Ethics Committee. All patients provided written informed consent before participation.
RESULTS

Paper I

*Isometric muscle strength:* Force values for the young and aged volunteers and the OA patients are presented in Figure 1 (I). Comparing means of all measurements, the young volunteers were stronger by 22% when compared to the healthy aged volunteers, and OA patients were weaker by 24% in their affected limb when compared to the healthy aged individuals (P<0.05; N/kg). Healthy males displayed an overall 44% larger force than healthy females. There was no difference (P=0.77) between left and right limb for either overall strength or individual muscle groups in healthy individuals.

No differences were found (P=0.38) in isometric force between the first and second test session, in either overall muscle strength or unilateral measurement of individual muscle groups (I, Fig 2). We did not see any differences in test reproducibility (CV%) between the two age groups of healthy individuals. These groups were therefore merged for comparisons between trials and sessions. The relative variation (CV%) varied between 7-12% for a specific muscle group when tested unilaterally (I, Tables 1 & 2), where knee extension seems to show the lowest values. Variation was somewhat lower when force values averaged for the two limbs were used for comparisons (6-11%). Variation of unilateral measurements was further reduced when averaged for the knee (4-5%) or hip (5-6%) or the total six measurements of the limb (3-4%; I, Table 2). Variation between individual trial repetitions (3-6%) on one test session was generally lower than between sessions (7-12%).

*Gait analysis:* Gait parameters for the group of healthy volunteers are presented in Table 3 (I). We observed no tendency for differences between the first and second test session in any parameter. Except for the double support phases, the relative variation (CV%) ranged between 5-8% (I, Table 3). Nominal values, including the single support phase, are similar to earlier reported data.

Paper II

Hip extension, flexion, abduction, adduction knee extension strength was reduced (11-29%; p<0.01) in the OA relative to the healthy limb (II, Table 1). Muscle CSA of hip extensors, flexors, adductors and knee extendors and flexors, but not hip abductors, was reduced (11-19%; p<0.01) in the OA limb, where RD of all muscle groups except the hip flexors was reduced (5-15 HU; p<0.01) relative to the healthy limb (II, Table 2). Intra observer reproducibility (coefficient of variation; CV%) for two separate CSA measurements varied between 0.4-4.1% and inter observer reproducibility between 1.4-6.2%. For RD measurements intra observer reproducibility was 0.3-2.0 and inter observer reproducibility 0.9-2.1. Duration of hip symptoms before surgery was 4.3 (SD 3) yrs and hip pain 5.2 (SD 2.5) on the visual analogue scale (VAS). The clinical scoring was similar to other studies, where EQ-5D showed 0.45 (SD 0.25) and HHS 51.6 (SD 9.2). Domains reported in SF-36 were, physical function 29 (SD 15), role physical 9 (SD 23), body pain 28 (SD 10), general health 65 (SD 21), vitality 47 (SD
20), social function 63 (SD 24), role emotional 36 (SD 44) and mental health 69 (SD 18).

**Paper III**

When compared to the healthy limb, the preoperative CSA was reduced by 4.5-15.2% (p<0.03) in all muscles except mm. gluteus medius/minimus and ankle plantar flexors, and RD was reduced by 2.7-13.8 HU in all muscles of the OA limb (III, Table 1). At the six month follow-up CSA was still reduced (3.7-11.3%) in all muscles except gluteus med/min, hamstrings and ankle plantar flexors, and RD reduced (3.6-13.7 HU) in all muscles except the ankle plantar flexors. At the two years follow-up a reduced CSA persisted in m. iliopsoas (7.0%; p=0.006) and hip adductors (8.4%; p=0.003) and a reduced RD in mm. gluteus maximus (10.1 HU; p<0.001), gluteus medius/minimus (5.6 HU; p=0.011), iliopsoas (3.9 HU; p=0.001) and adductors (2.4 HU; p=0.022). Changes in CSA and RD over time for OA and healthy limb are demonstrated in four graphs (III, Fig. 2). CSA increased in adductors (p=0.012), iliopsoas (p=0.030), vastii (p=0.001) and hamstrings (p=0.007) of the OA limb. RD increased in gluteus medius/minimus (p<0.001), adductors (p<0.001), vastii (p=0.001) and hamstrings (p<0.001), while it decreased in gluteus maximus (p=0.016) and back extensors (p=0.016) on the OA side. In the healthy limb, RD decreased in gluteus maximus (p<0.001), adductors (p=0.019), iliopsoas (p=0.023), vastii (p<0.001) and hamstrings (p=0.005), while CSA showed no change over 2 years. Back extensor muscles showed no side differences for CSA (p=0.129) or RD (p=0.643) at any test occasion (III, Table 1). Postoperatively no changes in CSA were demonstrated, whereas RD was lowered (2-3 HU) at the six months and two year follow-up (III, Table 1). No significant changes over time were observed in any of the individual water phantoms used at CT measurements. Intra-observer reproducibility (CV%) between two separate measurements varied 0.4-4.1% in CSA and 0.3-2.0% in RD, respectively. Inter-observer reproducibility was 1.4-6.2% and 0.9-2.1% in CSA and RD, respectively.

Mean duration of hip symptoms before surgery was 4.3 (1 to 10) years. The mean HHS, EQ-5D and VAS all improved (p<0.001) from 51.6 (33.6 to 65.1), 0.44 (0.03 to 0.69) and 5.2 (0 to 8) preoperatively to 86.2 (45.6 to 99.9), 0.85 (0.03 to 1.0) and 0.05 (0 to 1), respectively, at two years follow-up. Two years after surgery SF-36 had improved (p<0.001) for all domains except for general health (p=0.11). Preoperative values were: physical function (PF) 29.3 (10 to 60), role physical (RP) 9.1 (0-100), body pain (BP) 27.9 (10 to 41), general health (GH) 65.0 (25-97), vitality (VT) 46.6 (10 to 85), social function (SF) 63.1 (25 to 100), role emotional (RE) 36.4 (0-100) and mental health (MH) 68.9 (28-92). Two years postoperatively those values were: PF 72.7 (20 to 95), RP 77.3 (0 to 100), BP 79.8 (31 to 100), GH 71.9 (25-100), VT 70.6 (13.3-100), SF 89.8 (25 to 100), RE 86.4 (0-100) and MH 86.2 (52 to 100).

**Paper IV**

Preoperatively, all muscles except knee flexors showed a deficit of 9-27% (p<0.03) in OA compared to the healthy limb (IV, Table 1). Six months postoperatively that deficit was 8-16% (p<0.03) in all muscles except hip adductors and knee flexors. Two years after operation only the hip abductors showed a remaining 15% (p<0.001) deficit while
knee flexors were 11% stronger in the OA limb (p<0.015). Across 2 years after surgery all muscles in OA limb improved, except hip adductors and knee flexors which did not reach statistical significance. Healthy limb showed no significant postoperative changes. Recovery of the two groups; low and high force deficit (see Methods) are shown in Figure 1 (IV). At the six months follow-up the difference in force deficit between the groups was maintained (p<0.005) while after two years no significant difference could be demonstrated (p=0.12).

Gait analysis demonstrated a shorter single stance phase in OA limb compared to healthy limb preoperatively (p<0.001, IV, Table 2). At six months and two years follow-up there were no significant differences (p>0.045) between the limbs. Sway measurement of unilateral standing before and after operation demonstrated no significant differences between OA and healthy limbs (p>0.082) except for the 6 months follow-up of sagittal sway which was larger in OA limb (p=0.016, IV, Table 3). Measurement of bilateral standing showed a significant decreased lateral and sagittal sway postoperatively compared to preoperatively, although only significant for closed eyes (p<0.006, IV, Table 4). The sagittal sway was more pronounced than the lateral sway in both OA and healthy limb preoperatively as well as postoperatively.
GENERAL DISCUSSION

Muscle strength measurement

In order to be clinically applicable, a test procedure for lower limb function must meet certain requirements. First, the test should accurately assess relevant and important parameters. The measurement of voluntary force capacity of the major muscle groups of the hip and knee joints is suggested as a meaningful measure of the locomotive capacity in many patient groups (Rantanen et al. 1994). The test method must thereby accurately detect differences between groups of patients and healthy controls, changes over treatment time and side differences between the disabled and the healthy limb. Secondly, a test must be accepted by the elderly frequently frail individual, both in terms of the demanded body positions, and also the exhaustive effort required throughout a full test session. This requirement becomes obvious when the patient has severe arthritic or posttraumatic pain. Thirdly, any test must be time-effective in terms of both the duration of a single test session and the number of repeated sessions required obtaining accurate data. Our goal was to develop a test battery that could objectively evaluate physical performance capacity, although we anticipated that the ability to map out specific muscle groups would concur with the ability to evaluate over-all capacity.

Difficulties when measuring muscular strength about the hip constitute limitations to clinical research and to rehabilitation after hip arthroplasty, and it is essential to develop methods that are easy to apply and could be accepted by those typically sedentary and immobile individuals. Most patient studies report only isometric hip abduction force, which is readily obtained in the supine position using a hand held strain-gauge (Arokoski et al. 2002). Measurements of multiple muscle groups were typically performed in healthy individuals (Burnett et al. 1990, Markhede and Grimby 1980, Neumann et al. 1988), and only a few studies exist on OA patients (Arokoski et al. 2002, Horstmann et al. 1994, Shih et al. 1994). They used commercial isokinetic dynamometers with specific adaptors for hip torque measurement, where the patient is placed in the supine among other positions, and the resulting test protocol is extensive (Arokoski et al. 2002). It is a true challenge to reduce the number of physically demanding, painful and time consuming re-positionings of those frail patients, yet to still allow multiple measurements of muscular strength in both limbs. We used only two different body positions and tried to optimize comfort during test and rest periods. The seated position was used for knee extension and flexion, whereas for hip exercises subjects were in the upright position, using an abdominal trunk support and a foot support for the contra-lateral limb (see photos). Because limb segments below the measured joint are maintained in the vertical position, there is no need for gravity correction. Exhaustion when performing repeated maximal voluntary contraction is another major concern for the design of a test.

Although the isometric test situation does not resemble the typical dynamic joint movement during locomotion, previous studies have showed that isometric are comparable to dynamic force measurements, when describing deconditioning due to inactivity or disease (Arokoski et al. 2002, Berg et al. 1997). The lower energy demand, and joint load, of isometric muscle contractions allows the performance of
repeated trials with limited rest even by the untrained individual. With our strength test protocol measuring both knee and hip muscle force in both limbs, a full test session including twelve exercises was executed within 45 minutes and no one had to break due to fatigue. Clearly, the duration and exhaustion of isokinetic or other dynamic force measurements using our extensive and diverse protocol, would exclude repeated testing of frail patients, whether suffering from joint disease, muscular fatigue or cardiac limitation.

We also recognized that it was more difficult and therefore important to stabilize the hip than the knee joint when performing maximal voluntary contractions, where forces are impressive and comparable in hip and knee (Jensen et al. 1971). Insufficient familiarization to the method might be another source of variation, and could be counteracted by using several test sessions prior to an intervention (Berg et al. 1997). We noted, however in these individuals, that the learning effect between sessions was not as important as within the test session. In fact, when allowing five sub-maximal warm-up contractions before each maximal voluntary strength test, the present protocol suggested that there is no consistent improvement between sessions. We therefore conclude that only one test session is required to collect correct values when monitoring muscle function in these groups. It seems reasonable to hypothesize, however, that repeat baseline sessions could reduce variation even further when multiple comparisons are planned to evaluate changes over time. Using the same test procedure and vocal reinforcement during contractions is probably important and should be emphasized.

Earlier studies have reported similar results, in terms of reproducibility. Arokoski (Arokoski et al. 2002) used the Lido isokinetic rehab system for isometric and dynamic hip strength measurements and reported a reproducibility at 8-15% (CV). Markhede (Markhede and Grimby 1980) used the Cybex II isokinetic dynamometer with similar reproducibility (4-10%) for isometric hip muscle strength. These methodological errors, thus allow group studies that could detect clinically relevant changes due to age or disease. It should be remembered, however, that information for the individual patient would probably remain limited because of the large intra-individual variation. The reasons for the lower reproducibility in the hip compared to knee joint muscle assessment remains obscure, although the complex anatomy of the hip might be one important factor. One alternative approach to reduce variation could be to form average values from several measured muscle groups, accepting that detailed information on each specific muscle group would be lost. When CVs were recalculated for average values of measurements about the knee (extension and flexion; 4-6%) or hip (extension, flexion, abduction and adduction; 5-6%), or the average of all six measurements of the lower limb (4%), this notion was indeed supported (I, Table 2). If general muscle weakness of lower limbs is the monitored outcome, this approach might detect even minor differences in smaller groups, or in individuals. Variation could be reduced even further when the average of both limbs was formed (I, Table 1), and this might be a fruitful strategy to detect changes in small groups of heterogeneous patients where bilateral muscle weakness, or training effects, are evaluated, for example in geriatric training studies or cardiovascular or renal patient rehabilitation.

We conclude that our dynamometer system provides reliable measurements of hip and knee muscle strength in both limbs in young and aged individuals. This is supported by the fact that marked differences between males and females, aged and young individuals, of similar magnitude that have previously been reported, could be
demonstrated (I). The relative variation for unilateral measurements (7-12 %; I, Table 1) was comparable to previous studies that employed commercial dynamometers (Arokoski et al. 2002, Markhede and Grimby 1980). Moreover we could detect side differences (II) and changes over time (IV). We also found that a single test session is sufficient to assess maximal voluntary isometric strength, because a second test did not differ in absolute force values or variation. The substantial muscle weakness in limbs of OA hip patients reported here and by others (Arokoski et al. 2002, Horstmann et al. 1994, Shih et al. 1994) 20-50%, in relation to the presented methodological error, indicates that our dynamometer would be capable of detecting such differences in patient groups under treatment.

**Muscle strength**

Our study is the first to describe the relation between hip and knee muscle adaptation to OA in detail. A reasonable mechanism for the general decline in muscle strength would be that a chronic joint pain drastically reduces the load of daily weight-bearing, and therefore the whole limb suffers deconditioning. There could be multiple mechanisms for the reduced voluntary force output of the OA limb, including a reduced muscular mass, a diminished ability to recruit existing muscle, and possibly pain and fear on the test occasion.

Based on previous findings in inactivated healthy subjects (Berg et al. 1991, Berg et al. 1997), the greatest strength loss was anticipated in the weight-bearing extensor muscles, which seems confirmed considering the knee joint where extension strength was severely decreased while knee flexion strength was not reduced significantly. Differently, hip muscle strength was substantially compromised in all four test modalities (IV, Table 1), confirming data from a few existing studies in younger hip OA patients (Arokoski et al. 2002, Horstmann et al. 1994). Actually, there are currently no data at hand to support that hip abductors or extensors (supposedly important for gait and weight-bearing) are more compromised than other hip muscles in response to hip OA. It remains to be shown if other lower limb pathologies (i.e. knee OA) cause a similar pattern of muscular loss. These baseline data can help in understanding the mechanisms of muscular dysfunction in hip OA.

Arguments could be found to compare muscular adaptation both between the arthritic and healthy limb and within the individual limb over time. We thought the relevant clinical perspective is to evaluate whether or not the OA limb has the capacity to catch up with the healthy side after a successful THA, because a remaining muscular imbalance between the two limbs would probably be noticed and hamper the patient. It is however often assumed that also the healthy limb is weakened due to a general inactivity, and that a parallel recovery of both limbs should be anticipated after surgery (Adolphson et al. 1993, Arokoski et al. 2002). This could confound the interpretation of results. Interestingly, there turned out to be no significant postoperative changes in muscle strength of the healthy limb, and therefore it was tempting to regard that limb as the internal control to the OA limb. A group of external age- and sex-matched control subjects might be preferred for unbiased comparisons. However, the large number of healthy subjects requested to obtain statistical power impose major limitations to that experimental design. From a mechanistic perspective it is relevant to evaluate muscular adaptation over time in individual limbs and muscles; being their own preoperative control and data clearly show that hip muscles are slow to recover (IV, Table 1). The lack of muscular gain of the healthy limb merits an explanation. One might be that patients remain relatively
inactive even after a successful THA and traditional rehabilitation. Alternatively, it might be speculated that muscles of the healthy limb are relatively overloaded during the preoperative years of painful OA.

Patients suffering from knee OA show functional deficiency and quadriceps weakness in the OA compared to healthy limb before and after total knee arthroplasty (TKA), as described by several studies (Berman et al. 1991, Lorentzen et al. 1999, Mizner et al. 2005). It has been concluded that knee extensor force values will actually drop further the first months after operation and not return to preoperative values until 3-6 months postoperatively. It is even suggested that patients undergoing TKA will never recover their preoperative force deficit in OA compared to healthy limb or compared to healthy individuals (Berth et al. 2002, Walsh et al. 1998). We have found no hip muscle data in patients operated with total knee arthroplasty. Muscular strength in patients suffering from hip OA is less studied and the results are not conclusive. We (II) and others (Arokoski et al. 2002, Horstmann et al. 1994) have demonstrated a substantial preoperative force deficit in hip muscles of patients suffering from unilateral hip OA. Only one study (Horstmann et al. 1994) in young patients (age 30-67 years) reported a remaining hip abductor weakness 6 months after THA, while other studies could not demonstrate significant postoperative differences in OA compared to healthy limb (Shih et al. 1994, Trudelle-Jackson et al. 2002). One cross-sectional study (Bertocci et al. 2004) found weaker hip muscles of the OA limb compared to a small group of healthy individuals at 4-5 months after THA. The frequent lack of preoperative control data together with different measurement techniques and postoperative rehabilitation regimes may have affected previous studies.

This is the first prospective long-term study of aged OA patients, typical for the group receiving THA. We demonstrated a significant persisting strength deficit of hip muscles in OA compared to healthy limb after THA, including a 12% deficit after 6 months and a 6% deficit remaining 2 years after THA. These data were supported by muscular atrophy of hip muscles as shown by computerized tomography (III). No significant changes in force output or muscle mass were observed in the control limb across the 2 years. Within the gluteal muscles it seems that hip abductors have the least potential to recover. The clinical relevance of these data remains to be defined, but it might be speculated that the weakness 6 months after THA might affect both hip joint stability and the potential to regain ambulatory capacity. The two-year data might be interpreted so that muscles have indeed the capacity to recover if sufficient time is allowed for rehabilitation. The hip abductor weakness may on the other hand imply a long-standing insipient deficiency of hip muscles that might become critical to maintain everyday ambulation and an independent living if the marginal of physical capacity becomes reduced.

A traumatization of the abductors or other hip muscles at surgery might be one explanation for a delayed recovery or permanent loss of force capacity of those muscles. Lin et al (Lin et al. 2007) demonstrated faster recovery of hip muscle strength, walking speed and functional scores using minimal invasive technique compared to conventional anterior lateral approach, but other studies (Dorr et al. 2007) has shown shorter hospital stay but no long-term benefits. Long-term randomized prospective
studies of muscular strength comparing mini-incision to conventional incisions are still lacking.

A general inactivity or a catabolic effect of the surgical trauma might also interfere with short-term muscular recovery, as suggested by the delayed recovery of thigh muscles the first months after hip replacement (Suëtta et al. 2004). Thus, they found a 22% decrease in knee extensor strength 5 weeks after THA and a persisting 18% deficit in OA compared to healthy limb 3 months after surgery. No data on hip muscles were supplied however. Our measurements of knee extensor and flexor strength are at odds with those data and demonstrated a faster recovery of knee extensors compared to hip muscles. At six months follow-up about two thirds of the force deficit in knee extension had recovered but only one third of the deficit in total hip muscle force. Thus, in contrast also to the studies of knee OA patients, where knee extensors have shown poor postoperative recovery after TKA, we report a full recovery of knee extensors in hip OA patients two years after operation with THA.

Some authors claim that a deficient preoperative muscle function in hip OA patients predispose for a lowered postoperative rehabilitation potential (Kennedy et al. 2006). Similarly, a poor outcome was demonstrated one year after TKA in patients with low preoperative quadriiceps strength (Mizner et al. 2005). To evaluate if this also was the case in our patient group, the twenty patients were ascribed to either of two equal groups according to their deficit in total hip force (Htot; IV, Table 1) prior to surgery. The postoperative recovery of that deficit in OA compared to healthy limb for the two groups is displayed in a graph (IV, Fig. 1). We could demonstrate good recovery in OA limb also in patients with a large preoperative weakness, and two years after THA the difference in strength between the groups was not statistically significant and probably not clinically important. Thus our data do not confirm that a low preoperative function will predispose for a poor rehabilitation in the long perspective, although at six months the difference between the groups is significant. This concords with training studies of old sedentary subjects (Fiatarone et al. 1990) where an excellent training potential was demonstrated among the very weak individuals. The postoperative rehabilitation training in this study consisted of ten sessions of weekly group training led by a physiotherapist; where after home training was encouraged. In order to speed up the recovery process after THA, attempts have been made to modify the rehabilitation programs. More intense and targeted rehab training programs have shown good results in the early (Trudelle-Jackson and Smith 2004) and late phase (Jan et al. 2004) of muscular recovery after THA. It seems important to include also the abductor muscles.

Muscle strength data confirmed a maintained unilateral strength deficit in hip muscles and especially in hip abductors two years after THA. While the study showed that muscular recovery continued up to 2 years after THA, more detailed studies are needed to establish if the long-standing abductor muscle weakness is critical for joint stability and ambulatory function in individuals with a limited marginal of performance capacity.
Muscle atrophy

Our study, in contrast to previous OA studies, adds the measurement of radiological density (in Hounsfield units; HU) in all muscle groups, and could report a marked decline in density in most muscles of the OA limb (II, Table 2). Goodpaster et al. (Goodpaster et al. 2001) reported a low methodological error in such muscle density assessment. They concluded that fat content of muscle could be readily assessed using CT, and that each percent of increased tissue fat corresponded to a reduced density by 0.75-1 HU. In the gluteal muscles a reverse calculation would infer that fat was increased by approximately ten percent, indicating a similar relative loss of contractile muscle in the OA limb. Consequently, the total atrophic response of the gluteal muscles would be about two-fold compared to the estimation from the reduced CSA alone. The absence of a CSA reduction in the hip abductors on the OA side was an unexpected finding, but it is interesting to note that the prominent reduction in RD indicates a substantial net loss in contractile muscle; yet still larger in the hip extensors.

Studies using tomographic techniques (i.e. MRI, CT) to quantify muscle atrophy due to inactivity, trauma or disease by CSA or volume only, might have underestimated changes due to undetected alterations in extra- or intramuscular fat or other non-contractile components. Decreased muscle CSA could not fully explain the strength loss, confirming what is typically shown after unloaded inactivity (Berg et al. 1991, Berg et al. 1997). After compensating for non-contractile components in hip extensor muscles using the decreased RD, however, there seems to be no obvious mismatch between weakness and atrophy in the OA limb. In knee extensors, however, the small increase in non-contractile components does not seem to compensate for the gap between muscular atrophy and strength loss.

Healthy volunteers subjected to 5-6 weeks of experimental bed rest inactivity demonstrated a profound atrophy of the weight-bearing knee extensors and ankle plantar flexors whereas knee flexors (Berg et al. 2007) and gluteal muscles (Berg et al. 1997) showed a modest loss. Data were explained by local differences in gravitational load and hence the more severe response of the distal postural muscle groups. The present data in OA patients show rather the opposite pattern, with no differences in atrophy between extensor and flexor muscles of the calf, thigh or hip compartments, and the proximal hip muscles markedly affected both before and after THA. These findings suggest either that weight-bearing is not the prime determinant of muscular adaptation to hip OA, or that only muscles acting about the painful hip joint are unloaded while calf muscles maintain full weight-bearing even during severe limp.

While preoperative muscle atrophy along the arthritic limb in patients suffering from hip OA has been described previously by us and others (Adolphson et al. 1993, Arokoski et al. 2002), existing postoperative data are limited to thigh muscles. They suggested full recovery after traditional rehabilitation (Adolphson et al. 1993) or specific training (Suetta et al. 2004). Our long term data confirm those encouraging findings in muscles acting about the knee and ankle joints, whereas muscles acting about the hip do not seem to recover at the same rate. The explanation for this discrepancy remains obscure, and we have found no other data on hip muscles for comparison.
Fat infiltration seems more expressed in gluteal muscles (13-15 HU difference; III, Table 1) than in the thigh (5-8 HU) or calf (3-4 HU) of the OA compared to the healthy limb, and suggest an important added muscular atrophy especially around the affected hip that is not revealed by CSA measurement. In order to illustrate the full extent of atrophy and the time-course of postoperative recovery of contractile muscle in different muscle groups, the changes over time in cross-sectional area and radiological density are expressed in four graphs (III, Fig. 2). A less rapid recovery in RD than CSA is apparent, and this might be an important explanation for the slower recovery of hip muscle mass. After 6 months postoperative recovery there was in fact no change in hip RD, and thus only minor recovery of contractile muscle as indicated by increased CSA values. Differently, knee extensors and calf muscles which displayed less preoperative side differences in intramuscular fat, recovered about half their atrophy 6 months after THA, and almost in full after two years (III, Table 1). Our data expand and support the findings by shoulder surgeons; that fatty infiltration is a strong negative predictor of muscular recovery (Gladstone et al. 2007).

The surgical trauma of the THA procedure may negatively influence the immediate and long-term postoperative rehabilitation process. Suetta and co-workers (Suetta et al. 2004) reported a 13 and 9 % loss of quadriceps CSA one and three months, respectively, after THA and standard rehabilitation. We do not have those early data points and could only speculate that the modest recovery shown 6 months after THA was affected by the catabolic response of surgery. The operative technique may influence both the surgical trauma and the conditions for rehabilitation. All our patients were operated with the posterior (Moore) approach where muscle fibers of gluteus maximus were bluntly separated in the proximity of the motor nerve. A slower recovery of traumatized or denervated muscles might be expected, but it seems that the gluteus maximus showed the same delayed recovery as other hip muscles. This finding might even suggest that the size and type of surgical incision does not dictate the recovery of hip muscles atrophied after OA. Long-term studies on the different surgical approaches including less invasive techniques might shed further light to this issue.

These patients had suffered hip pain for an average of four years, and the atrophic process had probably developed for years. The demonstrated morphological abnormality including fat infiltration might be an important contribution to the impaired functional recovery after THA reported in patients with a low preoperative function (Kennedy et al. 2006). It could be speculated that a few years earlier operation might prevent the development of fat infiltration of hip muscles; while still allowing life-long survival of the joint prosthesis. Because our two-year data suggest that fat infiltration is gradually reversed, an alternative strategy might be to use intense rehab exercise to accelerate this process.

**Gait**

Gait function is an objective measurement of the functional status about the hip, and reflects the probable activity level (Bendall et al. 1989, Vaz et al. 1993). Gait pattern is typically measured using walkways instrumented with force plates (Olsson et al. 1986) or three-dimensional kinematics (Perron et al. 2000) in order to assess the temporal and spatial aspects of gait. Costs for this sophisticated and stationary equipment as well as for the necessary data processing and interpretation, limit such studies to centers.
specialized in biomechanics. More affordable and simple equipment has been suggested employing a conductive contact mat and electronic sensors on the used shoes (Kyriazis and Rigas 2001).

Tests with our technique for gait analysis are performed very quickly (less than 10 min) and are neither painful nor demanding for the majority of patients. The equipment could therefore be used in clinical practice to evaluate gait disturbances in many different patient categories. A methodological problem is that any photocell technique demands an extremely flat and non-flexing walkway. We used wooden boards adjusted to the somewhat uneven floor using wedges with good result. Alternative approaches include re-molded floors, although it would cause extra cost and make the equipment stationary.

Our values of the control group (I, Table 2) confirm earlier studies in great detail, where healthy subjects typically spend about 40% of the gait cycle supported on each foot; right or left single support phase, respectively, and the remaining 20% divided on the two double support phases (9-13% for each double support phase). Moreover, all gait parameters were equal for right and left side and also, no learning effect between the separate test sessions was observed. The relative coefficient of variation (CV%) between separate tests for the single support phase was 4-7% when expressed in relative length (per cent) of the gait cycle, and thus somewhat decreased compared to absolute values (sec; I, Table 2). This indicates that previously shown differences in response to disease (approximately 10%), including hip OA, would be detected.

Hip patients typically show a reduced single stance duration of the affected side (Isobe et al. 1998, Olsson et al. 1986, Tanaka 1998), which has been ascribed to pain and reduced ability to sustain load of the affected joint (Kyriazis and Rigas 2002). The double stance phases presented both methodological and theoretical problems. We found it difficult to accurately assess these phases, as indicated by a large variation (I, Table 2), especially at higher walking speeds. Previous studies (Kyriazis and Rigas 2002, Nilsson and Thorstensson 1987) confirm that these phases are indeed short and might, at higher speed or when using short steps, be less than 0.1 sec. It seems doubtful if assessments of the double support phase add further information to gait analysis. In our opinion, the assessment of the single support phases, whether in absolute time, per cent, or ratios between left and right side, seems the most intuitive and accurate measure of gait disturbance.

Previous studies have shown that patients with hip osteoarthritis have a reduced single stance phase of the OA limb. Our preoperative data confirm those studies and revealed a shorter single stance phase in OA compared to healthy limb. This indication of a limp was recovered already 6 months after operation, when the patients had received a pain-free THA, yet still showing muscular weakness and atrophy. This might implicate that joint pain is a more important factor than hip abductor strength to induce limp, as suggested by Horstmann et al. (Horstmann et al. 1994).
Postural stability

Postural sway of quiet bilateral standing was reduced after THA as previously shown by others (Wykman and Goldie 1989), and the natural interpretation would be that a preoperative impaired postural stability due to OA became improved after THA. In order to evaluate both limbs separately and also to stress the role of muscles for postural stability, we assessed sway of unilateral standing with a partial support of the contra-lateral arm. Unexpectedly, we could not prove any differences between the OA and healthy limb and no improvement after THA; at most a tendency for increased sway of the OA limb (IV, Table 3). In fact, a recent study (Arokoski et al. 2006) similarly concluded the lack of difference between OA and healthy limb in a similar unilateral sway test. Despite the speculations about the impact on proprioceptive pathways and muscular feedback about OA joints and their possible removal at THA surgery, it seems not yet proven that there is a clinically important impairment of postural stability due to hip osteoarthritis or after resulting THA.

Clinical scores

In order to get a broader perception of our patient group and to compare their self-reported health status with published populations, we also collected information on two generic (SF-36, EuroQoL) and one disease specific (HHS) health score. Preoperatively, our patient group scored lower in all SF-36 dimensions except for general health compared to an aged matched Swedish population (Sullivan et al. 1995) but comparable to previous studies of hip OA patients (Ostendorf et al. 2004). Harris hip score and EuroQoL were comparable to data collected in patients planned for THA reported to the National Swedish hip registry (www.jru.orthop.gu.se). Thus, our patients seem representative of the typical hip OA patient considered for THA, and self-reported function and quality of life as well as measured index of muscle mass and function are indeed lowered.

Muscular weakness in quadriceps has shown to be poorly correlated to patients perceptions of function but strongly related to actual performance before and after TKA (Mizner et al. 2005). Improvements of self reported scores have been strongly associated with improvement of pain rather than improvements in patients actual ability to perform (Stratford and Kennedy 2006). In our patient group we could confirm this by demonstrating a persisting muscular weakness in hip muscles but a full recovery of pain on the VAS scale and a full recovery of health scores, SF-36 and EuroQoL, as compared to a normal aged-matched population (Ostendorf et al. 2004, Sullivan et al. 1995). Self reported scores are probably not able to pick up moderate deficits in muscular strength.
CONCLUSIONS

Paper I

We conclude that our dynamometer provides reliable measurements of hip and knee muscle strength in young and aged individuals, and that a single test session is sufficient to assess maximal voluntary strength. The substantial muscle weakness reported for hip OA patients would be detected using our developed dynamometer system. We also conclude that our redesigned photocell technique for gait analysis is able to collect reliable data.

Paper II

Major muscles functioning around the hip and knee joints showed a substantial loss in strength and mass, which contributes to the reduced ambulatory capacity of OA patients. Decreased muscle CSA could not fully explain the strength loss. Infiltration with fat or other non-contractile components, as indicated by a decreased RD in OA limb muscles was substantial. If not adjusted for, there is a risk that muscle atrophy is underestimated in these aged and inactive individuals.

Paper III

The most striking finding was that the marked preoperative atrophy of muscles acting about the OA hip prevailed the first two years of recovery after THA, where a substantial fat infiltration of those muscles was slower to recover than muscular size. Lower leg muscles differently showed minor differences in size and fat infiltration.

Paper IV

Muscle strength data demonstrated a slow but full muscular recovery of muscles acting about the knee, but a maintained deficit of hip muscle strength two years after THA. Hip abductors were most affected. Gait and balance recovered after operation. To improve muscular function after THA postoperative training should probably be more intense and target hip abductors.
CONSIDERATIONS FOR FUTURE RESEARCH

Research about THA is massive and thousands of articles are published every year in this field. The majority of those articles focus on prosthesis design and materials with the ambition of improving long term survival of the prosthesis. Research about muscular function and soft tissue are scarce, which means there is much research to be done. Our ambition to map out natural history of muscle mass and function after standard THA will open the possibilities for future studies demonstrating the effect on muscle mass using different surgical approaches including minimal invasive surgery, where a small damage to soft tissue is emphasized. It would also be of interest to study tissue damages after operation with resurfacing prosthesis where tissue normally is more traumatized than in a standard THA.

Since recovery of hip muscle function after THA is slow it would be of interest to see if a more aggressive or prolonged physiotherapy, targeting hip abductors, could speed up the recovery after operation.

Dislocated hip fractures in elderly patients are today usually treated with THA or a hemiarthroplasty. Frequency of hip dislocations is higher in this patient group compared to OA patients operated with THA. Because it has been speculated that muscle function is associated with joint stability it would be of interest to characterize the postoperative changes in lower limb muscles in those often frail individuals compared to OA patients.
Artros i höftleden är en vanlig sjukdom hos äldre som orsakar ledvärk, stelhet och nedsatt rörlighet. Operation med höftledsprotes (THA) har i ett flertal studier visats vara en mycket framgångsrik operation när patienten själv får värdera resultatet. Kvantitativa studier av muskelstyrka och funktion är inte lika vanliga och resultaten är inte lika entydiga. Avlastning av artrosbenet p.g.a. smärta kan orsaka en muskelsvaghet och muskelförtvining som i sin tur kan leda till en hälta och troligen en sämre balans. Muskelförtvining kan mätas med skiktröntgen (CT) genom att bestämma tvärsnittsytan (CSA) och den radiologiska tätheten (RD) i muskulaturen, vilken mäts i Hounsfield units (HU). RD avspeglar hur mycket fett som finns i muskeln och en låg RD talar för en stor fettinfiltration. Målet med denna avhandling var att kartlägga muskelstyrka, muskelförtvining, gångförmåga och balans hos patienter med ensidig höftledsartros, före och efter operation med THA. Vår hypotes var att muskulaturen inte återhämtar sig fullt efter en operation.

Vi har genom upprepade mätningar utvärderat tillförlitligheten av en mätutrustning som mäter isometrisk viljemässig kraft i höft- och knämuskulatur samt av en gångbana som mäter hälta. Styrkan mättes hos tio unga och treton äldre friska försökspersoner samt hos elva patienter med ensidig höftledsartros. Tjugo försökspersoner genomgick gånganalys. Variationskoefficienten (CV%) varierade mellan 7-12 % för styrkemätningarna och mellan 4-8 % för gånganalysen.

Hos tjugo patienter med ensidig höftartros mättes höft- och knämuskelstyrka, gångförmåga, balans och hälsotillstånd med hälsosformulär före operation samt sex månader och två år efter. Med CT bestämdes CSA och RD i höft, lår, vad och ryggmuskulatur. Före operation var styrkan i artrosbenet jämfört med det friska benet nedsatt 9-27 %, förutom i knäböjarna. CSA var nedsatt 5-15 %, förutom i höftabduktorerna och fotledsböjarna och RD nedsatt 3-14 HU. Gånganalysen påvisade en hälta före operation. Ingen signifikant skillnad i balans mellan artros och friskt ben kunde påvisas.

Två år efter operation fanns fortfarande en svaghet i höftmuskulaturen på 6 % i artrosbenet jämfört med det friska benet. Innan operation var den svagheten 18 % och sex månader efter operation 12 %. Den största nedsättningen (15%) observerades i höftabduktorerna. Knästräckarna återhämtade sig helt. Efter två år fanns en nedsättning i CSA för höftbörjan iliopsoas (7%) och för höftadduktorerna (8,4%). RD var nedsatt i gluteus maximus (10,1 HU), gluteus medius/minimus (5,6 HU), iliopsoas (3,9 HU) och i adduktorerna (2,4 HU). Hälten försvann redan 6 månader efter operation. Balansmätningarna påvisade en förbättring balans vid stående på två ben efter operation. Hälsotillståndet förbättrades efter operation enligt samtliga hälsosformulär.

ACKNOWLEDGEMENTS

This study was carried out at the Department of Orthopaedics, Danderyd hospital, Karolinska Institutet. I would like to express my sincere gratitude to all who have supported me during my years of doctorial studies. In particular I would like to thank:

Hans Berg, MD, PhD, my supervisor and generous friend, for introducing me into the world of science and for your endless enthusiasm for research. Without your outstanding support and encouragement this work would not have been possible. I have very much appreciated your warm personality and great sense of humor and all round table chats (not always about science).

Nils Dalén, MD, Professor, my co-supervisor and generous friend, for your sympathetic and relaxed style and for all support and encouragement along the way.

Anders Byström and Nicholas Martinez-Carranza, MD, co-authors and friends, for your help with CT measurements.

Gustaf Neander and Ulf Lillkrona, MD, PhD, for giving me time and resources for research.

Gunnar Ordeberg, MD, PhD, my friend and clinical mentor at Danderyd Hospital during my residency, for introducing me to Danderyd neighbourhood and into the world of spine surgery.

Maria Frenne at the Radiology Department, for help with all x-rays in early mornings.

Helena Rohman and Suzanne Ahlström, for assistance in the laboratory.

Elisabet Berg, for all significant statistical help.

Rolf Andersson, for assistance with photography, layout and design of cover and posters.

Kathleen Norell, for taking your time to read my thesis and manuscripts and for correcting my English language.

Birgitta Lindén and Nina Ringart, for help with all administration at KI.

All volunteers who participated in these studies.

Colleagues at the Orthopaedic Department at Danderyd hospital, for creating a good atmosphere and for all fun we have had.
Colleagues at Stockholm Spine Center AB, Löwenströmska hospital, for being lovely friends and for creating a good working atmosphere.

Tycho Tullberg, MD, PhD, my boss and friend, for giving me the opportunity to work in a fantastic spine clinic.

True friends, for good times.

Ylva, my first teacher, for believing in me as a student and for your stubbornness in trying to learn me how to read.

Birgitta, my dear mother in law, for all help taking care of my family when I have been busy.

My late grand father John, for all support during my life and for being a good friend and companion. I miss you.

Johanna and Emma, my lovely sisters for your support and all fun we have had during all years. I’m always enjoying your company.

My father Carl-August and mother Katarina, for your lifelong support and for giving me the opportunities for doctorial studies and always believing in me. You are the best parents I could imagine and I am so lucky to be your son.

Annica, my beloved and beautiful wife, for your endless love and support. I love you so much.

Märtha and Ingrid, my wonderful two daughters and princesses, for being so sweet and make me feel warm and happy inside. You are the source of joy in my life.

This investigation was supported by grants from Anatomica, DePuy Johnson & Johnson, Stohnes, Osterman, Tore Nilssons foundations and the Swedish National Board of Health and Welfare.
REFERENCES


Burnett CN, Betts EF, King WM. Reliability of isokinetic measurements of hip muscle torque in young boys. Phys Ther 1990;70(4):244-9.


Stratford PW, Kennedy DM. Performance measures were necessary to obtain a complete picture of osteoarthritic patients. J Clin Epidemiol 2006;59(2):160-7.


