Rehabilitation outcome after total hip replacement; prospective randomized studies evaluating two different postoperative regimes and two different types of implants

PhD thesis

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PREFACE

This PhD thesis is carried out during my employment as Research assistant at the Department of Orthopaedics and the Department of Physiotherapy, Aarhus University Hospital in the period 2004-2007.

I am deeply indebted to a number of persons who have made this work possible. First of all I wish to express my sincere gratitude to my supervisors Professor Kjeld Søballe and MD, PhD Poul Mogensen. From the inception of this project Kjeld Søballe has provided valuable helpful advice on everything from design of the studies to writing process. I am grateful for his faith in my abilities to perform research and for giving me very good working conditions in terms of extensive freedom, much responsibility and guidance whenever needed. I wish to thank Poul Mogensen for his valuable and skilful guidance, discussion and support in the field of gait analysis.

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LIST OF ABBREVIATIONS

THR	Total hip replacement
OPC	Optimized perioperative care
CPC	Conventional perioperative care
LOS	Length of stay
RCT	Randomized controlled trial
SF-36	36-Item Short Form Health Survey
WOMAC	Western Ontario and McMasters University Osteoarthritis Index
HRS	Hip Resurfacing System
MHE	Mallory-Head Exeter
3D	Three dimensional
ROM	Range of motion
HHS	Harris hip score
EPI-SPI	Epidural-spinal
HEA	Hypotensive epidural anesthesia
VAS	Visual analogue scale
HB	Hemoglobin
PF	Physical function
RP	Role limitations caused by physical impairment
BP	Bodily pain
GH	General health
VT	Vitality
SF	Social function
RE	Role limitations caused by emotional problems
MH	Mental health
PCS	Physical Component Summary Scale
MCS	Mental Component Summary Scale
PADL	Personal activities of daily living
ASA	American Society of Anesthesiology

LIST OF PAPERS

This thesis is based on the following four papers, which will be referred to in the text by their Roman numerals (I – IV).

I. Petersen MK, Madsen C, Andersen NT, Soballe K: Efficacy of multimodal optimization of mobilization and nutrition in patients undergoing hip replacement: a randomized clinical trial. Acta Anaesthesiol Scand 2006; 50(6):712-717.

II. Petersen MK, Andersen KV, Andersen NT, Soballe K: "To whom do the results of this trial apply?" External validity of a randomized controlled trial involving 130 patients scheduled for primary total hip replacement. Acta Orthop 2007; 78(1):12-18.

III. Petersen MK, Andersen NT, Soballe K: Self-reported functional outcome after primary total hip replacement treated with two different perioperative regimes: a follow-up study including 61 patients. In press. Acta Orthop. Accepted for publication 23.10.2007.

IV. Petersen MK, Andersen NT, Mogensen P, Voigt M, Søballe K: Mechanics of gait after total hip replacement with Hip Resurfacing System or Mallory-Head Exeter prosthesis; a randomized controlled trial. In review.

ABSTRACT

Total hip replacement (THR) has evolved into a reliable and suitable surgical procedure to relieve pain and restore function among patients with damaged or degenerated hip joints and chronic pain.

The longevity of currently available implants is often considered as the main outcome after THR. However, outcome after THR depends not merely on a successful surgical procedure, but also on adequate postoperative rehabilitation. Multimodal rehabilitation, which evolved as a coordinated multimodal effort combining modern concepts of patient care with multimodal anesthetic and analgesic methods, has been introduced to improve rehabilitation after surgery.

The evolution of THR has been aided by information generated from gait analysis studies. Design criteria based on load magnitudes generated during gait have been used for both failure analysis as well as wear testing of new implants. A key to analysis of function following joint replacement is the ability to identify gait adaptations specific to design features.

The aims of this PhD thesis were in randomized controlled designs to evaluate rehabilitation outcome aspects after THR in terms of I) evaluating whether mobilization and nutrition could be optimized during admission, and if so to assess the effects on rehabilitation, II) evaluating the external validity of study I, III) evaluating the efficacy of optimized perioperative care on late phase rehabilitation outcome after THR, IV) evaluating mechanics of gait after THR with two different types of implants.

In study I, we evaluated 79 prospectively randomized patients undergoing elective primary THR. One group received optimized perioperative care (OPC); another group received conventional perioperative care (CPC). Epidural-spinal anesthesia and postoperative epidural analgesia with local anesthetics and opioids were used in all cases. Rehabilitation outcome was measured by length of stay (LOS), and process indicators were mobilization and nutrition. Although mobilization and energy intake were significantly increased in the OPC group compared with CPC group, LOS was moderately reduced (P=0.02). No differences in complications or readmission were seen.

In study II, we studied the distribution of preoperative characteristics and postoperative clinical variables among non-consenters and consenters in study I. In the randomized controlled trial (RCT), 130 patients were identified as potential participants, 18 patients were excluded, 33 enrolled participants declined to participate (non-consenters).

Significant differences were found in both preoperative characteristics and clinical outcome variables. The non-consenters were older, less healthy, and needed more help from the home care system. Furthermore, they were hospitalized longer and were more often transferred to a rehabilitation ward.

In study III, we evaluated the efficacy of two different peri-operative regimes after THR on self-reported functional outcome in 79 prospectively randomized patients. Rehabilitation outcome was measured by the 36-Item Short Form Health Survey (SF -36) and the Western Ontario and McMasters University Osteoarthritis Index (WOMAC). Patients' functional status 6 months postoperatively were compared with an age- and gender-matched healthy cohort. A representative sample of 4098 non-institutionalized Danish adults collected by the Danish National Institute of Public Health was used as controls. We found similar improvements in SF-36 and

WOMAC scores in the OPC group and the CPC group postoperatively, except for the total WOMAC score and the WOMAC sub-score function, which were statistically better in the CPC group. OPC and CPS group were similar with respect to score level. Six months after surgery, THR patients scored higher in the general health sub-scale and lower in three physical sub-scales of SF-36 [(P=<0.01), (P=0.01), P=0.05)] compared with the healthy controls.

In study IV, we evaluated 30 prospectively randomized patients undergoing elective primary THR. One group received Hip Resurfacing System (HRS) implant; another group received Mallory-Head Exeter (MHE) prosthesis. To examine whether one implant was superior to the other we evaluated mechanics of gait 6 and 12 weeks postoperatively. We also investigated whether gait adaptation normalized postoperatively. Laboratory three dimensional (3D) gait analyses were performed 6 and 12 weeks postoperatively. To compare patients with healthy controls, we used data from 22 age- and gender- matched healthy controls. We found similar postoperative improvements in mechanics of gait between the groups except for the peak abductor moments which changed more in the MHE group. HRS and MHE groups were similar with respect to level of peak values. Three months after surgery, most peak values were significantly different between the operated and non-operated hip in all THR patients. Mean curves of kinetic and kinematic variables of THR patients and healthy controls showed that gait adaptations were not normalized after 3 months.

Conclusion

Compared with conventional care, multimodal rehabilitation resulted in a moderate reduction in LOS. We found no differences between groups in relation to complications or pain.

Because the non-consenters did not include patients with contra indications for therapy, our data reinforce the need to provide additional information about recruitment process supplemented with readily available data in order to avoid biased estimates of treatments effects and misleading assessments regarding the degree to which the results may be generalized.

No evidence was found that enforced mobilization and nutrition during admission could affect self-reported functional outcome measured by SF-36 and WOMAC.

We found no evidence that dynamic range of motion (ROM) and muscle strength could be more affected in the early phase of rehabilitation and persisting impairments less in patients receiving a resurfacing implant compared with patients receiving a conventional prosthesis.

Although, THR patients improved considerably impairments in physical functioning and gait adaptation persisted.

1. INTRODUCTION

Since the publication of the initial studies on THR in the 1960s, THR has evolved into a reliable and suitable surgical procedure to relieve pain and restore function among patients with damaged or degenerated hip joints and chronic pain [1-5]. Indications for hip replacement include radiological evidence of joint damage, persistent pain, and/or functional disability that is not adequately relieved by non-surgical treatment such as analgesics or physical therapy [2;4;6;7]. Patients with deterioration due to primary osteoarthritis, fractures, or rheumatoid arthritis constitute the largest group of patients [8-10].

THR has been described as the greatest achievement in orthopedic surgery in the twentieth century [11], and the annual number of THR procedures has risen steadily worldwide during the last decades [1;3;5;10;12]. As the number of primary surgical interventions grows, the number of revisions is expected to increase. The predictability of the results of THR is excellent in the older age groups, whereas the longevity of the implant in young and active patients still remains unsatisfactory, with failure rates ranging from 20% to 42% [13-17]. Surface replacement is a bone-conserving alternative to standard THR. The theoretical advantages of this implant include less inflammatory debris and osteolysis, minimal resection of the femoral head, improved joint stability, and improved biomechanics [18-20]. Restoration of a normal movement patterns of the hip after THR provides better clinical function and reduced wear [18;20-26]. The evolution of THR has been aided by information generated from gait analysis studies. Design criteria based on load magnitudes generated during gait have been used for both failure analysis and wear testing of new implants. A key to analysis of function after joint replacement is the ability to identify gait adaptations specific to design features [27]. Several studies have used gait analysis to study functional outcome after THR [28-39].

When the outcomes of THR are evaluated, numerous factors other than the surgery itself should be taken into account. Outcome after THR depends not merely on a successful surgical procedure, but also on adequate postoperative rehabilitation. Multimodal rehabilitation or fast-track surgery has been introduced to reduce the surgical stress response, improve recovery, reduce hospitalization, and improve rehabilitation after surgery [40-42]. However, no current evidence suggests any single measure to improve postoperative rehabilitation after THR [43;44].

Although, the randomized controlled design is regarded as the gold standard for evaluation of the effect of an intervention, its external validity has been questioned [45;46]. RCTs can not be expected to produce results that are directly relevant to all patients and all settings, but they should at least allow patients and clinicians to judge to which groups of patients trial results can reasonably be applied.

The background for this thesis was, in a randomized design, to evaluate the efficacy of a perioperative multimodal optimization program on rehabilitation outcomes after THR, and to assess the external validity and generalizability of the trial result. Furthermore, we set out to evaluate gait characteristics after THR in relation to two different types of implants to examine whether one of the implants was superior to the other.

2. BACKGROUND

2.1 Osteoarthritis

In the hip joint, several biomechanical factors seem to be important in development of osteoarthritis, for instance, joint incongruence due to developmental or congenital malformations [47], excessive high loads [48;49], and subluxation. The initial symptoms of osteoarthritis are often vague, but typically present is noncharacteristic pain in the groin radiating to the anterior femur and the knee on loading the joint, especially at the end of a range position. The walking distance is reduced and some individuals experience locking, snapping, weakness, or instability of the hip joint [50]. When osteoarthritis progresses, most patients develop a loading triad: pain when a movement is initiated, followed by temporary alleviation, succeeded by worsening. The pain is often localized in the groin with pain radiating down the femur and the greater trochanter and possibly to the knee.

Even at an early stage of osteoarthritis, pain and pathological deformity in the hip joint lead to changes in joint moments and power around the ankle, knee, and hip joint during gait [51-53]. The overall hip function of patients referred to surgery is often measured with Harris Hip Score (HHS) [54].

The radiological symptoms of osteoarthritis are narrowing of the joint space, increased sclerosis of the head and acetabulum, cysts in the head or acetabulum, osteophytes, and later loss of sphericity of the femoral head (Figure 1). A method to estimate osteoarthritis radiological is measuring the minimal joint space width [55].

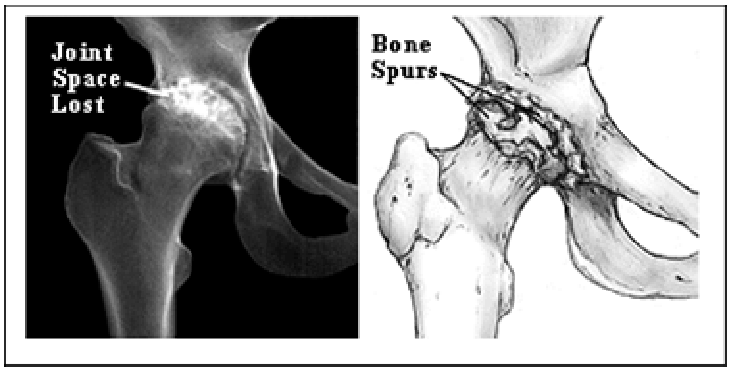


Figure1.

Radiograph of osteoarthritis in right hip joint with loss of sphericity of head and severe narrowing of the joint space.

2.2 Total hip replacement

THR is a surgical procedure which involves surgical removal of diseased cartilage and bone from the femoral head and acetabulum and replacing them with an artificial ball joint, which includes a stem inserted into the femur bone with a ball on the top and an artificial socket with plastic liner inside the acetabulum.

The artificial ball, stem, and socket are referred to as the prosthesis or the arthroplasty (Figure 2).

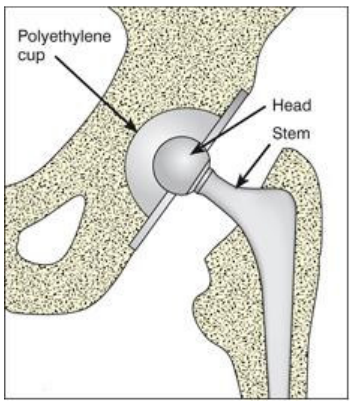


Figure 2. Total hip Replacement

The prosthesis consists of a cup which is fixed into the damaged acetabulum and a metallic ball which replaces the damaged head.
The ball is connected to a femoral prosthesis which is fixed inside the femoral shaft. A THR may be cemented or uncemented.
In a cemented THR the implant is fixed to bone by the use of special cement. In an uncemented THR both the cup and the femoral stem can have special coating which allows it to get fixed to bone without the use of cement.

The history of THR began in 1925 when Marius Smith-Peterson from Boston, Massachusetts, United States of America (USA) fitted molded glass over the ball of patients' hip joints [56].
In 1961, Sir Charnley from England was the first to demonstrate long-term success by using a prosthetic implant attached to bone with self-curing acrylic cement [57;58].
The performance of THR can be measured in different ways, including the occurrence of postoperative complications or the implant failure rate. The term implant failure is used when a part of or the whole implant is removed or exchanged. Aseptic loosening with or without osteolysis of the femur and/or the acetabulum component is the main cause of revision [9].
The longevity of currently available implants, the rate at which surgical revisions are needed to replace failed implants, and the ease with which implants can be replaced are of great concern in the orthopedic field [5;9;10;12;13;15-17;59-62].
THR in its current format has proved very effective in late middle-aged and elderly patients, with survival rates in excess of 90% at 10 years [10;12]. In relation to implant failure due to any reason, younger age and males have consistently been found to be associated with an overall higher risk after 5,10, 15, or 20 years' follow-up [10;60;63;64].
The development of new implant materials has primarily focused on extending longevity in order to avoid revision. A secondary consideration is preserving the integrity of the remaining bone, to make future revision surgery easier.

2.3 Metal on metal hip resurfacing arthroplasty

Hip resurfacing involves the removal and replacement of the surface of the femoral head with a hollow metal hemisphere. The hemisphere fits into a metal acetabular cup (Figure 3). Hybrid or all-cementless fixation is used. The technique retains the femoral head and avoids using the intramedullary devices that are implanted in standard THRs. Surface replacement represents a development in the evolution of hip arthroplasty, and it is a direct descendant of the cup arthroplasty originally conceived by Smith-Peterson [65]. Metal-on-metal surface replacement has been manufactured since the early 1990s [66;67].
It is a bone conserving alternative to total hip arthroplasty that restores normal joint biomechanic and load transfer and ensures joint stability [18-20;68-72].

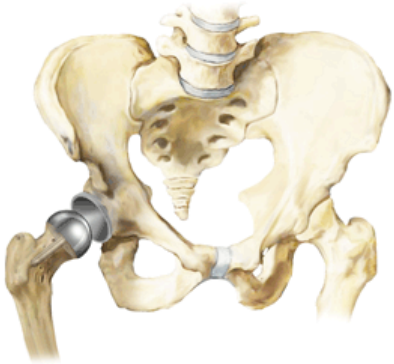


Figure 3. Hip resurfacing replacement.

The femoral head articulates with a matched acetabular component. The femoral head is prepared with bone cutting tools that enable the remaining femoral head to be capped.
The surgical approach is similar to that for standard THR, but with more dissection because the femoral head has to be preserved and displaced to visualize the acetabulum.

Because of the bone conservation, a theoretical advantage of resurfacing is that revision of the femoral component, when necessary, may be easier than revision of an intramedullary arthroplasty [73]. The surgical approach is similar to that for standard THR; however, more dissection is involved in resurfacing THR to prepare the acetabulum without excising the femoral head and neck. The femoral head has to be preserved and displayed to visualize the acetabulum [66;67].

Resurfacing is not appropriate in hips with loss of femoral head and neck bone stock or in hips with femoral cysts. In these patients, resurfacing may cause femoral neck fractures [74]. Therefore the best candidates for resurfacing are younger patients with a good bone stock. Although the early results of the resurfacing devices are encouraging [73;75-81], only a few randomized trials have been performed comparing the traditional techniques of THR with the resurfacing techniques [18;19;82;83]. These studies have primarily focused on the technical aspects of the procedure. There are currently no published results of RCTs that compare the two different techniques with respect to hip function, activity level, or patients' quality of life.

Because the resurfacing surgical technique is more invasive than conventional THR, we hypothesized that range of motion and muscle strength would be more affected during the early phase of rehabilitation in patients receiving a resurfacing implant than in patients receiving a conventional prosthesis. Furthermore, we expected persisting impairments of gait to be less in patients with resurfacing arthroplasty because of better joint stability and biomechanics.

2.4 Multimodal rehabilitation

Multimodal rehabilitation or fast-track surgery, which evolved as a coordinated multimodal effort combining modern concepts of patient education with multimodal anesthetic and analgesic methods, has been introduced to reduce the surgical stress response and minimize pain and discomfort [40;42;84-86]. The methods used have included epidural or regional anesthesia, aggressive postoperative mobilization, and early nutrition (Figure 4).

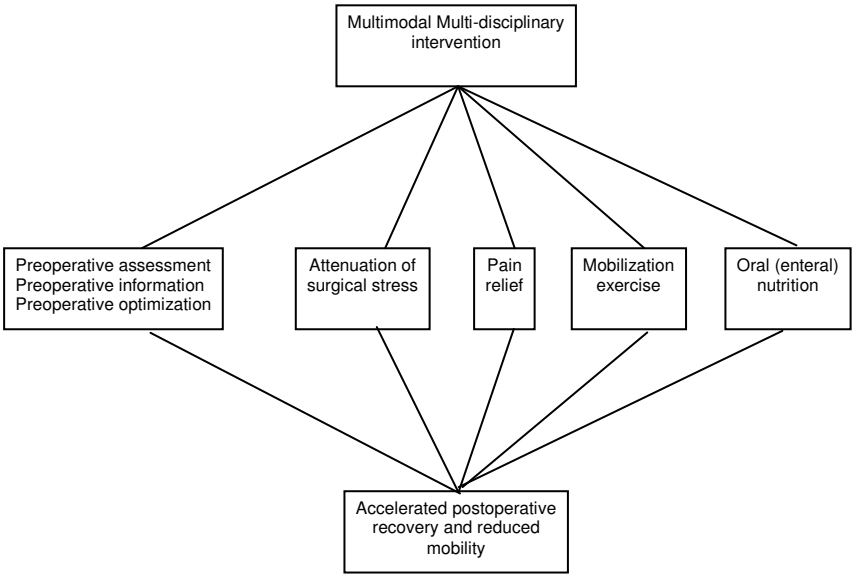


Figure 4.

Multimodal concept of early postoperative rehabilitation [85].

In controlled series of unselected patients, these advances in modern care with emphasis on oral nutrition and physical rehabilitation have been reported to enhance convalescence and reduce post surgical hospitalization [87-90]. It has been argued that the results of these trials could be largely attributed to the epidural analgesia and at best were applicable to a selected group of patients [89]

THR is a major surgical procedure that can be physically and psychologically stressful for patients [43].

In uncontrolled Danish studies it has been shown that multimodal fast- track programs did improve recovery and reduce length of stay after THR without an increase in complications and readmissions [91-93].

Furthermore, these advances in modern care with emphasis on early enforced mobilization and nutrition during admission have been reported to improve physical function and muscle strength in late phase rehabilitation after colorectal surgery [88;89;94].

Multimodal rehabilitation is a program that brings together a number of individually proven measures into a coordinated plan for rehabilitation. A solid evidence base would make the case for provision of the necessary conditions more powerful.

3. AIMS OF STUDIES

The aims of this thesis were as follows:

Study I: To evaluate in a prospective randomized design whether mobilization and nutrition in patients undergoing primary THR could be optimized, and if so, to assess the effects on rehabilitation.

Study II: To evaluate the external validity and generalizability of an RCT that investigated the efficacy of a multimodal optimization program after primary THR and to investigate to what extent results could be extrapolated to the population outlined by eligibility criteria.

Study III: To evaluate the efficacy of multimodal optimization of perioperative care during admission on self-reported functional outcome after THR and to compare patients' self-reported functional status after 6 months with that of an age-matched healthy cohort.

Study IV: To evaluate mechanics of gait after THR in patients with two different types of implants to examine whether one implant was superior to the other. Furthermore we set out to investigate to what extent adaptations to gait were normalized 3 months postoperatively.

4. METHODOLOGICAL CONSIDERATIONS

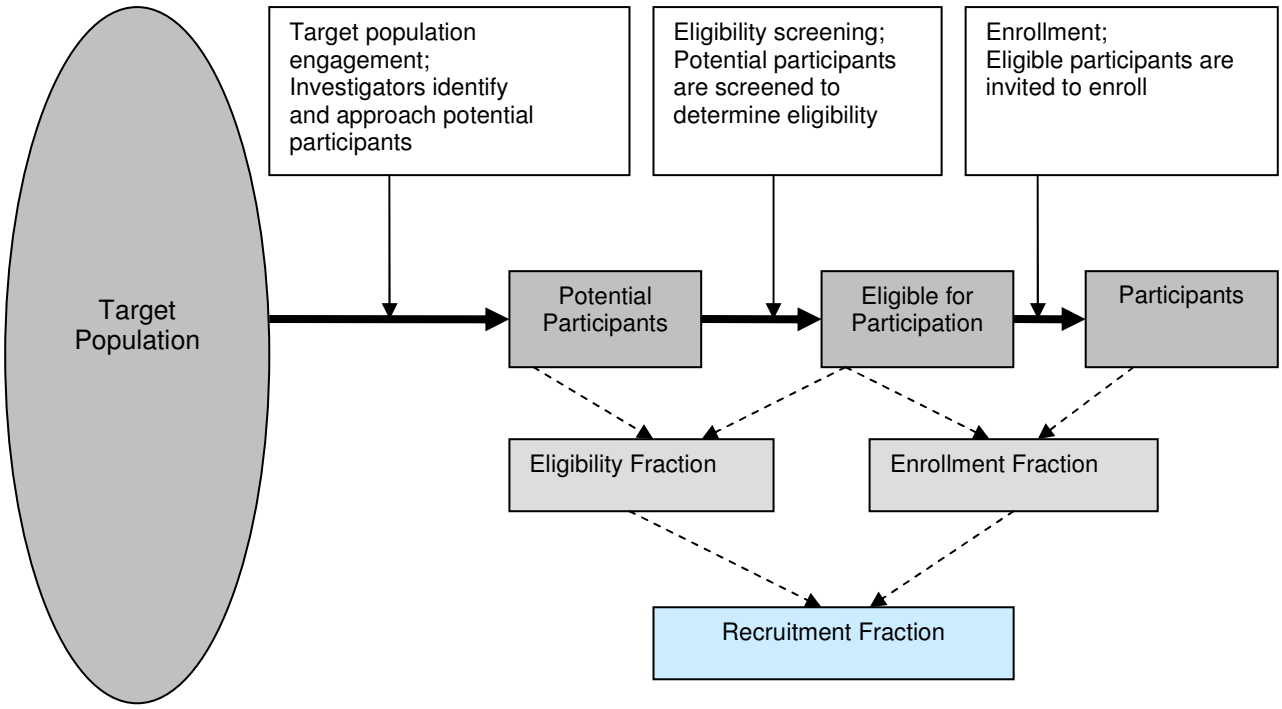
Several points must be considered when evaluating results from the present studies. Design errors, biological variations, and methods used to evaluate results may all influence the results obtained.

4.1 Experimental design

Evidence-based medicine has been defined as the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. This involves the translation of a clinical problem related to the care of a particular patient into an answerable clinical question [95]. In questions about therapy, a non-experimental approach can lead to false positive conclusions about efficacy. RCTs are frequently considered to be the gold standard of study designs for determining the efficacy of different interventions [45;46]. They must be internally valid (i.e. design and conduct must keep the possibility of bias to a minimum), but to be clinically useful the result must also be relevant to a definable group of patients in a particular clinical setting; this is generally termed external validity, applicability, or generalizability. When allocating individuals to a RCT, the intent is to include a strictly homogeneously sample of patients in order to reduce confounding factors. Strict eligibility can limit the external validity in RCTs, but the criteria should at least be available for scrutiny [46]. Even if the randomized comparison in clinical trials is not biased by exclusion per se, external validity of trial results depends on the representativeness of the study sample [96;97]. A step-wise model to describe the recruitment process (Figure 5) is recommended [45]

If only a proportion of potentially eligible patients are enrolled in a trial, it is important to evaluate how participants differ from non-participants as a result of eligibility criteria or other factors [45;98]. The external validity of an RCT also depends on whether the outcome measure is clinically relevant and on the duration of treatment and/or follow-up.

Figure 5. The steps in the recruitment process (Gross CP et al.2002) [45].



5. PATIENTS AND METHODS

5.1 Recruitment of patients Studies I, II, and III

Patients scheduled for elective primary unilateral THR and perioperative epidural analgesia were assessed for eligibility. Exclusion criteria were chronic opioid use, chronic pain syndrome, rheumatoid arthritis, and mental disorders. Randomization was carried out by means of opening sealed envelopes. Block randomization into blocks of eight was used. The sequences were computer generated, and the randomization was carried out by the investigator the day before surgery.

In the study period, 130 patients were identified as potential participants (patients enrolled in study II). Eighteen patients were excluded according to exclusion criteria, and 33 declined to participate. Seventy-nine patients were enrolled and randomized to receive OPC or CPC. Progress through the phases of study I and III is shown in (Figure 6). Demographic and surgical data did not differ between OPC and CPC group.

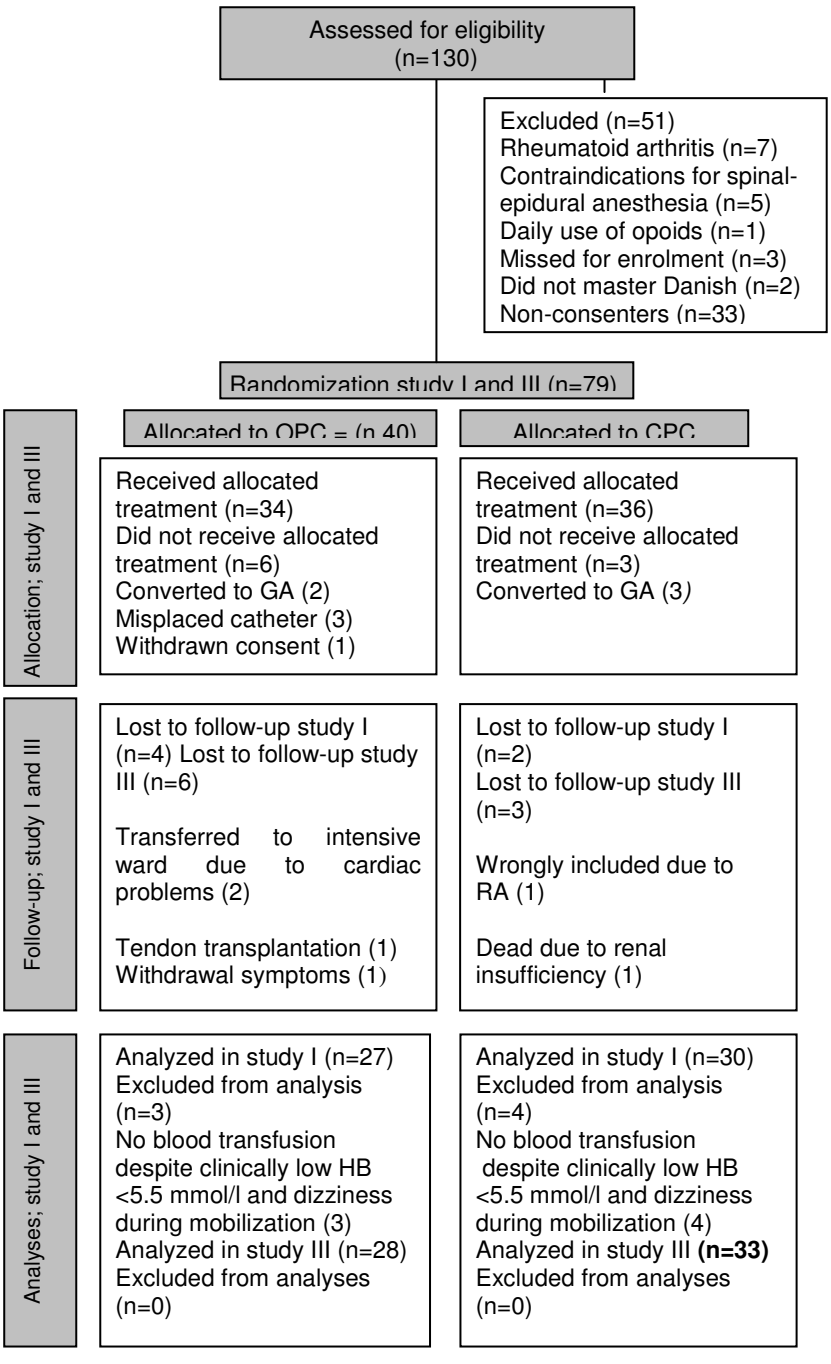


Figure6. Flowchart: progress through the phases of study I and III.

5.2 Recruitment of patients Study IV

Patients between the ages of 50 and 65 years with osteoarthritis scheduled for elective primary unilateral THR were assessed for eligibility. Exclusion criteria were insufficient bone density, exposure to chrome, cobalt, and/or molybdenum, kidney disease, fracture sequelae, hip dysplasia, sequelae to previous hip joint disorders in childhood, rheumatoid arthritis, patients with more than one joint affected by arthritis.

In the study period, 30 patients were included and randomized to receive HRS or MHE prosthesis. Three patients did not receive allocated intervention because of late discovery of conditions that precluded participation in the study (one patient due to bilateral hip arthritis, two patients due to insufficient bone density) and five patients were lost to follow-up (one patient had prolapsus intervertebralis, one patient had a deep wound infection, three patients withdrew consent). Twenty-two patients completed the study, 11 patients in each group. Patient characteristics and surgical data were similar except for the HRS group having a significantly longer surgical time [97.8 minutes (SD12.4)] compared with the MHE group [70.0 minutes (SD17.2), (P=0.01)]

6. SUMMARY OF STUDIES DESIGN

Different designs were used according to the particular question under investigation. Because all studies were experimental, they were longitudinal and prospective, and conducted in a randomized controlled design. All studies were approved by the local ethic committee and followed Helsinki Declaration guidelines.

6.1 Choice of experimental design Study I

The study was a non-blinded, prospective, randomized controlled study.

Patients were randomized to receive OPC or CPC.

All patients received standardized multimodal anesthesia and analgesia throughout the peri- and post-operative periods. According to departmental guidelines, all operations were performed using combined epidural-spinal anesthesia (EPI-SPI) or hypotensive epidural anesthesia (HEA). EPI-SPI was achieved with 3ml bupivacaine 0.5% plain (L_3-L_4). Epidural catheter was placed L_2–L_3. The systolic blood pressure was kept > 100 mm Hg, supported by injections of ephedrine if needed. HEA was achieved with ropivacaine 1 % by epidural catheter placed at level Th_{11}- Th_{12} to a fall in mean arterial blood pressure of 45 – 50 mm Hg.

Postoperatively, epidural analgesia was initiated when the motor blockage was equivalent to ≤ 2 on a modified Bromage scale (EPI-SPI) or thermalgesia under TH6 (HEA). No priming dose was given. Postoperative analgesia within the first 48 hours was attained with epidural ropivacaine 2 mg/ml with fentanyl 2 μ /ml 4 ml/hour or epidural ropivacaine 2 mg/ml with morphine 50 μ /ml 4ml/hour. A 4 ml bolus was given when the visual analogue scale (VAS) was >3 in rest and >5 mobilizing.

In addition to epidural infusion, 1 g of acetaminophen was given four times daily.

The epidural catheter was removed after 48 h, and Oxycontin® (oxycodonhydrochlorid) 10 mg twice a day and acetaminophen 1 g four times daily were given.

When the postoperative hemoglobin (HB) was <5.5 mmol/L and if the patient had clinical symptoms (dizziness during mobilization), a blood transfusion was given.

Disposal catheters were used when urine retention was > 350 ml documented by a bladder scan [99]

All patients received physiotherapy for ½ hour daily on weekdays and were discharged from hospital with a home-training exercise program. No further rehabilitation was established.

Because the department at which the study was conducted keeps all THR patients in one ward, it was not an option to randomize patients to two different wards. Another possibility could have been to use another hospital as a control, but this possibility would introduce new, possible bias due to differences in surgical techniques, management of anesthesia and analgesia, and postoperative regimes for physiotherapy.

In order to minimize bias caused by the attitudes of care takers, the optimization strategies were administrated by the investigators who were not members of the staff, and who were not involved in the decisions of patient discharge.

The OPC group got an optimization package that involved pre- and post-operative strategies. The optimization strategies are described in (Table1)

Table 1. Optimization strategies in the OPC group.

Preoperative education	Postoperative mobilization	Postoperative nutrition
➢Progressive fixed standard plans for mobilization and energy intake was introduced and delivered ➢Patients were informed about the optimization program and mutual expectations discussed ➢Transfer and walking techniques required after surgery were trained ➢Devices to be used postoperatively were introduced and delivered	➢Postoperatively patients were encouraged to follow written standard guidelines ➢Mobilization (sitting out of bed, and walking from bed to chair) was initiated the first postoperative day ➢Scheduled time out of bed increased by two hours a day, from 2 hours on the day after surgery to 12 hours on the sixth postoperative day ➢Patients were asked to walk the length of the ward corridor (2x50 m) a scheduled number of times increasing by 100 m on the 2 post.opr day to 500 m on the sixth postoperative day	➢Early and aggressive fluid and diet was introduced from the day of the operation ➢Eating and drinking despite lack of appetite was encouraged ➢Registration and calculation of energy intake was performed daily, and results discussed with the patients ➢Supplementary energy intake; 200 cc of a protein-rich drink was served 3x daily between the main meals

The control group received none of the optimized measures listed in the table (Table 1), and the team treating the patient responded to the will and condition of the patient with regard to providing post-operative care.

To control the efficacy of the optimization strategies, for the first 6 postoperative days all patients were asked to keep time records for leaving and returning to bed, walking distance was measured using a marked area of the ward corridor, and for the first 4 days all nutritional intakes were registered in a food record. Data were registered in a patient diary, and patients were assessed daily by one of the researchers. An analysis of the process indicators (mobilization and nutrition) showed that the optimization strategies worked.

6.2 Choice of experimental design Study II

The study was a prospective cohort study with an embedded RCT.

In order to evaluate the extern validity and generalizability of study I, we used a standardized abstraction instrument as recommended by Gross [45] . Trial recruitment terminology and population under investigation is described in (Table 2). We analyzed the available data to estimate differences between eligible consenters, eligible non-consenters, and excluded individuals. No patients were lost to follow-up.

Data for potential participants were collected prospectively. Preoperative baseline characteristics and postoperative clinical endpoint variables of eligible consenters, eligible non-consenters, and excluded patients were compared in order to assess to whom trial results could reasonably be applied.

Table 2. Trial enrollment terminology and description of study population in study II.

Term	Definition	The population under investigation
Target population	Location and characteristics of potentially eligible persons; represents the individuals to whom the trial results are expected to apply	Patients scheduled for elective primary unilateral THR and peri-operative epidural analgesia (N= 130)
Eligibility fraction	Proportion of potential participants who undergo screening and are eligible to enroll	Reason for exclusion of enrolment (N=18): • Rheumatoid arthritis (7) • Contraindications for epidural analgesia (5) • Daily use of opioids (1) • Missed for enrolment (3) • Unable to communicate in Danish (2)
Enrolment fraction	Proportion of patients who are eligible for participation and who actually enroll	Patients asked for informed consent (N=112)
Recruitment fraction	Proportion of potential participants who are actually enrolled and randomized	Enrolled and randomized patients (N=79)

6.3 Choice of experimental design Study III

The study was an explorative prolonged follow-up study of a cohort defined by the RCT described in Study I.

Preoperatively and 3 and 6 months postoperatively, data on self-reported functional outcome were collected from the recruitment fraction in study I. Postoperatively, questionnaires were mailed to patients with a stamped and addressed envelope. Three patients (4.7%) did not return the questionnaires. In order to compare THR patients self-reported functional status with healthy controls, we used data from a representative sample of 4098 non-institutionalized Danish adults. These data were collected in 1994 as a part of a population health survey carried out by the Danish National Institute of Public Health [100]. Six months postoperatively, self-reported physical scores of THR patients were compared with matching scores of the healthy population.

6.4 Choice of experimental design Study IV

The study was a non-blinded, prospective, randomized controlled study.

In all cases, an uncemented acetabular component and a cemented femur component were used.

The HRS from (Biomet ®) was used in the HRS group, and in the MHE group, a Mallory-Head cup (Biomet ®) and an Exeter stem (Stryker®) were used. Compared with the conventional prosthesis, the articulating surface of the resurfacing implant is much larger.

Surgery was performed in the lateral position, and a posterior approach was used in all cases. The resurfacing surgical procedure included a loosening of the of the gluteus maximus fibers from the bursa, and a release of the distal muscle insertion from the femoral bone.

All operations were performed by one senior surgeon, and all patients followed the same standardized postoperative rehabilitation program with full weight bearing allowed from the day after the operation. All patients were discharged with a home training exercise program, and no further rehabilitation was established. In order to assess patients' functional status preoperatively, WOMAC were completed the day before surgery.

All patients underwent 3D gait analysis 6 and 12 weeks postoperatively. Gait analyses were performed and processed by one examiner (physiotherapists) in the Movement Laboratory at the Hammel Neurocenter. All staff members involved in gait analysis were blinded as to type of prosthesis.

7. DESCRIPTION OF OUTCOME MEASURES

7.1 Patient based outcome measures

A number of trends in health care have resulted in the development and growing use of patient-based outcome measures to assess matters such as functional status and health-related quality of life [101;102]. It is recognized that traditional biomedical defined outcomes such as clinical and laboratory measures need to be complemented by measures that focus on patients' concerns in order to evaluate interventions and identify more appropriate forms of health care. Patient-based outcome measures provide a feasible and appropriate method for addressing the concerns of patients in the context of controlled trials [8;103]. In clinical research, outcome instruments are of major importance. They have to be valid, reliable, and responsive to changes [104-106]. Generic instruments are intended to capture a very broad range of aspects of health status and the consequences of illness, and they are considered suitable for comparison of health status between diseases. The disease-specific instruments provide patients' perceptions of a specific disease or condition and are useful for measuring clinically important changes in response to treatment [107]. Often, use of both a generic and a disease-specific instrument are recommended [103;108;109].

The SF -36 is a generic, self-administered instrument for measuring different aspects of the quality of life [110;111]. It consists of eight scales and 36 items that measure physical function (PF), role limitations caused by physical impairment (RP), bodily pain (BP), general health (GH), vitality (VT), social function (SF), role limitations caused by emotional problems (RE), and mental health (MH). The 36 items can be incorporated into a physical and mental summary scale (PCS and MCS). The SF-36 scores range from 0 to 100, with a higher score indicating better health status. Normalized values can be estimated to provide a reference value from the general population.

The WOMAC is a disease-specific, self-administered instrument developed to study patients with hip or knee osteoarthritis [105;112]. It has a multidimensional scale comprising 24 items grouped into three dimensions: pain, stiffness, and physical function. We used the Visual Analogue scaled formats (WOMAC VA3-series) rating from 0-10 cm, where 0 is no symptoms and 10 is worst possible symptoms.

The SF-36 and the WOMAC have been recommended as valid outcome measures to detect significant and meaningful clinical changes in trials evaluating outcome after THR [8;104;112-119].

7.2 Three dimensional gait analysis

Gait analysis in a laboratory consists of the collection of biomechanical data (kinematic, kinetic, and electromyography), and is often accompanied by videotaping to give an overall interpretation of the of the patient's walking ability. 3D gait analysis is a sophisticated laboratory technique by which modern electronics are used to incorporate information from a number of inputs.

Kinematic is the study of movement, requiring the recording of time and distance data, joint angles, and accelerations over time (temporal-spatial data). Kinetic is predominantly concerned with the forces and moments between the foot and the ground and can also interpret the position of the ground reaction force vector relative to each joint [120].

Multiple cameras are configured around a calibrated measurement volume and one or two force plates are placed in the middle of a walkway to measure ground reaction forces beneath one or two feet (Figure 7).

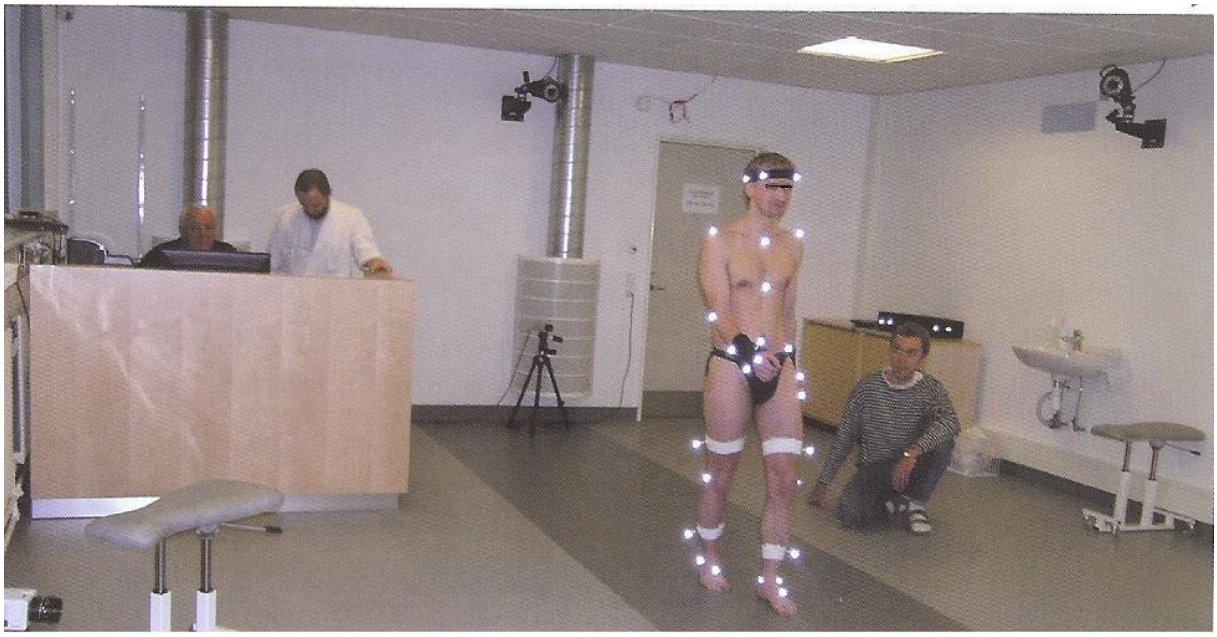
Figure 7.

A view of the Gait and Movement Analyses Laboratory, Hammel with walkway and positioned cameras.

The primary technology includes optica-electronic video camera-based systems that measure displacement of retroflective markers placed on the patient's skin and aligned in some fashion with bony landmarks and particular axes of joint rotation (Figure 8). Data from the cameras and force plates are send to a data station. Vicon Workstation (Oxford Metrics Limited, Oxford, and U.K) is an available motion measurement system of this type

Before each measurement session calibration has to be carried out. Calibration is the process that linearises each camera and measures each camera's position relative to the others. The calibration data is used in the reconstruction process to create a virtual 3D motion. 3D marker trajectory paths are stereometrically reconstructed from the two dimensional camera image data. The reconstruction is a calculation of the 3D position of each marker in each frame by using the two dimensional data from each camera and calibration parameters. A trajectory is the path of a marker during the trial. Vicon Workstation (Oxford Metrics Limited, Oxford, U.K) calculates the trajectories by joining the positions for each marker frame by frame.

Figure 8. Capture of data from a normal subject.



Fundamental in this approach is the definition of relation between the markers placed on the skin surface and the underlying bony geometry. In this way, the operator is able to establish a "technical coordinate system" associated with the externally placed markers and an "anatomical coordinate system" associated with the underlying bony structures for each body segment under examination [121] . An embedded or body-fixed coordinate system may be determined for any body segment (assumed to be ridged) that has at least three markers attached to it (Figure 9).

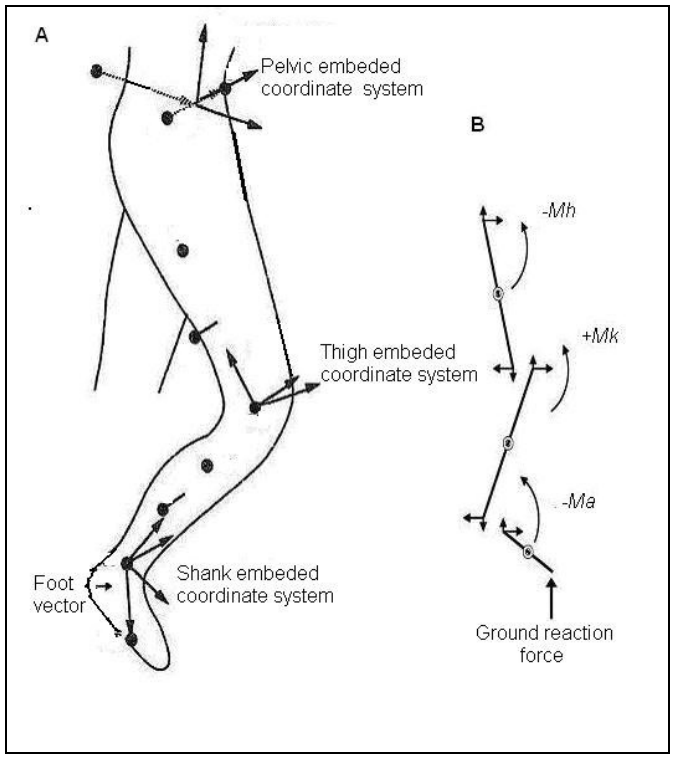


Figure 9.

A. Lower extremity, embedded coordinate systems used to compute the joint angles as frames of reference for the joint moment reactions.

B. Lower limb, free body diagram with the definition of positive directions of moments in the respective joint; hip joint (M_h), knee joint (M_k), and ankle joint (M_a) according to the gait model (Vicon Plug-In-Gait) (Oxford Metrics Limited, Oxford, U.K).

The combination of data from the force plate and kinematic data from the television system enables a mechanical analysis of the gait to be performed. In addition to the kinetic and kinematic data, these calculations require the mass and moment of inertia of each limb segment, and the location of its center of gravity. Such information is not directly available, but it must be estimated from body weight and a number of linear measurements.

Inverse dynamics are used to calculate the joint moments and power. Inverse dynamic is a fundamental and commonly used computational procedure for analysis of human movement. With anthropometric and kinematic information as the input, an inverse dynamic procedure calculates the force and torque reactions at various body joints [122]. A standard 3 D inverse dynamic approach to calculate joint torques as implemented in the Vicon Clinical Manager software package (Oxford Metrics Limited, Oxford, U.K.) can be used.

8. SUMMARY OF OUTCOME MEASURES

8.1 Choice of outcome measures Study I

LOS was registered from the day of admission to the day of discharge. Although other studies evaluating a multimodal approach in the management of surgical patients have used a reduction in the need for hospitalization as main outcome, the validity of LOS can be questioned. In order to minimize bias, we used standardized discharge criteria as recommended [41], and furthermore, discharge was considered by departmental surgeons who were blinded to randomization. Patients were considered for discharge if sufficient pain relief was obtained estimated as a VAS score< 3 cm resting and < 5 cm mobilizing, patients were able to maintain personal hygiene, walk with sticks and climb stairs. Pain intensity was estimated postoperatively using a VAS [123;124] every third hour during the first 24 h, subsequently every 8 hours until removal of the epidural catheter, and then once a day until discharge. Ability to perform personal activities of daily living (PADL) was estimated by the Katz index [125]. Independency was defined as ability to perform all six activities unassisted. Because we did not record data on decision to discharge, we have no explanation for what kept patients in hospital. However, our findings suggest that factors other than recovery of PADL and pain influence hospital stay, and support the criticism of the validity of LOS as an end-point measure.

In order to determine whether the use of different types of anesthesia and analgesia had an impact on recovery, a stratified analysis was made.

8.2 Choice of outcome measures Study II

Data for the study were abstracted from evaluation charts. The form included information on age, sex, type of anesthesia, American Society of Anesthesiology (ASA) classification, social and occupational factors, preoperative HHS [5;126], pre- and postoperative need of home care service, length of hospitalization, transfer to rehabilitation ward, and prevalence of postoperative complications. Postoperative complications and readmission were registered within the first 30 days after surgery. LOS, discharge criteria, and considerations about discharge were measured and registered in the same way as in study I.

Our data reinforce the need to collect and provide additional information about the recruitment process, supplemented with available quantitative data on all patients considered for enrollment.

8.3 Choice of outcome measures Study III

The SF -36 and the WOMAC were completed preoperatively and 3 and 6 months postoperatively. Changes in scores were calculated by subtracting the baseline scores from the follow-up scores. Changes over time and score level were compared between the two groups under investigation and tested statistically

Modern outcome assessment focuses on identifying reproducible and valid instruments that can be used to analyze patient outcomes after THR [5;126;127]. Validity and responsiveness are the most important criteria in deciding which particular instrument to use in a clinical trial [103;105]. Although generic instruments are useful in providing comprehensive health ratings that can be used across various disorders, they may be inferior to disease-specific instruments in their responsiveness in relation to intervention studies in which measurements are repeated. The lack of responsiveness may be caused by a ceiling or a floor effect, which means that improvements or deterioration can not be detected in patients with maximum respectively minimum score at baseline. We experienced that postoperatively, SF-36 showed a more conscious ceiling effect than WOMAC. On this basis we assume, in accordance with other studies [113;115-117], that WOMAC is more responsive to changes. A weakness of the study design is that we did not assess patients, clinical laboratory values, body composition, and muscle strength in order to be able to compare our results with other studies investigating enforced mobilization and nutrition[89;94].

8.4 Choice of outcome measures Study IV

The laboratory gait evaluation included simultaneous recording of body kinematic, kinetic, and muscle activation in patients walking unassisted at their natural cadence. The 3D gait analysis was carried out using a Vicon 612 8-camera system (Vicon, Oxford, UK), operating at 100 Hz and using a Helen Hayes marker set up [128;129]. Ground reaction forces were recorded using an AMTI force plate located in the middle of a 10-meter walkway. The sampling rate of the force plate data was set at 2000 Hz. Data from the force-plate and data from the cameras (frame rate 60 Hz) were synchronized and captured in a data station (Vicon Workstation). Before each measurement session, a static and dynamic calibration was carried out to allow the system to define the capture volume and the relative position and orientation of each camera. A reconstruction process was carried out to create virtual 3D motion, combining data from every camera by calculating the 3 D position of each marker in each frame and linking these points into a trajectory. On this basis, a 3D model for each segment of the body could be constructed. The relative angles between coordinate systems of each segment in the lower limb, the absolute angles between a coordinate system of pelvis and the laboratory coordinate system, and the moment of force in each joint from the kinematic data and the ground reaction force could then be calculated. Reconstruction and inverse dynamic calculations were carried out with the Vicon clinical manager software (Vicon workstation). Three of five trials of each leg were selected on the criteria of speed similarity as recommended by Vardaxis et al [130]. These trials were processed for further analysis with Vicon Plug-In-Gait soft ware (Vicon, Oxford, UK). The beginning of a gait cycle was defined as the moment of heel strike, and the end of the cycle was defined as the next heel strike of the same leg. The gait cycle was normalized on a time basis of 100%.

To compare patients self-reported functioning at baseline WOMAC scores were calculated preoperatively. End-point outcome measures were changes over time, changes in the magnitude of the peak values of gait parameter variables of the operated hip, and differences between operated and non-operated hip. The temporal-spatial variables analyzed were gait speed, cadence, stride length, step length, stance phase duration, and single support for both limbs. Kinematic and kinetic variables analyzed were ROM of the hip joint in all directions and the corresponding moments for both limbs. Positive, negative, and total work power during a gait cycle was calculated. To estimate to what extend normal gait adaptation was restored; the operated hip was compared with the non-operated healthy hip 12 weeks postoperatively. To evaluate whether it was reasonable to assume that the

non-operated hip was an appropriate reference, mean curves of kinematic and kinetic variables of the operated and non-operated hips were compared with values obtained from a matched healthy control group.

Despite widespread use, it is well recognized that inverse dynamic solutions are prone to errors. Errors can stem from a variety of sources, including inaccuracies in segmental parameters, ground reaction force measurements, inaccuracies related to locating joint centers, and inaccuracies caused by the relative motions between surface markers and underlying bones [131]. Because the inverse dynamic calculation is an interactive process starting from the ankle joint, the largest errors due to error propagation and error accumulation occurs at the most proximal joint in the model. Even though special care was taken to minimize bias, we can not eliminate the uncertainties in torque estimates derived through inverse dynamics, which can be substantial.

9. STATISTICS

9.1 Sample size

Elements of the sample size calculation were as follows:

- the alpha (Type I) error level
- the statistical power (Type II) error level
- the standard variation (SD) of the chosen effect variable estimated from the literature or pilot studies.
- the estimated minimal relevant difference in outcome between groups (MIREDIF)

For power calculations in Studies I and IV, we used the formula: $N= C_{2\alpha+} C_{\beta})^2 * S^2 / \Delta^2$.

Due to study design, sample size was not calculated in studies II and III.

9.2 Sample size Study I

We assumed that the intervention would not affect LOS in a negative direction.

Data for the sample size calculation was extracted from a database register at the Department of Orthopedics at Aarhus University hospital. Data on LOS from the year before the study was used to estimate MIREDIFF and SD. Mean LOS was estimated to 11.7 days (SD; 4.2). With a significance level of 5%, a power of 80%, and an expected reduction in LOS of 30%, sample size was estimated to be 50 patients. To compensate for patient dropout we planned to enroll patients until at least 25 patients per group had fulfilled the study protocol.

9.3 Sample size study IV

We expected gait adaptation in the early rehabilitation phase to be more affected in the HRS group. We especially expected hip ROM in the sagital plan to differ between the two implants.

Data from a previous study using gait analysis were used to estimate sample size. The estimate of the observed ROM in the sagital plan during one stride was 39.4 (SD 5.3). With a clinical relevant difference in ROM of 10%, a power of 80% and a significance level of 5%, sample size were estimated to 20 patients. To compensate for patient dropout we planned to enroll patients until at least 10 patients per group had fulfilled the study protocol. We ended up with 22 patients (11 in each group).

9.4 Statistical methods used

Statistical analyses were performed with SPSS 11.0 or SPSS 12.0 (Inc. Headquarters, 233 S. Walker Drive Chicago, Illinois 60606 USA) software package. Data normally distributed are described by means, SD, and 95 % CI, and statistically tested by Student's *t* test or by a repeated measurement model (Two-Way ANOVA). Non–parametric data are described by medians and range, and statistically tested by Mann-Whitney U test.

Frequency was compared using Fisher's exact test. Correlation between variables was tested using a weighted Spearman´s rho calculation from correlations within each of the groups.

Sf-36 and Womac variables are described by means or mean changes and 95% confidence interval (CI). Changes over time and score level were compared between the OPC and the CPC group, and were statistically tested for differences by a repeated measurement model (Two-Way ANOVA).

To compare the SF-36 sub-scales GH, PF, RP, and PCS in the THR group six months postoperatively with matching scores obtained in healthy controls, a weighted estimate of the differences between groups was calculated after stratification into six-age groups using the weights ($1/see^2$), where see is the standard error of the estimate within an age group.

Peak values of gait parameter variables are described by means and SD. Changes over time and changes in score level were compared between the HRS and MHE groups and were statistically tested for differences by a repeated measurement model (Two-Way ANOVA).

Peak values of gait parameter variables of the operated and the non-operated hip in the HRS and MHE groups were compared and analyzed for differences by a repeated measurement model (Two-Way ANOVA).

Mean curves of kinematic and kinetic values during a normalized gait were described but not analyzed statistically.

The level of significance was chosen to be 0.05. $P<0.01$ was considered highly significant.

10. SUMMARY OF RESULTS

10.1 Study I

Process Indicators (mobilization and nutrition PADL):

The analysis of the process indicators showed that mobilization and nutrition were highly significantly increased postoperatively in the group OPC group compared with the CPC group (Figure 10)

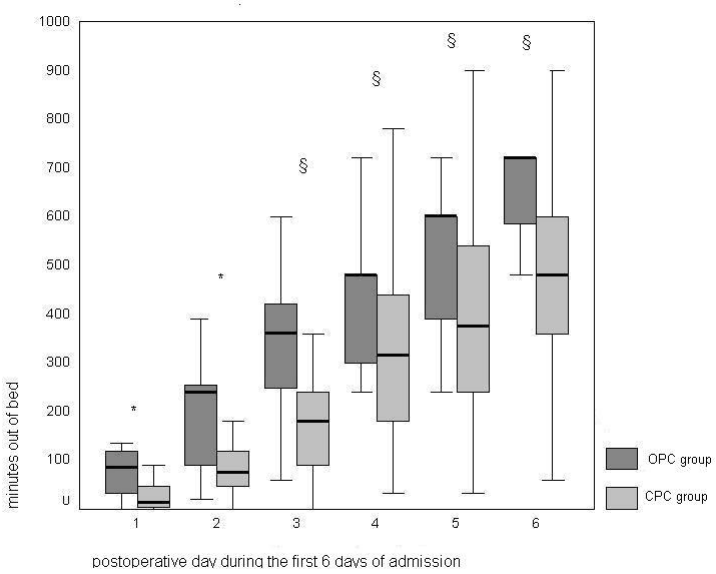


Figure 10.

During the first days of admission, mobilization in the OPC group was much more efficient than in the control group.
*= P<0.01 §=P<0.05.

The average total time out of bed was 37 h (SD 10) in the OPC group and 26 h (SD 14) in the CPC group (P=0.001). The median total walking distance was 1500 m (247-7900) in OPC group and 1200 m (247-7900) in CPC group. The average energy intake in the OPC group was 103.4 kj/kg (SD 25.9) compared with 76.1 kj/kg (SD 23.9) in the CPC group (P<0.001), and the average protein intake was 1.3 g/kg (SD 0.4) and 0.7 g/kg (SD 0.3), respectively (P<0.001).

The median day of independency in PADL was the third post-operative day (range 1-4) in the OPC group, and the fourth post-operative day (range 1-5) in the CPC group. The difference was not significant (P=0.22)

End-point outcome (LOS)

In the per-protocol analysis (n=57), the median LOS in the OPC group was 7 days (1-9) and in CPC group 8 days (1-10), (P=0.02). In the intention-to-treat analysis (n=64), no significant differences in LOS between groups were seen (P=0.2).

Confounders (complications and pain)

No differences in complications were found between groups. The relative risk in the intention-to-treat analysis was 1.6 (0.6-4.0), (P=0.4) and in the per-protocol analysis 1.7 (0.5-5.3), (P=0.5).

The median VAS pain score within the first 48 h after surgery was 1.8 (0-5.5) in the OPC group and 1.2 (0-4.1) in the CPC group. During the following days, it was 1.0 (0-5) in the OPC group and 1.0 (0-5.5) in the CPC group. A stratified analysis showed a vague positive (ρ 0.07) but not significant (P=0.62) correlation between ± pain and LOS, and a vague positive (ρ 0.06) but not significant difference between ± HEA and LOS.

10.2 Study II

Preoperative variables

Eligible non-consenters were older than eligible consenters (P=0.01), more often classified in ASA group 2 or 3 (P=0.01), had a lower Harris Hip Score (P=0.05) were more often on transfer income (P=<0.001), and received more often help from the home care service system preoperatively (P=0.001) (Table 3).

Table 3. Characteristics at baseline of eligible consenters, eligible non-consenters, and excluded.
Eligible consenters and eligible non-consenters are com-pared statistically. Excluded patients are described.

Variables	Eligible consenters (n=79)	Eligible non-consenters (n=33)	Excluded (n=18)	P value
Age (years)	57 (26; 84)	70 (27; 90)	56 (23; 80)	0.008
Gender				
Men	36/79 (0.5)	10/33 (0.3)	3/18 (0.2)	0.08
Women	43/79 (0.5)	23/33 (0.7)	15/18 (0.8)	
ASA Classification				
ASA class 1	40/79 (0.5)	9/33 (0.3)	3/18 (0.2)	
ASA class 2	30/79 (0.4)	16/33 (0.5)	12/18 (0.7)	0.01
ASA class 3	9/79 (0.1)	8/33 (0.2)	3/18 (0.2)	
Harris Hip Score	54.86 (14.3)	44.95 (18.5)	41.88 (14.6)	0.05
Social factors				
Married	40/79 (0.5)	21/33 (0.6)	9/18 (0.5)	0.2
Single	39/79 (0.5)	12/33 (0.4)	9/18 (0.5)	
Occupational factors				
Employed	48/79 (0.6)	8/33 (0.2)	7/18 (0.4)	
Old-age pensioner	23/79 (0.3)	17/33 (0.5)	6/18 (0.3)	<0.001
Invalidity pensioner	8/79 (0.1)	8/33 (0.2)	5/18 (0.3)	
Pre opr. home care				
Yes	3/79 (0.03)	9/33 (0.3)	3/18 (0.2)	0.001
No	76/79 (0.1)	24/33 (0.7)	15/18 (0.8)	

Postoperative variables

LOS differed significantly between eligible consenters and eligible non-consenters (P=<0.001), and more patients in the eligible non-consenter group needed help from the home care service system after discharge from hospital (P=< 0.001). A larger percentage of the eligible non-consenters were transferred to a rehabilitation ward (P=0.001). More patients in the eligible non-consenter group had urinary tract infections (P= 0.04) (Table 4).

Tabble 4. Postoperative end-point variables of eligible consenters eligible, non- consenters, and exclude. Eligible consenters and eligible non-consenters are compared statistically excluded patients are described.

Variables	Eligible consenters (n=79)	Eligible non-consenters (n=33)	Excluded (n=18)	P value
Length of stay	8.00 (1;17)	11.00 (6;53)	9.50 (3;28)	<0.001
Transfer to rehab ward				
Yes	3/79 (0.03)	9/33 (0.3)	3/18 (0.2)	0.001
No	76/79 (0.1)	24/33 (0.7)	15/18 (0.8)	
Wound infections				
Yes	2/79 (0.02)	3/33 (0.09)	1/18 (0.05)	0.15
No	77/79 (0.1)	30/33 (0.9)	17/18 (0.9)	
Urinary tract infections				
Yes	12/79 (0.2)	11/33 (0.3)	6/18 (0.3)	0.04
No	67/79 (0.8)	22/33 (0.6)	12/18 (0.7)	
Luxation of the hip				
Yes	0/79 (0)	1/33 (0.03)	3/18 (0.2)	0.29
No	79/79 (1)	32/33 (0.)	15/18 (0.8)	
Post opr home care				
Yes	4/79 (0.05)	15/33 (0.4)	5/18 (0.3)	<0.001
No	75/79 (0.9)	18/33 (0.5)	13/18 (0.7)	

10.3 Study III

No significant differences in change of score were seen between groups except for the total WOMAC score and the WOMAC sub- scale (function), the CPC group having a higher change in score (P=0.03 and 0.03).

The changes over time were all significant [all P values <0.001 except for two (0.007 and 0.009)].

There were no significant differences between the OPC and the CPC groups with respect to level (Table 5).

Table 5. Changes in WOMAC and SF 36 scores between baseline and follow-up 3- and 6 months postoperatively. Differences in changes over time (baseline and 3 month; baseline and 6 month) and differences between groups were analyzed and tested for significant differences by a repeated measurement model.

Variables	Intervention Group (N=28)			Control Group (N=33)			P-values
	Baseline score Mean (SD)	Changes at 3. months Mean (SD)	Changes at 6. months Mean (SD)	Baseline score Mean (SD)	Changes at 3. months Mean (SD)	Changes at 6. months Mean (SD)	Equal changes
WOMAC							
Pain	194 (142 - 245)	144 (98 - 191)	149 (100 - 199)	226 (184 - 269)	187 (145 - 229)	194 (153 - 235)	0.1
Stiffness	90 (69 - 111)	64 (43 - 85)	62 (42 - 82)	103 (85 - 121)	77 (60 - 94)	80 (61 - 99)	0.4
Function	658 (516 - 798)	374 (233 - 516)	456 (325 - 588)	794.7 (666 - 924)	575 (440 - 711)	620 (497 - 743)	0.03
Total WOMAC	941 (737 - 1146)	582 (389 - 776)	668 (476 - 859)	1126 (944 - 1308)	839 (661 - 1017)	894 (728 - 1061)	0.03
SF-36							
Physical functioning	44 (36 - 52)	25 (15 - 35)	31 (22 - 40)	41.7 (34 - 50)	27 (17-36)	32.3 (24 - 41)	1.0
Role physical	38 (22 - 53)	17 (-2.3 - 36)	30 (12 - 49)	24 (11 - 36)	30 (13 - 46)	39 (23 - 56)	0.6
Bodily pain	42 (33 - 50)	38 (29 - 47)	43 (35 - 52)	38 (31 - 45)	39 (28 - 49)	48 (39 - 56)	0.6
General health	61 (54 - 69)	11 (4 - 17)	11 (4 - 18)	70 (64 - 77)	6 (2 - 13)	7 (-1 - 15)	0.6
Vitality	55 (47 - 62)	11 (3 - 19)	18 (9 - 26)	53 (45 - 62)	16 (7 - 25)	19 (10 - 28	0.5
Social functioning	80 (70 - 90)	3.6 (-6 - 13)	12 (5 - 19)	71 (61 - 81)	12 (2 - 22)	17 (8 - 27)	0.5
Role emotional	61 (44 - 78)	18 (1 - 35)	23 (6 - 40)	52 (35 - 68)	8 (14 - 30)	27 (9 - 45)	0.2
Mental health	74 (67 - 80)	7 (0.1 - 13)	10 (3 - 17)	74 (67 - 80)	7.2 (-0.5 - 15)	8.4 (-0.3 - 17)	0.8
PCS	33 (30 -37)	11 (7 - 16)	14 (10 - 18)	33 (30 - 36)	13 (9 - 16)	15 (11 - 19)	0.9
MCS	53 (49 - 57)	1 (2 - 4)	-3 (-0.3 - 6)	51 (47 - 55)	1 (-4 - 5)	3 (-1 – 4.0)	0.9

WOMAC showed a minor ceiling effect 3 and 6 months postoperatively in all domains, and SF-36 presented both floor and ceiling effects preoperatively and 3 and 6 months postoperatively (Table 6).

Table 6. Psychometric properties of WOMAC and SF-36 at baseline and at follow-up 3 and 6 month postoperatively showing proportion of patients on lowest score (floor effect) and proportion of patients on highest score (ceiling effect). All values are number of patient

Variables	Study population N=61					
	Baseline		3 month postoperatively		6 month postoperatively	
	Proportion of patients on lowest score	Proportion of patients on highest score	Proportion of patients on lowest score	Proportion of patients on highest score	Proportion of patients on lowest score	Proportion of patients on highest score
WOMAC						
Pain	0	0	0	5	0	9
Stiffness	0	0	0	6	0	9
Function	0	0	0	3	0	4
SF-36						
Physical functioning	1	0	0	2	0	4
Role physical	32	9	20	24	13	30
Bodily pain	2	0	0	20	0	20
General health	0	1	0	8	0	11
Vitality	0	2	0	6	0	6
Social functioning	2	25	0	37	0	44
Role emotional	21	28	15	37	6	44
Mental health	0	2	0	10	0	11

A comparison of the stratified and weighted scores of the SF-36 sub-scales GH, PF, RP, and PCS between THR patients and healthy controls demonstrated that the THR group had an overall higher score in the sub-scale GH [(95% CI –0.1 - 1) (P=0.05)] compared with the healthy controls, but a lower score in all three physical subscales (PF, RP, and PCS) [(95% CI 4.0 - 13.), (P=<001)]; [95% CI (3.3 - 27.), (P=0.01)]; and [(95% CI 0.1 - 5.8),(P = 0.05)].

10.4 Study IV

No significant differences in changes in peak values of gait parameter values of the hip between 6 and 12 weeks were seen between groups except for peak abductor moments, which improved significantly more in the MHE group (P=0.01) (Table 7). The gait speed increased significantly with about 12% for all the patients in the period between 6 and 12 weeks after surgery. The change in walking speed was reflected as significant changes in most of the assessed gait parameters within the HRS and MHE groups (Table 7).

Table 7. Temporal-spatial, kinematic, and kinetic gait parameter variables of operated hips in the HRS and MHE groups 6 and 12 weeks postoperatively. Data are described by means and SD. Differences within and between groups are analyzed by a repeated measurement model; 1= difference in changes over time between groups; 2= difference in level between groups; 3= changes over time within groups.

Variables	HRS group (N=22)		MHE group (N=22)		P values		
	6 weeks Mean (SD)	12 weeks Mean (SD)	6 weeks Mean (SD)	12 weeks Mean (SD)	1	2	3
Temporal-spatial variables							
Gait speed (m/s)	1.2 (0.3)	1.3 (0.2)	1.1 (0.3)	1.3 (0.2)	0.9	0.4	<0.01
Cadence (steps/min)	113 (14)	118 (8)	110 (11)	116 (4)	0.9	0.5	0.01
Stride (m)	1.3 (0.2)	1.3 (0.1)	1.2 (0.2)	1.3 (0.1)	0.4	0.4	<0.01
Step length opr leg (m)	0.64 (0.1)	0.68 (0.1)	0.60 (0.1)	0.7 (0.1)	0.6	0.4	<0.01
Stance phase opr leg (%)	61.2 (1.6)	60.6 (0.8)	62.0 (2.9)	61 (1.9)	0.8	0.4	0.05
Single support opr leg (%)	37.6 (2.4)	38.9 (1.3)	36.5 (3.7)	39 (3.7)	0.4	0.6	0.01
Kinematic variables							
Max hip flexion angle (degrees)	35.2 (5.0)	34.5 (5.3)	31.9 (8.0)	32 (4.4)	0.9	0.1	0.7
Max hip extension angle (degrees)	5.5 (6.9)	1.5 (6.2)	3.0 (7.4)	-2.2 (4.2)	0.6	0.2	<0.01
ROM in sagital plane (degrees)	29.6 (7.2)	33.6 (5.9)	29.2 (5.6)	33.6 (4.)	0.8	0.9	<0.01
Max hip adduction angle (degrees)	4.5 (2.8)	4.2 (3.1)	4.9 (5.8)	6.0 (4.5)	0.4	0.5	0.6
Max hip abduction angle (degrees)	-5.4 (4.5)	-7.3 (4.3)	-4.6 (4.3)	-5.9 (2.3)	0.7	0.5	0.05
ROM in frontal plane (degrees)	9.8 (3.2)	11.5 (2.3)	9.5 (3.2)	12 (2.7)	0.5	1.0	<0.01
Max hip int. rotation angle (degrees)	8.1 (5.7)	7.3 (5.0)	9.4 (6.2)	10 (6.2)	0.7	0.3	1.0
Max hip ext. rotation angle (degrees)	-5.7 (5.8)	-9.0 (4.4)	-5.2 (4.5)	-8 (10.3)	0.8	0.7	0.2
ROM in transverse plane (degrees)	13.7 (2.9)	16.3 (6.0)	13.6 (4.8)	18 (5.8)	0.6	0.8	0.01
Kinetic variables							
Peak hip extensor moments (Nmm/kg)	689 (334)	863 (348)	665 (273)	817 (215)	0.8	0.8	<0.01
Peak hip flexor moments (Nmm/kg)	-636 (210)	-749 (212)	-513 (171)	-675 (238)	0.5	0.2	<0.01
Peak hip abductor moments (Nmm/kg)	718 (78)	733 (117)	652 (127)	774 (150)	0.01	0.8	<0.01
Peak hip adductor moments (Nmm/kg)	-101 (101)	-71 (31)	-107 (87)	-117 (48)	0.3	0.3	0.6
Peak hip ext. rotator moments (Nmm/kg)	63 (27)	66 (39.0)	61 (27)	78 (32)	0.2	0.7	0.06
Peak hip int. rotator moments (Nmm/kg)	-94 (37)	-125 (46)	-73 (51)	-98 (53)	0.6	0.2	<0.01
Work							
Total work (Joule)	19.5 (9.1)	27. (11.2)	17.8 (8.6)	25 (8.9)	0.9	0.6	<0.01

A significant difference between operated and non-operated hip was seen in all patients except for hip flexion, ROM in the frontal plane, ROM in transverse plane, flexor moments, adductor moments, and internal rotator moments (Table 8). No significant differences between the HRS and MHE groups were seen between operated and non-operated hip (Table 8).

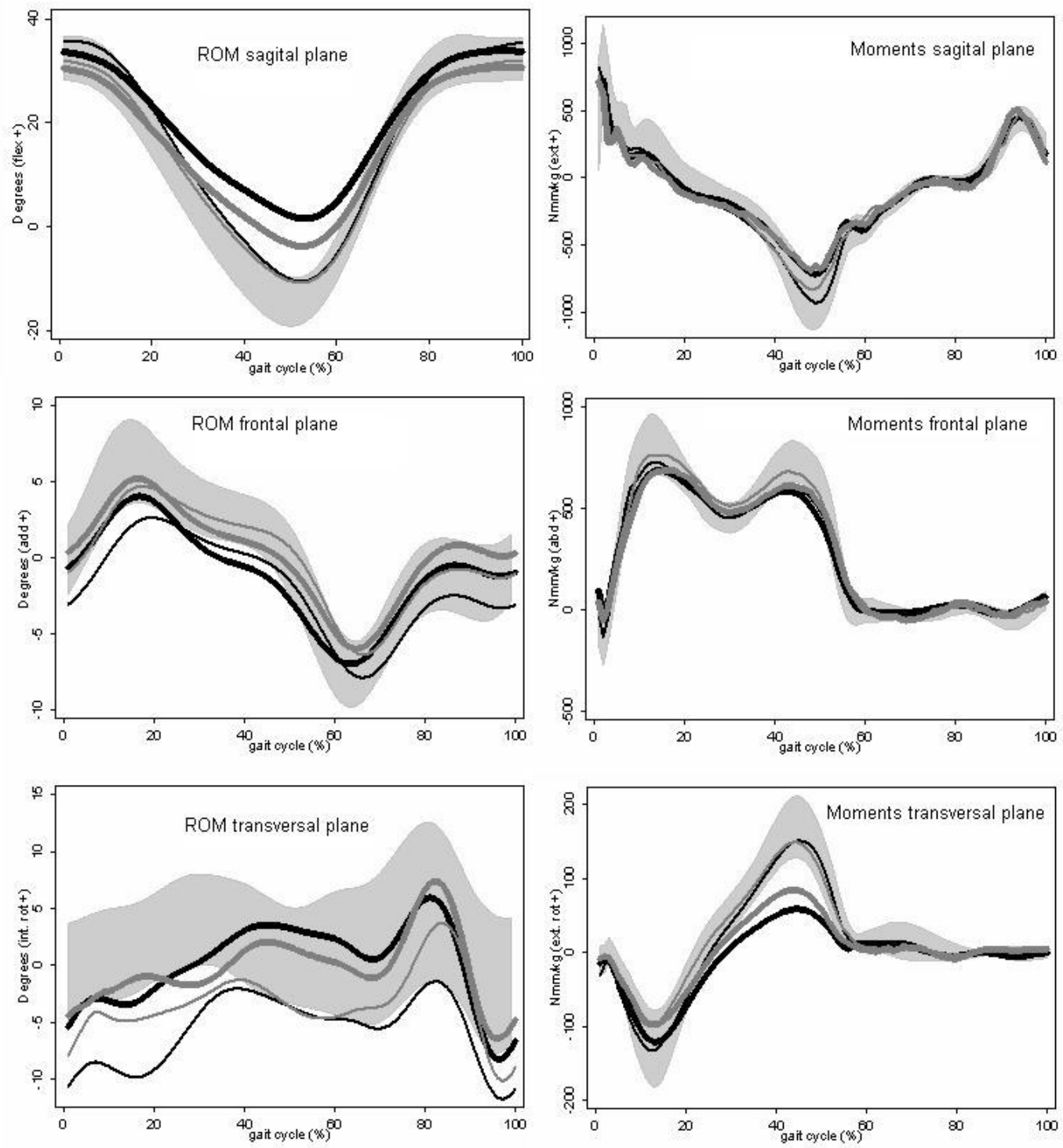
Table 8. Temporal-spatial, kinematic, and kinetic gait parameter variables of operated and non-operated hips 12 weeks postoperatively. Data are described by means and SD. Differences within and between groups are analyzed by a repeated measurement model; 1= differences in the difference between operated/ non-operated hip between groups; 2= difference in level between groups; 3= difference between operated/non-operated hip within groups.

Variables	HRS Group (n=11)		MHE Group (n=11)		P values		
	Opr. hip Mean (SD)	Non-opr hip Mean (SD)	Opr. hip Mean (SD)	Non-opr hip Mean (SD)	1	2	3
Temporal-spatial variables							
Step length (m)	0.68 (0.1)	0.64 (0.1)	0.66 (0.1)	0.63 (0.1)	0.5	0.6	<0.01
Stance phase (%)	60.6 (0.8)	61.0 (1.2)	61.2 (1.9)	62.0 (2.3)	0.6	0.3	<0.01
Single support (%)	38.9 (1.3)	39.3 (1.1)	38.9 (3.7)	39.9 (3.8)	0.2	0.8	<0.01
Kinematic variables							
Max hip flexion angle (degrees)	34.5 (5.3)	36.3 (6.0)	31.5 (4.4)	32.8 (5.3)	0.8	0.1	0.06
Max hip extension angle (degrees)	1.5 (6.2)	-10.7 (4.5)	-2.2 (4.2)	-12.6 (3.6)	0.4	0.1	<0.01
ROM sagital plane (degrees)	33.6 (5.9)	47.0 (4.9)	33.6 (4.0)	45.4 (6.4)	0.4	0.7	<0.01
Max hip adduction angle (degrees)	4.2 (3.1)	2.9 (3.7)	6.0 (4.5)	4.7 (3.6)	1.0	0.2	0.2
Max hip abduction angle (degrees)	-7.3 (4.3)	-8.0 (3.6)	-6.0 (2.3)	-7.1 (2.4)	0.8	0.3	0.3
ROM frontal plane (degrees)	11.5 (2.6)	10.9 (3.6)	11.9 (2.7)	11.9 (3.2	0.6	0.6	0.5
Max hip int. rotation angle (degrees)	7.3 (5.0)	0.8 (6.7)	10.0 (6.2)	2.3 (6.9)	0.8	0.2	<0.01
Max hip ext. rotation angle (degrees)	-9.0 (4.4)	-13.5 (9.2)	-7.5 (10.3)	-14.4 (7.4)	0.6	0.9	0.02
ROM transversal plane (degrees)	16.3 (6.0)	14.3 (6.1)	17.6 (5.8)	16.7 (5.4)	0.5	0.4	0.1
Kinetic variables							
Peak hip extensor moments (Nmm/kg)	8634 (348)	901 (323)	817 (215)	866 (386)	0.9	0.8	0.4
Peak hip flexor moments (Nmm/kg)	-749 (212)	-952 (337)	-675(238)	-931 (204)	0.5	0.7	<0.01
Peak hip abductor moments (Nmm/kg)	733 (117)	756 (121)	774 (150)	851 (152)	0.3	0.2	0.08
Peak hip adductor moments (Nmm/kg)	-71 (31)	-202 (183)	-117 (48)	-151 (98)	0.1	0.9	0.01
Peak hip ext. rotator moments (Nmm/kg)	66 (39)	152 (54)	78 (32)	163 (47)	1.0	0.5	<0.01
Peak hip int. rotator moments (Nmm/kg)	-125 (46)	-137 (68)	-98 (53)	-109 (39)	1.0	0.2	0.3
Work							
Total work (Joule)	27 (11.2)	41 (15.9)	25 (8.9)	35 (9.3)	0.2	0.4	<0.01

In the healthy control group, no statistical differences between left and right hip were seen in any gait parameter variables (all P values >0.05), therefore the left/right data were pooled.

Mean curves of kinetic and kinematic variables during a gait cycle (Figure 11) showed a reduction in dynamic ROM in extension, abduction, and external rotation and a reduction in corresponding moments in the THR groups compared with the healthy controls.

Figure 11. Ensembles averages of joint angle profiles (ROM) and moment profiles of the hip in all anatomical planes during a gait cycle walking at self-selected speed for the operated and non-operated hips in the HRS and MHE groups 12 weeks after surgery, and the average values of both hips in an age-matched healthy control group . The HRS group is represented by the black lines (bold= operated hip, narrow= non-operated hip), the MHE group by the gray lines (bold = operated hip, narrow = non-operated hip).The shaded areas represents equal boundaries of +/- 1 SD for the controls. Moments are normalized to body weight.



11. SUMMARY OF DISCUSSION

11.1 Study I

In the per-protocol analysis, the difference in median LOS was approximately one day shorter in the intervention group, whereas no difference was found in the intention-to-treat analysis.

A criticism of the study design is the lack of blinding. As a general reduction in LOS was observed during the study period, the effect of the multimodal optimization in this trial may be underestimated and biased.

Although the departmental surgeons who considered patients for discharge were blinded to randomization, patients and others involved in the study were not. To reduce bias, intervention and control patients were kept in different rooms, but they stayed on the same ward.

The validity of LOS as an end-point measure can be questioned. To minimize bias, standardized discharge criteria were used as recommended, and reducing LOS was not a part of the intervention [90]. Because data on decision to discharge were not recorded in the present study, we have no explanation for what kept patients in hospital. Our findings suggest that factors other than recovery of PADL and pain influence hospital stay.

Another criticism of the study design is the use of two different anesthetic regiments and two different opioids in not equipotent doses. A stratified analysis showed, however, no impact of the confounding factors on LOS.

The age of the participants was relatively low compared with an often older population in other studies. Because LOS in this trial did not differ from results obtained in older populations [93], it seems as if patients have to reach a sudden age before it effects LOS [132].

No significant difference in relative risk was observed; however the effect of fast-track programs on postoperative morbidity and complications can not be assessed with sufficient power in such a small-scale study.

Although the intervention succeeded, LOS was only moderately reduced compared with other studies of THR patients [91;92]. Unlike these studies, our study was conducted in a randomized controlled design and in a clinical setting in which fast-track programs and teambuilding had not been trained and implemented. Regarding the effect of optimized strategies on LOS, the result in the present study is in accordance with Dowsey et al. [133].

Adequate pain relief after THR is essential to enable functional recovery, and it is assumed that the success of fast-track surgery is due to the epidural analgesia [85;89]. In our study, both groups received optimal multimodal and identical epidural analgesia and no significant difference in pain score between groups was found. This finding suggests, in agreement with other studies [43;87;134], that pain relief in itself does not improve rehabilitation.

11.2 Study II

We found that eligible consenters differed significantly from eligible non-consenters with respect to important prognostic factors and subsequently to clinical outcome variables. The non-consenters constitute a subgroup of the screened population in which the trial therapy could be used, because this group did not include patients with contraindications to the trial therapy.

Because of the low number of patients in our study population, a possible bias as a result of lost information should be considered.

Despite the potentially important implications of disparities between eligible consenters and eligible non-consenters, only a few studies dealing with fast-track programs have previously supplied postoperative clinical end-point data in sufficient detail to allow a comparison. However, our results are in agreement with the findings of Husted et al. [132]. Furthermore, it has been shown in population based surveys [135-137], in primary preventive trials [138], and in clinical trials [139;140] that non-consenters are more frequent among subjects with increased risk for disease and mortality.

11.3 Study III

We found no evidence for an effect of the efficacy of optimization strategies during admission on self-reported functional outcome after THR.

No significant differences between groups in self-reported functional outcome was found except for the total WOMAC and the WOMAC sub-scale function. This result could be a coincidence caused by multiple testing (P values are close to 5 %), but in general the CPC group did better postoperatively than did the OPC group. We have no clear explanation for this finding, but in as much as the OPC group was hospitalized for a significantly shorter time than the CPC group [141], we can not eliminate that LOS could be a confounding factor.

Another explanation for the poor result of our intervention compared with the findings of others [142] could be that the intervention was only carried out during admission. In the study by Siggeirsdottir et al [142]., intervention was continued after discharge by offering home-visits during the first 2 weeks at home in order to ensure that the rehabilitation course was followed after hospitalization. Because of our study design, we do not know whether patients in the OPC group continued the optimization strategies after discharge.

A weakness of our study is the lack of blinding. Both caretakers and patients knew which treatment patients had received, and this could have introduced bias with regard to a general increase in mobilization and energy intake in the CPC group and thereby an underestimation of the efficacy of the optimization strategies.

The SF-36 showed a more conspicuous ceiling effect postoperatively than did the WOMAC. Validity and responsiveness are the most important criteria when deciding which particular instrument to use in a clinical trial [104]. In accordance with other studies [113;115-117], we found that the illness-specific instrument (WOMAC) is more responsive to changes over time than is the generic instrument (SF-36).

The functional outcome after 3 months in the THR group is in accordance with the results of other studies with a longer follow-up period [113;116;143]. This indicates that main improvements after THR are seen rather early in late-phase rehabilitation.

Although the THR patients after 6 months generally reached a higher score in the sub-scale GH compared with the healthy control group, their overall scores in the three physical sub-scales were lower, which indicates potential for further rehabilitation.

11.4 Study IV

We found no evidence for the hypothesis that dynamic ROM and muscle strength would be more affected in the early phase of rehabilitation and persisting impairments less in patients receiving a resurfacing implant compared with patients receiving a conventional prosthesis.

No significant differences between groups in temporal-spatial, kinematic, and kinetic gait parameter variables of the hip were found 6 and 12 weeks postoperatively with respect to changes in or levels of peak values except for peak abductor moments which changed more in the MHE group. The reason for this finding could be a faster recovery of the gluteal muscles due to the less invasive surgical procedure in the MHE group.

The change in walking speed in all the patients was reflected as significant changes in most of the assessed gait parameters within the HRS and MHE groups. Due to the fact that kinematic and kinetic parameters in the operated hip did not reach the level in the non-operated hip in both groups, it may be assumed that the power to perform the work must be produced in the knee and ankle joint.

A weakness of our study is that we did not perform a preoperative gait analysis in order to estimate whether patients in both groups had equal impairments of gait at baseline, but in as much as patients were included after fairly strict inclusion and exclusion criteria to assure a homogenous sample, patients were randomized between the groups, and because the preoperative WOMAC and HHS scores revealed no differences between groups in physical functioning, we believe that the results of our study are not biased by differences between groups due to the preoperative level in gait parameter variables.

In a study by Mont et al. [35], gait adaptation in patients receiving hip resurfacing arthroplasty was compared between patients receiving a standard prosthesis and healthy controls. In contrast to our study, Mont et al. showed that 1-year postoperative hip kinetic (abductor and extensor moments) and functionality (speed) normalized to greater degree in patients receiving a resurfacing implant compared with patients with a conventional prosthesis. Because this study used an uncontrolled retrospective design, and only one postoperative time point of evaluation, the study results could be biased because of a highly selected and motivated resurfacing group. Gore et al. [144] compared patients before and after resurfacing or conventional replacement and found that the group receiving resurfacing was younger and before surgery had less pain, slightly more hip motion, greater muscle strength, walked faster, and used fewer assistive devices during walking than did the group receiving the conventional replacement. After surgery, the group with resurfacing maintained its advantage in muscle strength and walking velocity.

Another weakness of our study is the short follow-up period. The argument for choosing a short follow-up period was that 3 months after surgery patients are expected to return to normal physical activities and work, and therefore after that period factors other than different types of implant could affect gait adaptations and bias results.

Patients with hip pathology may adapt to a certain gait pattern that consists of reduced dynamic ROM and joint moments in order to avoid pain and to reduce forces on the pathological hip joint [51-53]. Due to the lack of preoperative data, we can not evaluate to what extent changes in mechanics of gait persisted after THR. However, our findings after 3 months are in accordance with the residual hip impairments reported in other studies examining gait adaptations before and after THR [34;36;37;145-149].

An increased peak contact force of the hip joint has previously been shown in patients with disturbed gait patterns [150-153]. Information about loading of the hip joint can be achieved from actual gait moments. External moments provide a reflection of net agonist and antagonist muscle activity, and they can indicate which muscles are compromised during surgery. It is assumed that dysfunction of one muscle increases the joint contact force because a part of the required joint moments is taken over by other muscles with unfavorably short lever arms and therefore higher forces [151;154]. Several studies have reported postoperative extensor and abductor muscle weakness and have called for increased muscle strengthening regimes after THR surgery [145;155;156]. The results of our study support this need.

12. CONCLUSION

Compared with conventional care, optimized intensive mobilization and nutrition resulted in a moderate reduction in LOS. There were no differences regarding pain, complications, or time until independence in PADL. We found no evidence that the efficacy of optimization strategies during admission had an effect on self-reported functional outcome after THR. Multimodal rehabilitation is a program that brings together a number of individually proven measures into a coordinated plan for recovery. A solid evidence base would make the case for provision of the necessary conditions more powerful.

Our data on non-consenters reinforce the need for those conducting clinical trials to provide additional information about the recruitment process supplemented with readily available quantitative data in order to avoid biased estimates of treatment effects and misleading assessments regarding the degree to which trial results may be generalized [157]. Our findings demonstrated the importance of patient inclusion criteria in RCTs evaluating the efficacy of perioperative optimization strategies. Moreover, they may account for the lack of reproducibility of results in clinical practice dealing with fast- track programs.

We found no evidence for an effect of the efficacy of optimization strategies during admission on self-reported functional outcome after THR measured by SF-36 and WOMAC. Although patients improved considerably after THR, their physical functioning measured by self-reported functional outcome, and by mechanics of gait remained below the level of matched healthy controls. Our results indicate that the potential for improvement in physical function for THR patients has not yet been fully utilized.

We found no evidence for the hypothesis that dynamic ROM and muscle strength would be more affected in the early phase of rehabilitation and persisting impairments less in patients receiving a resurfacing implant compared with patients receiving a conventional prosthesis. Although, almost all gait parameter variables improved, impairments persisted. Especially ROM in extension, and extensor, abductor, and external rotator moments were reduced, which indicates extensor and abductor muscle weakness. Several studies have reported postoperative weakness and have called for increased muscle strengthening regimes after THR surgery. The results of our study support the need for such regimes. Gait retraining in conjunction with intensive muscle strengthening could prove beneficial for the function and longevity of the implant, especially among young patients.

13. Perspectives and future studies

Recent studies have documented that restoration of normal movement patterns of the hip after THR provides better clinical function and muscle strength as well as reduced wear [18;20-22;25;26]

More studies are needed to investigate how normal movement patterns in terms of ROM, muscle strength and neuromuscular activity can be achieved after THR. Failure to correct loading imbalances could be a factor in the development of implant failures in THR patients. It has been shown that hip loading or ground reaction force can be altered through gait retraining in subjects with THR [158]. However, it is unknown what the goals of gait training should be in order to obtain the best loading parameters for patient function and implant longevity.

Current levels of function achieved by THR patients may have been sufficient in the past, but younger and more physically active patients may place greater demands on the implant [159-162]. Gait retraining in conjunction with intensive muscle strengthening could prove beneficial for the function and longevity of the implant especially among young patients.

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15. PAPERS I - IV

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Efficacy of multimodal optimization of mobilization and nutrition in patients undergoing hip replacement: a randomized clinical trial

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Background: The aim of this trial was to assess the effects of optimization of mobilization and nutrition on patients undergoing primary total hip replacement (THR).
Methods: Seventy-nine patients undergoing elective primary THR were recruited prospectively. After randomization, one group received optimized pre-operative information and enforced mobilization and nutrition, another group received conventional peri-operative care. Epidural anaesthesia and post-operative epidural analgesia with local anaesthetics and opioids were used in all cases. Outcome related to length of stay, complications, pain, mobilization, energy intake, and physical activities of daily living (PADL).
Results: Although mobilization and nutrition were highly significantly increased in the intervention group, the reduction in length of stay was moderate (7.0 vs. 8.0 days $P = 0.019$). We found no differences between groups in relation to complications or pain. In the intervention group, the median day of independence in PADL was the third post-operative day (2 : 6 day) and the fourth post-operative day (2 : 7 day) in the control group. The difference was not significant.
Conclusion: Compared with conventional care, optimal and aggressive nutrition and mobilization resulted in a very moderate reduction in length of stay. There were no differences regarding pain, complications or time until independence in PADL.

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Key words: multimodal optimization; enforced nutrition and mobilization; prospective randomized trial; hospital stay; PADL.

MULTIMODAL rehabilitation or fast-track surgery, which evolved as a coordinated multimodal effort combining modern concepts of patient education with multimodal anaesthetic and analgesic methods, has been introduced to reduce the surgical stress response and minimize pain and discomfort (1–5). Methods used have included epidural or regional anaesthesia, aggressive post-operative mobilization and early nutrition.

In a controlled series of unselected patients, these advances in modern care with emphasis on oral nutrition and physical rehabilitation have been reported to enhance convalescence and reduce post-surgical hospitalization (6–9). It has been argued that the results of these trials could be largely attributed to the epidural analgesia and at best were applicable to a selected group of patients (8).

Total hip replacement (THR) is a major surgical procedure that can be physically and psychologically stressful for patients.

In uncontrolled Danish studies it has been shown that multimodal fast-track programmes did improve recovery and reduce length of stay after THR without an increase in complications and re-admission (10–12).

However, no current evidence suggests any single measure to improve post-operative recovery after THR (13,14).

The aim of this trial was to investigate in a prospective randomized design whether mobilization and nutrition in patients undergoing primary THR could be optimized, and if so to asses the effects on recovery.

Methods

The study was a non-blinded randomized controlled prospective study. The study was approved by the local Ethics Committee and fulfilled the Helsinki Declaration.

Patients scheduled for elective primary unilateral THR and peri-operative epidural analgesia were assessed for eligibility. Exclusion criteria were chronic opioid use, chronic pain syndrome, rheumatoid arthritis, and mental disorders.

In the study period, 18 patients did not meet the inclusion criteria, and 33 declined to participate.

Seventy-nine patients were randomized to receive multimodal optimization or conventional care.

On the day of admission, patients were randomized by means of opening sealed envelopes.

Block randomization into blocks of eight was used. The sequences were computer generated.

All patients received standardized multimodal anaesthesia and analgesia throughout the per- and post-operative period. According to departmental guidelines, and based on the judgement of the anaesthesiologist, all operations were performed using combined epidural-spinal anaesthesia (EPI-SPI) or a hypotensive epidural anaesthesia (HEA).

EPI-SPI was achieved with 3 ml of bupivacaine 0.5% plain (L_3–L_4). An epidural catheter was placed L_2–L_3. The systolic blood pressure was kept $>$ 100 mmHg supported by injections of ephedrine if needed. HEA was achieved with ropivacaine 1% with an epidural catheter being placed at level Th_{11}–Th_{12} to a fall in mean arterial blood pressure (MAP) at 45–50 mmHg.

Post-operatively, epidural analgesia was initiated when the motor blockage was equivalent to ≤ 2 on a modified Bromage scale (EPI-SPI) or thermalgesia under TH6 (HEA). No priming dose was given. Post-operative analgesia within the first 48 h was attained with epidural ropivacaine 2 mg/ml with fentanyl 2 μg/ml 4 ml/h or epidural ropivacaine 2 mg/ml with morphine 50 μg/ml 4 ml/h. A 4-ml bolus was given when the visual analogue scale (VAS) was $>$ 3 at rest and $>$ 5 mobilizing.

In addition to epidural infusion, 1 g of acetaminophen was given four times daily.

The epidural catheter was removed after 48 h and Oxycontin® (oxycodonhydrochlorid) 10 mg twice a day and acetaminophen 1 g four times daily were given.

When the post-operative haemoglobin (HB) was $<$ 5.5 mmol/l and if the patient had clinical symptoms (dizziness during mobilization) a blood transfusion was given.

Disposable catheters were used when urine retention was $>$ 350 ml documented by a bladder scan (15).

All patients received physiotherapy for half an hour daily on weekdays

The intervention group got an optimization package that involved pre- and post-operative strategies as described in Table 1.

Table 1

Optimization package.	
Pre-operative optimization	
Standard goals for mobilization and energy intake were described	Fixed standard goals for post-operative mobilization and nutrition were introduced and delivered to patients
Verbal and written supplementary information was standardized	Mutual expectations were discussed.
After surgery, transfer and walking techniques required were taught	Transfer out of bed
	Walking aids were introduced and delivered
	Walking with sticks was trained.
Post-operative mobilization	Mobilization out of bed for 2 h on the day after surgery.
Aggressive and progressive structured mobilization plans	Scheduled time out of bed increased by 2 h a day, from 2 h on the first post-operative day to 12 h on the sixth post-operative day
	Walking distance increased by 100 m a day from 100 m on the second post-operative day to 500 m on sixth post-operative day
Post-operative nutrition	
Early and aggressive fluid and diet re-introduction	Registration and calculation of daily fluid and energy intake
Eating and drinking despite lack of appetite was encouraged	Supplementary energy intake: 200 cc of a protein-rich drink (Fortimel®, Nutricia, Zoetermeer, The Netherlands) three times a day between the main meals
Post-operative rehabilitation	Sitting patients out of bed early on the first post-operative day
Early aggressive rehabilitation programme	Walking 100 m on the second post- operative day
Early introduction to exercise programme	Encouraged to follow fixed standard goals for mobilization and walking.

Pre-operative education was given by the investigators the day before surgery.

Patients were encouraged to follow written fixed standard goals on mobilization and nutrition.

The control group received none of the optimized measures listed in Table 1.

After surgery, mobilization, oral fluid and diet were re-introduced in a traditional stepwise manner.

The treating team responded to the will and condition of the patient in providing post-operative care, and no attempt was made to enforce mobilization or to encourage patients to eat and drink despite lack of appetite.

To control whether the optimization package had an effect on mobilization and nutrition, total energy intake was measured daily for the first 4 postoperative days, and time out of bed in minutes and walking distance in metres were measured daily for the first 6 postoperative days.

Outcomes

Length of stay was registered from the day of admission to the day of discharge.

Discharge was considered by departmental surgeons, who were blinded to randomization. Patients were considered for discharge if: sufficient pain relief was obtained estimated as a VAS score < 3 cm resting and < 5 cm mobilizing, patients were able to maintain personal hygiene, walk with sticks and climb stairs.

Pain intensity was estimated using a VAS (16, 17), every third hour during the first 24 h after surgery, subsequently every eighth hour until removal of the epidural catheter, and then once a day until discharge.

Physical performance was estimated daily using the Katz index (18). The index ranks adequacy of personal activities of daily living (PADL). Independence was defined as ability to perform all six activities unassisted.

Complications and re-admissions were registered within the first 30 days after surgery.

Statistical analysis

With a difference in hospitalization of 30%, expected standard deviation (SD) of 4.2 day, a power of 0.8 and significance level of 0.05, the minimum acceptable size of every group was calculated to be 25 patients.

Data normally distributed were described by means, standard error, and a 95% confidence interval (CI), and statistically tested using the Student's *t*-test. If not normally distributed, data were described by medians and range and the Mann–Whitney *U*-test was used. Frequency was compared using Fisher's exact test. Correlation between variables was tested using a weighted Spearman's rho calculation from correlations within each of the groups. The significance level was 0.05. Data were analysed using the Statistical Package for the Social Sciences (SPSS) for Windows version 11.0 (Chicago, IL).

Results

A total of 57 patients (27 in the intervention and 30 in the control group) completed the study protocol. The reasons for the early termination of nine patients and exclusion from the analysis of 13 patients are described in Fig. l.

Demographic and surgical data did not differ between groups (Table 2).

End-point outcome

In the intention-to-treat analysis, no significant differences in length of stay between groups were seen ($P = 0.20$).

In the per-protocol analysis ($n = 57$), more patients in the intervention group than in the control group were hospitalized for less than 8 days (59% and 33%, respectively). The median length of hospitalization in the intervention group was 7.0 days (range 1–9) and in the control group 8.0 days (range 1–10) ($P = 0.019$).

Process indicators (mobilization, nutrition, PADL)

The average total time out of bed was 37.4 h (SD 10.4) in the intervention group and 25.5 h (SD 14.4) in the control group ($P < 0.001$) (Fig. 2).

During the first 6 days of admission, mobilization in the intervention group was more efficient than in the control group, and the intervention group fulfilled the mobilization goals to a far greater extent than did the control group ($P < 0.001$) (Fig. 2).

Physical activity measured by daily walking distances in metres was found to correlate significantly with the ambulation time [$(\rho) = 0.397$, $P = 0.002$].

During the first 4 days, patients in the intervention group had an average energy intake of 103.40 kJ/kg (SD 25.86), compared with 76.08 kJ/kg (SD 23.88) in the control group. In the first 4 days, the average protein intake was 1.25 g/kg (SD 0.35) in the intervention group and 0.74 g/kg (SD 0.25) in the control group ($P < 0.0001$).

The median day of independence in PADL was the third post-operative day (range 1–4), in the intervention, and the fourth post-operative day (range 1–5) in the control group. The difference was not significant ($P = 0.22$).

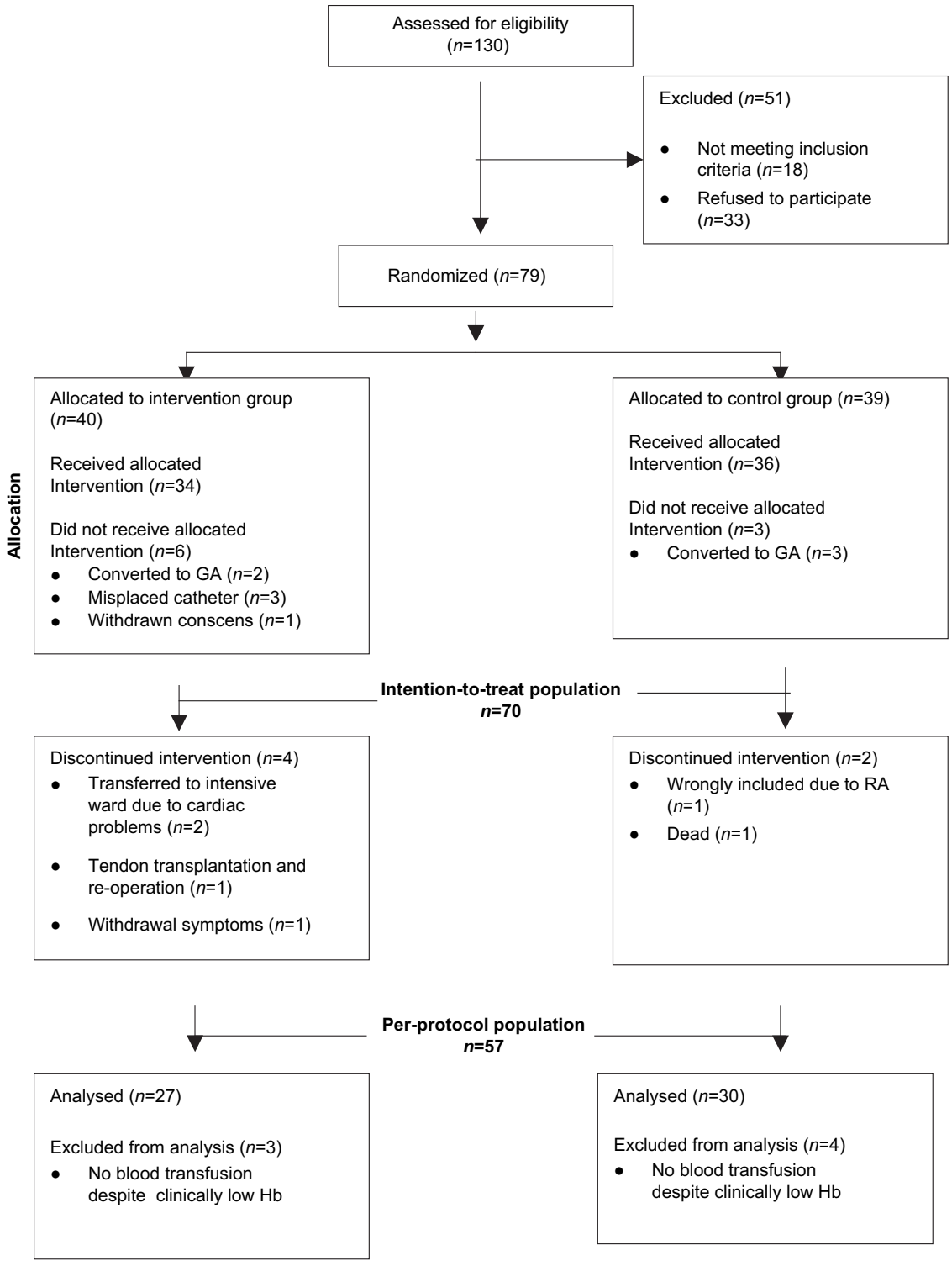

Fig. 1. Progress through the phases of the study.

Confounders (complications, pain)

There was found no difference in complications between groups. The relative risk in the in the intention to treat analysis was 1.6 (0.6–4.0) (P = 0.39) and in the per-protocol analysis 1.7 (0.5–5.3) (P = 0.49) and no patients were re-admitted.

Within the first 48 h after surgery, the median VAS pain score was 1.8 (0–5.5) in the intervention

Table 2

Demographic characteristics and surgical data distributed between groups.

Variables	Intention- to-treat $n = 70$		Per protocol $n = 57$	
	Intervention $n = 34$	Control $n = 36$	Intervention $n = 27$	Control $n = 30$
Gender (F/M)	20/14	19/17	15/12	14/16
Age (years)	55 (28–84)	58 (28–81)	55 (28–84)	58 (26–81)
Median				
ASA group I/II/III	19/13/2	19/11/6	16/11/0	16/10/4
Surgical time in min (mean)	75 (50, 180)	80 (50, 240)	75 (50, 120)	80 (50, 240)
Type of anaesthesia				
HEA/EPI-SPI	19/15	19/14	17/10	13/10
Type of drug				
RF/RM	18/16	18/18	15/12	14/16
Intra-operative bleeding (ml) mean	257.9 (204, 311)	360 (262, 457)	234.1 (182.8, 285.3)	387.9 (275.4, 500.4)
Post-operative HB (mmol/l)	6.82 (SD 0.909)	6.72 (SD 0.807)	6.94 (SD 0.751)	6.93 (SD 0.710)
Blood transfusion	3	2	3	2
Nausea/no nausea	12/22	15/21	8/19	10/20

HEA, hypotensive epidural anaesthesia; EPI-SPI, epidural-spinal anaesthesia; RF, ropivacain/fentanyl; RM, ropivacain/morphine; ASA, American Society of Anaesthesiologists' classification; HB, haemoglobin.

group and 1.2 (0–4.1) in the control group. During the following 4 days, it was 1.0 (0–5) in the intervention group and 1.0 (0–5.5) in the control group. There was no significant difference between groups concerning pain ($P = 0.949$) and ($P = 0.700$).

Correlation between variables

In order to control if the use of different types of anaesthesia and analgesia had an impact on recovery, a stratified analysis was made.

The analysis showed a vague positive (ρ 0.07) but not significant ($P = 0.62$) correlation between ± pain and length of stay, and a vague positive (ρ 0.06), but not significant ($P = 0.06$) difference between ± HEA and length of stay.

Fig. 2. Daily time out of bed in minutes during the first 6 days of admission in the two groups.

Discussion

In the per-protocol analysis, the difference in median length of stay was approximately 1 day shorter in the intervention group, whereas no difference was found in the intention-to-treat analysis.

A criticism of the study design is the lack of blinding. As a general reduction in length of stay was observed during the study period, the effect of the multimodal optimization in this trial may be underestimated and biased.

Although departmental surgeons, who considered patients for discharge, were blinded to randomization, patients and others involved in the study were not.

The validity of length of stay as an end-point measure can be questioned. To minimize bias, standardized discharge criteria were used as recommended (9).

Because data on decision to discharge were not recorded in the present study, we have no explanation for what kept patients in hospital. Our findings suggest that other factors than recovery of PADL and pain influence hospital stay.

Another criticism of the study design is both the use of two different anaesthetic regiments, and two different opioids in non-equipotent doses. However, a stratified analysis showed no impact of the confounding factors on length of stay.

The age of the participants was relatively low compared with a usually older population in other

studies. As length of hospitalization in this trial did not differ from results using older populations (14), it seems as if patients have to reach a certain age before it effects length of hospitalization (26).

No significant difference in relative risk was observed; however, the effect of fast-track programmes on post-operative morbidity and complications can not be assessed with sufficient power in such a small-scale study.

Although the intervention succeeded length of stay was only moderately reduced compared with other THR studies (10,11). Unlike these studies, our study was conducted in a randomized controlled design, and in a clinical setting where fast-track programmes and teambuilding had not been taught and implemented.

Adequate pain relief after THR is essential to enable functional recovery, and it is assumed that the success of fast-track surgery is due to the epidural analgesia (3,8). In our study, both groups received optimal multimodal and identical epidural analgesia and no significant difference in the pain score between groups was found. This finding suggests, in agreement with other studies (6,13,19), that pain relief in itself does not improve recovery.

Compared with conventional care, optimal and aggressive nutrition and mobilization resulted in a very moderate reduction in length of stay. There were no differences regarding pain, complications or time until independence in PADL.

Fast-track surgery is a programme that brings together a number of individually proven measures into a coordinated plan for recovery. A solid evidence base would make the case for provision of the necessary conditions more powerful.

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"To whom do the results of this trial apply?"

External validity of a randomized controlled trial involving 130 patients scheduled for primary total hip replacement

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Background **Although the randomized controlled trial (RCT) is regarded as the gold standard for evaluation of the effect of an intervention, its external validity has been questioned. RCTs cannot be expected to produce results that are directly relevant to all patients and all settings, but they should at least allow patients and clinicians to judge to whom trial results can reasonably be applied.**

We assessed the external validity of an RCT investigating the efficacy of a fast-track program after total hip replacement.

Methods **130 patients were identified as potential participants.18 patients were excluded, 33 enrolled patients declined to participate, and 79 patients were enrolled and randomized. We studied the distribution of preoperative characteristics and postoperative clinical variables in these 3 groups.**

Results **A significant difference was found in both preoperative characteristics and clinical outcome variables. The non-consenters were older, less healthy, and needed more help from the home care system. Furthermore, they were hospitalized longer and were more often transferred to a rehabilitation ward.**

Interpretation **Our findings demonstrate the importance of patient inclusion criteria in RCTs. Moreover, they may account for the lack of reproducibility of RCT results in clinical practice dealing with fast-track programs.**

In an unblinded RCT, we assessed the efficacy of a fast-track program after elective primary unilateral total hip replacement (THR) and perioperative epidural analgesia (Petersen et al. 2006). Randomized controlled trials (RCTs) are frequently considered to be the gold standard of study designs for determining the efficacy of different interventions (Gross et al. 2002, Rothwell 2005). They must be internally valid (i.e. design and conduction) in order to minimize bias, but to be clinically useful the result must also be relevant to a definable group of patients in a particular clinical setting; this is generally termed external validity or generalizability (Rothwell 2005). Even if the randomized comparison in clinical trials is not biased by exclusion per se, external validity of trial results depends on the representativeness of the study sample (Swanson and Ward 1995, Britton et al.1999). The beneficial effects of some interventions can be very dependent on factors such as the characteristics of patients (Altman et al. 2001, Gross et al. 2002, Rothwell 2005). If only a proportion of potentially eligible patients is enrolled in a trial, it is important to evaluate how participants differ from non-participants as a result of eligibility criteria or other factors (Charlson and Horwitz 1984, Gross et al. 2002). Knowledge of dissimilarities in the prevalence of risk factors in the population of participants and non-participants may therefore help to evaluate possible sources of bias, and show whether the effects of treatment, as observed in the trial, may be applied to the general population (Smith and Arnesen 1988, Smith and Arnesen 1990, van Bergen et al. 1995). A critical question is whether non-participants have similar susceptibility compared to participants for the out-

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Table 1. Trial recruitment terminology

Term	Definition [a]	The population under investigation
Target population	Location and characteristics of potentially eligible individuals; represents the individuals to whom the trial results are expected to apply.	Patients scheduled for elective primary unilateral THR and perioperative epidural analgesia (n = 130).
Eligibility fraction	Proportion of potential participants who undergo screening and are eligible to enroll.	Reason for exclusion of enrollment (n = 18): Rheumatoid arthritis (7) Contraindications for epidural analgesia (5) Daily use of opioids (1) Missed for enrollment (3) Unable to communicate in Danish (2)
Enrollment fraction	Proportion of patients who are eligible for participation and who actually enroll.	Patients asked for informed consent (n = 112)
Recruitment fraction	Proportion of potential participants who are actually enrolled and randomized.	Enrolled and randomized patients (n = 79)

[a] According to Gross et al. 2002

come events under study. If not, trial results may be difficult to extrapolate from the population outlined by the eligibility criteria (Charlson and Horwitz 1984). We assessed the external validity and generalizability of an RCT investigating the efficacy of a fast-track program after primary THR.

Patients and methods

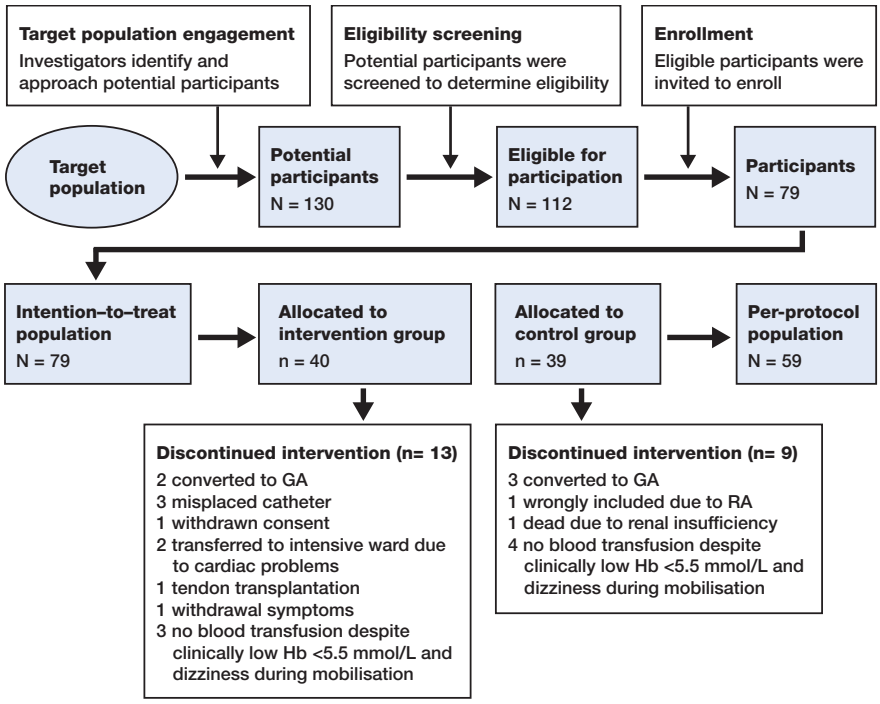
This study is a prospective cohort study with an embedded RCT. The study was approved by the local ethics committee and fulfilled the requirements of the Helsinki Declaration. Patients scheduled for elective primary unilateral THR and perioperative epidural analgesia were assessed for eligibility. Exclusion criteria were chronic opioid use, chronic pain syndrome, rheumatoid arthritis, and mental disorders. In order to estimate sample size for the RCT, we used data on length of hospitalization from the database register at Aarhus University Hospital. With a difference in hospitalization of 30%, expected standard deviation (SD) of 4.2 days, a power of 0.8 and significance level of 0.05, the minimum acceptable size of every group was calculated to be 25 patients.

130 patients were identified as potential participants.18 patients were excluded and 33 patients declined to participate (eligible non-consenters). 79 patients were enrolled and randomized (eligible consenters). The 3 groups (excluded, eligible consenters, and eligible non-consenters) represent the study population. Trial recruitment terminology and population data are described in Table 1.

In the recruitment period, all patients admitted for primary THR were identified as potential participants. Potential participants underwent eligibility screening to determine who was eligible for participation (eligibility fraction). Patients who were eligible for participation were asked to provide informed consent and to enroll in the study (enrollment fraction). The trial enrollment process and the progress through the phases of the RCT are illustrated in the Figure. In the event of ineligibility, the reason for exclusion was stated and described as in Table 1.

All patients in the eligible consenters group and eligible non-consenters group received standardized multimodal anesthesia and analgesia throughout the perioperative and postoperative periods. The epidural catheter was removed after 48 h. Disposal catheters were used when urine retention was > 350 mL, documented by a bladder scan. All patients received daily physiotherapy.

Data for the study were abstracted from evaluation charts that were completed for potential participants. No patients were lost to follow-up. The form included information on age, sex, type of



Flow diagram of the trial enrollment process and the phases of the study.

anesthesia, American Society of Anaesthesiology (ASA) classification, social and occupational factors, preoperative Harris hip score (HHS) (Soderman and Malchau 2001), pre- and postoperative need of home care service, length of hospitalization, transfer to rehabilitation ward, and prevalence of postoperative complications. Postoperative complications and readmission were registered within the first 30 days after surgery.

Length of stay was registered from the day of admission to the day of discharge. Discharge criteria were standardized according to departmental guidelines. In all cases, discharge was considered by departmental surgeons, who were blinded to randomization. Patients were considered for discharge when sufficient pain relief was obtained, estimated as VAS score of > 3 cm resting and > 5 cm moving, when patients were able to maintain personal hygiene, to walk with sticks, and to climb stairs.

The intervention in the RCT involved pre- and postoperative optimization strategies as described in Table 2; the control group received none of these optimized measures. Of 79 patients (the intention-to-treat population) 57 patients (per-protocol population) completed the study protocol (Figure).

Primary outcome of the RCT was length of stay. In the per-protocol analysis, more patients in the intervention group than in the control group were hospitalized for less than 8 days (16/27 (0.6) and 10/30 (0.3), respectively). The median length of stay in the intervention group was 7 (1–9) days, and it was 8 (1–10) days in the control group ($p = 0.02$). In the intention-to-treat analysis, the median length of hospitalization was 8 days in both groups ($p = 0.2$).

Secondary outcome of the RCT

The patients in the intervention group had an average energy intake of 103 kJ/kg (SD 26), compared to 76 kJ/kg (SD 24) in the control group ($p < 0.001$). The average protein intake was 1.25 g/kg (SD 0.35) in the intervention group and 0.74 g/kg (SD 0.25) in the control group ($p < 0.001$). The average total time out of bed was 37 h (SD 10) in the intervention group and 26 h (SD 14) in the control group ($p < 0.001$).

Safety endpoints

There was no difference in complications between groups. The relative risk of complications in the

Table 2. Pre- and postoperative optimization strategies

Preoperative optimization	
• Standard goals for mobilization and energy intake were described	Fixed standard goals for postoperative mobilization and nutrition were introduced and delivered to patients.
• Verbal and written supplementary information was standardized	Mutual expectations were discussed.
• Training in transfer and walking techniques required after surgery.	Transfer out of bed was trained. Walking aids were introduced and delivered. Training in walking with sticks.
Postoperative mobilization	
Aggressive and progressive structured mobilization plans.	Mobilization out of bed for 2 h on the day after surgery. Scheduled time out of bed increased by 2 h a day, from 2 h on the first to 12 h on the sixth postoperative day. Walking distance increased by 100 m a day from 100 m on the second postoperative day to 500 m on sixth postoperative day.
Postoperative nutrition	
Early and aggressive fluid and diet reintroduction. Eating and drinking despite lack of appetite was encouraged.	Registration and calculation of daily fluid and energy intake. Supplementary energy intake: 200 mL of a protein-rich drink (Fortimel; Nutricia, Zoetermeer, the Netherlands) 3 times a day between the main meals.
Postoperative rehabilitation	
Early aggressive rehabilitation program.	Sitting patients out of bed early on the first postoperative day Walking 100 meters on the second postoperative day. Early introduction to exercise program. Encouragement to follow fixed standard goals for mobilization and walking.

intention-to-treat analysis was 1.6 (0.6–4.0) (p = 0.4) and in the per-protocol analysis it was 1.7 (0.5–5.3) (p = 0.5). No patients were re-admitted.

Statistics

Data with normal distribution were described by means, standard error, and 95% CI, and statistically tested using Student's t-test. If not normally distributed, data were described by medians and range, and the Mann-Whitney U-test was used. Frequency was compared using Fisher's exact test or Kruskal-Wallis test. The crude and adjusted odds ratio (OR; adjusted for age and sex) for consenting was estimated by logistic regression. The significance level was 0.05. We used SPSS version 11.0 for Windows.

Results

Eligible non-consenters were older than eligible consenters (p = 0.01), more often classified in ASA group 2 or 3 (p = 0.01), had a lower Harris hip score (p = 0.05), were more often on transfer income (p < 0.001), and received help from the home care service system more often preoperatively (p = 0.001) (Table 3). The crude and adjusted (sex and age) odds ratio for consenting is given in Table 4. The unadjusted OR was not significantly different from the adjusted OR. Although no significant difference was seen with regard to sex, the unadjusted OR showed that consenting was higher for men than for women: 1.98 (0.84–0.99). Social status did not appear to have any influence on whether or not a patient would consent.

As the intention-to-treat analysis in the RCT showed no differences between intervention and control patients on length of stay and postoperative complications, the two groups were analyzed together. The length of stay was significantly different in eligible consenters and eligible non-consenters (p < 0.001) and more patients in the eligible non-consenter group needed help from the home care service system after discharge from hospital (p < 0.001). A larger proportion of the eligible non-consenters were transferred to a rehabilitation ward (p = 0.001). More patients in the eligible non-consenter group had urinary tract infections (p = 0.04) (Table 5).

Table 3. Characteristics at baseline of eligible consenters, eligible non-consenters, and excluded individuals

Variables	Eligible consenters (n = 79)	Eligible non-consenters (n = 33)	Excluded (n = 18)	P-value [a]
Age	57 (26–84)	70 (27–90)	56 (23–80)	0.008 [b]
Sex				
Male	36/79 (0.5) [f]	10/33 (0.3)	3/18 (0.2)	0.08 [c]
Female	43/79 (0.5)	23/33 (0.7)	15/18 (0.8)	
ASA classification				
ASA class 1	40/79 (0.5)	9/33 (0.3)	3/18 (0.2)	0.01 [d]
ASA class 2	30/79 (0.4)	16/33 (0.5)	12/18 (0.7)	
ASA class 3	9/79 (0.1)	8/33 (0.2)	3/18 (0.2)	
Harris hip score	54.9 (SD 14.3)	44.9 (SD 18.6)	41.9 (SD 14.6)	0.05 [e]
Social factors				
Married	40/79 (0.5)	21/33 (0.6)	9/18 (0.5)	0.2 [c]
Single	39/79 (0.5)	12/33 (0.4)	9/18 (0.5)	
Occupational factors				
Employed	48/79 (0.6)	8/33 (0.2)	7/18 (0.4)	<0.001 [c]
Old-age pensioner	23/79 (0.3)	17/33 (0.5)	6/18 (0.3)	
Invalidity pensioner	8/79 (0.1)	8/33 (0.2)	5/18 (0.3)	
Preoperative home care service				
Yes	3/79 (0.03)	9/33 (0.3)	3/18 (0.2)	<0.001 [c]
No	76/79 (0.1)	24/33 (0.7)	15/18 (0.8)	

[a] Eligible consenters and eligible non-consenters were compared statistically. Excluded patients are described.
[b] Mann-Whitney test; [c] Fisher's exact test; [d] Kruskal-Wallis; [e] Student's test
[f] Proportions are given in parentheses.

Table 4. Odds ratios (OR) for consenting

Variables	Unadjusted OR (95% CI)	Adjusted OR (95% CI) [a]
Age (year)	0.97 (0.94–0.99)	0.97 (0.94–0.99)
Gender		
Male	1.98 (0.84–4.7)	1.91 (0.79–4.60)
Female	1	1
ASA classification [a]		
ASA class 1	1	1
ASA class 2	0.42 (0.16–1.08)	0.61 (0.21–1.77)
ASA class 3	0.25 (0.08–0.84)	0.37 (0.10–1.43)
Harris hip score	1.04 (1.01–1.07)	1.03 (0.99–1.07)
Social factors [a]		
Married	0.59 (0.25–1.35)	0.49 (0.20–1.20)
Single	1	1
Occupational factors [a]		
Employed	1	1
Old-age pensioner	0.49 (0.16–1.47)	0.65 (0.13–3.30)
Invalidity pensioner	0.09 (0.03–0.26)	0.10 (0.02–0.45)
Preoperative home care service [a]		
Yes	0.10 (0.03–0.40)	0.17 (0.04–0.81)
No	1	1

[a] Adjusted for age and sex.

Discussion

We found that there was a significant difference between eligible consenters and eligible non-consenters with respect to important prognostic factors and subsequent clinical outcome variables.

Table 5. Postoperative clinical endpoint variables of eligible consenters, eligible non-consenters, and excluded individuals

Variables	Eligible consenters (n = 79)	Eligible non-consenters (n = 33)	Excluded (n = 18)	P-value [a]
Length of stay	8.00 (1–17)	11.00 (6–53)	9.50 (3–28)	<0.001 [b]
Transfer to rehabilitation ward				
Yes	3/79 (0.03) [d]	9/33 (0.3)	3/18 (0.2)	0.001 [c]
No	76/79 (0.1)	24/33 (0.7)	15/18 (0.8)	
Wound infections				
Yes	2/79 (0.02)	3/33 (0.09)	1/18 (0.05)	0.15 [c]
No	77/79 (0.1)	30/33 (0.9)	17/18 (0.9)	
Urinary tract infections				
Yes	12/79 (0.2)	11/33 (0.3)	6/18 (0.3)	0.04 [c]
No	67/79 (0.8)	22/33 (0.6)	12/18 (0.7)	
Luxation of the hip				
Yes	0/79 (0)	1/33 (0.03)	3/18 (0.2)	0.29 [c]
No	79/79 (1)	32/33 (0.)	15/18 (0.8)	
Postoperative home care service				
Yes	4/79 (0.05)	15/33 (0.4)	5/18 (0.3)	<0.001 [c]
No	75/79 (0.9)	18/33 (0.5)	13/18 (0.7)	

[a] Eligible consenters and eligible non-consenters were compared statistically. Excluded patients are described.
[b] Mann-Whitney test; [c] Fisher's exact test.
[d] Proportions are given in parentheses.

The non-consenters consisted of a subgroup of the screened population to whom the trial therapy could be applied, as this group did not include patients with contraindications to the trial therapy. Because of the low number of patients in our study population, possible bias as a result of lost information should be considered. The validity of length of stay as a clinical endpoint measure can be questioned. In order to minimize bias, we used standardized discharge criteria in all cases as previously recommended (Kehlet and Wilmore 2005).

Despite the potentially important implications of disparities between eligible consenters and eligible non-consenters, only a few studies dealing with fast-track programs have previously supplied postoperative clinical endpoint data in sufficient detail to allow a comparison. Our results are, however, in agreement with the findings of (Husted et al. 2004). Furthermore, it has been shown in population-based surveys (Bergstrand et al. 1983, Goldberg et al. 2001, Hasserius et al. 2002), in primary preventive trials (Wilhelmsen et al.1976), and in clinical trials (Smith and Arnesen 1988, 1990) that there is a higher frequency of non-consenters among subjects with increased risk of disease and mortality.

A basic prerequisite of clinical trials is that the study sample should be realistically representative of the target population for future treatment. Our data reinforce the need for those conducting clinical trials to provide additional information about the recruitment process, supplemented with readily available quantitative data as recommended in order to avoid misleading assessments regarding the degree to which the results may be generalized, and biased estimates of treatment effects (Altman et al. 2001). Our findings demonstrate the importance of patient inclusion criteria in RCTs. Moreover, they may account for the lack of reproducibility of results in clinical practice dealing with fast-track programs.

Contributions of authors

MP: participated in the entire process—planning and execution of the study, data collection, statistical analysis and preparation of the manuscript. KA: assisted in execution of the study, data collection, and in preparation of the manuscript. NA: participated in the planning process, and in the statistical analysis and preparation of the manuscript. KS: performed many of the THRs and participated in the entire process, especially in preparation of the manuscript.

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Self-reported functional outcome after primary total hip replacement treated with two different perioperative regimes

A follow-up study involving 61 patients

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Background and purpose **Fast-track surgery has been reported to improve rehabilitation outcome after major surgery, with length of hospitalization and muscle strength as outcome measures. We assessed the effect of optimization of perioperative care during admission on self-reported functional outcome, and compared patient status 6 months after THR with an age-matched healthy cohort.**

Patients and methods **79 THR patients were randomized to optimized perioperative care (OPC) or conventional perioperative care (CPC). 61 patients fulfilled the requirements of the study protocol. Endpoint outcome was measured by SF-36 and WOMAC. To compare functional outcome in the THR group with that in healthy controls, we used data from a representative sample of 4,098 non-institutionalized Danish adults collected by the Danish National Institute of Public Health.**

Results **We found similar improvements in SF-36 and WOMAC scores for the OPC and CPC groups postoperatively, except for the total WOMAC score and the WOMAC subscore "function"—in which the CPC group did statistically significantly better. The OPC and CPS groups had similar score levels. 6 months after surgery, THR patients scored higher overall in the general health subscale and lower in three physical subscales of SF-36 compared to age-matched healthy controls.**

Interpretation **We found no evidence for the effect of optimization strategies during admission on self-reported functional outcome after THR. Although THR patients improved considerably after treatment, their physical status remained below the level of the healthy controls. Our results may indicate that the potential for functional improvement in THR patients is not fully realized, but this must be studied further.**

Multimodal rehabilitation or fast-track surgery combine modern concepts of patient care with multimodal anesthetic and analgesic methods. It has been introduced to improve recovery, reduce hospitalization, and improve rehabilitation after surgery (Wilmore and Kehlet 2001, Henriksen et al. 2002, Kehlet and Wilmore 2002, 2005, Anderson et al. 2003, Gatt et al. 2005, Kehlet and Husted et al. 2006a, b, c, Petersen et al. 2006).

Preoperative education followed by postoperative home-based rehabilitation appears to be effective in reducing the length of stay and in improving function and quality of life after THR (Siggeirsdottir et al. 2005). Whether perioperative enforced mobilization and nutrition during admission can affect postoperative self-reported functional outcome in late-phase rehabilitation after total hip replacement (THR) has, however, not yet been demonstrated in any controlled study.

We assessed the usefulness of optimization of perioperative care during admission on self-reported functional outcome after THR, and compared patients' self-reported functional status after

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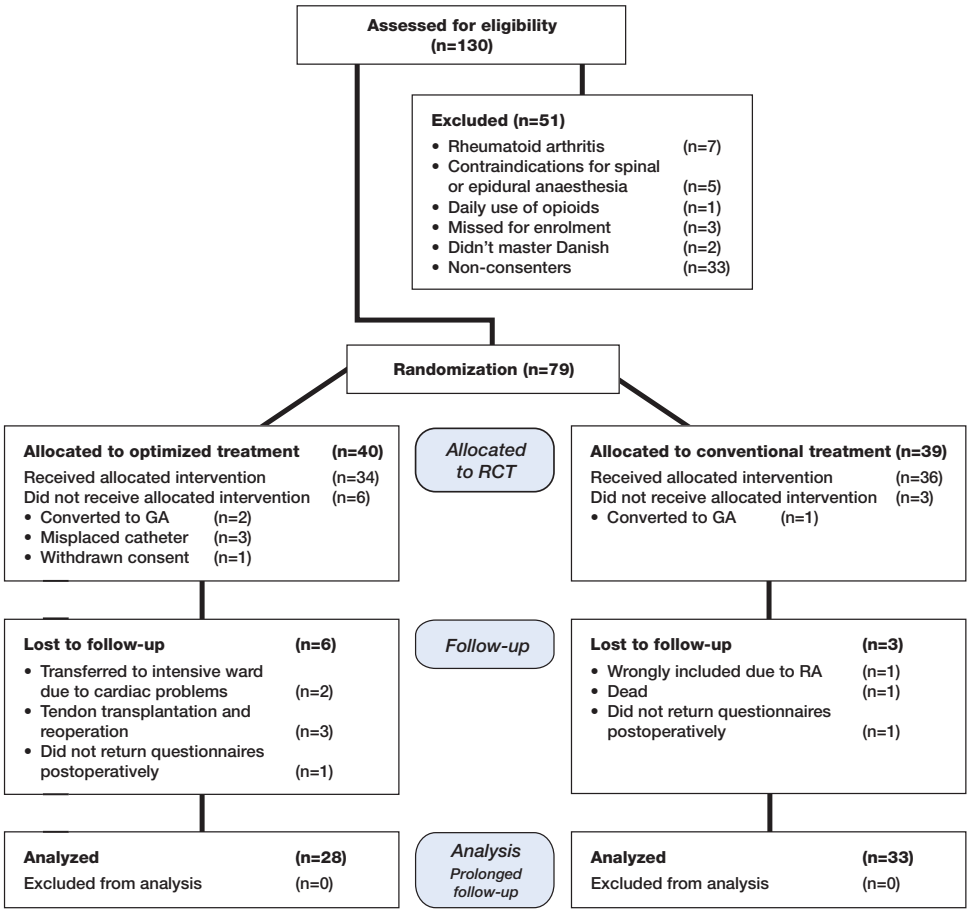

Figure 1. Flow chart showing progress through the different phases of the study.

6 months with that of an age-matched healthy cohort.

Patients and methods

In this paper we present our findings from prolonged follow-up of a cohort defined by a previous randomized controlled trial (RCT) (Petersen et al. 2006). The study was approved by the local ethics committee and was carried out in accordance with the Helsinki Declaration.

Patients with osteoarthritis who were scheduled for elective primary unilateral THR and perioperative epidural analgesia were assessed for eligibility. Exclusion criteria were chronic opioid use, chronic pain syndrome, rheumatoid arthritis, fractures, and mental disorders.

Randomization was carried out on the day of admission by the use of sealed envelopes. Block randomization into blocks of 8 was used. The sequences were computer-generated.

130 patients were identified as potential participants, 18 patients did not meet the inclusion criteria, and 33 declined to participate (Figure 1). Thus, 79 patients were randomized to receive optimized perioperative care (OPC) or conventional perioperative care (CPC). 61 patients, 28 in the OPC group and 33 in the CPC group, constituted the study population of this prolonged follow-up study.

In order to compare the self-reported functional status of the THR patients with that of the healthy controls, we used data from a representative sample of 4,098 non-institutionalized Danish adults. These data were collected from February through August 1994 as a part of a population health survey car-

ried out by the Danish National Institute of Public Health (Bjorner et al. 1997). All THR patients and healthy controls were classified into 6 age-matched groups.

All patients received standardized multimodal anesthesia and analgesia throughout the perioperative and postoperative period. The epidural catheter was removed after 48 h and Oxycontin (oxycodon hydrochloride) 10 mg twice a day and acetaminophen 1 g 4 times a day were given.

When the postoperative hemoglobin (HB) was < 5.5 mmol/L and if the patient had clinical symptoms (dizziness during mobilization), a blood transfusion was given.

All patients received physiotherapy for half an hour daily on weekdays. All of them were discharged with an exercise program for home training. No further rehabilitation was done. Patients were considered for discharge when sufficient pain relief had been achieved (estimated as a VAS score of < 3 cm while resting and < 5 cm during mobilization), and when the patient was able to maintain personal hygiene, to walk with sticks, and to climb stairs. Discharge was at the discretion of departmental surgeons.

The OPC group

The OPC group was given an optimized treatment regime involving pre- and postoperative strategies. Patient education was given the day before surgery by the investigators. The patients were introduced to standard plans for mobilization and energy intake. They were informed about the optimized treatment regime and the expectations they had in common were discussed. Transfer and walking techniques that would be required after surgery were trained. Devices to be used postoperatively were introduced and given to the patient.

Postoperatively, patients were encouraged to follow the written standard goals as follows. Mobilization was started on the first postoperative day. Scheduled time out of bed increased by 2 h a day, from 2 h on the day after surgery to 12 h on the sixth postoperative day. Furthermore, patients were asked to walk the length of the ward corridor (2 × 50 m) a scheduled number of times, increasing by 100 m a day from 100 m on the second postoperative day to 500 m on sixth postoperative day.

Eating and drinking despite lack of appetite was encouraged from the day of the operation. Registration and calculation of energy intake was performed on a daily basis. Supplementary energy intake: 200 mL of a protein-rich drink (Fortimel; Nutricia, Zoetermeer, the Netherlands) was served 3 times a day between the main meals.

The CPC group

The CPC group received none of the optimized measures listed. After surgery mobilization, oral fluid, and diet were introduced in a stepwise manner. The treating team responded to the wishes and condition of the patient in providing postoperative care, and no attempt was made to enforce mobilization or to encourage patients to eat and drink despite their lack of appetite.

To control the efficacy of the optimization strategies, all patients were asked to keep time records for leaving and returning to bed. Distance walked was measured using a marked area of the corridor in the ward, and all intake of nutrients was registered in a food record. Data were registered in a patient diary and patients were assessed by one of the researchers on a daily basis.

Process indicators

Analysis of the process indicators (mobilization and nutrition) showed that patients in the OPC group were mobilized to a far greater extent than patients in the CPC group (Figure 2). The average total time out of bed was 37 h (SD 10) in the OPC group and 26 h (SD 14) in the CPC group ($p < 0.001$). The median total walking distance was 1,500 (255–4,050) m in OPC group and 1,200 (247–7,900) m in CPC group ($p = 0.04$). The average energy and protein intake in the OPC group was 103 kJ/kg (SD 26) and 1.25 g/kg (SD 0.35), respectively, as compared to 76 kJ/kg (SD 24) and 0.74 g/kg (SD 0.25) in the CPC group ($p < 0.001$).

Endpoint outcome

The 36-item Short Form Health Survey (SF-36) and the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) were completed preoperatively, and 3 and 6 months postoperatively. Endpoint outcome measures were: changes in scores over time and changes in score level of the SF-36 and WOMAC variables.

The SF-36 is a generic, self-administered instru-

ment for measuring different aspects of quality of life (Ware and Sherbourne 1992, Ware and Gandek 1998). The SF-36 scores range from 0 to 100, with a higher score indicating better health status.

The WOMAC is a disease-specific, self-administered instrument developed for the study of patients with osteoarthritis of the knee or hip (Bellamy 1997, 2002). It has a multidimensional scale comprising 24 items grouped into 3 dimensions: pain, stiffness, and physical function. We used the visual analog scale formats (WOMAC VA3 series) from 0–10 cm, where 0 represents no symptoms and 10 represents the worst possible symptoms.

Table 1. Overall comparison of demographics and perioperative data for the study population

Variables	Intervention (n = 28)	Control (n = 33)
Sex (F/M)	17/11	17/16
Age in years: median (range)	56 (28–84)	58 (26–81)
ASA classification [a] (n)		
I (normal healthy)	16	18
II (mild systemic disease)	12	11
III (severe systemic disease)	0	4
Harris hip score preoperatively [b]	53.7 (48.6–58.8)	57.0 (51.4–62.7)
Type of prosthesis (n)		
Uncemented	19	19
Hybrid	6	4
Cemented	3	10
Surgical time in min. [b]	77 (69–85)	92 (79–106)
Preoperative hemoglobin (mmol/L) [b]	8.4 (8.1–8.6)	8.8 (8.5–9.1)
Postoperative hemoglobin (mmol/L) [b]	6.7 (6.4–7.0)	6.7 (6.5–7.0)
Blood transfusion	3	2
Nausea (n)	11	14
Pain at rest [b]	1.3 (1.0–1.6)	1.5 (1.1–2.0)
Pain during mobilization [b]	3.1 (2.3–3.8)	3.2 (2.4–4.1)
Wound infection (n)	1	1
Urinary tract infection (n)	7	4

[a] American Society of Anaesthesiology classification.
[b] Mean (95% CI)

Statistics

SF-36 and WOMAC variables are described by means or mean changes and 95% confidence intervals (CIs), and analyzed by a repeated measurements model. Changes over time (parallel curves) and score level (average over time) were compared between the OPC group and the CPC group, and tested for significant differences.

6 months postoperatively, scores of the SF-36 subscales "general health", "physical functioning", "role physical", and "physical component summary scale" for the THR patients were compared with matching scores for the healthy controls.

A weighted estimate of the differences between groups was calculated after stratification into 6 age groups using the weights (1/SEE2), where SEE is the standard error of the estimate within a particular age group. The significance level was $p = 0.05$. We used SPSS software version 11.0 for Windows.

Results

61 patients completed the study (Table 1, Figure 2). No significant differences in change of score were seen between groups, except for the total WOMAC score and the WOMAC subscale "function", where the CPC group had a higher change in score ($p = 0.03$ for both comparisons) (Table 2). The changes over time were all significant (all p-values were < 0.001 except for two (0.007 and 0.009)), and there were no significant difference between the OPC group and the CPC group regarding level.

WOMAC showed a minor ceiling effect 3 and 6 months postoperatively in all domains, and SF-36 showed both floor and ceiling effects preoperatively, and also 3 and 6 months postoperatively (Table 3).

A comparison of the stratified and weighted scores of the SF-36 subscales "general health" (GH), "physical functioning" (PF), "role physical" (RP), and "physical component summary" (PCS) between THR patients and healthy controls showed that the THR patients had an overall higher score in the subscale GH (95% CI: 0.1–1, $p = 0.05$) than the healthy controls, but a lower score in all three physical subscales (PF, RP, and PCS) (95% CI: 4.0–13, $p \leq 001$; 95% CI: 3.3–27, $p = 0.01$; and 95% CI: 0.1–5.8, $p = 0.05$, respectively).

The differences in scores were more distinct among the younger and the older age groups, especially in relation to the variables RP and PCS

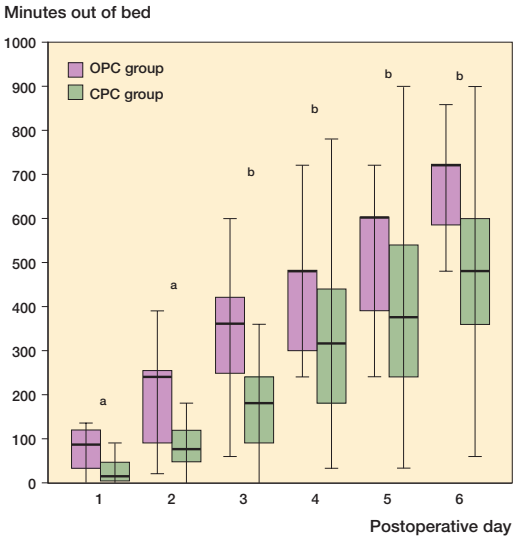

Figure 2. Daily time out of bed (in min) during the first 6 postoperative days after admission in the two groups (mean and SEM). a = p ≤ 0.05; b = p ≤0.01.

Discussion

In this follow-up study investigating the usefulness of two different perioperative treatment regimes after THR on self-reported functional outcome 3 and 6 months postoperatively, we found that there were no significant differences between groups except for the total WOMAC result and the WOMAC subscale "function". This result could be a coincidence caused by multiple testing (p-values were close to 0.05), but generally speaking the CPC group did better postoperatively than the OPC group. We have no clear explanation for this finding, but as the OPC group was hospitalized for a significantly shorter time than the CPC group (Petersen et al. 2006), we cannot eliminate the possibility that length of stay was a confounding factor.

Another explanation for the poor result of our intervention compared to that of others (Siggeirsdottir et al. 2005) may be that the intervention was only carried out during hospitalization. In the study by Siggeirsdottir et al., intervention was continued after discharge by offering home visits during the first 2 weeks after discharge, in order to ensure that the rehabilitation course was being followed after hospitalization. As a result of our study design, we do not know whether patients in the OPC group continued the recommended regimes after discharge.

Another weakness of our study was the lack of blinding. Both caretakers and patients knew which treatment patients were receiving, and this could have introduced bias regarding a general increase in mobilization and energy intake in the CPC group—and thereby an underestimation of the efficacy of the optimization strategies. Yet another weakness was that we did not assess patients' biochemistry, body composition, or muscle strength in order to be able to compare our results with those of other studies (Henriksen et al. 2002, Gatt et al. 2005).

The SF-36 showed a more conspicuous ceiling effect postoperatively than the WOMAC. Validity and responsiveness are the most important criteria when deciding which particular instrument to use in a clinical trial (Bellamy et al. 1997). Although generic instruments are useful in providing comprehensive health ratings that can be used with various disorders, they may be inferior to disease-specific instruments in their responsiveness in relation to intervention studies where measurements are repeated. The lack of responsiveness may be caused by a ceiling effect, which means that improvements cannot be detected in patients with a maximum score at baseline.

In accordance with other studies (Angst et al. 2001, Bachmeier et al. 2001, Patt and Mauerhan 2005, Quintana et al. 2005), we found that the illness-specific instrument (WOMAC) was more responsive to changes over time than the generic instrument (SF-36).

The functional outcome after 3 months in the THR group was in accordance with the results of other studies with a longer follow-up period (Bachmeier et al. 2001, Juul et al. 2006, Quintana et al. 2005). This indicates that the main improvements after THR are seen rather early in late-phase rehabilitation.

Although the THR patients generally achieved a higher score in the subscale "general health" than the controls after 6 months, their overall scores in the 3 physical subscales were lower. Our results may indicate that the potential for improvement in function for THR patients is not fully realized, but this must be studied further. The difference was

Table 2. Changes in WOMAC and SF 36 scores between baseline and follow-up 3 and 6 months postoperatively. Differences in changes over time baseline and 3 months; baseline and 6 months between groups were analyzed and tested for statistically significant differences by a repeated measurements model

Outcome variables	Intervention group (n = 28)			Control group (n = 33)			P-value
	A	B	C	A	B	C	D
WOMAC							
Pain, mean	194	144	149	226	187	194	0.1
95% CI	142–245	98–191	100–199	184–269	145–229	153–235	
Stiffness, mean	90	64	62	103	77	80	0.4
95% CI	69–111	43–85	42–82	85–121	60–94	61–99	
Function, mean	658	374	456	795	575	620	0.03
95% CI	516–798	233–516	325–588	666–924	440–711	497–743	
Total WOMAC, mean	941	582	668	1126	839	894	0.03
95% CI	737–1146	389–776	476–859	944–1308	661–1017	728–1061	
SF-3							
Physical functioning, mean	44	25	31	42	27	32	1.0
95% CI	36–52	15–35	22–40	34–50	17–36	24–41	
Role physical, mean	38	17	30	24	30	39	0.6
95% CI	22–53	-2–36	12–49	11–36	13–46	23–56	
Bodily pain, mean	42	38	43	38	39	48	0.6
95% CI	33–50	29–47	35–52	31–45	28–49	39–56	
General health, mean	61	11	11	70	6	7	0.6
95% CI	54–69	4–17	4–18	64–77	2–13	-1–15	
Vitality, mean	55	11	18	53	16	19	0.5
95% CI	47–62	3–19	9–26	45–62	7–25	10–28	
Social functioning, mean	80	4	12	71	12	17	0.5
95% CI	70–90	-6–13	5–19	61–81	2–22	8–27	
Role emotional, mean	61	18	23	52	8	27	0.2
95% CI	44–78	1–35	6–40	35–68	14–30	9–45	
Mental health, mean	74	7	10	74	7	8	0.8
95% CI	67–80	0.1–13	3–17	67–80	-0.5–15	-0.3–17	
Physical component summary scale, mean	33	11	14	33	13	15	0.9
95% CI	30–37	7–16	10–18	30–36	9–16	11–19	
Mental component summary scale, mean	53	1	-3	51	1	3	0.9
95% CI	49–57	2–4	-0.3–6	47–55	-4–5	-1–4	

A Baseline score
B Change in score after 3 months
C Change in score after 6 months
D Equal changes between groups

more conspicuous in the young and the old age groups, which seems important when the need for a course of postoperative rehabilitation is considered because the young THR patients are expected to return to full working capacity and ideally the old patients should stay out of domiciliary care.

Contributions of authors

MP participated in the entire planning process and execution of the study, data collection, statistical analysis, and preparation of the manuscript. NA participated in the planning process and in the statistical analysis and preparation of the manuscript. KS performed many of the THRs and participated in the entire process, especially in preparation of the manuscript.

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Table 3. Psychometric properties of WOMAC and SF-36 at baseline and at follow-up 3 and 6 months postoperatively, showing the number of patients with the lowest score (floor effect) and the number of patients with the highest score (ceiling effect). Study population was 61 patients

Variables	Baseline		3 months postop.		6 months postop.	
	A	B	A	B	A	B
WOMAC						
Pain	0	0	0	5	0	9
Stiffness	0	0	0	6	0	9
Function	0	0	0	3	0	4
SF-36						
Physical functioning	1	0	0	2	0	4
Role physical	32	9	20	24	13	30
Bodily pain	2	0	0	20	0	20
General health	0	1	0	8	0	11
Vitality	0	2	0	6	0	6
Social functioning	2	25	0	37	0	44
Role emotional	21	28	15	37	6	44
Mental health	0	2	0	10	0	11

A Number of patients with lowest score
B Number of patients with highest score

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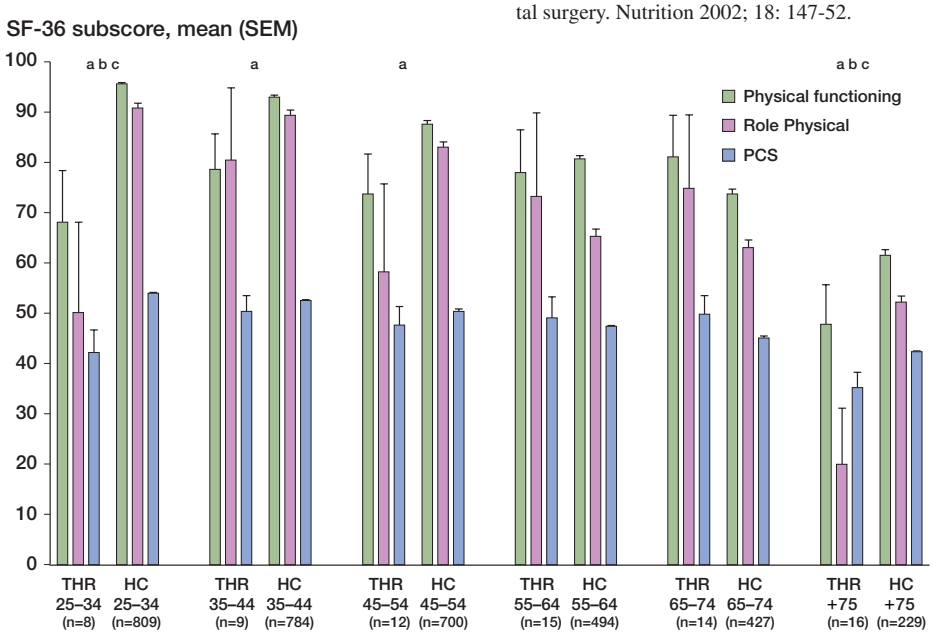

Figure 3. Scores of THR patients and healthy controls in the SF-36 subscales physical functioning (PF), role physical (RP), and physical component summary scale (PCS) broken down according to patient age. Scores are presented as mean an SEM. Statistically significant differences in mean scores between patients and controls are shown as follows: a = PF: $p < 0.05$; b = RP: $p < 0.05$; c = PCS: $p < 0.05$.

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Mechanics of gait after total hip replacement with Hip Resurfacing Implant or Mallory-head Exeter prosthesis: a randomized controlled trial

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Attached 2 figures, 3 tables

Abstract

Background and purpose

A key to the analysis of function after joint replacement is the ability to identify gait adaptations specific to design features. In a prospective controlled design, we evaluated mechanics of gait after total hip replacement (THR) with use of two different types of implants. We also investigated whether adaptations to gait normalized postoperatively.

Patients and methods

Thirty patients were randomized to receive a hip resurfacing system (HRS group) or conventional hybrid prosthesis (MHE group). Twenty-22 patients underwent three-dimensional gait analysis 6 and 12 weeks postoperatively. To evaluate normalization of gait after THR, we used data from 22 age- and sex-matched healthy controls.

Results

We found similar postoperative improvements in mechanics of gait between the groups, except for peak abductor moments, which improved more in the MHE group. HRS and MHE groups were similar with respect to level of peak values. Three months after surgery, most peak values were significantly different between operated and non-operated hip in all THR patients. Mean curves of kinetic and kinematic variables of THR patients and healthy controls showed that gait adaptations were not normalized after 3 months.

Interpretation

We found no evidence for the hypothesis that one implant was superior to the other in normalizing gait adaptation. Although THR patients improved considerably and significantly in almost all gait parameter variables, gait impairments persisted. Our results may indicate the need of gait retraining in conjunction with intensive muscle strengthening to improve function and longevity of implants, especially among young patients.

Introduction

The predictability of the results of total hip replacement (THR) is excellent in the older age groups, whereas the longevity of the implant in young and active patients still remains unsatisfactory, with failure rates ranging from 20% to 42% (Beaule and Dorey, 2001,Duffy et al., 2001).

Surface replacement is a bone-conserving alternative to standard THR. The theoretical advantages of this implant include less inflammatory debris and osteolysis, minimal resection of the femoral head, improved joint stability, and improved biomechanics(Girard et al., 2006,Ong et al., 2006). Restoration of normal movement patterns of the hip after THR provides better clinical function and reduced wear (Yamaguchi et al., 2004, Asayama et al., 2005, Girard et al., 2006,Ong et al., 2006) . A key to analysis of function after joint replacement is the ability to identify gait adaptations specific to design features (Andriacchi and Hurwitz, 1997). Several studies have used gait analysis to study functional outcome after THR (Gore et al., 1985, Perron et al., 2000, Bach et al., 2002, Kyriazis and Rigas,

2002, Madsen et al., 2004, Mont et al., 2007). Impairments of gait adaptation in the hip are believed to be caused by reduced muscle strength in the gluteal muscles, reduced range of hip extension especially in the late stance phase (Hurwitz et al., 1997, Hulet et al., 2000) . Because the resurfacing surgical technique is more invasive than conventional THR, we hypothesized that range of motion and muscle strength would be more affected during the early phase of rehabilitation in patients receiving a resurfacing implant than in patients receiving a conventional prosthesis. Furthermore, we expected persisting gait impairments to be less in patients with resurfacing arthroplasty because of better joint stability and biomechanics.

In a prospective randomized controlled study, we evaluated mechanics of gait after THR in patients with two different types of implant to examine whether one implant was superior to the other. Furthermore, we set out to investigate to what extent adaptations to gait were normalized 3 months postoperatively.

Material and methods

This study is a prospective randomized controlled trial. The study was approved by the local ethic committee and fulfilled the Helsinki Declaration. Patients between the ages of 50 and 65 years with osteoarthritis scheduled for elective primary unilateral THR were assessed for eligibility. Exclusion criteria were insufficient bone density; exposure to chrome, cobalt, and molybdenum; kidney disease; fracture sequelae; hip joint dysplasia; sequelae to previous hip joint disorders in childhood; patients with rheumatoid arthritis; and patients with more than one joint affected by arthritis.

Patients were randomized by means of opening sealed envelopes. Block randomization into blocks of six was used. The sequences were computer generated, and the randomization was performed by a nurse who was not a part of the research group.

In the study period, 30 patients were included and randomized to receive the hip resurfacing system (HRS group) or conventional hybrid prosthesis (MHE group).

In all cases, an uncemented acetabular component and a cemented femur component were used.

The hip resurfacing system (HRS) from (Biomet ®) was used in the HRS group, and in the conventional group, a Mallory-Head cup (Biomet) and an Exeter stem (Stryker®) were used. Compared to the conventional prosthesis (MHE), the articulating surface of the HRS is much larger. A posterior approach was used in all cases. The resurfacing surgical procedure included a loosening of the of the gluteus maximus fibers from the bursa and a release of the distal muscle insertion from the femoral bone.

All operations were performed by one senior surgeon, and all patients followed the same standardized postoperative rehabilitation program with full weight bearing allowed from the day after the operation. All patients were discharged with a home training exercise program, and no further rehabilitation was established.

In order to assess patient's self-reported functional status preoperatively, The Western Ontario and McMasters University Osteoarthritis Index (WOMAC) were completed.

All patients underwent three-dimensional (3D) gait analysis 6 and 12 weeks postoperatively.

The laboratory gait evaluation included simultaneous recording of body kinematics, kinetics, and muscle activation patterns in patients walking unassisted at their natural cadence. Gait analyses were performed by one examiner (physiotherapist) in the Gait and Movement Laboratory at the Hammel Neurocenter. All staff members administrating gait analysis were blinded to the type of prosthesis.

The 3D gait analysis was carried out using a Vicon 612 8-camera system (Vicon, Oxford, UK), operating at 100 Hz and using a Helen Hayes marker set up (Kadaba et al.,1990, Davis et al.,1991). Ground reaction forces were recorded using one AMTI force plate located in the middle of a 10-meter walkway. The sampling rate of the force plate data was set at 2000 Hz. Data from the force-plate and data from the cameras (frame rate 60 Hz) were synchronized and captured in a data station (Vicon Workstation). Before each measurement session, a static and dynamic calibration was carried out to allow the system to define the capture volume and the relative position and orientation of each the camera. A reconstruction process was carried out to create a virtual 3D motion, combining data from every camera by calculating the 3D position of each marker in each frame and linking these points into a trajectory. On this basis, a 3D model for each segment of the lower body could be constructed. The relative angles between coordinate systems of each segment in the lower limb, the absolute angles between a coordinate system of pelvis and the laboratory coordinate system, and the moment of force in each joint from the kinematics data and the ground reaction force could then be calculated. Reconstruction and calculations were carried out by the Vicon clinical manager software (Vicon workstation).

Three of five trials of each leg were selected on the criteria of speed similarity as recommended by Vardaxis et al (Vardaxis et al.,1998). These trials were processed for further analysis with Vicon Plug-In-Gait soft ware (Vicon, Oxford, UK). The beginning of a gait cycle was defined as the moment of heel strike, and the end of the cycle was defined as the next heel strike of the same leg. The gait cycle was normalized on a time basis of 100%.

Twenty-two age- and sex-matched healthy adults from the normal-material database of the Hammel Neurocenter Gait Laboratory following the same procedure were used as healthy controls (HC).

Outcome measures

End-point outcome measures were changes over time, changes in the magnitude of the peak values of gait parameter variables of the operated hip and differences between operated hip and non-operated hip.

Temporal-spatial variables analyzed were gait speed, cadence, stride length, step length, stance phase duration, and single support for both limbs.

Kinematic and kinetic variables analyzed were range of motion (ROM) of the hip joint in all directions and the corresponding moments for both limbs. Positive, negative, and total work power during a gait cycle were calculated.

To estimate to what extend normal gait adaptation was restored; the operated hip was compared with the non-operated hip 12 weeks postoperatively. To evaluate whether it was reasonable to assume that the non-operated hip was an appropriate reference, mean curves of kinematic and kinetic variables of the operated and non-operated hips were compared with hip values obtained from a matched healthy control population.

To compare patient's self-reported physical functioning at baseline, WOMAC scores were calculated preoperatively.

Statistics

Data from previous studies were used to estimate sample size. The estimate of the observed ROM in the sagital plane during one stride was 39.4 (SD 5.3). With a clinical relevant difference in ROM of 10%, a power of 80% and a significance level of 5%, sample size were estimated to consist of 20 patients.

Data normally distributed are described by means and standard deviation (SD), and statistically tested using Student's *t* test. Frequency was compared using Fisher's exact test.

Peak values of gait parameter variables are described by means and SD, and analyzed by a repeated measurement model. Changes over time and score level were compared between the HRS and the MHE groups and tested for significant differences by a repeated measurement model (Two- Way ANOVA). Peak values of gait parameter variables of operated and non-operated hip in the HRS and MHE groups were compared and analyzed for differences by a repeated measurement model (Two-Way ANOVA). Mean curves of kinematic and kinetic values during a gait cycle of HRS, MHE, and HC are described but not analyzed statistically.

The significance level was set at 0.05. We used the Statistical Package for the Social Sciences (SPSS) version 11.0 for Windows.

Results

Twenty-two patients completed the study. Progress through the phases of the study is illustrated in Fig. 1. Patient characteristics and perioperative data (Table1) were similar except for the HRS group having a significantly longer surgical time of 97.8 minutes (SD12.4) compared with 70.0 minutes in the MHE group (SD17.2) (P=0.01).

The gait speed increased significantly with about 12% for all THR patients in the period between 6 and 12 weeks after surgery, but with no significant differences between groups. The change in walking speed was reflected as significant changes in most of the assessed gait parameters within the patient groups (Table 2).

No significant differences in changes in peak values of gait parameter values of the hip at 6 and 12 weeks were seen between groups except for peak abductor moments, which improved significantly more in the MHE group (P=0.01) (Table 2).

A significant difference between operated and non-operated hips was seen except for hip flexion, ROM in the frontal plane, ROM in transverse plane, flexor moments, adductor moments, and max internal rotator moments (Table 3).

No significant differences between the HRS and MHE groups were seen between operated and non-operated hips (Table 3).

In the HC group, no statistical differences between left and right hip were seen in any gait parameter variables (all P values >0.05), and therefore the left/right data were pooled.

Mean curves of kinetic and kinematic variables during a gait cycle (Figure 2) showed a reduction in dynamic ROM in extension, abduction, and external rotation and a reduction in corresponding moments in both THR groups compared with the HC group.

Discussion

In this prospective randomized study, we investigated gait adaptations of the hip in patients after THR in which two different types of implants were used. No significant differences between groups in kinetic, kinematic, and temporal-spatial gait parameter variables of the hip were found 6 and 12 weeks postoperatively with respect to changes in or levels of peak values, except for peak abductor moments which changed more in the MHE group. The reason for this finding could be a faster recovery of the gluteal muscles due to the less invasive surgical procedure in the MHE group. Because differences between groups regarding level of ROM in hip extension and abduction and corresponding moments were minor and not significant, we found no evidence for the hypothesis that dynamic ROM and muscle strength would be more affected in the early phase of rehabilitation and persisting impairments less in patients receiving a resurfacing implant compared with patients receiving a conventional prosthesis.

A weakness of our study is that we did not perform a preoperative gait analysis in order to estimate whether patients in both groups had equal impairments of gait at baseline, but in as much as patients were included after fairly strict inclusion and exclusion criteria to assure a homogenous sample,

patients were randomized between the groups, and because the preoperative WOMAC and Harris Hip scores revealed no differences between groups in physical functioning, we believe that the results of our study are not biased by differences between groups due to the preoperative level in gait parameter variables.

In a study by Mont et al. (Mont et al., 2007) gait adaptation in patients receiving hip resurfacing arthroplasty was compared between patients receiving a standard prosthesis and healthy controls. In contrast to our study, Mont et al. showed that 1-year postoperative hip kinematics (abductor and extensor moments) and functionality (speed) was normalized to greater degree in patients receiving a resurfacing implant compared with patients with a conventional prosthesis. Because this study used an uncontrolled retrospective design, and only one postoperative time point of evaluation, the study results could be biased because of a highly selected and motivated resurfacing group. Gore et al. (Gore et al., 1985) compared patients before and after resurfacing or conventional replacement and found that before surgery the group receiving resurfacing was younger, had less pain, slightly more hip motion, greater muscle strength, walked faster, and used fewer assistive devices during walking than did the group receiving the conventional replacement. After surgery, the group with resurfacing maintained its advantage in muscle strength and walking velocity.

Another weakness of our study is the short follow-up period. The argument for choosing a short follow-up period was that 3 months after surgery patients are expected to return to normal physical activities and work, and therefore after that period factors other than different types of implant could affect gait adaptations and bias results. Furthermore, it has previously been reported that the greatest improvements in mechanics of gait occurred within the early rehabilitation phase (Murray et al., 1981,Wall et al., 1981).

Patients with hip pathology may adapt to a certain gait pattern that consists of reduced dynamic ROM and joint moments in order to avoid pain and to reduce forces on the pathological hip joint (Hurwitz et al., 1997, Pedersen et al., 2004, Hulet et al., 2000). Due to the lack of preoperative data, we can not evaluate to what extent changes in mechanics of gait persisted after THR.

However, our findings after 3 months are in accordance with the residual hip impairments reported in other studies examining gait adaptations before and after THR (Murray et al.,1981, Perron et al., 2000, Miki et al., 2004, Madsen et al., 2004, Foucher et al., 2007).

An increased peak contact force of the hip joint has previously been shown in patients with disturbed gait patterns (Bergmann et al., 2001,Heller et al., 2005,McGrory et al., 1995). Information about loading of the hip joint can be achieved from actual gait moments. External moments provide a reflection of net agonist and antagonist muscle activity, and they can indicate which muscles are compromised during surgery. It is assumed that dysfunction of one muscle increases the joint contact force because a part of the required joint moments is taken over by other muscles with unfavorably short lever arms and therefore higher forces (Bergmann et al., 2001,Bergmann et al., 2007). Several studies have reported postoperative extensor and abductor muscle weakness and have called for

increased muscle strengthening regimes after THR surgery (Long et al., 1993,Shih et al., 1994,Sicard-Rosenbaum et al., 2002). The results of our study support this need.

Failure to correct loading imbalances could be a factor in the development of implant failures in THR patients. It has been shown that hip loading or ground reaction force can be altered through gait retraining in subjects with THRs (White and Lifeso, 2005). However, it is unknown what the goals of gait training should be in order to obtain the best loading parameters for patient function and implant longevity. Current levels of function achieved by THR patients may have been sufficient in the past, but younger and more physically active patients may place greater demands on the implant (Healy et al., 2001,Kuster, 2002,Naal et al., 2007,Yun, 2006). Gait retraining in conjunction with intensive muscle strengthening could prove beneficial for the function and longevity of the implant especially among young patients.

Contributions of authors

MP participated in the entire planning process and execution of the study, data collection, statistical analysis, and preparation of the manuscript. NA participated in the planning process and in the statistical analysis and preparation of the manuscript. PM participated in the entire planning process, the execution of the gait analysis and preparation of the manuscript. MV participated in the data analysis and preparation of the manuscript. KS participated in the entire process, especially in preparation of the manuscript.

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Table 1. Patient characteristics and surgical data in HRS and MHE group

Variables	HRS group (N=11)	MHE group (N=11)	p values
Age in years (mean / SD)	59 (4.6)	61 (3.0)	0.5
Sex (F/M)	7/4	8/3	0.6
Weight in kilograms (mean / SD)	77.9 (9.1)	76.5 (10.8)	0.7
Height in meters	168.07 (6.9)	169.02 (7.4)	0.8
BMI	28 (3.6)	27 (3.5)	0.5
Surgical time in min (mean / SD)	97.8 (12.4)	70.0 (17.2)	0.01
Harris Hip Score (mean / SD)	52.3 (12.7)	48 (13.9)	0.5
WOMAC pain (mean / SD)	28 (7.3)	26 (10.6)	0.7
WOMAC stiff (mean / SD)	11 (5.2)	11 (5.4)	0.9
WOMAC function (mean / SD)	83 (23.8)	94 (35.3)	0.4
WOMAC total (mean / SD)	122 (26.1)	132 (48.7)	0.6

Table 2. Temporal-spatial, kinematic, and kinetic gait parameter variables of operated hips in the HRS and MHE groups 6 and 12 weeks postoperatively. Data are described by means (SD).
Differences within and between groups are analyzed by a repeated measurement model;
1= difference in changes over time between groups; 2= difference in level between groups; 3 = changes over time within groups.

Variables	HRS group (N=22)		MHE group (N=22)		P values		
	6 weeks Mean (SD)	12 weeks Mean (SD)	6 weeks Mean (SD)	12 weeks Mean (SD)	1	2	3
Temporal-spatial variables							
Gait speed (m/s)	1.2 (0.3)	1.3 (0.2)	1.1 (0.3)	1.3 (0.2)	0.9	0.4	<0.01
Cadence (steps/min)	113 (14)	118 (8)	110 (11)	116 (4)	0.9	0.5	0.01
Stride (m)	1.3 (0.2)	1.3 (0.1)	1.2 (0.2)	1.3 (0.1)	0.4	0.4	<0.01
Step length opr leg (m)	0.64 (0.1)	0.68 (0.1)	0.60 (0.1)	0.7 (0.1)	0.6	0.4	<0.01
Stance phase opr leg (%)	61.2 (1.6)	60.6 (0.8)	62.0 (2.9)	61 (1.9)	0.8	0.4	0.05
Single support opr leg (%)	37.6 (2.4)	38.9 (1.3)	36.5 (3.7)	39 (3.7)	0.4	0.6	0.01
Kinematic variables							
Max hip flexion angle (degrees)	35.2 (5.0)	34.5 (5.3)	31.9 (8.0)	32 (4.4)	0.9	0.1	0.7
Max hip extension angle (degrees)	5.5 (6.9)	1.5 (6.2)	3.0 (7.4)	-2.2 (4.2)	0.6	0.2	<0.01
ROM in sagital plane (degrees)	29.6 (7.2)	33.6 (5.9)	29.2 (5.6)	33.6 (4.)	0.8	0.9	<0.01
Max hip adduction angle (degrees)	4.5 (2.8)	4.2 (3.1)	4.9 (5.8)	6.0 (4.5)	0.4	0.5	0.6
Max hip abduction angle (degrees)	-5.4 (4.5)	-7.3 (4.3)	-4.6 (4.3)	-5.9 (2.3)	0.7	0.5	0.05
ROM in frontal plane (degrees)	9.8 (3.2)	11.5 (2.3)	9.5 (3.2)	12 (2.7)	0.5	1.0	<0.01
Max hip int. rotation angle (degrees)	8.1 (5.7)	7.3 (5.0)	9.4 (6.2)	10 (6.2)	0.7	0.3	1.0
Max hip ext. rotation angle (degrees)	-5.7 (5.8)	-9.0 (4.4)	-5.2 (4.5)	-8 (10.3)	0.8	0.7	0.2
ROM in transverse plane (degrees)	13.7 (2.9)	16.3 (6.0)	13.6 (4.8)	18 (5.8)	0.6	0.8	0.01
Kinetic variables							
Peak hip extensor moments (Nmm/kg)	689 (334)	863 (348)	665 (273)	817 (215)	0.8	0.8	<0.01
Peak hip flexor moments (Nmm/kg)	-636 (210)	-749 (212)	-513 (171)	-675 (238)	0.5	0.2	<0.01
Peak hip abductor moments (Nmm/kg)	718 (78)	733 (117)	652 (127)	774 (150)	0.01	0.8	<0.01
Peak hip adductor moments (Nmm/kg)	-101 (101)	-71 (31)	-107 (87)	-117 (48)	0.3	0.3	0.6
Peak hip ext. rotator moments (Nmm/kg)	63 (27)	66 (39.0)	61 (27)	78 (32)	0.2	0.7	0.06
Peak hip int. rotator moments (Nmm/kg)	-94 (37)	-125 (46)	-73 (51)	-98 (53)	0.6	0.2	<0.01
Work							
Total work (Joule)	19.5 (9.1)	27. (11.2)	17.8 (8.6)	25 (8.9)	0.9	0.6	<0.01

Table 3. Temporal-spatial, kinematic, and kinetic gait parameter variables of operated and non-operated hips 12 weeks postoperatively. Data are described by means (SD). Differences within and between groups are analyzed by a repeated measurement model;
1= differences in the difference between operated/non-operated hip between groups; 2 difference in level between groups; 3= difference between operated/non-operated hip within groups.

Variables	HRS Group (n=11)		MHE Group (n=11)		P values		
	Opr. hip Mean (SD)	Non-opr hip Mean (SD)	Opr. hip Mean (SD)	Non-opr hip Mean (SD)	1	2	3
Temporal-spatial variables							
Step length (m)	0.68 (0.1)	0.64 (0.1)	0.66 (0.1)	0.63 (0.1)	0.5	0.6	<0.01
Stance phase (%)	60.6 (0.8)	61.0 (1.2)	61.2 (1.9)	62.0 (2.3)	0.6	0.3	<0.01
Single support (%)	38.9 (1.3)	39.3 (1.1)	38.9 (3.7)	39.9 (3.8)	0.2	0.8	<0.01
Kinematic variables							
Max hip flexion angle (degrees)	34.5 (5.3)	36.3 (6.0)	31.5 (4.4)	32.8 (5.3)	0.8	0.1	0.06
Max hip extension angle (degrees)	1.5 (6.2)	-10.7 (4.5)	-2.2 (4.2)	-12.6 (3.6)	0.4	0.1	<0.01
ROM sagital plane (degrees)	33.6 (5.9)	47.0 (4.9)	33.6 (4.0)	45.4 (6.4)	0.4	0.7	<0.01
Max hip adduction angle (degrees)	4.2 (3.1)	2.9 (3.7)	6.0 (4.5)	4.7 (3.6)	1.0	0.2	0.2
Max hip abduction angle (degrees)	-7.3 (4.3)	-8.0 (3.6)	-6.0 (2.3)	-7.1 (2.4)	0.8	0.3	0.3
ROM frontal plane (degrees)	11.5 (2.6)	10.9 (3.6)	11.9 (2.7)	11.9 (3.2	0.6	0.6	0.5
Max hip int. rotation angle (degrees)	7.3 (5.0)	0.8 (6.7)	10.0 (6.2)	2.3 (6.9)	0.8	0.2	<0.01
Max hip ext. rotation angle (degrees)	-9.0 (4.4)	-13.5 (9.2)	-7.5 (10.3)	-14.4 (7.4)	0.6	0.9	0.02
ROM transversal plane (degrees)	16.3 (6.0)	14.3 (6.1)	17.6 (5.8)	16.7 (5.4)	0.5	0.4	0.1
Kinetic variables							
Peak hip extensor moments (Nmm/kg)	8634 (348)	901 (323)	817 (215)	866 (386)	0.9	0.8	0.4
Peak hip flexor moments (Nmm/kg)	-749 (212)	-952 (337)	-675(238)	-931 (204)	0.5	0.7	<0.01
Peak hip abductor moments (Nmm/kg)	733 (117)	756 (121)	774 (150)	851 (152)	0.3	0.2	0.08
Peak hip adductor moments (Nmm/kg)	-71 (31)	-202 (183)	-117 (48)	-151 (98)	0.1	0.9	0.01
Peak hip ext. rotator moments (Nmm/kg)	66 (39)	152 (54)	78 (32)	163 (47)	1.0	0.5	<0.01
Peak hip int. rotator moments (Nmm/kg)	-125 (46)	-137 (68)	-98 (53)	-109 (39)	1.0	0.2	0.3
Work							
Total work (Joule)	27 (11.2)	41 (15.9)	25 (8.9)	35 (9.3)	0.2	0.4	<0.01

Figure 1. Flowchart: progress through the phases of the study

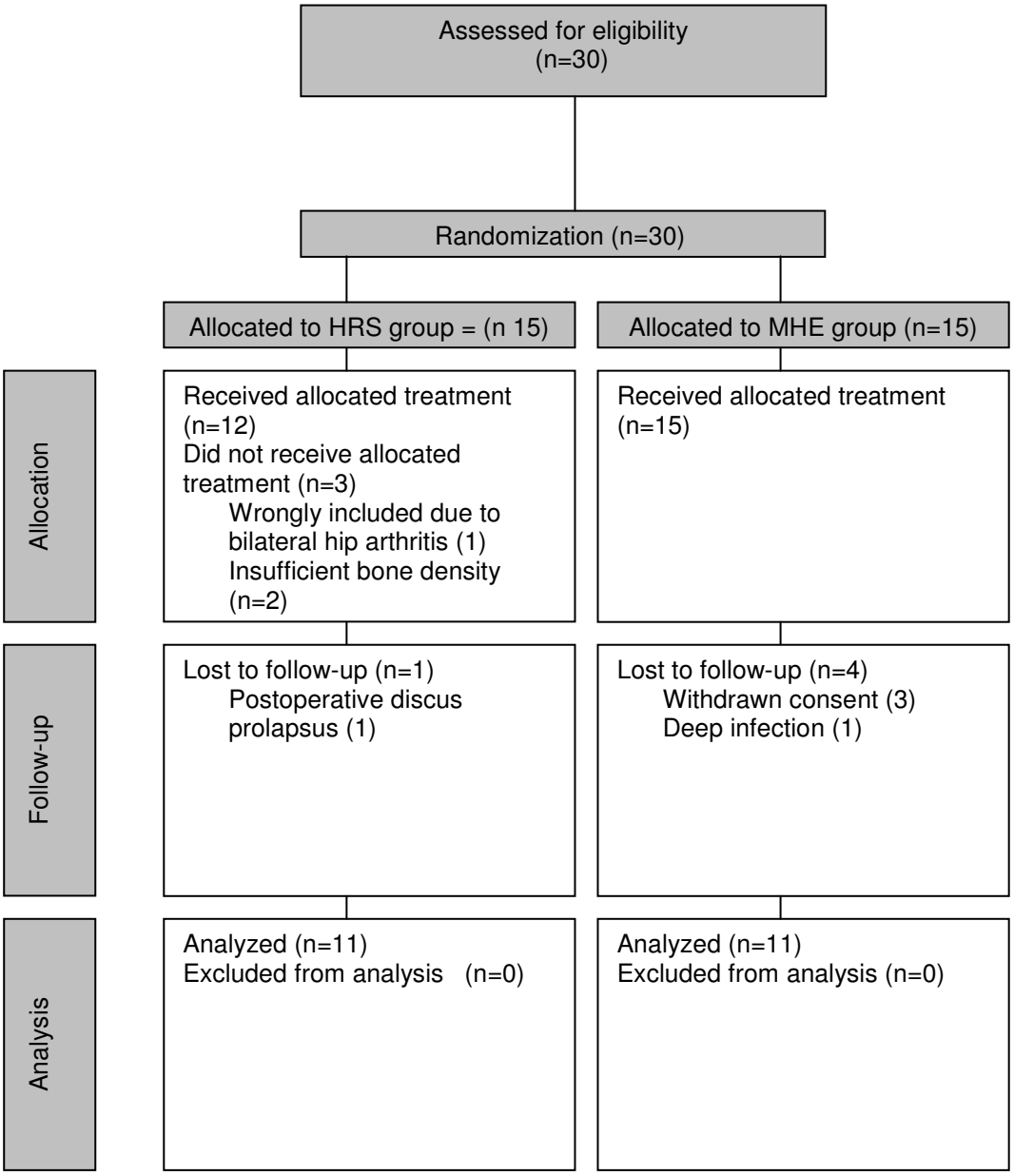

Figure 2. Ensembles averages of joint angle profiles (ROM) and moments in all anatomical planes during a gait cycle walking at a self-selected speed for the operated and non-operated hips in HRS group and MHE group 12 weeks after surgery, and the average values of both hips in HC group.
The HRS group is represented by the black lines (bold = operated hip, narrow = non-operated hip); the MHE group is represented by the grey lines (bold = operated hip, narrow = non-operated hip).
The shaded areas represent equal boundaries of +/- 1 SD for controls.