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Early rehabilitation after fast-track total hip replacement

Effect of early, supervised, progressive resistance training and influence of movement restrictions and assistive devices on functional recovery

PhD dissertation

Lone Ramer Mikkelsen

Health
Aarhus University
2014

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Preface

This PhD thesis was accomplished during my employment at the Elective Surgery Centre (former Department of Orthopaedic Surgery) at Silkeborg Regional Hospital. It was carried out in close corporation with Orthopaedic Research Aarhus (www.orthoresearch.dk) led by my main supervisor Professor Kjeld Søballe.

First of all I would like to thank all the participating patients who have investigated time and energy in participating in these studies, without them: no studies!!

I am grateful to my three academic supervisors for their belief in me and the projects. I would like to thank Professor Kjeld Søballe for his encouragement and advices, especially concerning the design of the studies, and for sharing with me his impressive knowledge within hip replacement surgery and clinical research methods. I send my gratitude to my supervisor Inger Mechlenburg, PhD, for her role as a mentor, giving me encouragement during hard times and counselling concerning scientific questions as well as the difficult balance between work and family life. I would like to praise her always constructive and very rapid response to scientific texts send to her for review. I thank my supervisor Mette Krintel Petersen, PhD, for suggesting that I should carry out this PhD in the first place, and for sharing her widespread experience on physiotherapy research and the execution of clinical intervention studies.

I wish to express my sincere gratitude to the management at Elective Surgery Centre for supporting this work, especially Søren Mikkelsen, executive consultant, for making this project possible, always believing in me and giving me optimal working conditions. Likewise Line Jespersen, head of physiotherapy department, for excellent collaboration. There are many colleagues I wish to thank for making a huge positive difference during this work: Lene Bastrup Jørgensen, PhD, for friendship, endless encouragements and scientific discussions, Martin Vesterby, MD for great support and many inspiring scientific discussions and Mette Farstad, PT, for convincing me that I should leap into this PhD project and supporting me on the way. Furthermore, my appreciation goes to all the physiotherapists in Elective Surgery Centre, especially those taking part in the studies. I thank you all for enthusiastic participation with great sense of responsibility. I also wish to thank the project staff for helping with patient screening and inclusion. Finally, my dear colleagues at the Interdisciplinary Research Unit deserve a warm thank you for creating a positive atmosphere and giving lots of encouragement.

My gratitude also goes to Niels Trolle Andersen for helpful statistical supervision on several occasions and senior researcher Thomas Bandholm for fruitful collaboration and several valuable advices. Furthermore, I thank my sister Ulla Ramer Mikkelsen, phD, who has generously shared her extensive research experience within the field of sports medicine. Last, but definitely not least, I send thanks and lots of love to my husband Claus for supporting me and making this project possible by taking care of our children Freja, Malte and Selma and all the practical issues when I left on congresses and several writing stays away from home.

I am grateful for the financial support received from the Lundbeck Foundation Centre for Fast-Track Hip and Knee Arthroplasty, the Health Research Fund of Central Denmark Region, the Danish Rheumatism Association, the Health Foundation, Aase and Ejnar Danielsens Foundation and the Association of Danish Physiotherapists.

Lone Ramer Mikkelsen, 2014

List of papers

This thesis is based on the following papers, which will be referred to by their Roman numerals (I-III) throughout this thesis.

I. Mikkelsen LR, Petersen MK, Søballe K, Mikkelsen S, Mechlenburg I. Does reduced movement restrictions and use of assistive devices affect rehabilitation outcome after total hip replacement? A non-randomized, controlled study. *Eur J Phys Rehabil Med.* 2014; 50: 383-93

II. Mikkelsen LR, Mikkelsen S, Søballe K, Mechlenburg I, Petersen AK. A study of the inter-rater reliability of a test battery for use in patients after total hip replacement. *Clin Rehabil.* 2014 May 21 [Epub ahead of print]

III. Mikkelsen LR, Mechlenburg I, Søballe K, Jørgensen LB, Mikkelsen S, Bandholm T, Petersen AK. Effect of early supervised progressive resistance training compared to unsupervised home-based exercise after fast-track total hip replacement applied to patients with preoperative functional limitations. A single-blinded randomised controlled trial. Submitted to *Osteoarthritis and Cartilage*, Apr 2014, re-submitted after revision, August 2014

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Abbreviations

ADL	Activities of daily living
ANOVA	Analysis of variance
ASA	American Society of Anesthesiologists. Physical status classification: I-Healthy patient, II-Patient with mild systemic disease, III+IV-Patient with severe systemic disease.
CG	Control group (Study III)
CI	Confidence interval
HADS	Hospital anxiety and depression scale
HOOS	Hip dysfunction and osteoarthritis outcome score questionnaire
HRQOL	Health-related quality of life
ICC	Intraclass correlation coefficient
IG	Intervention group (Study III)
IQR	Interquartile range
MANOVA	Multivariate repeated measurement analysis of variance
MDC	Minimal detectable change (equation: $1.96 \times \sqrt{2} \times SEM$)
MDC (%)	MDC in per cent of the grand mean (mean of the two test sessions)
Nm	Newton x meter
OA	Osteoarthritis
PRO	Patient-reported outcome
PRT	Progressive resistance training
QOL	Quality of life
RG	Restricted group (Study I)
RM	Repetition maximum
ROM	Range of motion
SD	Standard deviation
SEM	Standard error of measurement (equation: $SD/\sqrt{2}$)
SEM (%)	SEM in per cent of the grand mean (mean of the two test sessions)
THR	Total hip replacement
TKR	Total knee replacement
UG	Unrestricted group (Study I)
VAS	Visual analogue scale
W	Watt

1. English summary

Total hip replacement (THR) surgery results in substantial pain relief and functional gains. However, deficits in muscle strength and physical function after THR persist. Progressive resistance training (PRT) commenced early after THR can potentially reduce these deficits and thereby enhance recovery. Traditionally, rehabilitation after THR has included movement restrictions to prevent hip dislocations. Improvements in surgical techniques and increase of femoral head size may have changed the rationale for these restrictions.

The objectives of this thesis were I) to evaluate the influence of movement restrictions and assistive devices on rehabilitation after fast-track THR, II) to assess the inter-rater reliability of a test battery of functional performance, muscle strength and leg extension power on THR patients and III) to examine whether two weekly sessions of supervised PRT in combination with home-based exercise is more effective than unsupervised home-based exercise alone in improving leg-extension power of the operated leg 10 weeks after THR in patients with perceived functional limitations.

The thesis consists of three studies (I-III) including patients undergoing primary THR due to hip osteoarthritis (OA) at Silkeborg Regional Hospital in the period September 2010 to November 2012. In Study I, 146 patients treated with movement restrictions and a standard package of assistive devices (restricted group) was compared to 219 patients treated with less movement restrictions and use of assistive devices according to individual needs (unrestricted group) in a non-randomised, comparative study. Questionnaires on function, pain, quality of life (HOOS), anxiety, depression (HADS), working status and patient satisfaction were completed before THR, 3 and 6 weeks after. At the 3-week follow-up independency in four different activities of daily living (ADL) tasks was evaluated. In Study II, two raters performed test and re-test on two samples of 20 patients 3 months after THR. The test battery included sit-to-stand performance, 20-metre maximum walking speed, stair climb performance, isometric muscle strength (hip abduction/flexion), and leg extension power. In Study III, patients were randomly assigned to a control group (n=30) performing home-based exercises 7 days/week or an intervention group (n=32) performing PRT 2 days/week and home-based exercises the remaining 5 days/week. The PRT consisted of four lower extremity exercises performed with loads of 8-12 repetition maximum (RM) from week 1 to 10 after THR. Outcome was assessed before THR and 10 and 26 weeks after by the test battery presented in Study II and patient-reported outcome (HOOS). The primary outcome was change in leg extension power from baseline to 10-week follow-up.
Study I showed slightly slower recovery in patient-reported function in the unrestricted group compared to the restricted group, but the difference was

eliminated after 6 weeks and potentially biased by missing answers. The unrestricted group was more independent in ADL after 3 weeks and returned earlier to work compared to the restricted group, with no differences in the other patient-reported outcomes. The reliability study (II) documented acceptable relative and absolute inter-rater reliability of the test battery on a group level, but not on an individual level. In Study III, the supervised PRT in addition to home-based exercise was not superior to home-based exercise alone in improving leg extension power of the operated leg after THR. A few secondary outcomes favoured PRT but seemed clinically insignificant.

2. Danish summary

Total hoftealloplastik (THA) operation fører til betydelig smertelindring og forbedring af funktionsniveauet. Der er dog vedvarende deficits i muskelstyrke og fysisk funktionsevne efter operationen. Progressiv styrketræning påbegyndt tidligt efter THA kan potentielt reducere disse deficits og dermed forbedre kvaliteten af rehabiliteringen. Traditionelt har rehabilitering efter THA indbefattet bevægerestriktioner for at forebygge hofteluksation. Forbedringer i operationsteknik og brugen af større ledhoveder har muligvis ændret rationalet for disse restriktioner.

Formålene med denne ph.d. afhandling var, I) at undersøge betydningen af bevægerestriktioner og brugen af hjælpemidler på rehabiliteringen efter fast-track THA, II) at bestemme inter-tester reliabiliteten af et testbatteri til måling af funktionsevne, muskelstyrke og ekstensionskraft i benet hos patienter der er opereret med THA og III) at undersøge om progressiv styrketræning to gange ugentligt i kombination med hjemmetræning er mere effektivt end ikke-superviseret hjemmetræning alene til at forbedre ekstensionskraften i det opererede ben 10 uger efter THA hos patienter med selv-vurderede funktionsbegrænsninger.

Afhandlingen består af tre studier (I-III) der inkluderede patienter, som fik foretaget en THA operation på grund af hofteartrose på Regionshospitalet Silkeborg i perioden september 2010 til november 2012. I Studie I blev 146 patienter behandlet med bevægerestriktioner og en standard pakke med hjælpemidler (restriktiv gruppe) sammenlignet med 219 patienter der fik færre restriktioner og hjælpemidler ud fra individuelle behov (ikke-restriktiv gruppe) i et ikke-randomiseret, sammenlignende studie. Spørgeskemaer vedrørende funktion, smerte, livskvalitet (HOOS), angst/nervøsitet, depression (HADS), tilbagevenden til arbejde og patienttilfredshed blev udfyldt før, samt 3 og 6 uger efter THA operation. Ved 3 ugers opfølgning blev patienternes uafhængighed i fire dagligdags aktiviteter endvidere vurderet. I Studie II udførte to testere test og re-test på to grupper af 20 patienter 3 måneder efter THA. Testbatteriet inkluderede følgende tests: rejse-sætte sig, 20 meter maximal ganghastighed, trappegang, isometrisk muskelstyrke (hofteabduktion og -fleksion) og ekstensionskraft i benet. I Studie III blev patienterne randomiseret til enten en kontrolgruppe (n=30) der lavede hjemmetræning 7 dage/uge eller en interventionsgruppe (n=32) der lavede styrketræning 2 dage/uge og hjemmetræning de resterende 5 dage/uge. Styrketræningen bestod af fire øvelser for ben muskulaturen udført med en relativ belastning af 8-12 repetition maximum (RM) fra uge 1-10 efter THA. Effektmålinger blev udført før operationen samt 10 og 26 uger efter med testbatteriet fra Studie II og spørgeskema (HOOS). Det primære effektmål

var ændringen i ekstensionskraft i det opererede ben fra præoperativt til 10 uger postoperativt.

Studie I viste en smule langsommere fremgang i selv-vurderet funktion i den ikke-restriktive gruppe sammenlignet med den restriktive gruppe, men forskellen var udlignet efter 6 uger og resultatet er potentielt skævvredet af manglende besvarelser. Den ikke-restriktive gruppe havde højere grad af uafhængighed i dagligdags funktioner efter 3 uger og tidligere tilbagevenden til arbejde sammenlignet med den restriktive gruppe. Der var ingen forskelle i de øvrige patient-rapporterede målinger. Reliabilitetsstudiet (II) dokumenterede acceptabel relativ og absolut reliabilitet af testbatteriet på gruppeniveau, men ikke på individniveau. I Studie III var superviseret styrketræning 2 gange ugentligt i tillæg til hjemmetræning ikke mere effektivt end hjemmetræning alene til at forbedre ekstensionskraften i det opererede ben efter THA. Enkelte af de sekundære effektmål viste effekt af interventionen men blev ikke vurderet klinisk relevante.

3. Introduction

3.1 Total Hip Replacement

Total hip replacement (THR) is primarily offered to patients with end-stage osteoarthritis (OA) to reduce pain and improve function.[1] The effect of THR is well documented; the majority of the patients experience significant pain relief and functional improvements and are very satisfied with the procedure.[2-7] The procedure is so effective, that THR has been termed the surgery of the century in *The Lancet*.[8]

The surgical procedure involves removal of cartilage and bone from the femoral head and acetabulum and replacing it with artificial joint components: a stem inserted into the femoral bone with a ball on the top and an artificial socket with a polyethylene liner inside the acetabulum (see Figure 1).

Figure 1. Total hip replacement: artificial joint components and position in the pelvis and femoral bone.

Photo from: Protesekompagniet (Depuy Synthes).

The era of THR surgery as it is known today began in the 1960s when Sir John Charnley introduced THR with the prosthetic implant fixated to the bone by cement and was the first to demonstrate long-term success.[9] Since then, numerous studies have investigated different materials, designs and surgical methods to optimise the outcome and longevity of THR. The prosthetic survival rates in Denmark demonstrate that 92% of the implants are still functioning 10 years after THR and 84% after 17 years.[10] The most common indication for THR is OA, which is the cause for 79% of the operations. Other indications are femoral fractures, femoral head necrosis, congenital hip disorders, and rheumatoid arthritis.[10] Currently more than 8000 primary THR and more than 1400 revision THRs are performed annually in

Denmark – and the incidence is increasing due to a longer lifespan and a general expectation of having an active lifestyle, even in old age.[10] The posterior approach is most commonly used especially in Denmark, with 95% of the THR surgeries being performed using the posterior approach.[10] At Silkeborg Regional Hospital, the implants used are predominantly metal stems articulating with polyethylene liners as is most commonly used in Denmark.[10] When patients are below 75 years of age, cementless prostheses are primarily used, and for the older patients cemented prostheses are primarily used.

3.2 Fast-track surgery

During the last decade, an increasing focus has been on fast-track surgery (also called enhanced recovery programme) aimed at gaining rapid functional recovery, as well as reduced hospital stay and reduced postoperative morbidity through evidence-based optimisation within all areas of patient management.[11-13] These areas include pre-operative patient education, peri-operative pain management (including spinal anaesthesia), reduction of surgical stress response, optimal nutrition, early mobilisation, well-adjusted blood management and thromboembolic prophylaxis.[11-13] The fast-track concept involves implementing well-described pathways for these procedures, which often requires a revision of the organisational factors. Thus, adoption of multimodal pathways by dedicated elective centres has been suggested.[13] The outcomes after fast-track THR have demonstrated substantial reduction in length of stay, with no increase in readmission rates and with subsequent high patient satisfaction at lower health care costs.[13-15] Fast-track programmes including mobilisation on the day of surgery instead of the day after decreases length of stay and results in lower pain scores.[13] Well-described functional discharge criteria are crucial within the fast-track concept to assure that the timing of hospital discharge depends on functional recovery rather than routines at the department and organisational factors at the hospital.[16] At the Elective Surgery Centre (former Department of Orthopaedic Surgery) at Silkeborg Regional Hospital, a fast-track methodology was implemented in 2004, at first for a subgroup of THR patients with a family relative joining them during 5 days of hospital admission (known as the Joint Care concept) and from 2006 this was reduced to 3 days. Since 2010, all THR surgeries have been performed in a fast-track setup, with admission on the day of surgery and 1-2 days of postoperative hospitalisation.

3.3 Recovery after THR

As described earlier, undergoing THR surgery results in substantial pain reduction and gains in quality of life and function.[7] Nevertheless, there are some deficits documented in the literature: unfavourable long-term pain outcome in 7-23% of patients,[17] deficits in lower extremity muscle strength,[18-20] deficits in functional capacity,[20, 21] long-term deficits in perceived function[2, 22] and inactive lifestyle.[23, 24]

3.3.1 Function

It is well established in the literature that perceived function and functional performance reflect different aspects of functioning.[21, 25, 26] A definition of these aspects of functioning is given in Table 1 and used throughout this thesis.

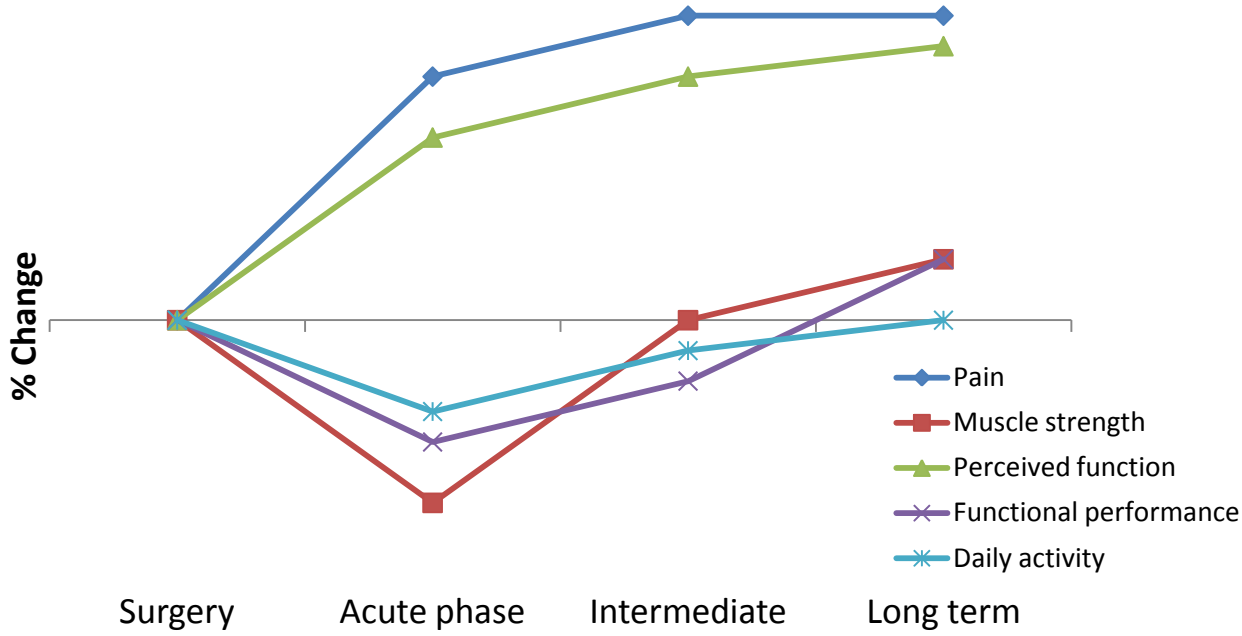
Table 1. Different aspects of functioning

Aspects of functioning	Meaning	Measurements
Perceived function[a]	How impaired the patients feel	Patient-reported outcome questionnaires
Functional performance[b]	What the patients can actually do	Performance tests, for example: Walking test, chair rise test, stair test, timed-up-and go
Daily activity	What the patients actually do in their daily life	Directly measured by accelerometers, pedometers etc. Indirectly measured by questionnaires or activity diary

[a]Also termed patient-reported function, [b]Also termed functional capacity and physical function

The pace of recovery differs significantly between different outcome measurements, as illustrated in Figure 2. Pain and perceived function improves rapidly, with significant improvement from preoperative already within the first week after THR.[27, 28] Physical performance, as measured with tests of muscle strength or functional performance, decreases early after THR and reaches preoperative levels within 1 to 3 months after surgery.[18, 20, 21, 29, 30] Concerning actual daily activity (what the patients actually do), the literature is sparse.[21] It seems that THR patients reach their preoperative level of activity within 3 months after surgery.[30, 31] A recent systematic review indicates that 8 months after surgery, THR patients have recovered to about 80% of the levels of healthy controls in all three aspects of functioning, but it remains unclear whether and when patients fully recover to the level of controls.[21] There seems to be consensus that it is crucial to include measurements of both perceived function and functional performance when evaluating functional outcome after THR due to the distinct discrepancy between these, functional performance recovery being less and latest to occur.[21, 26, 32]

Figure 2. Illustration of the pace of recovery in different aspects of functioning (Figure constructed on the basis of the literature covered in section 3.3)



3.3.2 Muscle strength

Hip muscle strength is reduced in patients with hip OA compared to the contralateral leg and to healthy controls.[33, 34] THR surgery leads to further acute loss of muscle strength,[27] potentially caused by post-surgical catabolism,[35] immobilisation,[36] diminished neural drive to muscle fibres[36] and arthrogenic muscle inhibition (AMI).[37] AMI is a well-known phenomenon in knee surgery that reflects failure in muscle activation close to the operated joint possibly due to intra-articular swelling, inflammation, pain and structural joint damage. AMI may appear after hip surgery as well.[38] Recent reports indicate that hip muscle strength is significantly decreased 1 month after surgery but regained within 3 months. (Figure 2).[18, 20] However, THR patients experience prolonged muscle weakness up to 2 years after surgery compared to healthy controls, especially in hip flexion and abduction.[19, 39] Likewise, substantial between-limb asymmetry in hip muscle strength has been documented to be present during the first 6 months after THR, and these deficits persist in some muscle groups up to 1 year, primarily in hip flexion.[18] These studies on post-surgical muscle strength have presumably included THR patients undergoing conventional surgical procedures; at least fast-track procedures are not reported. A few recent reports suggest less muscle strength loss and significant strength increases from preoperative levels within 3 months after fast-track THR.[29, 30]

3.4 Rehabilitation after THR

3.4.1 Movement restrictions and use of assistive devices

Hip dislocation is a rare but severe complication after THR, and studies have reported dislocation rates of ~0.5 to 4.5% after THR performed through the posterior approach.[15, 40, 41] A multitude of factors contribute to dislocation after THR, including component malposition, patient education, femoral head size and preoperative range of motion (ROM).[42-45] Rehabilitation during the initial months after THR, when the risk of dislocation is greatest, has traditionally included many restrictions on hip range of motion and patient activity as a preventive measure.[42, 46, 47] The movement restrictions typically include maximum 90° of hip flexion and no adduction and internal rotation beyond the neutral position. To comply with these restrictions, patients are often provided with assistive devices such as elevated toilet seats, elevated chairs (or wedge pillows), abduction pillows and ergonomic reachers. Activity restrictions include driving a car and sleeping on the side. Such restrictions are often applied the first 1-3 months postoperatively.[42, 46] Improvements in surgical techniques and increase in the femoral head size of the hip implants have decreased the risk of hip dislocation,[48] and this may have changed the rationale for these restrictions.[49] Studies including patients undergoing THR performed through the anterolateral surgical approach demonstrate continuously low dislocations rates when movement restrictions are eliminated or reduced (Table 2).[46, 47, 49, 50] Furthermore, some of these studies have demonstrated benefits of less restricted rehabilitation in terms of earlier ambulation, higher patient satisfaction and earlier return to work.[46, 47] As shown in Table 2, the literature concerning THR using the posterior approach is sparse; only conference abstracts or small-sample studies have compared restricted versus unrestricted rehabilitation. The only peer-reviewed article reports better patient reported outcome (PRO) using no restrictions in combination with enhanced physiotherapy.[31] In that study, only patients with hip resurfacing implants were included; thus applying the results to standard THR might be inappropriate.[31] The positive findings they report could be caused by enhanced physiotherapy interventions as well as unrestricted movements, and their sample size is too small to reach any conclusion regarding dislocations risk. The study by Skettrup *et al.*[51] is not powered to conclude concerning risk of dislocations, they find neither benefit nor harm of unrestricted rehabilitation on patient-reported outcomes and functional performance. Gromov *et al.*[52] reports comparable hip dislocation rates with and without movement restrictions (3.4% versus 3.1%) in a retrospective trial on a larger sample. But, these conference abstracts should be interpreted with caution in light of their unpublished status. Thus, the possible benefits or harm of unrestricted rehabilitation after THR using the posterior surgical approach remains unknown.

Table 2: Studies regarding rehabilitation with or without movement restrictions after THR using the anterolateral or posterior surgical approach

Study	Design / *n*	Intervention	Follow-up	Dislocations	Conclusions
Posterior surgical approach					
Barker, 2013[31]	RCT / 80	+/- precautions and enhanced rehab	1 year	0%	Accelerated rehab + no restrictions→↑PRO
Gromov, 2013[52] (conf.abstract)	Retrospective / 985 + 685	+/- precautions	3 months	3.4%/ 3.1%	No restrictions→ →dislocation rate
Skettrup, 2011[51] (conf abstract)	RCT / 80	+/- restrictions	3 months	0%	No restrictions → →dislocations →function
Anterolateral surgical approach					
Restrepo, 2011[49]	Cohort /2.532	- restrictions	6 months	0.15%	Low dislocation rate with no restrictions
Ververelli, 2009[46]	RCT / 81	+/- restrictions	1 year	0%	No restrictions → →dislocations + earlier ambulation
Peak, 2005[47]	RCT / 265	↑/↓ restrictions	6 months	0.66%/ 0%	Less restrictions→ →dislocations ↑satisfaction + earlier return to work
Talbot, 2002[50]	Cohort / 499	- restrictions	6 weeks	0.6%	Low dislocation rate with no restrictions

PRO: Patient reported outcome, → comparable, ↑ many/increase, ↓few/decrease

3.4.2 Exercise therapy after THR

One of the first studies to investigate the effect of exercises after THR was Sashika *et al* in 1996.[53] In a non-randomised controlled study initiated ½-2 years after THR, they found a 6 week home-based exercise program with strengthening exercises effective in improving hip abduction strength compared to a control group with no prescribed exercises. Since then, numerous studies have been published on the subject postoperative exercise in relation to THR. In Table 3, randomised controlled trials investigating efficacy of postoperative exercises on muscle strength, functional performance and/or PRO are listed.

Table 3: Randomised controlled trials concerning exercise interventions after discharge following total hip replacement

Study	*n* (THR)	Comparison†	Training initiation	Training dosage	Intervention focus	Blinding / Follow-up	Effect on primary outcome
Monticone, 2014[54]	100	Supervised functional exe + weight bearing vs ROM exe	4-7 days post THR	90 min x 5/week for 3 weeks	Function, balance, ↓use of walking aids	Yes/ 1 year	↑PRO
Heiberg, 2012[55]	68	+/- Supervised group-based functional exe	3 months post THR	70 min x 2/week for 6 weeks	Neuromuscular functional exe	Yes/ 1 year	↑Walking distance
Liebs, 2012[56]	465 (280)	Supervised early vs late aquatic exe	6 days vs 14 days post THR	30 min x 3/week until 5 week post THR	Proprioception, coordination, strength*	Unspe-cified / 2 year	→PRO
Mikkelsen, 2012 (pilot study)[30]	44	Home-based rubber band vs no resistance exe	1 day post THR	Daily for 12 weeks	Strength*, function	Yes / 12 week	→Walking speed
Aprile, 2011 (pilot study)[57]	27 (15 THR)	Supervised group-based vs individual	3 weeks post THR	1-2 h daily for 15 days	Proprioception, strength*, flexibility	Yes /15 days	→PRO
Liebs, 2010[58]	362 (203)	+/- Stationary bike during rehab	2 weeks post THR	3 times/week ≥ 3 weeks.	Stationary bike at low intensity	Unspe-cified / 2 year	↑PRO
Giaquinto, 2010[59]	64	Hydrotherapy vs land-based exe	<10 days post THR	40 min x 6/week for 3 weeks	Gait in water (unspecified)	Yes /6 months	↑ PRO
Husby, 2010[60] **+ Husby, 2009**[61]	24	+/- Strength training	1 week post THR	1 hour x 5/week for 5 weeks	Strength training at 5 RM	Unspe-cified /1 year	5 week: ↑Mm strength. 1 year:→Mm strength →PRO
Stockton, 2009[62]	57	2 vs 1 daily physiotherapy session	1 day post THR	Daily for ~ 8 days	Mobilisation + transfer	Partly /6 days	↑ADL independency at day 3 not day 6
Rahmann, 2009[63]	65 (27)	Supervised aquatic vs land-based exe	4 days post THR	Daily for 14 days	Function and strength*	Yes / 14 days	↑Mm strength → function

Abbreviations: Exe: exercise, vs: versus, ROM: Range of motion, PRO: Patient reported outcomes, ADL: Activities of daily living, RM: Repetition Maximum, Mm: muscle, † Intervention group mentioned first, *No information on training load, → comparable, ↑ increase, ↓decrease

Table 3 (continued) Randomised controlled trials concerning exercise interventions after discharge following total hip replacement

Study	n	Comparison†	Training initiation	Training dosage	Intervention focus	Blinding/ Follow- up	Effect on primary outcome
Suetta, 2008[64] **+ Suetta 2004 a+b**[65, 66]	30	Strength training vs electrical mm stimulation vs home-based exe	~1 week post THR	Strength training 3 days/week for 12 weeks	Quadriceps muscle strength at 20 to 8 RM	Yes /12 week	↑Mm strength, ↑Mm size ↓hospitalisation, ↑→function
Gremeaux, 2008[67]	29	+/- electric mm stimulation	< 2 weeks post THR	1 hour x 5/week for 5 weeks	Electrical stimulation quadriceps + calf mm	Unspecified /45 days	↑Mm strength
Smith, 2009[68]	60	+/- bed exe	1 day post THR	Daily for 6 weeks	ROM + static muscle exe	Yes /1 year	6 week + 1 year: →ADL independency, →PRO
Galea, 2008[69]		Supervised vs home-based exe	1 day post THR	Daily + in centre 45 min x 2/week for 8 weeks	Functional tasks + individual progression	Unspecified /8 week	→PRO, →function
Unlu, 2007[70]	26	Supervised vs home-based exe vs walking	1-2 years post THR	2 times/days for 6 weeks	ROM + low intensity strength (10-30% of max) vs only walk	Yes /6 weeks	↑Mm strength
Trudelle-Jackson, 2004[71]	28	Home-based strength + stability vs ROM + isometric exe	4-12 months post THR	3-4 times/week for 8 weeks	Weight bearing + strength* + stability	Yes /8 week	↑PRO ↑Mm strength
Jan, 2004[72]	53	Home-based exe vs no intervention	>1.5 years post THR	Daily exe + 30 min walk for 12 week	ROM + hip strength* + walk	No /12 week	→Mm strength (↑ in per-protocol analysis)
Hesse, 2003[73]	80	+/- Treadmill training	~ 3 weeks post THR	45 min/day for 10 days	Treadmill walking	Yes /1 year	↑ Harris hip score (>60% drop out at 1 year)
Jesudason, 2002[74]	42	+/- bed exe	1 day post THR	2-3 times/day for 7 days	ROM	Yes /7 days	→ADL independency

Abbreviations: Exe: exercise, vs: versus, ROM: Range of motion, PRO: Patient reported outcomes, ADL: Activities of daily living, RM: Repetition Maximum, Mm: muscle, † Intervention group mentioned first, *No information on training load, → comparable, ↑ increase, ↓decrease

In Table 3, 22 papers are briefly described representing 19 studies. In general the existing exercise intervention studies clearly indicate beneficial effects of training after THR. However, there are several shortcomings to the design, scientific methodology, sample size and intervention descriptions in a number of the studies.

Several studies have investigated the effect of additional training interventions or intensifying traditional interventions.[30, 54, 55, 58, 60-62, 64-68, 71-74] The majority of these report superior effect of more training/higher intensity on perceived function, muscle strength or functional performance.[54, 55, 58, 60-62, 64-67, 71, 73] However, adding low intensity bed exercises in the early rehabilitation did not provide additional effects.[68, 74] Two studies did not prove additional effects of intensifying or adding exercises to existing rehabilitation.[30, 72] The study by Mikkelsen *et al* is a pilot study[30] and the study by Jan *et al*[72] reported low compliance and did find effect of the intervention in a per-protocol analysis. Especially interventions aiming at increasing muscle strength seems appropriate since muscle strength is markedly reduced early after surgery, and persisting deficits have been documented as described in section 3.3.2. Often strengthening exercises are reported with no information on training load, as marked with * in Table 3. Likewise, information on progression and dose are often lacking as well as the description of the regime in the control groups.

Some studies in Table 3 compare different settings, timing or delivery type of exercises.[56, 57, 59, 63, 69, 70] There seems to be no differences when comparing outpatient to home-based exercise[69, 70] or group-based to individual exercise[57] or early initiation (day 6) to late initiation (day 14) of exercise.[56] However, two studies indicate water-based exercises to be superior to land-based exercise.[59, 63]

The timing of the training interventions in the studies vary between immediate start-up after surgery to initiation of training interventions years after THR (Table 3). Bandholm & Kehlet suggest that exercise therapy after fast-track THR should be initiated early after surgery, before the most pronounced decline in muscle strength and function appears.[75] Nonetheless, it seems reasonable to conclude that intensifying exercises and/or adding exercises in the rehabilitation after THR have a beneficial effect on perceived function, muscle strength or functional performance.
However, it remains unknown weather this applies after fast-track THR as well, since none of the studies specifically reports the participants to be treated in a fast-track setup. Thus, several studies are conducted in post-discharge rehabilitation units and do not report length of stay in hospital and others report hospitalisation periods up to 10-16 days.[66]

3.4.3 Progressive resistance training

The principle of progressive resistance training (PRT) is to continually increase load in the resistance exercises, thereby inducing increased stress to the muscles that respond by increasing the ability to produce strength.[76] In order to assess and describe the relative load during PRT, the term repetition maximum (RM) is used. RM describes the maximum possible repetitions at a given load, for example 10 RM describes the heaviest load possible for 10 consecutive exercise repetitions. It is recommended to use high loads (>70% of 1 RM, corresponding to 12 RM) during resistance training in musculoskeletal rehabilitation.[77]

In healthy older adults the effect of PRT in increasing muscle strength, power and functional performance is well documented.[81, 82] In recent years, PRT has frequently been applied in musculoskeletal rehabilitation, e.g. after orthopaedic surgery.[77] A recent systematic review concludes that PRT is safe and effective in increasing muscle strength, reducing pain and improving functional performance in musculoskeletal rehabilitation, specifically after THR.[77]

The conclusions drawn in the previous section (3.4.2) are supported by a newly published systematic review on PRT before and after total hip and knee replacement.[78] They report a weak-to-moderate evidence of a beneficial effect of pre- and postoperative progressive resistance training interventions on muscle strength and functional capacity in THR patients.[78] This conclusion is based on one study (two papers) investigating a peri-operative intervention with exercise before and after THR.[79, 80] and the two studies on postoperative PRT included in Table 3[60, 61, 64-66] Details regarding these two studies are reported in Table 4.

Table 4: Randomised controlled studies on postoperative progressive resistance training after total hip replacement

Study details	**Suetta**[64-66]	**Husby**[60, 61]
n (PRT group)	30 (11)	24 (12)
Training initiation post THR	When possible Median 7 days	1 week
Warm-up	10 min stationary bike	10 min stationary bike
Exercise	Leg pres Knee extension	Leg pres Hip abduction
Sets and repetitions	Week 1-6: 3-5 sets of 10 rep Week 6-12: 3-5 sets of 8 rep	4 sets of 5 rep
Intensity	Week 1: 20 RM Week 2-4: 15 RM Week 5-6: 12 RM Week 6-12: 8 RM	Week 1-4: 5 RM
Frequency	3 days/week	5 days/week
Duration	12 weeks	4 weeks
Results after intervention period (PRT versus control)		
Muscle strength	↑ isokinetic quad. strength (60 °+ 180°/seconds) ↑ isometric quad. strength ↑RFD	↑ 1RM in leg press + hip abduction, →peak force, ↑RFD
Muscle size	↑ cross-sectional area (muscle + muscle fiber)	Not measured
Performance tests	↑ Sit-to-stand test, →stair test, →walk speed, ↑Stair walking power	→ gait parameters (step length, stance time) ↑work efficiency →max oxygen consumption
PRO	Not measured	→SF-36 →hip function score

PRT: Progressive resistance training, rep: repetitions, Quad: Quadriceps, RM: Repetition Maximum, PRO: patient reported outcome, SF-36: Short form-36 (generic health status questionnaire), RFD: rate of force development, → comparable, ↑ increase, ↓decrease

The literature reveals that PRT can be initiated early after THR on quadriceps and hip abduction muscles and is more effective in improving muscle strength and muscle size compared to less intensive training interventions (Table 4). Concerning functional performance and PRO the results are more divergent. Due to the small sample sizes, few exercises included and inconclusive results concerning patient-reported and functional outcomes, these promising results need to be confirmed in larger studies and on additional muscle groups around the hip. As earlier mentioned also the implementation of fast-track treatment programmes makes it relevant to further investigate the efficacy of PRT after THR.

4. Objectives and hypothesis

The overall objective of this thesis was to investigate whether improvement in rehabilitation after fast-track THR can be achieved through reduced movement restrictions and less use of assistive devices and the application of supervised PRT in addition to home-based exercise. The specific objectives and hypotheses for each study are covered below.

Study I

Objective: To evaluate the influence of assistive devices and movement restrictions during early rehabilitation after fast track total hip replacement on 1) Patient-reported function, pain and quality of life, 2) Functional capacity evaluated by physiotherapists and 3) Patient-focused variables: anxiety/depression, return to work and patient satisfaction.

Hypothesis: Reduction of movement restrictions and use of assistive devices result in superior outcomes on 1), 2) and 3) during the first 6 weeks after THR.

Study II

Objective: To assess the inter-rater reliability of a proposed test battery that included four lower-extremity performance tests, two isometric muscle strength tests and one test of leg extension power in THR patients 3 months after surgery. Furthermore, the aim was to determine which is the more reliable of two commonly used sit-to-stand tests in THR patients: five repetitions sit-to-stand or 30-second sit-to-stand.

Hypothesis: The test battery shows acceptable absolute and relative reliability with intraclass correlation coefficients (ICC) above 0.80 and standard error of measurements (SEM) above 10% of the mean of the two test sessions.

Study III

Objective: To examine whether two weekly sessions of supervised progressive resistance training (PRT) in combination with five weekly sessions of unsupervised home-based exercise is more effective than seven weekly sessions of unsupervised home-based exercise in improving leg-extension power of the operated leg 10 weeks after total hip replacement (THR) in patients with perceived functional limitations.

Hypothesis: The PRT intervention results in larger improvement in leg extension power as well as in the secondary outcomes compared to the unsupervised home-based exercise.

5. Methodological considerations

5.1 Ethical issues

All the studies were conducted in accordance with the Declaration of Helsinki II, and the Danish Data Protection Agency approved the studies (Journal numbers: Study I: 2007-58-0010, studies II and III: 2010-41-4907). The Central Denmark Region Committee on Biomedical Research Ethics reviewed Study I as non-notifiable (Inquiry 41/2011) and accepted initiation of the study. The same committee approved Study II and Study III in a combined application (M-20090231). The randomised controlled trial (RCT) (Study III) was pre-registered at ClinicalTrials.gov (NCT01214954).

In Study I, all patients undergoing total hip replacement surgery in the inclusion period were asked to fill out questionnaires as part of the quality assessment in the department. Since no informed consent was obtained directly in relation to this study, the Danish Health and Medicines Authority permitted access to the patients' medical journals (3-3013-196/1/). In Study II, patients were contacted before their scheduled 3-month postoperative outpatient visit at the hospital. They were given written and verbal information, and if they were willing to participate in the study, the tests were performed on the day of their hospital visit. In Study III, eligible patients were informed about the study during preoperative ambulant visit at the hospital, and a minimum of 2 days of consideration time was offered. Written informed consent was obtained in studies II and III.

In Study I, we found it necessary to pre-define a stopping guideline, since the safety-issues of removing movement restrictions with regard to hip dislocation were unknown. It was decided that occurrence of five hip dislocations among the first 100 patients without movement restrictions, and subsequently a dislocation rate of $\geq 5\%$ should result in a change of the procedure.

5.2 Design of studies

The choice of study design for the three studies is described below.

In Study I, we used a non-randomised controlled design with 6-week follow-up. The study compared patients before and after implementation of a less restricted rehabilitation regimen. This comparative before-after design was chosen instead of parallel group design to avoid potential contamination of the intervention in the two groups. When hospitalised in the same department, patients will inevitably gain

knowledge of the movement restrictions in the other group, and this could affect their compliance to group assignment. Furthermore, willingness to participate in a RCT might be low due to safety issues, i.e. that patients fear dislocation, as in the study by Peak *et al.* where 42% of the eligible patients refused to participate.[47] The relatively short follow-up time was chosen to augment participation and because it reflects the time-frame of the movement restrictions. The enrolment period for the study was pre-defined. The restricted group was enrolled consecutively from 3 May to 19 August 2011, hereafter the rehabilitation regimen was changed, and the unrestricted group was consecutively enrolled from 25 August to 30 November 2011. During the change of procedures, a pre-defined intermediate sample of 20 patients was excluded from the study (20 to 25 August 2011).

In Study II, we tested inter-rater reliability in an intra-day test-retest design. Inter-rater test was chosen instead of intra-rater since we anticipated that more than one rater would be required in Study III. Test-retest on the same day was chosen to eliminate the day-to-day variation. Consequently, fatigue could introduce a bias, and therefore we divided the test battery into two sections applied on two samples as an attempt to minimise this problem.

Study III was a single-blinded RCT with 6-months follow-up. We chose the RCT design since it is considered the optimal design when evaluating effects of an intervention.[84] Block randomisation was performed to ensure a continuous flow into the PRT group. Alternate block sizes of 4-6 patients were used to avoid the option of predicting the group assignment at any time. Stratification for contralateral THR was performed to ensure an equal distribution between the groups. Sequence in permuted blocks with equal numbers of "intervention" and "control" assignments was obtained using a simple "shuffling envelope" procedure before study initiation by a secretary not otherwise involved in the study. Blinding of patients, assessors and the physiotherapists supervising in PRT would be optimal, but this is not possible with this type of intervention. We blinded the outcome assessors throughout the study and the patient and in-hospital staff during hospital admission. We chose 10-week follow-up at the primary measurement time as it reflects the immediate effect of the intervention, but a 6-month follow-up was added in order to investigate the persistence of a potential effect. Furthermore, 1-year follow-up by mailed questionnaire measured the long-term PRO.

5.3 Patients

Participants in all three studies were recruited from Elective Surgery Centre at Silkeborg Regional Hospital in the period September 2010 to November 2012. All patients followed a multimodal fast-track surgical program for THR including

patient information, spinal anaesthesia, optimised multimodal pain management, enforced mobilisation and nutrition. Patients were invited to an information day prior to surgery where they were thoroughly informed about the expected course of their operation and rehabilitation and encouraged to take active part in the treatment and rehabilitation. On the day of surgery patients were admitted to the hospital, and the surgery was performed using the posterior approach.[85] The Moore incision was used to expose the hip joint; only standard incisions were used (no minimal incisions). Primarily, cementless prostheses were used with femoral head sizes ranging from 28 to 44 mm, with the majority being 36-40 mm (shown in Paper I). Patients were subsequently discharged to their homes when they met pre-defined functional discharge criteria: independency in gait, transfer, personal care and home-based exercise as well as sufficient pain treatment and no exceptional wound oozing. The length of hospital stay was typically 1 to 2 postoperative days.

The uniform inclusion criteria used in all three studies included primary unilateral THR for hip OA and age > 18 years. Uniform exclusion criteria were resurfacing hip implant and inability to speak or read Danish.

In addition to this, some study-specific in- and exclusion criteria were used in studies II and III as described below.

Study II: Additional inclusion criteria: 55 to 80 years of age. Additional exclusion criteria: neurological diseases, cognitive problems/dementia or major postoperative complications (e.g. infection, fracture or hip dislocation). The last being possible because patients were included 3 months after surgery. We excluded patients with specific comorbidities because this was assumed to affect the reliability due to fatigue or not understanding the instructions.

Study III: Additional inclusion criteria: preoperative HOOS activities of daily living (ADL) subscale score ≤ 67, residence within 30 km from the hospital, motivated for training twice a week for 10 weeks and absence of mental or physical conditions that would impede the intervention. Additional exclusion criteria: body mass index (BMI) >35, pre-planned supervised postoperative rehabilitation and pre-planned contralateral THR within 6 months. The geographical criterion was to decrease the need for transportation to the bi-weekly training sessions. We excluded the patients with very high BMI, because it was estimated that it would be problematic for them to use the training machines.

Due to the longevity of patient inclusion into the RCT, we chose to accept an overlap between the inclusion period in studies I and III. This was possible due to the non-

randomised design of Study I. Study I was carried out as part of the quality assessment in the department, and thereby the questionnaires were administered as standard practice for all patients undergoing THR in the inclusion period. Thus, the patients gave no informed consent to participate.

5.4 Intervention

In the following section, the interventions used in the studies are described. The rationale behind the intervention is described when considered relevant for understanding the study.

5.4.1 Study I

Patients in the restricted group (RG) underwent the traditional rehabilitation in the department including restrictions of hip movement (maximum 90° of flexion, no adduction beyond neutral position and no internal rotation) during the first 6 weeks postoperatively. To obey to these restrictions patients were provided with the following standard package of assistive devices: elevated toilet seat, shoe horn, bath bench, ergonomic reacher, sock aid and wedge pillow. The unrestricted group (UG) had no movement restrictions apart from avoiding the combination of full hip flexion, internal rotation and adduction. To illustrate this for the patients, they were advised to bend between their knees when flexing the hip, e.g. to put on shoes. In the UG, assistive devices were only distributed when needed for the patient to perform activities of daily living (ADL), e.g. if a patient could not rise from a normal toilet, an elevated toilet was lent to them. Walking devices, generally crutches, were administered to all patients in both groups, as these were not considered a device to ensure adherence to movement restrictions but solely to support the walking ability. Information on the rehabilitation regimen was provided at the information day prior to surgery and in a patient brochure concerning several aspects of the surgery, hospitalisation and rehabilitation. The contents of the information day and brochure were similar for all groups, except regarding issues concerning movement restrictions and assistive devices.

Rationale for the unrestricted regimen

As described in section 3.4.1, there is some evidence to support unrestricted rehabilitation after THR using the anterolateral surgical approach. These results cannot be directly transferred to THR patients operated via the posterior approach, but it indicates that there might be a window for improving recovery. Clinical experience and a pilot study at our department imply that movement restrictions are an issue of concern for the patients. The unrestricted regimen was developed by an interdisciplinary team with representatives from the following professions: orthopaedic surgeon, physiotherapist, nurse and occupational therapist. Handling of

the safety-issues arising with the unrestricted rehabilitation is described in the ethic section 5.1.

5.4.2 Study II

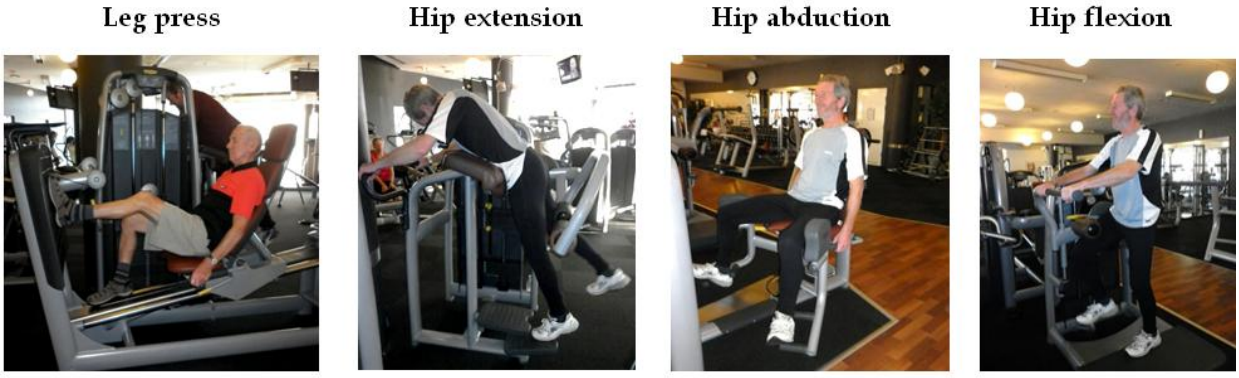
All patients were tested twice on the same day by two physiotherapists (rater A and B) with a 2-hour break between the tests. The test battery was divided into two for this reliability study to reduce the impact of fatigue due to performance of all tests twice on the same day. Thus, we performed the reliability study on two patient samples. The physiotherapists underwent training and pilot testing of the standardised test procedures before the study was initiated. Sealed envelopes were used for randomisation to rater A or rater B (1:1) as the first tester for each patient. During the second test, the rater was blinded to the results of the previous test. Sample 1 performed test-retest of each of the following tests: five repetitions sit-to-stand, 30 second sit-to-stand, stair-climb test and isometric strength test in hip abduction and flexion. Sample 2 performed the leg extension power test and a 20 meter walk test.

5.4.3 Study III

Progressive resistance training

In the intervention group (IG) patients performed biweekly sessions of supervised progressive resistance training (PRT) in combination with unsupervised home-based exercise the remaining 5 days, using the exercise program as described for the control group (CG). The PRT was initiated within the first week after surgery and performed until 10 weeks after surgery in a public fitness centre with one-to-one supervision by a physiotherapist from the department. Patients warmed up on a stationary bike for 5-10 minutes and then performed unilateral PRT of the operated leg for 30-40 minutes. The resistance exercises are illustrated in Figure 3 and consisted of hip extension, leg press (replaced by knee extension the first 5 weeks), hip flexion and hip abduction in strength training machines. The relative load was increased from 10-12 repetition maximum (RM) at commencement to 8 RM during the intervention period. The absolute training load (kilograms lifted) was adjusted on a set-by-set basis for all exercises, using contraction to failure in every set. For further details on PRT, see Paper III. The PRT was combined with 10 minutes of simple functional task exercises from week 4, consisting of walking, chair rising, one-legged stance and stair performance. In the functional task exercises the focus was on quality and symmetry in the executions of the function.

Figure 3. The exercises used in the progressive resistance training



Rationale for PRT

In section 3.4.2 the principles of PRT and the literature concerning PRT early after THR are described. However, strength deficits have been reported for muscle groups beyond those targeted in these studies, e.g. hip flexor and extensor muscles[18-20, 27, 86] and therefore PRT should likely target these muscle groups as well to enhance recovery after THR. Hence, in Study III we included PRT exercises of all the major muscle groups surrounding the hip joint. The frequency and duration were established by balancing between feasibility and effect. However, we considered it important to limit the frequency and duration of the intervention in order to foster willingness to participate as well as compliance to the intervention, especially for those with difficulties in relation to transportation and those returning to work. We chose a relatively high intensity (> 70% of 1 RM) since it is superior to lower intensities in increasing muscle strength in older adults[82] and during musculoskeletal rehabilitation.[77] Power training (high-velocity exercises) appears to result in superior functional gains compared to PRT in the elderly; findings, however are inconsistent.[82] We chose PRT at low velocities instead of power training in order to use an intervention that was comparable with the previous studies on the subject and to use the most evidence-based approach to gaining strength. It is unknown whether power training is feasible and safe early after THR. The PRT programme is further described in Paper III according to strength training descriptors as suggested by Toigo and Boutoiller.[87] The functional task exercises were included in an attempt to optimise the transferability of strength gains into functional performance.

Home-based exercise program

In the CG, patients performed daily sessions of unsupervised home-based exercise. The exercise programme consisted of unloaded exercises in the movement directions: hip flexion, extension, abduction and knee flexion/extension. Patients were recommended to perform one set of 10 repetitions of the exercises twice a day in their maximum possible range of motion. At the outpatient visit 4 weeks after surgery, the

physiotherapist asked the patients to perform the exercises with a sports rubber band to increase the relative load in the movement directions described above. Furthermore, exercises were individually adjusted if needed, for example, if a flexion contracture was identified, muscle stretching was prescribed.

Rationale for home-based exercise program

The intervention in the CG reflects the standard practice at our institution. We have previously investigated the effect of intensifying these unsupervised exercises from the first postoperative day, e.g. by using rubber band resistance.[30] In that study we found no additional effect but a higher patient satisfaction when intensifying the program. Thus in the present study, and as our standard practice, we use a pragmatic approach in which we do intensify the unloaded exercises, but only after the outpatient visit 4 weeks after surgery.

5.5 Outcomes

In this section, the chosen outcomes in the studies are shortly covered; the outcomes are described in more detail in the papers. The rationale for the choice of outcomes is evaluated when considered relevant.

5.5.1. Baseline variables

In all three studies the following baseline variables were collected: age, gender and body mass index (BMI). In Study II, only a few baseline variables were considered relevant to report. In Study I and Study III this was supplemented with the American Society of Anesthesiologists (ASA) classification (physical status classification), length of stay in hospital, status of the contralateral hip, prosthesis type. Finally, in Study I some further baseline variables were included due to the non-randomised design and the nature of the intervention: marital status, educational level, working status and femoral head size of the prosthesis.

5.5.2 Study I

In Study I, we collected data as part of the standard care for all patients undergoing THR surgery, thus it had to be outcome measures reasonable and acceptable in light of the patients not having consented to participation. The measurement times were preoperative, 3 and 6 weeks after surgery. The preoperative questionnaires were handed out to patients when they were assigned to the operation and returned prior to surgery. At 3-week follow-up, data were collected in connection with patients attending an outpatient visit at the hospital and 6 week follow-up data were conducted by mail. The primary outcome was perceived limitations in ADL measured by the ADL subscale of the hip dysfunction and osteoarthritis outcome score questionnaire (HOOS 2.0).[88] This was chosen as the primary outcome since we

wanted to measure the perceived function and thereby whether the patients' perception of functional constraints was affected by movement restrictions and use of assistive devices. Secondary outcomes included the remaining subscales of HOOS (except from function in sport and recreation which was considered irrelevant at this early stage after THR), and the Hospital Anxiety and Depression Scale (HADS). The HADS questionnaire was included to elucidate whether the different regimens had different effects on anxiety or depression. It was hypothesised that the unrestricted regimen might lead to less distress due to less worrying about hip dislocation and about violating the restrictions. As a simple measure of early functional capacity, an ADL evaluation (ability to perform stair climbing, getting dressed, bath/shower and house cleaning) was performed by physiotherapists 3 weeks after surgery. This approach was chosen in an attempt to include a more objective measure of what the patients could actually do (different aspects of functioning is explained in Table 1). The dislocation rate within the first 6 weeks was followed closely throughout the study, and return to work and patient satisfaction was measured by questionnaire at 6-week follow-up. For further description of the measurements, see Paper I.

5.5.3 Study II

Study II investigated the inter-rater reliability of the physical tests we planned on using in the effect study (III). For a specific description of how the tests were executed, see Paper II. The measurement time was 3 months after THR in connection with an outpatient visit at the hospital.

Leg extension power and hip muscle strength

During the test of muscle strength and power, we used a sound file with a verbal command to avoid the voice and accentuation of the rater to affect the test performance. This was chosen as a preventive measure to counteract the influence of using more than one rater.

Leg extension power was used as a proxy measure of functional performance. Leg extension power is highly correlated with functional performance and the risk of falling,[89-92] and it has been used in hip OA patients[93] and after total hip replacement.[94] The Nottingham Power Rig (University of Nottingham Mechanical Engineering Unit, UK) was used to measure leg extension power, which was expressed as the product of force and velocity in a single-leg simultaneous hip and knee extension. The power was recorded for several pushes until a plateau was reached. A minimum of six trials to minimise learning effect, and a maximum of 12 trials to minimise fatigue were obtained, and the highest measurement in Watts (W) was used. In Figure 4 the test setup is illustrated.

Figure 4. Test of leg extension power

Isometric hip muscle strength was tested with a hand-held dynamometer Power Track II Commander (JTECH Medical, Salt Lake City, UT, USA). Measuring muscle strength in hip abduction and flexion was chosen because previous studies have shown large deficits in these muscles groups,[18, 19] and they were directly trained in the PRT exercises in the intervention group in Study III. It could have been relevant to measure hip extension strength as well, but we did not manage to establish a suitable position for this test in THR patients where ROM in hip extension often are limited. Hand-held dynamometer testing of lower extremity muscle strength is suggested as a valid measurement for evaluating orthopaedic patients,[95] and it is applied in OA patients[96] and after total joint replacement surgery.[30, 89] We used standardised test procedures as described by Thorborg *et al*.[97] The test was repeated until a plateau was reached, with a minimum of four tests to minimise the learning effect and a maximum of 10 to minimise fatigue. Hip abduction was measured in a supine position and hip flexion in a sitting position.[97] In Figure 5, the test setup for isometric strength testing is illustrated.

Figure 5. Test of isometric muscle strength using hand-held dynamometer in hip abduction (left) and hip flexion (right)

Functional performance test

In all the functional performance tests, the better of two trials was used. The patients performed the tests without walking aid if it was possible and safe, and if a walking aid was considered necessary, the patients used the device they would normally use.

Walking ability is considered by the patients to be the most important functional skill to improve when undergoing THR, hence it is essential to include a measure of walking ability when evaluating functional outcome after THR.[98] Maximum walking speed over a short distance was chosen, because it is associated with independency in ADL[99, 100] and considered a highly relevant task in order to participate in activities outside the home, e.g. navigate in traffic. The 20-meter walking test was used as it is a part of the Osteoarthritis Initiative[101] and is used in recent studies on patients with hip and knee OA.[94, 102] Patients walked as fast as possible on a 20-meter lane that included the acceleration phase (standing start) but not deceleration (walking past end line). When measuring maximum walking speed over short distances, the 10-meter walk test is often used. We decided not to use this test because previous results on the same patient group have shown that the patients obtain fast walking speeds so rapidly that the accuracy of the test could be affected by the short time frame, and a longer walking test is suggested.[30] This is in line with newly published recommendations for functional testing of patients with hip or knee OA, where 40 meter walk test is recommended.[103] In this recommendation it is emphasised that maximum walking speed should be used instead of a self-selected pace.[103] It is relevant to include a measure of gait quality, as better muscle function might positively affect the gait pattern. We did measure asymmetry during walking speed and stair testing in a subgroup of the patients in Study III using inertia measurement

unit. However, these results will be analysed and published separately and are not included in this thesis.

Chair rise performance is an important functional skill in everyday life, and high performance is associated with independency in ADL.[99, 100] As a measure of chair rise performance, two tests were included in the reliability study (II); the five repetitions sit-to-stand and the 30-second sit-to-stand test. This was to evaluate which of these tests to include in the effect study (III) as the literature at that time was inconclusive. The five repetitions sit-to-stand test was chosen because it is a part of the Osteoarthritis Initiative[101] and often used in patients with hip OA and after total hip replacement.[66, 94, 102] The 30-second sit-to-stand is also widely used to measure chair rise performance in patients with hip OA and after THR,[89, 104-106] furthermore it is recommended to use in functional testing of patients with hip and knee OA.[103]

Stair-climb performance has been suggested and used when measuring functional performance in hip OA patients[107, 108] and after total hip replacement.[6, 66, 109] Furthermore, it is also part of the new recommendations for functional testing of patients with hip and knee OA.[103] There is no standardisation of stair tests concerning, e.g. number of steps, step heights and measurement of ascending, descending or a combination. In the present study, focus was solely on ascending stairs. It was presumed that descending stairs would be affected by balance, coordination and nervousness to a larger extent than ascending. Patients ascended nine steps (16.5 cm high) as fast as possible without using the handrail.

5.5.4 Study III

In Study III, the test described for Study II was used for effect evaluation. The primary outcome was defined as change in leg extension power from preoperative level to 10 weeks after surgery when the intervention period was completed. There are a few deviations in the secondary outcomes between Study II and Study III. The stair climb test was changed to a longer test, 18 steps instead of nine steps, in the RCT (Study III) on the basis of preliminary results found in the reliability study (II). It was speculated that the accuracy of the test could be affected by the short time frame (mean ~4 seconds). The measurement of chair rise performance was performed using a 30-second sit-to-stand test in Study III, based on preliminary findings from Study II, and the possibility to score the weakest patients, even if five repetitions was impossible (the disparity between the two chair rise tests is further described in Paper II). The choice of 30-second sit-to-stand test was validated by the recommendations for functional testing on patients with hip and knee OA published after commencement of this study.[103]

When measuring strength gains after PRT, a simple approach is to use 1RM testing of the trained exercises, as done by Husby *et al*.[60, 61] We did not use this approach, as we wanted our effect measurement to vary from the trained exercise in order to minimise the influence of improved technique attained through the exercises. By measuring leg extension power and isometric hip muscle strength, we measured whether strength gains achieved during slow, dynamic muscle contractions are transferred to these other types of muscle function.

The PRO questionnaire HOOS was used repeatedly to evaluate differences between the groups during early recovery while the intervention was on-going. Furthermore, HOOS was administered by mail 1 year after surgery as an extended follow-up beyond the period of the follow-up visits at the hospital. The HOOS questionnaire is described in section 5.5.1 and in Paper I and III. In the earliest measurements, the subscale function in sport and recreation was considered irrelevant because of the questions regarding for instance running. The immediate effect of the intervention was measured at 10-week follow-up. Furthermore, early changes and long-term follow-up measurements were conducted when considered feasible and relevant, e.g. the less demanding physical tests were performed early. The outcomes applied at the different measurement times are presented in Table 5.

Table 5. Overview of outcome measures and measurement times in Study III, primary outcome and time frame coloured blue

	Baseline	2 week	4 week	6 week	10 week	6 month	1 year
Physical tests							
Leg extensor power	X				X	X	
Walking speed	X		X		X	X	
Chair rise	X				X	X	
Stair climb	X				X	X	
Isometric hip strength	X		X		X	X	
Patient-reported outcomes							
HOOS	X	X*	X*	X	X	X	X
Training diary (weekly)		X	X	X	X		

Abbreviations: HOOS: Hip dysfunction and osteoarthritis outcome score questionnaire, *Not including the subscale concerning function in sport and recreation.

Rationale for primary outcome

The leg extension power was chosen as the primary outcome because it serves as a proxy for functional performance. It was chosen over functional testing as it seems possible to standardise the power test to a larger degree, and it is potentially less influenced by habits, experience, anxiety, balance, etc. We chose to focus on functional performance rather than perceived function because PRO measures may fail to capture actual changes in functional performance as measured by functional

performance tests, and it possibly reflects pain level as much as function.[21, 25, 26] However, it is considered essential that the physical testing is supplemented with measurement of perceived function.

Process indicators

In order to evaluate the progression in training load and occurrence of potential side effects consisting of exacerbation of hip pain, we assessed these variables closely during the first 4 weeks of training in the first 20 patients in the IG. The absolute training load was measured in kilograms (kg). For each exercise at each training session, the highest load in a completed set was used as the data point. Hip pain in the operated leg was measured using a 100 mm mechanical visual analogue scale (VAS) with endpoints of 0 mm ("no pain") and 100 mm ("worst imaginable pain"). After the final set of an exercise, the patient scored hip pain corresponding to that experienced during the set. By default, the VAS was set at 0 mm, and the patient placed the marker according to their perceived pain. The corresponding value to the nearest mm-VAS was used at the data point.

Exploratory subgroup analysis

On selected baseline variables the effect of the intervention was further explored in a subgroup analysis on the primary outcome. We selected the variables age, gender, BMI and the preoperative muscle function (measured by leg extension power). These variables were chosen as they are known to influence the outcome after THR[29, 110-112] and/or the response to resistance training.[113-115] When continuous baseline variables were used, the subgroups were defined by the median value.

5.6 Statistics

5.6.1 Sample sizes

In all studies, the significance level was set at 0.05. In Study I, we chose a power of 95%, because of the non-randomised design, we aimed at gaining as much certainty as possible in the results. In Study II and Study III the power was set at 80% as is most commonly used in clinical trials.

In Study I, we used data on perceived function from a Danish study comparing outcome after large-head THR with no movement restrictions to standard THR with standard movement restrictions applied.[116, 117] The mean score 8 weeks after surgery were 12.7 (SD 10.3) versus 17.9 (SD 11.2), and based on expecting the same difference, we needed a sample of 121 patients in each group. The actual sample in Study I was larger than anticipated (n=146 in RG and n=219 in UG), because we had to pre-define the enrolment period and the date for change of procedures.

In the reliability study (II), we defined a conservative level of acceptable intra-class correlation coefficient (ICC) > 0.8. With two raters and a 95% confidence interval (CI) of ± 0.2, a sample size of 13 subjects was required.[118] To decrease the uncertainty of the results and to increase generalisability, we decided to include 20 subjects for each sample.

In the RCT (Study III), the sample size calculation was based on earlier obtained leg extension power data from pilot testing patients 3 months after THR (mean ± SD: 1.78 ± 0.49 Watt/kg). The minimal relevant difference in effect between intervention and control group was defined as 20%, which is suggested in musculoskeletal intervention research,[119] resulting in a required sample size of 60. Based on an expected 10-15% drop out, we aimed at including 70 patients.

5.6.2 Statistical evaluation

In all studies, the significance level was set at 0.05. The statistical analyses were performed using STATA 12.1 (StataCorp, College Station, TX, USA) software package. Data was entered in Excel 2010 (Microsoft Coorporation, Redmond, WA, USA) or EpiData 3.1 (Epidata association, Odense, Denmark), depending on the complexity of data. In Study III, data were double entered and validated in EpiData, and in Study I, double entry was performed on a random subsample of 100 patients, showing low error rate (0.3%). The reliability data were entered and validated in Excel.

Normal distribution was determined using probability plots and histograms. Normally distributed data were described by means and standard deviation (SD), and data not normally distributed by medians and range or interquartile range (IQR). Simple comparison of normally distributed data between or within groups was performed using unpaired or paired t-tests, respectively. On data not normally distributed, the groups were compared using the non-parametric Wilcoxon rank-sum test. When analysing changes over more than two measurement times, the groups were compared using multivariate repeated measurement analysis of variance (MANOVA), with group and time as factors. The assumption of homogeneity in standard deviations and correlations was tested, and an approximate test allowing for heterogeneity was used when appropriate. For model validation, histograms and probability plots of the differences between measurement times in each group were inspected and approved.

Study I

The primary analysis was a comparison between the groups regarding change in HOOS function score over time (MANOVA). The remaining subscales from HOOS

were analysed identically. The functional capacity evaluation, return to work and patient satisfaction were compared using chi^2 test or Fisher's exact test. The hip dislocation rates were compared between the groups using Fisher's exact test due to the very low number of events. The baseline variables were analysed according to the type of data: dichotome or grouped variables with chi^2 test, normally distributed variables with unpaired t-test.

Study II

Differences in test results between the two raters were analysed with a paired t-test. In accordance with published guidelines for reporting reliability and agreement studies, reliability was investigated in terms of test–retest reliability and measurement error.[120] The agreement between the tests was examined by Bland Altman plots.[120] Identification of the mean difference with 95% CI and limits of agreement were included in the plots. The standard error of measurement (SEM), which represents the typical error in a single measurement,[121] was calculated by the equation $SD/\sqrt{2}$. The minimal detectable change defined as the measure of statistically significant change between two measurements,[121] was calculated by the equation $1.96 \times \sqrt{2} \times SEM$. For a statistically significant change between two observations to be detected, the change must be at least the minimal detectable change. SEM and minimal detectable change (MDC) are presented in actual units, but they are also expressed as a percentage of the mean of the two test sessions (grand mean), making comparisons between tests and studies possible.[122] The relative reliability was calculated using the ICC model 2.1. The ICC is a ratio of the variance between subjects over the total variance. The ICC 2.1 is a fixed model addressing both systematic and random error.[123] The ICC is affected by sample variability in the sense that with large variability an excellent ICC can be achieved even with a large measurement error. Thus both absolute and relative reliability are reported. Yet, ICCs are used in most comparisons between tests and between studies because of their wide-spread use and unit-less nature.

Study III

The primary analysis followed the intention-to-treat principle including all randomised participants on the primary outcome: leg extension power. Data were analysed by a mixed model with a random person level and systematic effects of time, group and the interaction between time and group. The remaining group comparisons were conducted as extended per-protocol analyses using non-missing values only (no imputations). Patients who discontinued the intervention were encouraged to participate in the follow-up test anyway, and those who accepted were included in the analyses according to their original group assignment. The groups were compared regarding changes over time on the continuous variables

using MANOVA with group and time as factors. The within-group changes between baseline and 10-week follow-up were tested using a paired t-test.

To investigate changes in absolute training loads and patient-reported disability over time, repeated measures analyses of variance (ANOVAs) with Box's conservative correction for unstructured covariance were used. For changes in hip pain during exercise and at rest, the correspondent non-parametric Friedman's test was used.

6. Results

In the results section, selected parts of the results from each study are presented and combined when considered appropriate.

6.1 Patient characteristics

The uniform baseline characteristics in the studies are presented in Table 6. As described in section 5.5.1, not all baseline variables were considered relevant in the reliability study (II), and additional variables are included in Paper I.

Table 6. Baseline characteristics for participants in Study I, II and III.

	Study I		**Study II**		**Study III**	
	RG	**UG**	**Sample 1**	**Sample 2**	**IG**	**CG**
	(*n*=146)	(*n*=219)	(*n*=20)	(*n*=20)	(*n*=32)	(*n*=30)
Age mean (SD)	69.0 (10)	68.4 (10)	66.2 (8)	68.4 (5)	64.8 (8)	65.1 (10)
BMI (kg/m^2) mean (SD)	27.2 (5)	26.5 (4)	27.8 (4)	28.0 (3)	27.5 (4)	25.4 (4)
Female *n* (%)	68 (47)	106 (48)	9 (45)	9 (45)	14 (44)	12 (40)
Contralateral THR *n* (%)	34 (23)	49 (23)			8 (25)	7 (23)
Cementless prosthesis *n* (%)	125 (86)	190 (87)	Not reported		29 (91)	28 (93)
ASA I *n* (%)	42 (30)	69 (32)			15 (47)	15 (50)
LOS = 1 day post THR *n* (%)	98 (67)	173 (79)			22 (69)	20 (67)

RG: Restricted group, UG: Unrestricted group, IG: Intervention group, CG: Control group BMI: Body Mass Index, THR: Total hip replacement, ASA: American Society of Anesthesiologists physical status classification: ASA I = Healthy patient, LOS: length of stay in hospital.

6.2 Study I

We included 146 THR patients in the RG and 219 in the UG. The response rate varied between groups, variables and measurement times. The response rates in RG and UG were 83-85% and 84-88% at baseline, 71-85% and 91-96% at 3-week follow-up and 87-93% and 85-93% at 6-week follow-up. Patient inclusion and response rates are further described in Paper I.

6.2.1 Primary outcome HOOS

The primary outcome was perceived function measured by the HOOS ADL subscale. The scores at baseline, 3 and 6 weeks after surgery were (mean ± SD); RG: 43±16 – 81±14 – 83±13 compared to UG: 46±17 – 76±9 – 83±14 (p = 0.004). The RG showed the

fastest increase (p=0.004). At 3-week follow-up the percentage of missing values on the HOOS ADL subscale was 29% in the RG versus 9% in the UG. In the remaining HOOS subscales, no significant differences between the groups were present (see Paper I for further description).

6.2.2 Secondary outcomes

In Table 7 the secondary outcomes are presented as dichotome variables; some of the variables are described more comprehensively in Paper I.

Table 7. Secondary dichotomised outcomes of THR patients in the restricted group (RG) and in the unrestricted group (UG)

	RG (n=146)	**UG (n=219)**	**p (Chi²)**
Independent* in ADL 3 weeks post THR			
Stairs	33% (40/122)	51% (103/201)	0.003[F]
Getting dressed	40% (50/124)	72% (148/205)	<0.001
Bath/shower	68% (84/124)	88% (181/205)	<0.001
House cleaning	38% (47/124)	60% (123/205)	0.001
Outcomes at 6 week post THR			
Return to work	32% (12/37)	54% (29/54)	0.045
Hip dislocation	1.4% (2/146)	2.7% (6/219)	0.48
Satisfied/very satisfied with treatment	96% (132/138)	96% (194/202)	0.86

Abbreviations: THR: Total hip replacement, ADL: Activities of daily living. *Independent of both assistive device and help from others, [F] Fisher's exact test

Table 7 reveals that a significantly higher proportion of patients in the UG were independent in the four ADL tasks at the 3-week follow-up compared to the RG. Furthermore, a higher proportion had returned to work at the 6-week follow-up in the UG than in the RG. Hip dislocation rates and patient satisfaction was comparable between the groups.

HADS results

In Table 8, the continuous HADS results are presented in accordance with the data distribution being not normally distributed. The scale goes from 0 to 21, with scores >7 representing above normal level of anxiety/depression. In Paper I, the HADS results were dichotomised for simplicity.

Table 8. Results from Hospital anxiety and depression scale (HADS) in the restricted group (*n*=146) and the unrestricted group (*n*=219), values are median (IQR), (% non-responders)

	Restricted group		**Unrestricted group**		***p* value***
HADS Anxiety					
Baseline	6 (3;10)	(17%)	5 (2;8)	(15%)	0.007
3 week	1 (0;3)	(19%)	1.5 (0;4)	(7%)	0.88
6 week	1 (0;4)	(10%)	1 (0;2)	(15%)	0.30
HADS Depression					
Baseline	3 (1;6)	(18%)	2 (0;4)	(15%)	0.036
3 week	1 (0;2)	(20%)	1 (0;2)	(6%)	0.85
6 week	1 (0;2)	(10%)	0 (0;1)	(16%)	0.13

Scale range: 0-21 (0-7: normal, 8-10: mild, 11-15: moderate, 16-21: severe depression/anxiety) *Wilcoxon rank-sum test of between group difference

The level of anxiety and depression was higher in the RG at baseline compared to the UG. At the follow-up measurements there were no between-group differences.

Assistive devices

The amount of assistive devices handed out by the hospital was reduced by 37-79% after changing to the unrestricted regimen, with the elevated toilet seat as the assistive devices mostly reduced (presented in Paper I).

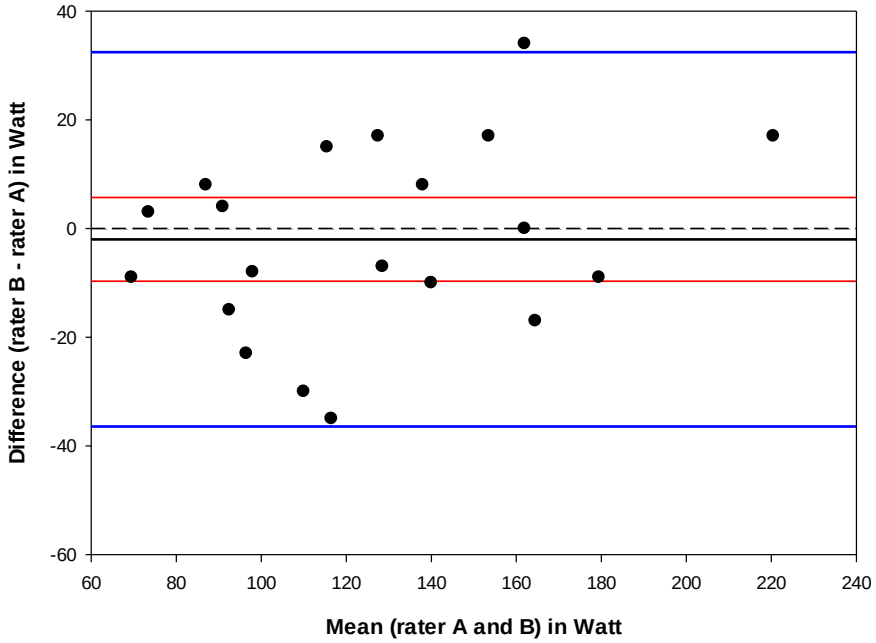
6.3 Study II

We included 40 THR patients in the reliability study and divided them into two samples each consisting of 20 patients.

The difference (bias) between the test results from rater A and rater B concerning the 20-metre walk test was 0.32 seconds (p=0.03) and 0.18 seconds (p=0.003) in the stair-climb test. In the remaining tests, no significant differences occurred, meaning that there were no systematic difference in the results from rater A and rater B.

Bland Altman plot for leg extension power is shown in Figure 6, and plots of the remaining tests are presented in Paper II.

Figure 6. Bland Altman plot on data from leg extension power test.



Mean difference between raters (black line) with 95% CI (red lines) and limits of agreement (blue lines). The dotted black line, Y=0 indicates perfect average agreement.

Bland Altman plots on data from leg extension power and hip abduction showed sign of heteroscedasticity; consequently, the absolute measurement error is larger at higher scores on these measurements.

The SEM in per cent of the grand mean (SEM(%)) ranged from 3% to 10%, indicating the measurement error on a group level. The MDC in per cent of the grand mean (MDC(%)) ranged from 10% to 27%, indicating the measurement error on an individual level. The relative reliability measured by ICC was above 0.80 in all tests, ranging from 0.83 to 0.95. The measurement properties of the specific tests are presented in Paper II. The absolute and relative reliability of the 30-second sit-to-stand compared with five repetitions sit-to-stand was ICC: 0.88 versus 0.84, SEM(%): 7 versus 8, MDC(%): 20 versus 22.

6.4 Study III

In Study III, 73 THR patients were consecutively included and randomised to either IG (n=37) or CG (n=36). After randomisation, two patients in each group withdrew consent, and seven were excluded due to major events such as hip fracture and hip dislocations. None of these events were considered to be associated with the rehabilitation (presented in flowchart in Paper III). The 11 patients that did not complete the study tended to be older: mean age 70.8 (SD 9), weaker: mean leg extension power at baseline: 1.26 W/kg (SD 0.6) and more often female (64%). We

pre-planned to include 70 patients but chose to continue inclusion until 73 participants in order to secure achievement of the estimated sample size of 30 in each group despite the drop outs.

6.4.1 Training compliance and adverse effects

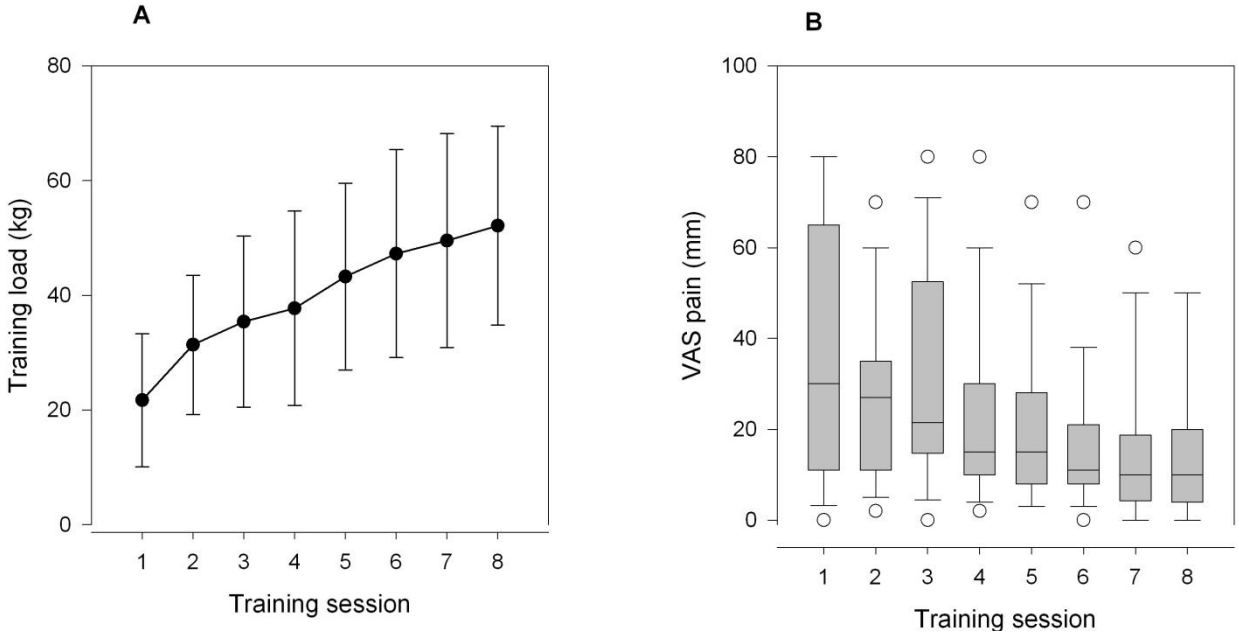
The patients in the IG attended a median of 19 training session (range: 1-22) during the 10-week intervention period. The resistance training was initiated at a median of 5 (range: 4-9) days after surgery. Patients reported that they performed the home-based exercises a median of 5 (range: 0-7) days a week in the IG as prescribed and 6 (range: 0-7) days a week in the CG, where 7 days a week was prescribed.

Five patients experienced adverse effects during or after PRT sessions that were related to hypotension, sequelae after brain tumour, rupture of a haematoma and knee pain. None of these adverse effects resulted in continuing complications; however, two patients discontinued the intervention due to discomfort, but they participated in follow-up visits and are included in the analysis according to their group assignment.

6.4.2 Process indicators: Training load and pain

In Figure 7, the training load and hip pain during hip flexion exercise in the first 4 weeks of training are presented for a subgroup of the IG.

Figure 7. Absolute training load (A) and hip pain (B) during hip flexion exercise at each session during the first 4 weeks of PRT applied on 20 patients after THR. Values are mean ±SD in plot A and median (IQR) in plot B.



Training load increased over time in all the exercises, $p<0.001$ (repeated measures ANOVA), while hip pain during exercise decreased in all the four exercises ($p<0.0001$, Friedman's test).

6.4.3 Physical tests

Change in leg extension power from baseline to 10-week follow-up were mean (95% CI) IG: 0.29 (0.13;0.45) and CG: 0.26 (0.10;0.42) W/kg, with no between-group difference, $p=0.79$ (mixed effect model). These changes correspond to relative improvements of 21% and 17% in the IG and CG groups, respectively. In Table 9, the results on all the physical performance tests at the three main measurement times are presented. The results from the intermediate test 4 weeks postoperatively and change-estimates from baseline to 10 week follow up are presented in Paper III.

Table 9. Results from the physical outcome measures in the intervention group (IG, $n=32$) and control group (CG, $n=30$) during 6 months' follow-up after THR

Measurement	Baseline		10 week		6 month		*p*-value
	IG	CG	IG	CG	IG	CG	
Leg extension power (W/kg)§	1.44(0.6)	1.55(0.7)	1.72(0.6)*	1.78(0.6)*	2.04(0.7)	1.97(0.6)	0.23
Walking speed (seconds)	14.0(4.8)	13.6(3.5)	11.1(2.4)*	12.0(2.6)*	10.8(2.8)	11.0(2.6)	0.008[a]
Hip abduction strength (Nm/kg)	0.82(0.3)	0.92(0.4)	1.03(0.3)*	1.03(0.3)*	1.08(0.3)	1.15(0.3)	0.26[a]
Hip flexion strength (Nm/kg)	1.07(0.3)	1.27(0.4)	1.25(0.3)*	1.32(0.4)	1.33(0.3)	1.41(0.4)	0.29
Sit-to-stand test (repetitions)§	11.6(3.9)	11.9(4.6)	14.4(3.9)*	13.1(4.3)*	15.5(4.5)	15.1(5.1)	0.12
Stair climb test (seconds)	12.8(7.9)	13.1(7.2)	9.5(3.2)*	10.5(4.0)*	9.1(3.0)	9.0(2.8)	0.04[a]

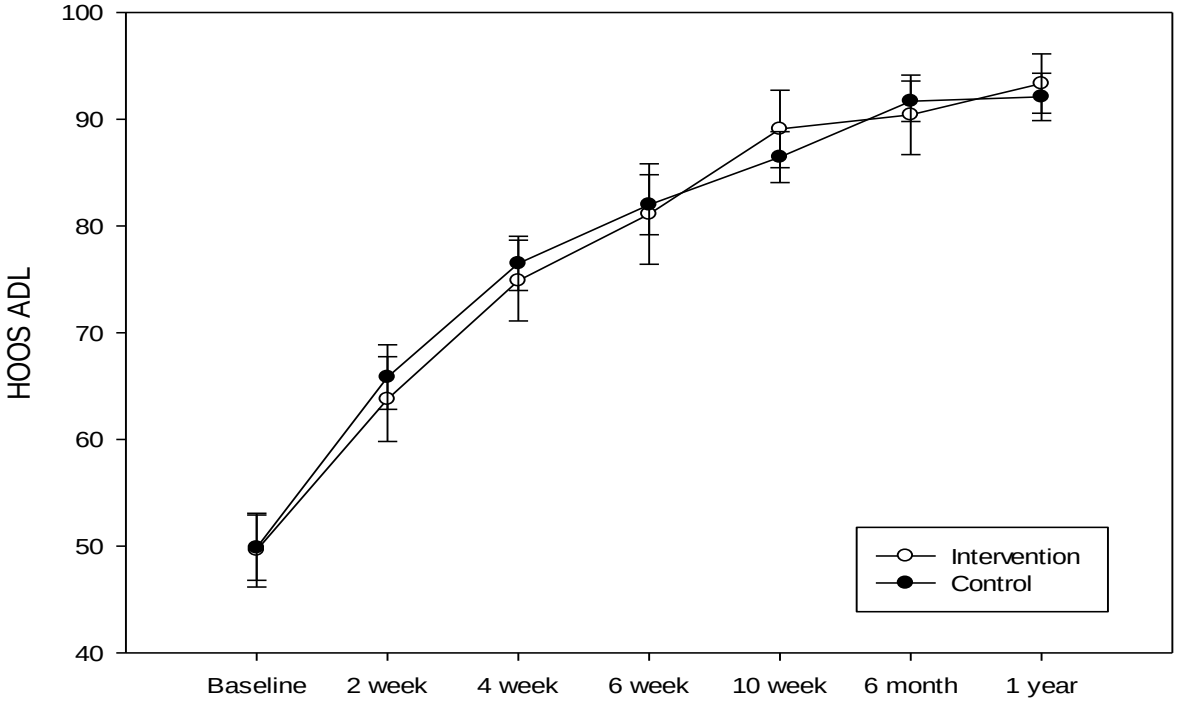
Abbreviations: THR: Total hip replacement, diff: difference, W/kg: Watt/kilogram bodyweight, Nm/kg: Newton*meter/kilogram bodyweight, §1 missing at baseline, the patient was not able to perform the test due to pain, †Multivariate repeated measurement analysis, testing the difference between groups over time, *Significant within group difference from baseline to 10 week follow-up ($p<0.05$), [a]Approximate test, allowing for heterogeneity

All the physical outcomes improved significantly from baseline to 10-week follow-up in both groups, except for hip flexion strength in the CG. In maximum walking speed and stair climb performance there was significantly better improvement over time in the IG compared to the CG (Table 9).

6.4.4 Patient reported outcome HOOS

In both groups, a rapid and large improvement was seen in all the HOOS subscales, with no between group differences (*p*-value range: 0.31-0.90). Ceiling effect, defined as maximum score (100 points) in ≥ 20% of patients, was present in the pain subscale at 10-week follow-up and in the other subscales at 6-month follow-up, except in the subscale sport/recreation, where ceiling effects appeared only at 1-year follow-up. In Figure 8, the results from the HOOS ADL subscale are presented; the results from the remaining HOOS subscales are presented in Paper III.

Figure 8. Results from the HOOS ADL subscale in intervention group (*n*=32) and control group (*n*=30), values are mean ± 95% CI.



6.4.5 Exploratory analysis

In Table 10, the results from the exploratory subgroup analysis are presented.

Table 10. Exploratory subgroup analysis on the primary outcome: Changes in leg extension power from baseline to 10-week follow-up, values given as means [95% CI]

	Intervention	*n*	Control	*n*	*p* value
All (*n*=61)	0.28 [0.12;0.44]	32	0.25 [0.02;0.48]	29	0.82
Gender					
Female (*n*=25)	0.37 [0.16;0.59]	14	0.001 [-0.24;0.24]	11	0.019
Male (*n*=36)	0.21 [-0.04;0.46]	18	0.40 [0.06;0.75]	18	0.35
Age (years)					
<65	0.28 [-0.41;1.02]	17	0.21 [-0.86;1.37]	13	0.73
≥65	0.29 [-0.86;1.24]	15	0.29 [-0.78;1.27]	16	0.99
Baseline leg extension power					
<1.5 W/kg	0.46 [-.13;1.24]	17	0.51 [-.38;1.37]	13	0.79
≥1.5 W/kg	0.08 [-.86;1.02]	15	0.04 [-.86;1.36]	16	0.85
Body mass index					
<26 kg/m^2	0.28 [-0.08;0.65]	11	0.15 [-0.17;0.46]	19	0.56
≥26 kg/m^2	0.28 [0.09;0.47]	21	0.45 [0.09;0.81]	10	0.33

The subgroup analysis revealed a significant effect of the intervention among women with an opposite, yet insignificant, effect among men. The remaining subgroups showed no significant effects.

7. Discussion

7.1 Key findings

Study I

The patients in the RG group attained more rapid improvement than those in the UG group with regard to the primary outcome: patient-reported function measured by the HOOS ADL subscale (p=0.004). However, the validity of the results is uncertain due to a large and potentially non-random proportion of missing answers in the RG group, 29% versus 9% in the UG, at the 3-week follow-up when the between-group difference occurred.

Study II

The proposed test battery showed acceptable relative and absolute inter-rater reliability on a group level, with measurement errors of 3-10%, but not on an individual level, with MDCs of 10-27%. The relative reliability was excellent in the entire test battery, with ICCs above 0.8. The absolute and relative reliability of 30-seconds sit-to-stand was slightly better than the five repetitions sit-to-stand.

Study III

The main finding was no superior effect of two weekly sessions of supervised PRT in addition to five weekly sessions of unsupervised home-based exercise in improving leg extension power of the operated leg 10 weeks after surgery, when compared to seven weekly sessions of unsupervised home-based exercise in patients with THR who had lower pre-operative function. All secondary outcomes improved significantly from baseline to 10-week follow-up in both groups, except with regard to hip flexion muscle strength in the CG (Table 9). There was a statistically significant difference between groups over time in maximum walking speed (p=0.008) and stair climb performance (p=0.04) (Table 9). We question the clinical relevance of these findings because of the small differences and the diminishing of the effect after 6 months. In all the remaining secondary outcomes, there was no between group differences over time (p>0.05).

7.2 Less restricted rehabilitation (Study I)

7.2.1 Perceived function in relation to response rates

The result with regard to perceived function was surprising, since we hypothesised that fewer restrictions would result in less perceived functional limitations. At the 3-week follow-up there was a substantial difference in response rate between groups and variables. This is partly explained by less attendance at the ambulant visit 3-weeks after surgery in the RG group, which we speculate could be related to the movement restrictions and extensive use of assistive devices, but the cause of non-attendance remains unknown. However, there was an additional number of missing answers specific on the HOOS ADL subscale in the RG group, with 29% missing, whereas the subscale QOL had only 18% and the functional evaluation only 15%. In the UG group, the numbers of non-responders on the HOOS ADL subscale was only 9%. This suggests that the nature of the questions is part of the explanation. If a patient has movement restrictions, it might be difficult to answer questions concerning activities like "rising from a chair" or "reaching to the floor". If the missing answers are non-random, e.g. among the patients with more severe conditions as shown in other studies,[124] the result would overestimate the difference. We consider the difference found on the HOOS ADL subscale at the 3-week follow-up to be clinically insignificant and potentially invalid due to the missing answers, the difference being below 5 points, and the diminished difference after 6 weeks. This is supported by the results on the remaining HOOS subscales with less missing values in which no significant differences between groups occurred. In future studies on movement restrictions, we suggest that a physical performance test might be a better functional measure than patient-reported outcomes due to these response problems. Before commencement of this trial, we considered use of the patient-reported outcomes to be an advantage, since it could reveal how limited the patients felt, when for instance they had to use an assistive device to perform a functional task. Conversely, our results indicate that instead of reflecting these limitations, the patients tend to not answer these questions.

7.2.2 Secondary outcomes

We found significant results in favour of the UG on the secondary outcomes concerning functional capacity (p<0.005) and return to work (p=0.045). It seems that reducing movement restrictions and the use of assistive devices can lead to an earlier independent ambulation in the four ADL tasks measured in Study I. This difference between the groups can be caused by less movement restrictions and less use of assistive devices; it is not possible to distinguish between these effects. Some caution should be taken in the interpretation due to the unblinded assessment of functional capacity; however, the evaluation was standardised and kept very simple to avoid

assessor influence. Patient satisfaction was comparable between groups, indicating that the unrestricted regimen did not affect the perceived quality of the treatment when evaluated 6 weeks after surgery. The RG had a higher score of both anxiety (p=0.007) and depression (p=0.036) at baseline compared to the UG (Table 8). This difference can be caused by the preoperative information because the restricted group was informed about movement restrictions and the use of assistive devices to prevent hip dislocation. After surgery, there were no between-group differences and a very low level of anxiety and depression occurred in both groups (Table 8). Even though median values were low, this finding corresponds to 30-38% having above normal level of anxiety and 10-13% above normal level of depression before scheduled THR surgery, indicating that this could be a topic of concern (Paper I). There are safety concerns when implementing the unrestricted regimen with regard to the risk of hip dislocation. We found comparable hip dislocation rates in the two groups; 1.4% in RG versus 2.7% in UG, p=0.48. This indicates that the unrestricted regimen could increase the dislocation risk, but the study is underpowered to draw any conclusions concerning dislocation risk. Thus, it remains crucial to determine the safety of unrestricted rehabilitation in relation to risk of hip dislocation in THR using the posterior surgical approach.

The number of assistive devices handed out by the hospital was markedly reduced (37-79%) after implementation of the unrestricted regimen. This is considered a component of the intervention (individual evaluation of patients need for assistive devices in combination with reduced movement restrictions) rather than a result. But it is highly relevant for clinical practice that it seems reasonable to individually evaluate the patients need for assistive devices rather than using standard packages.

7.2.3 Comparison with relevant findings from other studies

Apart from perceived function, the results in Study I are in line with earlier studies indicating better or equal outcomes after less restricted rehabilitation after THR using the anterolateral surgical approach.[46, 47, 49, 50] The hip dislocation rates in the present study (1.4 and 2.7%) are comparable to findings from a large sample of THR performed with fast-track programmes for peri-operative care (3.5%),[15] and to the unpublished, retrospective Danish study (Table 2) showing hip dislocation rates of 3.4% with movement restrictions and 3.1% without.[52] However, prospective large-scale studies are needed to confirm the safety of unrestricted rehabilitation after THR using the posterior approach in relation to risk of hip dislocation.

We found a large and rapid recovery on perceived function in both groups as measured by the HOOS ADL subscale. A recent study by Barker *et al.*[31] found greater gains in the HOOS ADL score after enhanced recovery that included no hip precautions compared to conventional rehabilitation with hip precautions in a

sample of hip resurfacing patients. They improved from baseline score ~50 in both groups to 6 weeks postoperatively ~70 and ~80, respectively. In our sample both groups had lower scores at baseline and improved more than in their study: 43 and 46 at baseline improved to 83 after 6 weeks in both groups.

7.3 Inter-rater reliability of physical tests (Study II)

The presented systematic differences between raters are considered small and clinically irrelevant (0.3 and 0.18 seconds). We found overall acceptable relative reliability and measurement errors on a group level, as expected. These findings confirmed the appropriateness of using this test battery as an effect measure in the RCT (Study III). There is no consensus concerning cut-off levels for acceptable absolute reliability, but a SEM (%) of 10% has been suggested[125] and was used in this study together with an MDC (%) of 10% to indicate acceptable measurement error on an individual level. However, the MDC (%) was only acceptable for the 20-metre walk test and the stair-climb test, with an MDC of 0.4 and 1.2 seconds, corresponding to 10% in both tests. This means that in a clinical setting, the remaining tests should be considered inappropriate.

The present study reveals better reliability in leg extension power (ICC 0.91 and MDC 34 W) than a recent intra-rater study on hip OA patients (ICC 0.72 and MDC 43 W).[93] This difference could be explained by the disparity between the included patients (pre versus post total hip replacement) or it could be a result of the standardised verbal commands in the present study or differences in test procedures. Concerning the functional tests, our results are in line with their findings.[93]

Previous studies on inter-rater reliability of isometric strength measurements on healthy adults using a hand-held dynamometer have discovered that problems associated with strength of the rater can influence the results.[126, 127] In contrast, we found no systematic differences between raters in the hand-held dynamometer measurements. A possible explanation is that when measuring patients with affected lower-limb strength, as after total hip replacement, the problem of adequate rater-strength might be less marked. In an inter-rater study using hand-held dynamometer performed on hip OA patients, Poulsen *et al.*[128] found lower ICCs in hip abduction strength (0.38-0.85) and hip flexion strength (0.55) than in our study. As in the previous comparison concerning leg extension power, this difference could be caused by the sound file, a more pronounced standardisation of test procedures, or the differences between the study populations. The relative reliability of isometric strength test in the present study is comparable to findings from a pilot test of inter-rater reliability in connection with an intervention study on total hip replacement

patients.[31] With regard to hip abduction strength, the two studies found identical ICCs of 0.93, and with regard to hip flexion ICCs were comparable: 0.83 versus 0.88.

In summary, our reliability results are comparable to previous studies and superior on the leg extension power test. The results indicate that it is feasible to use more than one assessor when applying this test battery in THR patients at a group level as is done in intervention studies. The standardisation of verbal commands by use of a simple sound file played on a computer is considered an easy and effective method to reduce the impact from the rater's voice and accentuation.

7.3 Effect of progressive resistance training (Study III)

7.3.1 Muscle function results

Contrary to our hypothesis, we found no additional effect of the PRT in improvements in leg extension power. This is in contrast to the previous studies on effectiveness of PRT early after THR.[60, 61, 64-66] There might be various explanations for this, as discussed in the following section.

Lack of effect in exercise studies is often explained by insufficient intensity or dose of the exercises, in other words poor therapeutic validity is suggested to result in negative study findings.[129] In the present study, we applied the recommended intensity, sets and frequency of the exercises,[77, 81] controlled by comprehensive supervision and high training compliance. The planned progression of absolute load was achieved without exacerbating pain, as shown in Figure 4. Thus we judge the execution, intensity and frequency of the intervention to be sufficient. The applied duration of the PRT is debatable though, since there is no conclusive evidence concerning the optimal training period of PRT for elderly[81] or after THR.[130] Commonly, a minimum of 12 weeks of PRT are applied.[82] We wanted a short training period in order to enhance patient inclusion, which was expected to be difficult because of the need for transportation to biweekly training sessions shortly after surgery. Short training duration would also improve the possibility of implementation in the clinic if successful results were obtained. Since earlier studies have shown an effect of resistance training over shorter time frames (5-8 weeks),[61, 71] we considered 10 weeks to be an acceptable compromise, knowing that it would result in 8-9 weeks of actual training, depending on how early start-up was accomplished. However, in light of our results showing tendencies of effect but no convincing between-group differences, our results may have been affected by the training period being too short.

In Table 11 the relative improvements from the present study concerning muscle power and strength are compared to the two previous studies on PRT after THR.

Table 11. Strength gains during intervention period in studies on PRT after THR

Study	**Mikkelsen**			**Suetta**[64-66]	**Husby**[60,61]	
Weeks of PRT	10			12	5	
Strength measurement	Leg extension power + isometric			Isokinetic +isometric	1 RM test of the trained exercises	
Muscle group	Leg extension	Hip abduction	Hip flexion	Knee extension	Leg press	Hip abduction
Immediate effect of PRT						
PRT group	+21%*	+26%*	+18%*	+22-28%*	-11%†	+59%†
Control group	+17%*	+12%*	4%^{NS}	-1.5-0%^{NS}	-36%†	+4%†
Long term effect (½ year)						
PRT group	+42%	+32%	+24%	Not	+6%	+ 85%
Control group	+27%	+25%	+11%	reported	+10%	+75%

PRT: Progressive resistance training, THR: Total hip replacement, *Significant different from preoperative ($p<0.05$), ^{NS} Not significant different from preoperative ($p>0.05$), †Difference to preoperative not tested

In the present study, the strength gains are slightly smaller but comparable to those found by Suetta *et al*.[64-66] This is judged to be a satisfactory result of the training in light of their intervention and effect being solely on the quadriceps muscle, which is probably less influenced by surgery than the muscles surrounding the hip. Furthermore, the implementation of fast-track procedures and general improvements in surgery potentially forms a different basis for training after surgery. In their study from 2004, the length of hospital stay was dramatically longer, with 10 and 16 days in the two groups compared to 1-2 days in our study. This suggests that their control group was more immobilised, thereby making larger differences possible because of a better potential for improvements. This speculation is confirmed by the difference in strength development in the control groups of these two studies, where our CG shows greater improvements during 10 weeks after surgery than their CG during 12 weeks. When comparing to the study by Husby *et al*.[60,61] it should be noticed that their intervention period was only 5 weeks and the strength measurements used was 1RM of the trained exercise. This effect measure might reflect further issues than only muscle strength improvements; the patients in the IG probably improved their technique during training and not just their muscle strength. However, they report

much larger gains in hip abduction strength intermediately and in the long term compared to our study, and much less strength gains in leg press compared to our results on leg extension power.

In comparison to a recent Danish study concerning preoperative exercises, we found less improvements in leg extension power, their follow-up being 3 months after THR and all patients receiving outpatient physiotherapy post discharge (~30% compared to 21% in the IG in the present study).[94] An explanation could be the different baseline levels: ~74 watts in their study compared to ~117 watts in or study. It seems that the samples of THR patients recruited are very different concerning leg extension power, even though both studies are randomised training studies performed in the same time period in Denmark. This difference in baseline power is surprising since we aimed at excluding the best functioning patients, which was not the case in the study by Villadsen *et al*.[94]

Effect modification by gender
Interestingly, it seems that gender modifies the effect of PRT on leg extension power of the operated leg. As shown in Table 10, there is significant effect of the intervention among the females, whereas among males the direction of the effect is opposite, though not significant. This could be speculated to be caused by a lower power at baseline and thereby larger potential for improvements, but baseline level in leg extension power does not modify the effect of PRT (Table 10). Neither does age nor BMI modify the effect of the intervention. The literature on gender differences are divergent, with studies claiming that gender does not affect the response to resistance training[114] and others claiming that men achieve larger responses.[113, 131] Our results are contrary to this, with the women showing the best response to PRT. The explanation of this finding remains unknown, but it might be explained by the hypothesis that strength adaptations in women are less dependent on hypertrophy and to a larger extent depend on neuromuscular adaptations compared to men.[113, 115] If this is the case, it could explain this surprising finding, since the surgical stress response results in catabolism,[35] which might blunt hypertrophy and thereby decrease the response to PRT in men more than in women. It must be emphasised that these analysis and speculations are solely explorative and hypothesis generating.

7.3.2 Functional performance

The functional tests performed in Study III are comparable to those used in the study by Suetta *et al*.[66] Some of the functional tests improved significantly more with PRT compared to home-based exercises: sit-to-stand performance in their study, walking speed and stair climb performance in the present study. In their study, PRT resulted in comparable but slightly larger improvements compared to our study (walking speed: 30% versus 21%, stair test; 28% versus 26% and sit-to-stand test: 30% versus

25%).[66] As mentioned before, we believe that the patient's potential for improvement was larger in their study. This is supported by comparison of the two control groups that both received home-based rehabilitation. The functional performance in the CG in the present study improved significantly (12-20%, $p<0.05$), which was not the case in the previous study (-16% to +22%, $p>0.05$).[66] The maximum walking speed improved more in our IG (21%) than in the before-mentioned study[94] on preoperative exercises (14-18%), even though baseline speed was slightly slower and their follow-up period slightly longer. All together, the functional performance gains after PRT found in the present study comply well with expectations based on current literature, but the CG improved more than expected.

7.3.3 Patient reported outcome

There were no significant between-group differences on the HOOS subscales in Study III. The HOOS results indicate a rapid and substantial recovery in both groups, comparable with intervention groups in other studies.[31, 94] It is surprising that this intervention, with a considerably larger amount of supervision than in the CG, did not affect the patient-reported outcome. An explanation could be that the substantial improvements in the CG make it impossible to attain significantly larger improvements by new interventions. The present study showed slightly larger improvement on the HOOS ADL scores in both groups compared to the study by Villadsen *et al.* on preoperative training.[94] After 10 weeks the IG improved by 40 points and the CG by 37 compared to their 3-month improvement of ~30 points, with comparable baseline values.[94] Ceiling effects of ≥20% at maximum scores were observed for all HOOS subscales (except sport/recreation) from the 6 month's follow-up and forward, indicating that the suitability of the questionnaire in long-term follow-up after THR might be disputed.

7.3.4 Summary on findings in Study III

Overall, a comparison with earlier studies indicates that the IG in the present study achieved the expected gains after PRT; the surprising finding is the comparable improvements in the CG. All outcome measures improved slightly more in the IG than in the CG, indicating that there might be an effect of the intervention that did not reach statistical significance in the present study. However the differences are considered too small to be clinically meaningful in light of the rather comprehensive and expensive intervention, with 20 sessions of high intense one-to-one supervised PRT.

7.4 Limitations

7.4.1 Selection bias

We consecutively included all THR patients in Study I as part of the quality assessment in the department and with relatively high response rates. Accordingly, we assume that there is a minimum of selection bias in that study population. In Study I, the patients tended to be slightly older, more females, less healthy and less frequently received cementless prosthesis than in Study III, where informed consent was obtained (Table 6), indicating presence of selection bias in Study III. This is underlined by comparing the baseline mean HOOS ADL score in Study I (~45) to Study III (~50), implying that the patients in Study III perceived less functional limitations even though the best functioning patients were excluded. This selection bias is probably caused by the demands for participation. The patients should be willing to participate in training twice a week and attend one extra follow-up visit at the hospital. The transportation to the training was a crucial point for participation since 58 patients refused participation for that specific reason (shown in Paper III). We believe that the exclusion of the best functioning patients to some degree counteracts the typical selection bias in intervention studies, i.e. that participants are less disabled than non-participants.[132, 133] However, the comparisons to Study I reveal that Study III is probably affected by some selection bias, and we assume that we had an over-representation of motivated patients. In the reliability study (II), we do not consider the selection to be crucial; thus we used convenience sampling. The samples in Study II do not deviate notably from the other studies with regard to age, gender and BMI (Table 6).

7.4.2 Blinding

In Study I, the physiotherapists performing the ADL evaluation were unblinded to intervention due to the before-after design of the study. This could cause information bias if the physiotherapists considered one intervention to be superior to the other and unknowingly evaluated that group better. This was prevented by keeping the evaluations and answers very simple and giving thorough instructions on how to evaluate the tasks. Furthermore, it was emphasised that it was unknown which rehabilitation regimen that was superior in improving independency in ADL functions.

In Study II, the rater of the second test was blinded to the first test results.

Blinding of the assessors in Study III was secured through randomising late during hospital stay and reminding the patients not to mention their group assignment, and by performing the PRT in other facilities and with other personnel than the tests.

However, blinding of the patients was impossible; thus a positive expectation could influence the outcome after PRT in a positive direction.

7.4.3 Other limitations

In both Study I and Study III multiple comparisons were made, and this induces a risk of type I error. Hence, the significant differences found in secondary outcomes should be interpreted with caution and in relation to the clinical relevance of the findings.

An overlap in inclusion period between Study I and Study III caused a procedure change concerning movement restrictions during patient inclusion in Study III. Equal distributions into the two groups in Study III were secured through block randomisation. Furthermore, it resulted in a larger burden of outcome measurement for a subsample of 20 participants in Study III. We attempted to minimise this by collecting data on the studies jointly; the double-participants attended the 4-week follow-up visit as used in Study III, this visit counted as the 3-week follow-up in Study I. We deemed this to be feasible since the double-participant group was a fairly small number of the sample in Study I, and since the timing of this follow-up visit also could vary by a week in normal practice. The HOOS questionnaire was used in both studies, and the same answer was used in both studies, with extra measurement times in Study III.

Study I

The missing answers regarding the primary outcome in the RG limited the conclusions that could be drawn concerning perceived function. The non-randomised design could affect the validity of the group comparisons. We cannot eliminate the possibility that unmeasured confounders biased the results. However it strengthens the design that baseline variables were reasonably distributed between groups and that the inclusion period was fairly short, hence minimising the influence of general developments in surgery and treatment practice. The short follow-up period limits the conclusions to the first 6 weeks of recovery. Since movement restrictions and use of assistive devices was only part of the rehabilitation within the first 6 weeks, we found that a follow-up period of this length was adequate.

Study II

It is recommended that around 50 participants are included in reliability studies.[134] Hence, the sample size is considered a limitation in the present study even though calculated sample size requirements were fully met.

Study III

Besides the before-mentioned selection bias, the limitations of this study encompass risk of attention bias due to a considerable difference in the amount of supervision provided in the compared groups. To comply with the possible risk of attention bias, it would have been optimal to perform supervised placebo training in the CG, but this was not deemed feasible. However, the results do not indicate presence of attention bias since the primary outcome and the patient reported outcome was not superior in the IG. During the study period, 15% of the participants dropped out. Drop outs were distributed equally between the groups and predominantly related to major complications or emerged diseases. Results from the intention-to-treat and extended per protocol analysis on leg extension power were similar, indicating no systematic bias due to drop outs. Hence the drop outs are considered unrelated to the intervention and not affecting the internal validity of the study. In addition, two patients had to discontinue the intervention, implying that a subgroup of patients might not tolerate the PRT. However, we did include all participants in all analysis regardless of their training attendance.

7.5 Generalisability

The results from Study I we believe to be highly generalisable to the general population of patients with OA going through THR surgery. This is based on the consecutive enrolment of all patients at the department, without asking for participation. However, the results on the variables at 3-week follow-up with low response rates have questionable generalisability.

In Study II, we selected patients of a certain age group (55-80 years) and without musculoskeletal comorbidities, thus our results are only generalisable to that group of patients. Many patients refused to participate in the study (51%), which could further affect the generalisability if the non-participants were systematically different from participants. We do not believe the patient selection to be problematic in this case because to the reasons for non-participation were mostly practical (time issues at the specific test day), and because the study investigated reliability of the tests, no comparison between patients were made.

Selection bias seemed to be a problem in Study III, as described in section 7.4.1, and thereby the generalisability is affected. We may have included motivated patients with a positive attitude towards training. Drop outs among the weakest patients might further decrease the generalisability of the results to the most disabled group of THR patients. Patients that did not complete the study tended to be older, weaker and more were women compared to those who completed. All together, the results can presumably be generalised to motivated THR patients with an intermediate level

of perceived function, meaning that the patients with the highest level were excluded and patients with the lowest level tended to refuse participation or drop out of the study.

8. Conclusion

Study I

We found slightly slower but equal recovery on perceived function in the UG compared to the RG, but potential bias leads to inconclusive results. However, less restricted rehabilitation led to earlier return to work, more independence in functional capacity, and a substantial decrease in the use of assistive devices, while hip dislocation rates, levels of anxiety, depression and patient satisfaction were comparable to the restricted group.

Study II

The tests battery showed acceptable relative and absolute inter-rater reliability on a group level, but not on an individual level, because only tests of walking speed and stair climb performance proved acceptable absolute reliability. After THR, the 30-second sit-to-stand test is recommended over the five repetitions sit-to-stand test.

Study III

Supervised progressive resistance training 2 days/week in combination with home-based exercise 5 days/week was not superior to daily home-based exercise in improving leg extension power of the operated leg 10 weeks after THR. For some of the secondary outcomes, results were in favour of PRT but were deemed clinically insignificant. Significant improvements in muscle function, functional performance and patient-reported outcomes were achieved 10 weeks after THR, despite group assignment, except regarding hip flexion muscle strength in the CG.

9. Perspectives and future research

Most of the previous literature on outcome and rehabilitation after THR is based on patients undergoing conventional THR surgery. The results covered in this thesis underline the need for future research to establish the functional performance and muscle strength outcomes after fast-track surgery without supervised rehabilitation. This could indicate whether there is need for supervised rehabilitation and form the basis for an impairment-based approach in future rehabilitation studies. To establish the need for supervised rehabilitation, it is necessary to define what is full recovery – or acceptable recovery – after fast-track THR. This is a complex issue to address, because increases from the preoperative level do not reflect whether or not the patients are sufficiently recovered, since the preoperative level of muscle function and functional performance are affected by pain and disuse. The contralateral leg has been used as a measure for recovery,[18] but it can hardly be considered an unaffected leg due to OA often being bilateral. Furthermore, between-limb comparisons are mainly relevant concerning muscle function, and the functional tests do seldom distinguish between legs. Comparison to healthy peers is an alternative approach and has been used previously.[19, 20] If patient satisfaction and patient-reported outcomes were to determine full recovery then the goals seem to be achieved for the vast majority of patients. However, there is a discrepancy between what THR patients perceive they can do physically and what they actually can do as described in the introduction. Thus, it is relevant to consider all these aspects of functional recovery in future studies.

Before this thesis there was a general consensus in the literature that high-intense resistance training would probably be a solution to overcome the documented deficits after THR since they were mainly muscle strength related. Several authors requested studies on PRT after THR.[75, 130, 135] However, the results from this thesis indicate that the PRT is not as effective as expected. These findings do not claim to be exhaustive, but need to be confirmed or contradicted in future research. There might be a subgroup of patients profiting from PRT and maybe different timings and dosages could change the conclusions. Based on this thesis, it is speculated that women might benefit from PRT after THR, but this needs to be verified in future studies. Different rehabilitation strategies could also be investigated, for instance, general physical activity. The current literature is sparse but suggests that THR patients do not fully utilise their functional gains from surgery in the form of increasing their daily activity level to that of healthy controls.[21] Maybe interventions aiming at increasing general physical activity and returning to sport rather than specific hip exercises would be beneficial. Another approach is functional task exercises, and recent studies support the effect of these interventions as shown in

Table 3. In the future, personalised rehabilitation might be a possibility if it is possible to identify subgroups of patients that benefit the most from specific intervention. There is large variation in all the physical and patient-reported outcomes used in this thesis, indicating that THR patients are heterogeneous when it comes to their health status before surgery, their gain from THR and their response to rehabilitation interventions. It seems that some recover well with use of unsupervised home-based exercises and return to an active lifestyle. It is speculated that some patients need PRT to fully recover – and this could be women – while some need functional exercises and maybe some need quite different approaches. In future training studies, the transportation to the training sessions should be considered since it was a general reason for non-participation in Study III. In an optimal design, the patients should have easy access to the training facility, and it should not require driving a car. This is specifically important early after surgery, and it could counteract some of the selection problems.

Concerning movement restrictions after THR, the optimal regimen needs to be established. This thesis indicates beneficial effects of fewer restrictions, but the evidence is still inconclusive concerning the safety in relation to risk of hip dislocation. Large scale prospective studies with complete follow-up are needed. This is challenging, since register-studies involve potential problems with the coding procedures, and in clinical studies non-response can be associated with higher dislocation risk. Thus a meticulous effort should be made to attain complete follow-up.

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List of appendices

Appendix 1: Paper I

Mikkelsen LR, Petersen MK, Søballe K, Mikkelsen S, Mechlenburg I. Does reduced movement restrictions and use of assistive devices affect rehabilitation outcome after total hip replacement? A non-randomized, controlled study. *Eur J Phys Rehabil Med.* 2014; 50: 383-93

Appendix 2: Paper II

Mikkelsen LR, Mikkelsen S, Søballe K, Mechlenburg I, Petersen AK. A study of the inter-rater reliability of a test battery for use in patients after total hip replacement. *Clin Rehabil.* 2014 May 21 [Epub ahead of print]

Appendix 3: Paper III

Mikkelsen LR, Mechlenburg I, Søballe K, Jørgensen LB, Mikkelsen S, Bandholm T, Petersen AK. Effect of early supervised progressive resistance training compared to unsupervised home-based exercise after fast-track total hip replacement applied to patients with preoperative functional limitations. A single-blinded randomised controlled trial. Submitted to *Osteoarthritis and Cartilage*, Apr 2014, re-submitted after revision, August 2014

Appendix 4: List of theses from the orthopaedic research group

Appendix 1

Paper I

EUR J PHYS REHABIL MED 2014;50:383-93

Does reduced movement restrictions and use of assistive devices affect rehabilitation outcome after total hip replacement? A non-randomized, controlled study

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***Background*. Improvements in surgical techniques and increase of femoral head size might have changed the rationale for movement restrictions after total hip replacement (THR).**
***Aim*. To evaluate the influence of movement restrictions and assistive devices on rehabilitation after fast track THR.**
***Design*. Non-randomized, controlled study.**
***Setting*. Inpatient.**
***Population*. 365 consecutively included THR patients.**
***Methods*. Patients included the 3 initial month of the study underwent rehabilitation with restrictions in hip movement and a standard package of assistive devices (restricted group). This group was compared to patients included the following 3 months with less restricted hip movement and use of assistive devices according to individual needs (unrestricted group). Questionnaires on function, pain, quality of life (HOOS), anxiety (HADS), working status and patient satisfaction were completed before THR, 3 and 6 weeks after.**
***Results*. The HOOS function score at the 3 measurement times was (mean±SD); unrestricted group: 46±17 - 76±9 - 83±14 compared to restricted group: 43±16 - 81±14 - 83±13. Changes over time was significantly higher in the restricted group (P=0.004). Return to work 6 weeks after THR for the unrestricted group compared to restricted group was: 53% *versus* 32% (P=0.045). No significant differences between groups in pain, symptoms, quality of life, anxiety/depression, hip dislocations and patient satisfaction.**
***Conclusion*. This study showed slightly slower recovery in patient-reported function after reduction in movement restrictions and use of assistive devices, but the difference was eliminated after 6 weeks. Reduced movement restrictions did not affect the other patient-reported outcomes and led to earlier return to work.**
***Clinical Rehabilitation Impact*. It is possible to reduce movement restrictions and use of assistive devices considerably. More research on safety issues is needed to elucidate the effect of unrestricted rehabilitation on hip dislocation.**

KEY WORDS: Arthroplasty, replacement, hip - Rehabilitation - Self-help devices.

Total hip replacement (THR) is a common and successful procedure to relieve pain and increase function in patients with osteoarthritis in the hip.[1-3] Traditionally, rehabilitation strategies after THR have included several hip movement restrictions to prevent hip dislocation.[4] The improvements in surgical techniques and increase in the femoral head size of the hip implants have decreased the risk of hip dislocation [5] and this might have changed the rationale for these restrictions.[6]

Several studies on THR patients operated with the anterolateral surgical approach indicates that movement restrictions and use of assistive devices are unnecessary in preventing hip dislocation and might

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delay rehabilitation.[6-9] Peak *et al*. (2005) showed a faster return to normal activities, higher patient satisfaction and a continued low dislocation rate in an unrestricted group compared to a restricted group in a randomized controlled trial including 265 THR patients. The restricted group had additional movement restrictions and used more assistive devices than the unrestricted group. The same research institution confirms their findings of low dislocations rates (0.15%) after unrestricted rehabilitation in a pragmatic trial on a larger sample of patients (N.=2532).[6] Likewise, Ververelli *et al*. (2009) found a less restricted group of THR patients to be faster to ambulate with a cane, without a cane, and without a limp compared to patients randomized to traditional rehabilitation with restricted hip movement. Changing to an unrestricted rehabilitation after THR also led to a continuous low dislocation rate (0.6%) in an earlier study on 499 THR patients.[8] It has been suggested that movement restrictions might also be unnecessary after THR performed through the posterior approach.[6]

Some studies indicates a different risk profile concerning hip dislocation between different surgical techniques; the posterior surgical approach leading to a higher risk than the anterolateral approach,[4, 10] but evidence on the subject is inconclusive.[11] The possible benefits or harms of reducing movement restrictions and the use of assistive devices in rehabilitation after THR using the posterior approach, remains unknown. We hypothesized that a less restricted rehabilitation protocol after THR (less movement restrictions and less use of assistive devices) would result in a faster functional recovery after hip surgery. Thus the objective of this trial was to evaluate the influence of assistive devices and movement restrictions during early rehabilitation after fast track total hip replacement on: 1) patient reported outcome on function, pain and quality of life; 2) functional capacity evaluated by physiotherapists; and 3) patient focused variables: anxiety/depression, return to work and patient satisfaction.

Materials and methods

Trial design

The study compared patients before and after a change in clinical practice in a non-randomized controlled trial as part of a quality assessment. The restricted group was enrolled consecutively from May 3 to August 19, 2011, hereafter the rehabilitation regime was changed, and the unrestricted group was consecutively enrolled from August 25 to November 30, 2011. During the change of procedures a pre-defined intermediate period of 20 patients was excluded from the study (20-25 August 2011).

Study population

The study was carried out at Center for Planned Surgery at Silkeborg Regional Hospital. The regional ethical committee accepted initiation of the study and reviewed the study as non-notifiable (Inquiry 41/2011). The Danish Data Protection Agency approved the study (2007-58-0010) and the Danish Health and Medicines Authority permitted access to the patients' medical journals (3-3013-196/1/). All patients undergoing total hip replacement surgery in the inclusion period were asked to fulfill the questionnaires in the study as part of the quality assessment in the orthopedic department. Exclusion criteria were; patients undergoing revision THR, THR due to femoral fractures and other diagnosis than osteoarthritis as the primary indication for surgery, *e.g*. rheumatoid arthritis. The participant flow is shown in Figure 1.

All surgeries were performed through the posterior approach in spinal anesthesia by 7 experienced surgeons. The Moore incision was used to expose the hip joint, only standard incision, no minimal incisions was used. This approach splits the fibers of gluteus maximus, then the small internal rotator muscles (piriformis, gemmelli's and obtoratorius internus) is detached and the posterior aspect of the capsule is cut through. The capsule and small rotator muscles were re-inserted. A radiological control of the prosthetic positioning was performed on the first postoperative day and all patients were allowed full weight bearing from the day of surgery. Perioperative treatment followed a fast-track program for THR using multimodal optimization of care including: patient information, anesthesia, pain management, mobilization and nutrition.[12, 13] All patients were invited to an information day prior to surgery where they learned about the expected course of their operation and rehabilitation and they were encouraged to take active part in the treatment and rehabilitation. Patients were admitted to the hospital on the

day of surgery and were discharged to their home when meeting predefined functional discharge criteria such as independency in mobilization and toilet visits, typically on the first or second postoperative day. During admission physiotherapy was provided 1-2 times a day to ensure following goals: mobilization, independency in daily activities and ability to perform a home-based hip exercise program. The prescribed home-based training program consisted of unloaded hip exercises combined with stationary bicycling and walking activities. Three weeks after surgery all participants were offered a physiotherapy consultation where the exercise program was progressed using rubber band resistance in the movement directions: Knee extension and hip flexion, extension and abduction and functional exercises, *e.g.*, one-legged-stance, step up. The exercise program is developed according to the accessible evidence [14, 15] and adjusted for local conditions, such as no standard physiotherapy after discharge, therefore home-based exercise is used. No further supervision was carried out, unless the physiotherapist considered it necessary to refer the patients to rehabilitation in the municipality after discharge (17.2 % of the sample).

Interventions

Patients in the restricted group (RG) underwent the traditional rehabilitation in the department including movement restrictions (maximum 90° of flexion, no adduction beyond neutral position and no internal rotation) the first 6 weeks postoperatively. To obey to these restrictions patients were provided with the following assistive devices: elevated toilet seat, shoe horn, bath bench, ergonomic reacher, sock aid and wedge pillow. The unrestricted group (UG) had no movement restrictions apart from avoiding the combination of full hip flexion, internal rotation and adduction. To illustrate this for the patients, they were advised to bend between their knees when flexing the hip, *e.g.*, to put on shoes. In the UG assistive devices were only distributed when needed for the patient to perform activities of daily living, *e.g.*, if a patient could not rise from a normal toilet, an elevated toilet was lent. Walking devices, generally crutches, were administered to all patients in both groups, as this is not considered a device to ensure adherence to movement restrictions but solely to support the walking ability. Information on the rehabilitation regime was provided at the above mentioned information day and in a patient brochure concerning several aspects of the surgery, hospitalization and rehabilitation. The content of the information day and brochure was similar between the groups, except from issues concerning movement restrictions and assistive devices.

Outcomes

The primary outcome was activities of daily living (ADL) measured by the subscale of the hip dysfunction and osteoarthritis outcome score questionnaire (HOOS 2.0).[16] Secondary outcomes included the following subscales of HOOS; Pain, symptoms, and hip related Quality of life (QOL). The subscale function in sport and recreation was not considered relevant at this early stage after THR. HOOS is a valid and reliable patient-reported outcome questionnaire when evaluating patients undergoing THR.[16] Scores range from 0 to 100, where 100 represent the best possible score. The Danish version of HOOS 2.0 was administered at baseline (before surgery), 3- and 6 weeks postoperatively. At these time points the patients also completed The Hospital Anxiety and Depression Scale (HADS). HADS is a psychological screening tool to detect states of anxiety and depression in a hospital setting, it is sensitive to changes and can be used in clinical research.[17] The HADS is also found to perform well in both somatic, psychiatric and primary care patients and in the general population, thus we found it suitable to use after discharge.[18] At the consultation 3 weeks after surgery physiotherapists evaluated patients' ability to perform 4 different activities of daily living independently (stair climbing, getting dressed, bath/shower and house cleaning). Patients were placed in 4 categories for each activity: "capable independently", "capable with use of assistive device", "capable with help from another person" and "incapable". The ADL evaluation was a direct testing of the stair climbing ability at the consultation. The other activities were not possible to test directly, but were evaluated on the basis of information from the patient. The evaluation distinguished between not being able to perform an activity or getting help due to indolence, thus patients were not asked if they did perform an activity, but whether they could perform the activity independently. Other secondary outcomes were: return to work, patient satisfaction, willingness-to-repeat surgery and use of assistive devices. Hip dis-

location within the first six weeks was registered. From the medical charts and patient questionnaires the following baseline variables were collected: age, gender, body mass index (BMI), American Society of Anaesthesiologists (ASA) classification (physical status classification), marital status and educational level.

Sample size

We performed a sample size calculation based on a study comparing two types of THR surgeries where one group had no movement restrictions due to the type of implant (large head-head THA) and the other group had movement restrictions as described in our restricted group.[19] The calculation was based on patient-evaluated ADL scores from the Western and Ontario McMasters University Osteoarthritis Index (WOMAC) questionnaire which includes the same questions as the HOOS used in the present study, but with the scale reversed; 0-100 (best/worst). The mean score 8 weeks post-surgery was 12.7 (SD 10.3) and 17.9 (SD 11.2), in favor of the less restricted group (data not shown in paper, obtained through personal contact). With a significance level of 5% and a power of 95%, we needed 121 patients in each group. The required sample size was predefined, but we also had to predefine the enrollment period due to practical and organizational reasons. Based on the expected number of THR surgeries we decided on a seven months period of enrollment to ensure inclusion of the required sample size, and the date for changing procedures was defined as August 20, 2011.

Stopping guideline

The consequences of changing the movement restrictions after THR surgeries using the posterior approach is unknown, thus we found it necessary to predefine a guideline for discontinuing the study. In collaboration with two senior surgeons (authors SM and KS), it was decided that occurrence of five hip dislocations among the first 100 patients end thereafter a dislocation rate of 5% or above in the UG would result in a change of the intervention.

Blinding

Neither investigators nor patients could be blinded to the intervention. The patients were however not aware of the focus on hip movement restrictions and assistive devices; they were merely informed that the questionnaires were used for quality control in the department.

Statistical analysis

The primary analysis was a comparison between the groups regarding their HOOS function score using multivariate repeated measurement ANOVA with group and time as factors. The assumption of homogeneity in standard deviations and correlations in the groups was tested. The other HOOS subscales were analyzed identically. With this statistical model we analyzed both early (3 weeks) and later (6 weeks) occurrence of differences between the groups, and the P-value refers to differences in change over time between the two groups. The functional capacity evaluation, return to work and patient satisfaction was compared using χ^2 test. The hip dislocation rates were compared between the groups using Fisher's exact test due to the very low number of events. The baseline variables were analyzed according to the type of data; dichotome or grouped variables with χ^2 test, normally distributed variables with unpaired *t*-test.

Results

Thirty-one patients were excluded from the study due to other indications for surgery than arthritis: revision of an earlier THR (N.=20), femoral head fracture (N.=8), rheumatoid arthritis (N.=1), femoral head necrosis (N.=1), polymyalgia rheumatica (N.=1) (Figure 1). Baseline characteristics are presented in Table I. There was no significant differences between the groups in the baseline characteristics, except from educational level where a greater proportion of the UG had a higher level of education (46% *versus* 33%, P=0.02). The median length of hospital stay was 1 day (range: 1-8), with the majority of patients being discharged on the first postoperative day, N.=271~74%.

Patient evaluated function and functional capacity

There was significant difference between the groups in the change in HOOS ADL score, with the RG having the fastest increase (Table II) (P=0.004).

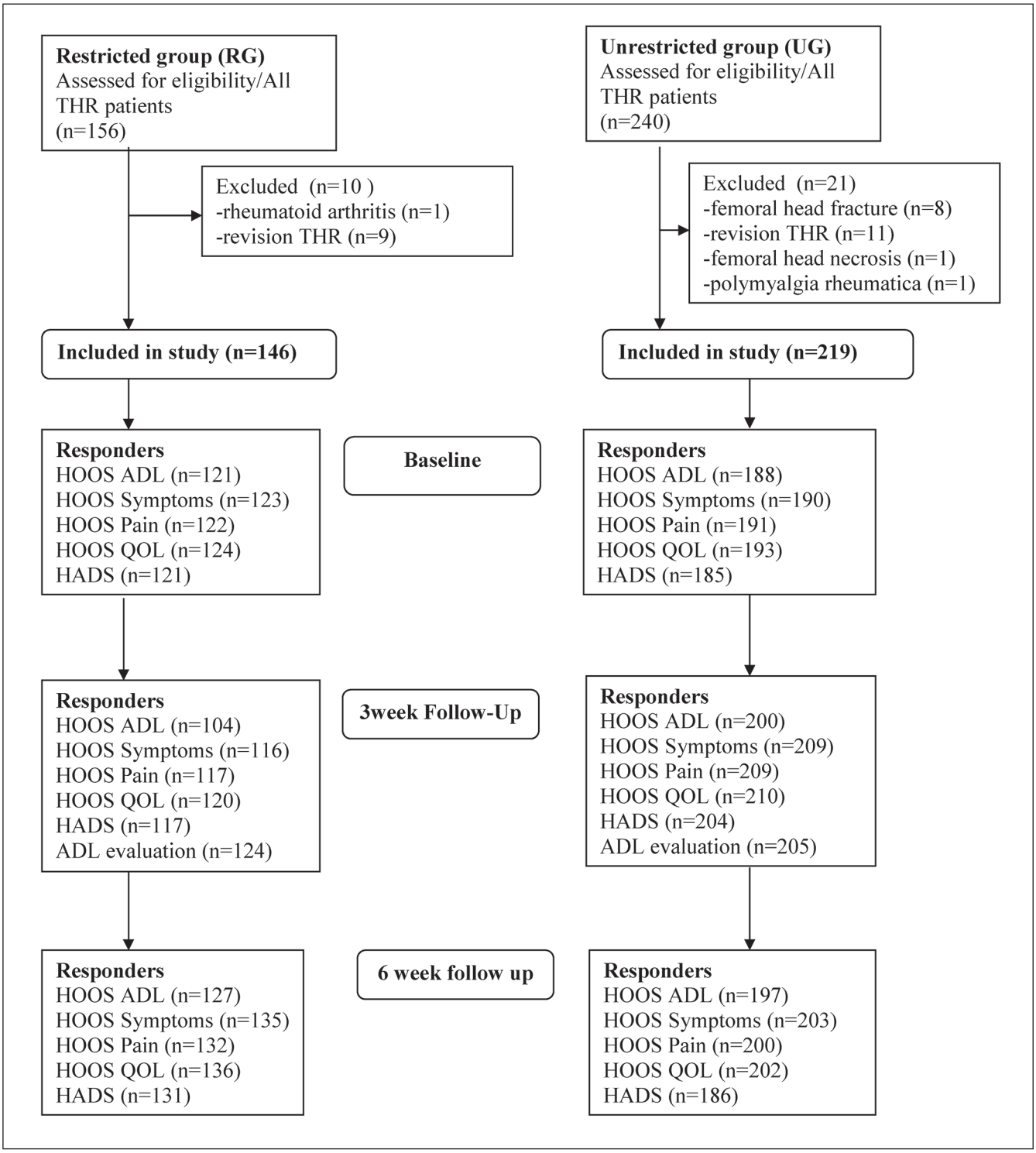

Figure 1.—365 patients with primary THR for osteoarthritis were consecutively included. Patients included the 3 initial months were allocated to the restricted group (RG) and patients included the following 3 months were allocated to the unrestricted group (UG).

TABLE I.—*Baseline characteristics of 365 patients consecutively included and followed in respect to the influence of assistive devices and movement restrictions after fast track total hip replacement.*

	All N.=365	RG N.=146	UG N.=219	P value*
	Values are number (%) unless otherwise stated			
Age (year), mean (SD)	68.7 (10.0)	69.0 (10.1)	68.4 (9.9)	0.58‡
BMI (kg/m²), mean (SD)	26.8 (4.5)	27.2 (5.1)	26.5 (4.1)	0.15‡
Male	191 (52.3)	78 (53.4)	113 (51.6)	0.73†
Married/cohabiting (10 missing)	258 (72.7)	104 (71.7)	154 (73.3)	0.74†
Retired from work (9 missing)	264 (74.2)	105 (73.9)	159 (74.3)	0.94†
Contralateral THR	83 (23.0)	34 (23.3)	49 (22.8)	0.91†
Femoral head size (31 missing)				
≤32 mm	14 (4.2)	5 (4.1)	9 (4.2)	0.20†
36 mm	213 (63.8)	85 (69.7)	125 (59.0)	
40 mm	95 (28.4)	29 (23.8)	66 (31.1)	
≥44 mm	12 (3.6)	3 (2.5)	9 (4.2)	
Prosthesis type (1 missing)				
Cementless	315 (86.5)	125 (86.2)	190 (86.8)	0.97†
Cemented	13 (3.6)	5 (3.5)	8 (3.7)	
Hybrid	36 (9.9)	15 (10.3)	21 (9.6)	
Physical status (11 missing)§				
ASA I	111 (31.4)	42 (30.0)	69 (32.2)	0.13†
ASA II	210 (59.3)	79 (56.4)	131 (61.2)	
ASA III+IV	33 (9.3)	19 (13.6)	14 (6.5)	
Educational level (40 missing)				
Compulsory school/skilled worker	190 (58.5)	79 (67.0)	111 (53.6)	0.02†
Higher education	135 (41.5)	39 (33.1)	96 (46.4)	—

RG: restricted group; UG: unrestricted group; BMI: body mass index; THA: total hip replacement.
*: Difference between groups, ‡: t-test, †: chi² test, §: American Society of Anesthesiologists physical status classification: I-Healthy patient, II-Patient with mild systemic disease, III+IV-Patient with severe systemic disease.

TABLE II.—*Scores for the subscales ADL, symptoms, pain and quality of life measured with Hip Osteoarthritis Outcome Scale (HOOS).*

Measure	Restricted group N.=146		Unrestricted group N.=219		P value
	Mean (SD)	Missing %	Mean (SD)	Missing %	
HOOS ADL					
Baseline	42.87 (16.3)	17	46.48 (17.1)	14	
3 weeks post	80.96 (14.0)	29	76.19 (15.0)	9	
6 weeks post	83.3 (13.3)	13	82.58 (14.2)	10	0.004*
HOOS symptoms					
Baseline	40.96 (18.8)	16	41.47 (17.0)	13	
3 weeks post	79.37 (14.9)	21	74.43 (16.2)	5	
6 weeks post	82.49 (14.6)	8	80.78 (14.8)	7	0.29*
HOOS pain					
Baseline	43.59 (17.3)	16	43.57 (14.8)	13	
3 weeks post	82.07 (14.8)	20	79.12 (15.9)	5	
6 weeks post	85.74 (14.6)	10	85.04 (14.8)	9	0.17*
HOOS QOL					
Baseline	26.58 (16.8)	15	27.86 (14.6)	12	
3 weeks post	66.32 (21.5)	18	63.52 (19.6)	4	
6 weeks post	70.83 (19.7)	7	68.97 (20.0)	8	0.37*

Scale 0-100 (worst-best); HOOS: Hip Osteoarthritis Outcome Scale; QOL: Quality of Life. *Multivariate repeated measurement ANOVA with group and time as factors, the p-value refers to difference s in change over time between the two groups.

At 3 week follow up the difference between the groups was 4.7 points in favor of the RG and at 6 weeks follow up there was no difference. In the other HOOS subscales there were no significant differences between the groups (Table II). A higher proportion of the UG was capable of performing

TABLE III.—*Functional capacity of 146 patients in the restricted group (RG) and 219 in the unrestricted group (UG) 3 weeks after total hip replacement.*

ADL function	Capable % (number)	With assistive devices % (number)	Incapable* % (number)	P value
Stair climbing				
RG (24 missing)	32.8 (40)	65.6 (80)	1.6 (2)	
UG (18 missing)	51.2 (103)	47.3 (95)	1.5 (3)	0.003‡
Getting dressed				
RG (22 missing)	40.3 (50)	35.5 (44)	24.2 (30)	
UG (14 missing)	71.5 (148)	12.7 (26)	15.1 (31)	<0.001†
Bath/shower				
RG (22 missing)	67.7 (84)	19.4 (24)	12.9 (16)	
UG (14 missing)	88.3 (181)	6.8 (14)	4.9 (10)	<0.001†
House cleaning				
RG (22 missing)	37.9 (47)	22.6 (28)	39.5 (49)	
UG (14 missing)	60.0 (123)	14.2 (29)	25.9 (53)	0.001†

ADL: activities of daily living. *Incapable independently, including the answers: "capable with help" and "incapable", ‡: Fisher's exact test comparing the distribution in the two groups, †: Chi2 test comparing the distribution in the two groups.

the four different ADL functions independently 3 weeks postoperative as presented in Table III ($p<0.005$).

Anxiety and depression

In the RG 38% of the participant (N.=46) were categorized as having anxiety at baseline (HADS anxiety score>7), at 3 weeks follow up this was decreased to 4% (N.=5) and 8% at 6 weeks follow up (N.=10)

The corresponding numbers in the UG were 30% (N.=55), 9% (N.=19 and 4% (N.=8). There was no significant differences between the groups according to the HADS scores (P>0.10). In the HADS depression score the tendency was the same (data not shown).

Distribution of assistive devices

The distribution of all the different assistive devices was reduced with 37-79% in the UG compared to the RG (Figure 2).

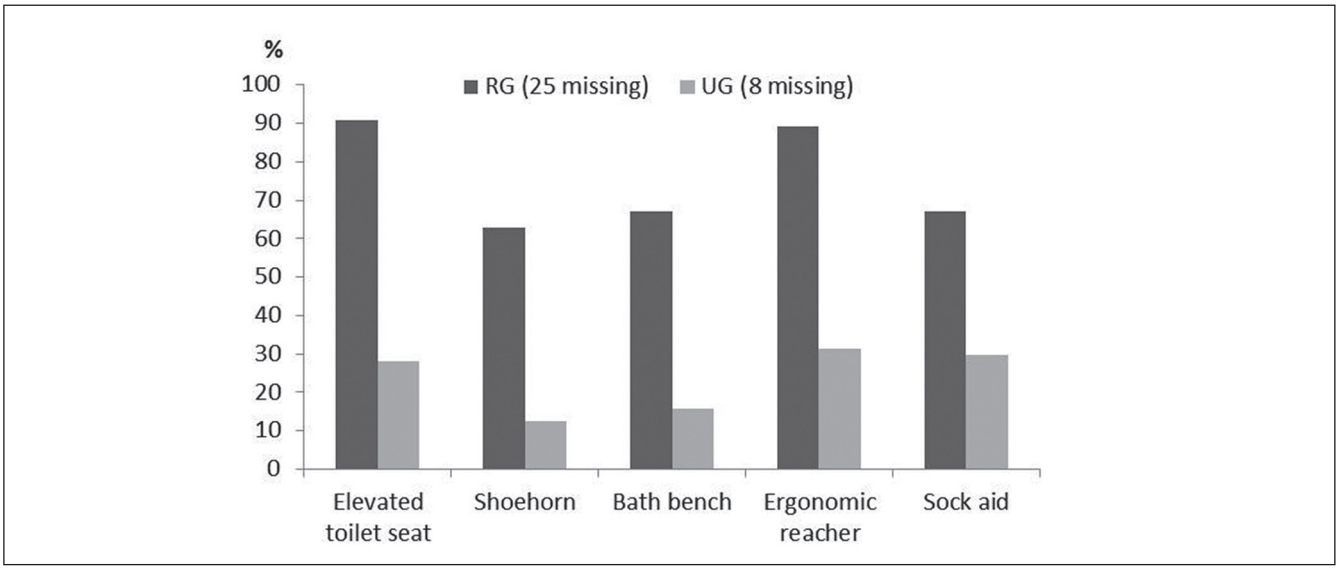

Figure 2.—Distribution of assistive devices handed out from the hospital in the restricted group (RG, N.=146) and in the unrestricted group (UG, N.=219).

Return to work

In the study population 24.9%, N.=91 (RG: N.=37~26%, UG: N.=54~26%, 9 missing) was still working or at sick leave at the time of surgery. Six weeks after surgery 32.4% (12/37) had returned to work in the RG compared to 53.7% (29/54 – 1 missing) in the UG (P=0.045).

Patient satisfaction

In the RG 95.7% (132/138) were satisfied or very satisfied with the course of treatment in the UG the corresponding number was 96% (194/202) (P=0.86, 25 missing). The willingness to repeat surgery after six weeks was 91% (N.=182/200) in the UG compared to 90% (N.=124/138) in the RG (P=0.37, 27 missing)

Hip dislocation

There was no significant difference between the hip dislocation rate in the two groups. During the 6 weeks follow up hip dislocations occurred in 2/146 (1.4%, 95%CI: 0.2; 4.9) in the RG and 6/219 (2.7%, 95% CI: 1.0; 5.9) in the UG (P=0.48). For detailed information concerning the hip dislocations, see Table IV.

Discussion

This study did not reveal beneficial effect of rehabilitation without movement restrictions on the primary outcome, patient evaluated function, as oppose to our hypothesis. The RG had the fastest improvement, but the difference was neutralized six weeks postoperative. However, the validity of this result is threatened by the substantial amount of missing values at 3 weeks follow up were the difference is present. Furthermore the amount of missing values is different in the two groups (29% in the RG *versus* 9% in the UG). If these missings are non-random, *e.g.* among the patients with more severe conditions as shown by Hutchings *et al.*[20] the results could be biased in the direction of an overestimation of the difference. In the other HOOS subscales there is no significant difference in the development over time between the groups (Table II). Missing answers seems to be selective on HOOS ADL scale with 29% missing whereas the subscale QOL has only 18%. This suggests that the nature of the questions is a part of

TABLE IV.—*Patient characteristics and circumstances for hip dislocation.*

Patient	Dislocation circumstances	Gender, age, BMI	Comorbidity	Marital status	Days after THA	Femoral head size	Prosthesis type	Surgery time	Outpatient physio
RG – 1	Lying in bed	Male, 72 years, BMI: 24 kg/m^2	ASA I Musculoskeletal disorder	Living alone	33	40 mm	Cementless	32 min	No
RG – 2	During fall out of bed	Male, 80 years, BMI: 23 kg/m^2	ASA II Thrombus + cognitive deficits	Married	3	36 mm	Hybrid	45 min	Yes
UG – 1	Putting on sockings in standing position	Female, 75 years, BMI: 28 kg/m^2	ASA II Heart/lung disease	Living alone	14	36 mm	Hybrid	40 min	No
UG – 2	Sitting down on knees	Male, 80 years, BMI: 27 kg/m^2	ASA I	Living alone	37	40 mm	Cementless	23 min	No
UG – 3	Raising from low chair that is turning at the same time	Male, 51 years, BMI: 29 kg/m^2	ASA II Musculoskeletal disorder. Later fall related dislocations under influence of alcohol consumption	Living alone	8	36 mm	Cementless	25 min	No
UG – 4	Unknown	Male, 70 years, BMI: 26 kg/m^2	ASA III Musculoskeletal disorder+ Heart/lung disease Very low functional capacity	Married	40	40 mm	Cementless	30 min	Yes
UG – 5	Unknown	Male, 66 years, BMI: 35 kg/m^2	ASA II	Married	9	36 mm	Cementless	23 min	No
UG – 6	Sitting in wheelchair	Female, 73 years, BMI: 25 kg/m^2	ASA II Musculoskeletal disorder	Married	0 – on surgery day	32 mm	Cemented	91 min	No

RG: restricted group; UG: unrestricted group; BMI: body mass index; ASA: American Society of Anesthesiologists.

the explanation; if more than 2 questions are left unanswered the subscale is defined as missing. When having movement restrictions it might be difficult to answer questions concerning activities like "getting up from a chair". All differences between the groups are below 5 points, in some studies 8-10 points has been suggested as the minimal clinical relevant difference on the HOOS ADL subscale, thus the difference in this study is not considered clinically relevant.[21, 22]

When functional capacity was evaluated by physiotherapists the results were quite different. The proportion of patients capable of performing the four ADL functions independently at 3 weeks follow-up was substantially higher 18% in the UG compared to 31% the RG. In line with results in other studies we found that perceived daily functioning (how limited the patient feels) and functional capacity (the patients' ability to perform a given activity) reflect different aspects of functioning.[23-25] We recommend the use of both patient-evaluated function and functional capacity in future studies measuring functional outcome after THR. The differences between the groups concerning functional capacity can be influenced by both less movement restrictions and less use of assistive devices, we cannot separate these effects. We found a substantial decrease in the amount of assistive devices handed out by the hospital (37-79% reduction) in the UG compared to the RG. This reduction is a component of the intervention rather than a result, but we find it relevant for clinical practice and further research that it was possible to substantially reduce the distribution of assistive devices when movement restrictions was reduced and the need for assistive devices individually evaluated. However, continued evaluation of patients' need for assistive devices seems required, since up to 30 % of the UG lent an assistive device.

There was no difference between the groups concerning anxiety and depression. Apparently, going through surgery and early rehabilitation decreased the proportion of patients with anxiety or depression, already 3 weeks after THR and hence we found a prevalence of anxiety and depression below the results from Singh *et al.*[26] measuring these conditions 2 and 5 years post THR. Also the patient satisfaction and willingness to repeat surgery was comparable and high in the two groups (90-96%), thus our study contradicts negative effect on patient satisfaction or anxiety and depression levels during unrestricted rehabilitation.

Limitations and strengths of the study

In this study multiple comparisons were made which increases the risk of type I error. Hence, the significant differences we found should be interpreted with caution and in relation to the clinical relevance of the findings. The non-randomized design induces risk of bias due to unequal distribution of confounding factors between the groups. However, the baseline characteristics indicates an equal distribution at least among the measured variables, only the educational level is significant different between the groups, but with 40 missing in this variable the conclusions are uncertain. Furthermore the short inclusion period decreases the risk of any unknown factors to have changed in the department during the study period, thus we believe that no other changes in the perioperative treatment than the investigated have influenced the results. A non-randomized design was chosen to avoid potential contamination of the intervention in the two groups. When hospitalized in the same department patients will inevitably build knowledge on the movement restrictions in the other group and this could affect their compliance to group assignment. Furthermore, willingness to participate in a randomized controlled trial (RCT) might be low due to safety issues; *i.e.*, that patients fear dislocation, as in the study by Peak *et al.* (2005) where 42% of the eligible patients refused to participate.[6]

Another disadvantage is the inability to draw conclusions concerning the safety issues regarding hip dislocation risk when using the unrestricted rehabilitation. Due to the low dislocation rates and the non-inferiority design of such a trial, it would require a very large sample size to investigate this issue. Our study found no difference between the dislocation rates among the two groups, but this should be investigated in a future study with a much larger sample size. Alternatively, the safety issue could be investigated in the national hip arthroplasty register since more orthopedic departments in Denmark have implemented unrestricted rehabilitation after THR. The lack of blinding in the study is also a concern leading to conservative conclusions concerning the ADL evaluations. However, the physiotherapist performed this evaluation as part of the standard clinical control without special focus on the regime that was ongoing at the time. In this study the follow up period is very short, thus we can only conclude

on the first 6 weeks recovery. The scope of the study was to evaluate the influence of movement restrictions and use of assistive devices, and since this was only part of the rehabilitation within the first 6 weeks we found it adequate to have this length of follow up period. There are also strengths to emphasize in this study. We included a high number of patients (N.=365) in a short time period (7 months). All THR patients in the department were asked to answer questionnaires as part of the standard hospital procedure, this we believe might decrease the risk of information bias, the patients being unaware of the study focus, thus their attitude towards unrestricted rehabilitation will not influence the results. It might also result in a broader inclusion where patients who would refuse participation in a RCT actually are included. When we report response rates it is thus the proportion of all the patients going through surgery (within the inclusion criteria) and it ranged from 71% to 93% in the RG and 85-96% in the UG (Figure 1). Overall we find these response rates satisfactory, it is when systematic differences occur between the groups in response rates we conclude it might affect the results.

We have not been able to find literature concerning rehabilitation without movement restrictions after THR using the posterior surgical approach, thus comparison can only be made to other surgical techniques. Apart from the patient evaluated function the results from this study are in line with earlier studies indicating better or equal outcomes after less restricted rehabilitation after THR using the anterolateral surgical approach.[6-9] A recent study by Barker *et al.*[27] found greater gains in the HOOS ADL score after enhanced recovery including no hip precautions compared to conventional rehabilitation with hip precautions in a sample of hip resurfacing patients. They improved from baseline score ≈50 in both groups to 6 weeks postoperative ≈70 and 80, respectively. In our sample both groups had lower scores at baseline and improved more than in their study (Table II), this indicates that we found a fairly large and rapid recovery on patient-reported function in both our groups. Our hip dislocation rates (1.4% and 2.7%) is comparable to findings from a large sample of THR performed with fast track programs for peri-operative care 3.5% (95% CI:2.49-4.85).[28] Our study was not powered to conclude concerning hip dislocations, but our results is encouraging in the sense that it seems relevant to investigate the impact of movement restrictions on hip dislocation in a larger sample. More research is needed concerning movement restriction and assistive devices when using the posterior surgical approach to make clinical recommendations. Nevertheless the great reduction in use of assistive devices we found can be useful in clinical practice; we recommend reconsidering standard packages used for this patient group.

Conclusions

This study suggests slightly slower recovery in patient reported function after reduction in movement restrictions and use of assistive devices, but the difference is eliminated after 6 weeks. Neither beneficial nor harmful effects of the less restricted rehabilitation are evident concerning patient-evaluated pain and hip-related quality of life. Yet, there is a clear trend of a beneficial effect of the unrestricted regime concerning; earlier return to work, more independency in functional capacity tests and a substantial decrease in the use of assistive devices while the dislocation rate and level of anxiety and depression is comparable to the restricted group. It seems possible to reduce the use of assistive devices considerably. More research concerning safety issues is needed to elucidate the effect of unrestricted rehabilitation on hip dislocation rates. Furthermore studies concerning the influence on patient evaluated outcomes are needed and blinded assessment of functional capacity in ADL functions is recommended.

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The present study was presented at the 8th Combined Meeting of Orthopedic Research Societies, 13-16 October 2013 and at the Danish Orthopedic Society Congress, 23-25 October 2013.

Funding.—The study was supported by the Health Research Fund of Central Denmark Region.

Acknowledgements.—The authors would like to thank the orthopedic surgeons, nurses and physiotherapists at the department for their involvement in planning and carrying out the procedure change, and the physiotherapists furthermore for their participation in the data collection.

Received on August 12, 2013.
Accepted for publication on January 22, 2014.
Epub ahead of print on January 30, 2014.

Appendix 2

Paper II

Article

CLINICAL REHABILITATION

Clinical Rehabilitation
1–10
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DOI: 10.1177/0269215514534088
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A study of the inter-rater reliability of a test battery for use in patients after total hip replacement

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Abstract

Objective: To assess the within-day inter-rater reliability of a test battery of functional performance, muscle strength and leg extension power on total hip replacement patients.
Design: A test–retest design was used.
Setting: Orthopaedic department at a Regional Hospital in Denmark.
Subjects: Two convenience samples of 20 total hip replacement patients were included.
Intervention: The tests were performed three months after total hip replacement. Two raters performed test and re-test, with two hours rest in-between.
Main measures: The test battery included: sit-to-stand performance, 20-metre maximum walking speed, stair climb performance, isometric muscle strength (hip abduction/flexion), and leg extension power. Absolute reliability was assessed with Bland Altman plots, standard error of measurement (SEM), and minimal detectable change. Relative reliability was assessed with intra-class correlation coefficient.
Results: Systematic differences between testers were seen in tests of walking speed (0.32 seconds p = 0.03) and stair climb performance (0.18 seconds p = 0.003). In per cent of the grand mean, the standard error of measurement was 3%–10%, indicating the measurement error on a group level, and the minimal detectable change was 10%–27%, indicating the measurement error on an individual level. The intra-class correlation coefficients were above 0.80 in all tests (range 0.83–0.95).
Conclusions: The tests showed acceptable relative and absolute inter-rater reliability on a group level, but not on an individual level (except from test of walking speed and stair climb performance). Systematic differences between testers were considered clinically irrelevant (0.3 and 0.2 seconds).

Keywords

Arthroplasty, measurement error, muscle strength, reliability, walking

Received: 13 January 2014; accepted: 12 April 2014

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Introduction

Total hip replacement is offered to patients with end-stage osteoarthritis to reduce their pain and improve their function.[1] Although it is generally a successful procedure, both acute and long-term deficits in muscle strength and functional performance have been documented.[2–4] No clear evidence exists to support the effect of rehabilitation interventions aimed at reducing these deficits.[5] Reliable, objective performance measures are needed in rehabilitation research and to ensure proper clinical evaluation of therapeutic outcomes. To appraise the efforts of current rehabilitation research devoted to intensive strength training after total hip replacement[6,7] it is essential to measure changes in muscle strength and lower-extremity power as well as functional performance.

Previous studies of the reliability of muscle strength and performance tests have focused on patients with osteoarthritis.[8–12] To our knowledge, no previous studies have aimed specifically at evaluating the reliability of functional performance tests after total hip replacement.

The aim of this study is to assess the inter-rater reliability of a proposed test battery that includes four lower-extremity performance tests, two isometric muscle strength tests, and one test of leg extension power in total hip replacement patients three months after surgery. Furthermore, the aim is to determine which is the more reliable of two commonly used sit-to-stand tests in total hip replacement patients: five repetitions sit-to-stand or 30 seconds sit-to-stand.

Methods

Eligible patients were contacted before their scheduled three-month postoperative outpatient visit at the hospital (convenience sample). They were given written and verbal information; and if they were willing to participate in the study, the tests were performed on the day of their hospital visit. Inclusion criteria were: 55–80 years of age and primary, unilateral total hip replacement surgery at Silkeborg Regional Hospital, Denmark, three months before testing. Exclusion criteria were: neurological diseases, inability to read or speak Danish, cognitive problems/dementia or major postoperative complications (e.g. infection, fracture, or hip dislocation). The study was conducted in accordance with the Declaration of Helsinki II and approved by the Central Denmark Region Committee on Biomedical Research Ethics (M-20090231).

All patients were tested twice on the same day by two physiotherapists (rater A and B) with a two-hour break between the tests. The test battery was divided into two for this reliability study to reduce the impact of fatigue owing to performance of all tests twice on the same day. Thus, we performed the reliability study on two patient samples. The physiotherapists underwent training and pilot testing of the standardised test procedures before the study was initiated. Each patient was randomized to whichever physiotherapist performed the initial testing. Sealed envelopes were used for randomization to rater A or rater B as the first tester (1:1). During the second test, the rater was blinded to the results of the previous test. Sample 1 performed test–retest of each of the following tests: five repetitions sit-to-stand, 30 seconds sit-to-stand, stair-climb test and isometric strength test in hip abduction and flexion. Sample 2 performed the leg extension power test using the Leg Extensor Power Rig and a 20 metre walk test.

Measurements

Five repetitions sit-to-stand

The test is a part of the Osteoarthritis Initiative[13] and it is often used in patients with osteoarthritis and after total hip replacement.[14–16] Patients were seated on a standard chair (seat height: 44 cm) with their arms crossed over the chest and the back touching the back rest. They were instructed to rise to a fully extended position and to sit again, five times as quickly as possible. The better of two trials, with 30 seconds rest in-between, measured to the nearest 0.01 second was used as the data point. If the patient was unable to rise from the chair five times, the test could not be completed.

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30 seconds sit-to-stand

The 30 seconds sit-to-stand test is widely used in patients with osteoarthritis and after total joint replacement.[17–21] The chair and the starting position were as described above. The patient was instructed to perform as many rises as possible in 30 seconds. The physiotherapist counted the rises out loud and stopped the patient after 30 seconds. The number of rises to a fully extended position was used as the data point. If a single rise was impossible, the score was 0. The better of two trials, with 30 seconds rest in-between, was used as the data point.

20 metre walking test

The test is a part of the Osteoarthritis Initiative[13] and is used in recent studies on patients with hip and knee osteoarthritis.[14,15] Patients started in a standing position behind the starting line and walked 20 metre as fast as possible towards a cone two metres beyond the end-point line. This procedure measures acceleration, but not deceleration. The better of two trials, with 30 seconds rest in-between, measured to the nearest 0.01 seconds, was used as the data point.

Stair-climb test

Stair-climbing performance has been suggested and used when measuring functional performance in hip osteoarthritis patients[12,22] and after total hip replacement.[16,23,24] Participants were instructed to ascend nine steps (16.5 cm high) as fast as possible without using the handrail. The better of two trials, with 30 seconds rest in-between, measured to the nearest 0.01 seconds, was used as the data point.

Leg extensor power

Leg extension power is highly correlated with functional performance and the risk of falling[17,25–27] and it has been used in hip osteoarthritis patients,[8] and after total hip and knee replacement.[15,17,18] The Nottingham Power Rig (University of Nottingham Mechanical Engineering Unit, UK) was used to measure leg extension power that was expressed as the product of force and velocity in a single-leg simultaneous hip and knee extension. Patients were seated with their arms crossed, the operated leg placed on the footplate, and the other foot resting on the floor. They were asked to push the pedal down as hard and fast as possible; we used a sound file with the verbal command to avoid that the voice and the accentuation of the tester would affect the test performance. The power was recorded for each push (30 seconds rest between trials) until they reached a plateau defined as two successive measurements below the highest measurement. A minimum of six trials to minimise learning effect, and a maximum of 12 trials to minimise fatigue, were obtained and the highest measurement in watt was used as the data point.

Isometric strength test in hip abduction and flexion

Isometric hip strength was tested with the handheld dynamometer, Power Track II Commander (JTECH Medical, Salt Lake City, UT, USA). Handheld dynamometer testing of lower extremity muscle strength is suggested as a valid measurement for evaluating orthopaedic patients,[28] and it is applied in osteoarthritis patients[10] and after total joint replacement surgery.[17,29] We used standardised test procedures as described by Thorborg et al.[30] Additionally, we used a sound file with the verbal command to avoid that the voice and the accentuation of the tester would affect the test performance. The test consisted of a five-second isometric maximum voluntary contraction against the dynamometer. The test was repeated with a 30-second rest in-between until a plateau was reached, which was defined as two successive measurements below the highest. A minimum of four tests were required to minimise the learning effect and a maximum of 10 to minimise fatigue. The highest score, measured in Newtons, was used as the data point.

Hip abduction was measured in a supine position with the participants stabilising themselves with their hands holding on to the sides of the table.[30] The participant pressed as hard as possible

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Table 1. Patient characteristics in two samples of patients three months after total hip replacement.

	Sample 1 (n = 20)	Sample 2 (n = 20)
Sex, men/women	11/9	11/9
Age, mean ±SD	66.2 ± 8.2	68.4 ± 5.1
BMI, mean ±SD (kg/m^2)	27.8 ± 4.1	28.0 ± 3.1
THR side, right/left	12/8	12/8

BMI: body mass index; THR: total hip replacement.

towards the dynamometer placed 5 cm proximal to the lateral malleolus with the hip in neutral position. Hip flexion was measured in a sitting position with the hip at 90° of flexion and the participant holding on to the sides of the table with both hands. The resistance was applied 5 cm proximal to the proximal edge of the patella against hip flexion.

Sample size

We defined an intra-class correlation coefficient (ICC) level >0.8 to be satisfactory. Often 0.7 is defined as acceptable,[31] but owing to expected variability in the scores, we decided on this more conservative cut-off level. With two raters, acceptable ICCs of 0.8, and a 95% CI (confidence interval) of ±0.2, a sample size of 13 subjects is required.[32] To decrease the uncertainty of the results and to increase generalisability, we decided to include 20 subjects for each sample.

Statistics

Statistically significant differences in test results between the two trials were analysed with paired t-tests as data were normally distributed. In accordance with published guidelines for reporting reliability and agreement studies, reliability was investigated in terms of test–retest reliability and measurement error.[33] The agreement between the tests was examined by a Bland Altman plots.[33] Identification of the mean difference with 95% CI and limits of agreement were included in the plots. The standard error of measurement (SEM), which represents the typical error in a single measurement,[34] was calculated by the equation SD/√2. The minimal detectable change defined as the measure of statistically significant change between two measurements,[34] was calculated by the equation $1.96 \times \sqrt{2} \times$ SEM. For a statistically significant change between two observations to be detected, the change must be at least the minimal detectable change. SEM and minimal detectable change (MDC) are presented in actual units, but they are also expressed as a percentage of the mean of the two test sessions (grand mean), making comparisons between tests and studies easier.[35] The relative reliability was calculated using the ICC model 2.1. The ICC is a ratio of the variance between subjects over the total variance. The ICC 2.1 is a fixed model addressing both systematic and random error.[36] The significance level was 0.05. A STATA 12.1 (StataCorp, College Station, TX) software package was used for data analysis.

Results

Two samples, each consisting of 20 subjects, were included in the period November 2010–May 2011. Of 87 eligible total hip replacement patients, 44 (51%) refused to participate in the study, the majority owing to lack of time on the scheduled day. Three patients withdrew consent to participate before commencement of the tests, leaving 40 patients (20 in each sample) that completed the study. Patient characteristics concerning the two samples are presented in Table 1. One patient in Sample 1 was not able to complete the last test (stair-climb test) in the second test session owing to fatigue; thus, 19 participants are included in the analysis on stair-climb test. Otherwise there was no missing data.

As seen in Table 2, there were systematic differences between the test results from rater A and B concerning the 20 metre walk test (0.32 seconds, p = 0.03) and stair-climb test (0.18 seconds p = 0.003). In the remaining tests, no significant differences

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Table 2. Power, muscle strength, and functional performance in two samples of 20 patients three months after total hip replacement measured by two raters.

Test	Rater A mean±SD	Rater B mean±SD	Difference mean±SD	*P* value (*t*-test, diff.)
Leg extension power (Watt)	127.3±37.2	125.3±42.6	–2.0±17.6	0.62
Hip abduction strength (Newton)	93.7±24.2	97.1±25.7	3.4±9.2	0.11
Hip flexion strength (Newton)	221.9±55.0	227.9±50.3	6.0±30.9	0.40
20 metre walk test (seconds)	12.4±2.3	12.1±2.1	–0.3±0.6	0.03
Stair test (n = 19) (seconds)	3.8±0.6	4.0±0.7	0.18±0.2	0.003
Sit-to-stand-30 seconds (repetitions)	14.4±2.9	14.3±2.8	–0.2±1.4	0.64
Sit-to-stand-5 repetitions (seconds)	10.6±2.1	10.5±2.1	–0.2±1.2	0.52

were present; test results and differences with corresponding SDs and *p*-values are shown in Table 2. Bland Altman plots with 95% limits of agreement for all seven tests are shown in Figure 1. The plots for leg extension power and hip abduction strength test showed signs of heteroscedasticity. Data on absolute and relative reliability are presented in Table 3. The SEM in per cent of the grand mean ranged between 3% to 10%, indicating the measurement error on a group level. The MDC in per cent of the grand mean ranged between 10% and 27%, indicating the measurement error on an individual level. The relative reliability measured by ICC were above 0.80 in all the tests (range 0.83–0.95) with the 20 metre walk test having the highest ICC and hip flexion strength the lowest. The absolute and relative reliability of the 30 seconds sit-to-stand compared with five repetitions sit-to-stand was; ICC: 0.88 vs. 0.84, SEM(%): 7 vs. 8, MDC(%): 20 vs. 22.

Discussion

The proposed test battery showed acceptable relative and absolute inter-rater reliability on a group level when applied on patients three months after total hip replacement. The most important limitation of the present study is the small sample size, and a probable selection of the well-functioning patients potentially affecting the generalisability of the findings. The strengths of the study encompass its randomization, blinding, same-day test and re-test, and repetitive test procedures to counteract learning effect.

Study strength and limitations

It is recommended to include around 50 participants in reliability studies.[31] Hence, the sample size is considered a limitation in the present study even though calculated sample size requirements were fully met. Furthermore, the generalisability of the results may be influenced by potential selection of well-functioning patients, because patients older than 80 years and patients with neurological or cognitive co-morbidity were excluded. Only 49% of the eligible patients accepted participation, and often the frailest patients decline participation, which may compromise the external validity of the study. However, the main reason for non-participation in the present study was lack of time on the test day, indicating this selection bias may be less pronounced. A study strength is that the test battery was divided and applied on two samples of patients to counteract the influence of fatigue, which is a well-known problem in this type of testing.[8] The standardisation of verbal commands by use of a simple sound file played on a computer is considered an easy and effective method to reduce the impact from the rater's voice and accentuation. Problems with inter-rater reliability using a hand-held dynamometer on healthy adults have been reported owing to influence of gender and strength of the rater.[37,38] When measuring patients with affected lower-limp strength, as after total hip replacement, the problem of adequate rater-strength might be less outspoken.

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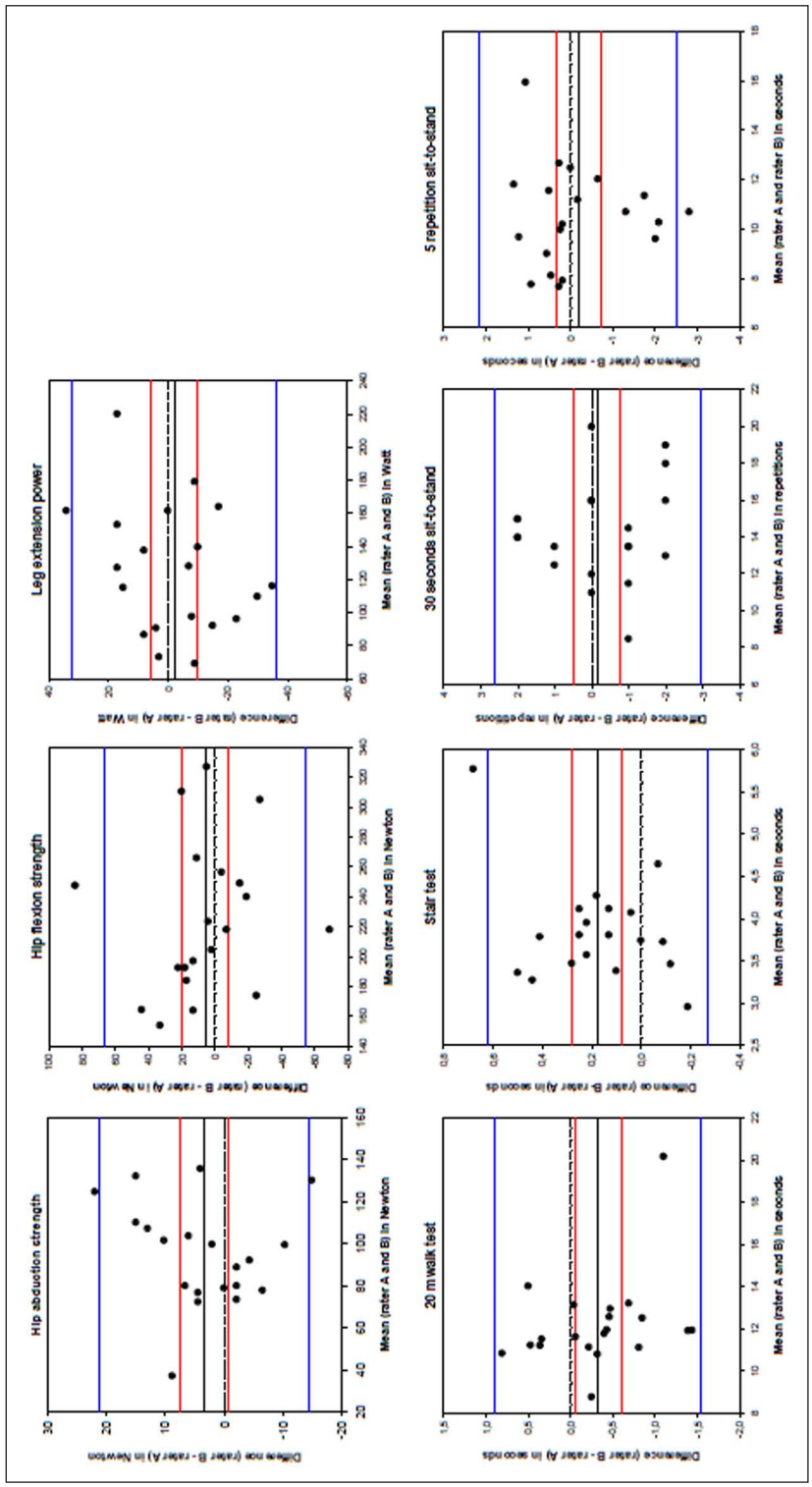

Figure 1. Bland Altman plots with limits of agreement for seven different performance tests.
Mean difference between testers (black line) with 95% CI (red lines) and limits of agreement (blue lines). The dotted black line, Y = 0 indicates perfect average agreement.

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Table 3. Measures of relative and absolute inter-rater reliability of seven tests of power, muscle strength, and functional performance in two samples of 20 patients three months after total hip replacement.

Test	ICC [95% CI]	SEM (%)	MDC (%)
Leg extension power (Watt)	0.91 [0.83;0.99]	12.4 (10)	34.4 (27)
Hip abduction strength (Newton)	0.93 [0.86;0.99]	6.5 (7)	18.0 (19)
Hip flexion strength (Newton)	0.83 [0.69;0.97]	21.8 (10)	60.5 (27)
20 m walk test (seconds)	0.95 [0.91;0.99]	0.4 (3)	1.2 (10)
Stair test (n=19) (seconds)	0.90 [0.81;0.99]	0.2 (5)	0.4 (10)
Sit-to-stand-30sec (repetitions)	0.88 [0.78;0.98]	1.0 (7)	2.8 (20)
Sit-to-stand-5rep (seconds)	0.84 [0.71;0.97]	0.8 (8)	2.3 (22)

ICC: intra class correlation coefficient; MDC: minimal detectable change; MDC(%): MDC in per cent of the mean of two test sessions; SEM: standard error of measurement; SEM(%): SEM in per cent of the mean of two test sessions.

The relative reliability of the entire test battery, estimated with ICCs, ranged from 0.83 to 0.95 (Table 3). This would, by most suggested ranking systems, be classified as excellent reliability.[32,39,40] Systematic differences between raters were seen in the 20 metre walk test and stair-climb test ($p < 0.05$), which indicates that these tests might be influenced by raters. However, these differences are considered small and clinically irrelevant (0.3 and 0.18 seconds). There is no consensus concerning cut-off levels for acceptable absolute reliability, but a SEM(%) of 10% has been suggested[41] and is used in this study. The absolute reliability in the functional performance tests was acceptable with SEM less than one second in the timed tests and one repetition in the 30 seconds sit-to-stand, corresponding to measurement errors of 3%–8% of the grand mean (Table 3). Likewise, the absolute reliability of the power and strength measurements is considered acceptable on a group level with measurement errors of 7%–10% (Table 3). Thus, changes on a group level above these values can be considered real changes and not a result of measurement error. When measuring changes on an individual level, as in a clinical setting, only the 20 metre walk test and the stair-climb test are considered suitable with a MDC of 0.4 and 1.2 seconds, corresponding to changes of 10% in both tests. The remaining tests were considered inappropriate to measure changes on an individual level owing to the large values of MDC (19%–27%) (Table 3).

This study revealed comparable but slightly better absolute and relative reliability of 30 seconds sit-to-stand than of the five repetitions sit-to-stand (Table 3). An advantage of the 30 seconds sit-to-stand is the possibility to score frail patients who may be unable to complete five chair rises. Furthermore, the possible result '0' (not being able to perform a single chair stand) from the 30 seconds sit-to-stand test result enables analysis on a ratio scale rather than an interval scale allowing for extended statistical evaluations. Thus, the 30 seconds sit-to-stand test is recommended as the preferred chair stand performance test after total hip replacement, especially if weak patients or early postoperative measurements are included. This finding is in line with the newly published recommendations for functional testing on patients with hip and knee osteoarthritis, where the 30 seconds sit-to-stand test is recommended.[42]

Comparison with other studies

This study presents better reliability in the leg extension power test (ICC 0.91 and MDC 34 W) than a recent study on hip osteoarthritis patients (ICC 0.72 and MDC 43 W).[8] This is surprising because their study is an intra-rater study where reliability is usually higher than in inter-rater studies. This difference could be explained by the disparity between the included patients (pre vs. post total hip replacement) or it could be a result of the standardised verbal commands in the present study. In the functional tests, our results are in line with their findings; 20 metre walk test (ICC: 0.95 vs. 0.98, MDC: 1.2 vs. 1.7 seconds) and five repetitions sit-to-stand (ICC: 0.84 vs. 0.89, MDC: 2.3 vs. 2.7 seconds).[8]

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The relative reliability of isometric strength test in the present study is comparable with those from a pilot test of inter-rater reliability in connection to an intervention study on total hip replacement patients.[43] We found equal ICCs of 0.93 for hip abduction strength and comparable ICCs for hip flexion 0.83 vs. 0.88. The hip abduction strength test showed slightly better relative reliability than the hip flexion in both studies and also the absolute reliability is superior for the hip abduction test compared with the hip flexion test in the present study (Table 3). It is difficult to compare stair climbing tests because of differences in the local facilities, for example concerning step height and number of steps.

There is a need for standardisation of functional measurements in the field of rehabilitation research after total hip replacement to enable comparison of study results in meta-analyses.[23,44] This study adds to the sparse literature on this field and suggests a reliable test battery for evaluating physical performance after total hip replacement. More research is needed to establish which tests have the highest validity and reliability in measuring different aspects of functioning after total hip replacement.

Clinical message

- A test battery of the 20 metre walk test, sit-to-stand test, stair-climb test, leg extension power, and isometric strength in hip abduction and flexion showed acceptable relative and absolute inter-rater reliability on a group level (3%–10% measurement error), but not on an individual level (10%–27% measurement error).

Contributors

All authors were involved in initiating and designing the study. LRM was responsible for collecting and analysing the data, and overall responsible for the decisions made in this study. IM, KS, and AKP contributed with supervision on the overall use of methods, the data analysis, and interpretation of data. SM had special focus on the patients and was involved in the practical, organizational parts of the study. LRM wrote the initial draft of the article, and all co-authors contributed to critical revision of the article.

Acknowledgements

The authors would like to thank the physiotherapists and patients that participated in the tests during this study. We also thank Thomas Bandholm, Senior Researcher, PhD, for valuable feedback.

Conflict of interest

All authors declare that they have no conflicts of interest

Funding

The study was supported by grants from The Lundbeck Foundation Centre for Fast-Track Hip and Knee Arthroplasty, The Health Research Fund of Central Denmark Region, The Danish Rheumatism Association, The Association of Danish Physiotherapists, The Health Foundation and Aase and Ejnar Danielsens Foundation.

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Appendix 3

Paper III

Title page

Title

Effect of early supervised progressive resistance training compared to unsupervised home-based exercise after fast-track total hip replacement applied to patients with preoperative functional limitations. A single-blinded randomised controlled trial

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Running title

Resistance training early after THR

Abstract

Objective

To examine if 2 weekly sessions of supervised progressive resistance training (PRT) in combination with 5 weekly sessions of unsupervised home-based exercise is more effective than 7 weekly sessions of unsupervised home-based exercise in improving leg-extension power of the operated leg 10 weeks after total hip replacement (THR) in patients with lower pre-operative function.

Method

A total of 73 patients scheduled for THR were randomised (1:1) to intervention group (IG, home based exercise 5 days/week and PRT 2 days/week) or control group (CG, home based exercise 7 days/week). The primary endpoint was change in leg extension power at 10 week follow up. Secondary outcomes were isometric hip muscle strength, sit-to-stand test, stair climb test, 20 meter walking speed and patient-reported outcome (HOOS).

Results

Sixty-two completed the trial (85%). Leg extension power increased from baseline to the 10 week follow up in both groups; mean [95% CI] IG: 0.29 [0.13;0.45] and CG: 0.26 [0.10;0.42]W/kg, with no between-group difference (primary outcome) (P=0.79). Maximal walking speed (P = 0.008) and stair climb performance (P = 0.04) improved more in the IG compared to CG, no other between-group differences existed.

Conclusions

In this trial, supervised PRT twice a week in addition to 5 weekly sessions of unsupervised exercise for 10 weeks was not superior to 7 weekly sessions of unsupervised home-based exercise for 10 weeks in improving the primary outcome, leg-extension power of the operated leg, at the primary endpoint 10 weeks after surgery in THR patients with lower pre-operative function.

Trial registration: NCT01214954

Keywords

- Total hip replacement
- Progressive resistance training
- Rehabilitation
- Randomised controlled trial

Introduction

Loss of muscle strength and functional performance as well as long term postoperative deficits has been reported after total hip replacement (THR)[1-9]. These deficits include reduced; muscle strength[1, 2], walking symmetry[6, 8, 10], patient-reported outcomes[4, 5, 9] and functional performance such as walking speed and chair rise performance[3, 4]. No clear evidence exists on how to reduce these deficits[11], and rehabilitation strategies after THR are often experience-based[11, 12]. Given the immediate loss of muscle strength[7, 13-15] and muscle mass post-surgery,[14, 16]progressive resistance training (PRT) has been advocated to be initiated shortly following surgery[2, 6, 7, 10, 17]. Studies indicate that PRT can be initiated early after THR, and that it seems to be more effective in improving muscle strength compared to less intensive training interventions[14, 18]. However, these studies[14, 18] have had small sample sizes (11 and 12 in the PRT group, respectively) and include few exercises (knee extension[14], leg press[14, 18] and hip abduction[18]). Since loss of muscle strength has been reported for the hip flexor and extensor muscles[1, 2, 7, 13, 19] PRT should likely address these muscle groups in addition. Muscle impairment measured as leg extension power is closely related to functional performance in elderly with functional limitations and among total knee replacement patients[20, 21]. Because THR patients with low levels of perceived function preoperatively achieve inferior levels of perceived function postoperatively, it has been suggested to target supervised rehabilitation to this subgroup of patients[22, 23].

Consequently, the objective of this trial was to examine if 2 weekly sessions of supervised PRT in combination with 5 weekly sessions of unsupervised home-based exercise is more effective than 7 weekly sessions of unsupervised home-based exercise in improving leg-extension power of the operated leg 10 weeks after THR in patients with lower pre-operative function

Methods

The study is an assessor-blinded randomised controlled trial, with 1:1 allocation ratio.

Participants

Eligible patients attending the Elective Surgery Centre, Silkeborg Regional Hospital, Denmark were consecutively included in the study. Inclusion criteria were: Primary unilateral THR for hip osteoarthrosis (OA), preoperative HOOS ADL ≤ 67, age > 18 years, residence within 30 km from the

hospital and willing to participate in training twice a week for 10 weeks. The cut off level on The hip dysfunction and osteoarthritis outcome score questionnaire (HOOS 2.0) ADL score (described in method section) was specified according to the 75th percentile in a previous study[15]. The rationale for choosing this cut-off was a settlement between including the most disabled patients while maintaining a feasible patient inclusion. Exclusion criteria were: Resurfacing hip implant, body mass index (BMI) >35, pre-planned supervised rehabilitation, pre-planned contralateral THR within 6 months, inability to speak or read Danish and mental or physical conditions impeding the intervention. Eligible patients were informed about the study during preoperative ambulant visit at the hospital and a minimum of two days of consideration time was offered. Written informed consent was obtained and ethical approval was obtained from the Central Denmark Region Committee on Biomedical Research Ethics (VEK M-20090231). The study was approved by the Data Protection Agency (Journal number: 2010-41-4907) and pre-registered at ClinicalTrials.gov (NCT01214954).

Randomisation

Block randomisation was performed using random block sizes of 4 or 6 patients. Stratification for contralateral THR was performed to ensure an equal distribution between the groups. Sequence in permuted blocks with equal numbers of “intervention” and “control” assignments was obtained using a simple “shuffling envelope” procedure before study initiation by a secretary not involved in the study. During admission, staff and patients were blinded to randomisation. Shortly before discharge a project nurse obtained the sequentially numbered, opaque, sealed envelope containing the patient’s assigned intervention and informed the patients about group assignment.

Standard peri-operative care

All patients followed a multimodal fast-track surgical program for THR including: patient information, spinal anesthesia, optimized multimodal pain management, enforced mobilization and nutrition. All patients were prior to surgery thoroughly informed about the expected course of their operation and rehabilitation, and encouraged to take active part in the treatment and rehabilitation. On surgery day patients were admitted to hospital and the surgery was performed by one of seven experienced orthopaedic surgeons using the posterior approach[24]. Patients were

subsequently discharged to their home when meeting pre-defined functional discharge criteria; independency in gait, transfer, personal care and home-based exercise and sufficient pain treatment – typically on the second postoperative day (Table 2). During admission, physiotherapy was provided daily aiming at achievement of the discharge criteria. After discharge two outpatient visits with the physiotherapist was offered to all patients (four and 10 weeks after surgery).

Rehabilitation interventions

Progressive resistance training

The PRT was initiated within the first week after surgery and performed twice a week for 10 weeks in the intervention group. The training duration was established by balancing feasibility and effect. The PRT sessions were conducted in a public fitness centre near the hospital with one-to-one supervision by physiotherapists from the hospital sub-specialized in PRT. Patients warmed up on a stationary bike for 5-10 minutes and then performed unilateral PRT of the operated leg for 30-40 minutes. Resistance exercises consisted of hip extension, knee extension (replaced by leg press at week six), hip flexion and hip abduction in strength training machines (Technogym, Pedan A/S, DK). The relative load increased during the 10 weeks, (10-12 repetition maximum (RM) to 8 RM). The absolute training load (kilograms lifted) was adjusted on a set-by-set basis for all exercises, using contraction to failure in every set. The PRT training modality is documented in Table 1, using the strength training descriptors suggested by Toigo and Boutellier.[25]

Home-based exercise

The standardised exercise program consisted of unloaded exercises in the movement directions: hip flexion, -extension, -abduction and knee flexion/extension. Patients were recommended to perform one set of 10 repetitions twice a day in their maximum possible range of motion. The control group (CG) was recommended to perform the exercises seven days a week and the intervention group (IG) was recommended to perform the same exercises 5 days a week and omit these exercises on the days with PRT. All patients were encouraged to supplement the hip exercises with aerobic training on a stationary bike or by walking. At the outpatient visit four week postoperative, the physiotherapist introduced the patients to perform the exercises with a sports rubber band to increase the relative load in the movement directions described above.

Furthermore, exercises were individually adjusted if needed, for example if a flexion contracture was identified, then muscle stretching was prescribed. At the 10 week follow up visit patients in both groups were encouraged to continue their home-based training and gradually return to their usual activities. The rehabilitation in the control group reflected standard care at the hospital.

INSERT Table 1

Outcome measures

Three physiotherapists collected all data (tests and questionnaires) at the hospital. Blinding of assessors was accomplished by randomising late during hospital stay, performing the PRT in other facilities than the tests and requesting the patients not to mention their group assignment to the assessors. These physiotherapists were trained and calibrated before study initiation. All outcome measurements were performed at baseline, typically 1-2 weeks prior to surgery, after the intervention period to investigate immediate effects (primary endpoint), and after six months to evaluate follow-up effects. Furthermore, the least demanding physical tests (isometric muscle strength and gait speed, see description below) were performed four weeks postoperative in order to evaluate early changes in physical performance. The methods used in the physical tests have acceptable relative and absolute inter-rater reliability (ICC>0.8 and SEM<10%)[26].

Primary outcome measure

The primary outcome was defined as the change in leg extension power from baseline to 10 week follow up in the unit W/kg body mass. Leg extension power was chosen as the primary outcome to capture changes in muscle performance relevant for functional performance, because it is highly correlated with functional performance, mobility and risk of falling[20, 21, 27, 28]. Shortly after knee replacement surgery significant correlations to walking speed and chair rise performance have been reported: rho= 0.82, P<0.001 and 0.74, P<0.001[20]. The Nottingham Power Rig (University of Nottingham Mechanical Engineering Unit, UK) was used to measure leg extension power expressed as the product of force and velocity in a single-leg simultaneous hip and knee extension[29, 30]. Subjects seated in the rig with arms folded gave maximal push against a footplate attached to a flywheel. Power output was derived from the acceleration of the flywheel and was

recorded in Watts. This measurement has previously been used to assess muscle power in hip OA patients[31] and after total hip and knee replacement[20, 32, 33]. A sound file with the verbal command was used to avoid voice and accentuation affecting the test performance. The test was repeated with 30 seconds rest between trials until a plateau was reached, defined as two successive measurements below the highest. A minimum of six trials to minimize learning effect, and a maximum of 12 trials to minimize fatigue were obtained and the highest measurement in watt was normalized for body weight in kg and used as the data point. The inter-tester reliability of this measurement procedure is acceptable with ICC=0.91 (95% CI: 0.83;0.99) and measurement error (SEM) of 10 % (corresponding to 12.4 W)[26].

Secondary outcome measures

Maximum walking speed was measured with the 20-m walk test, which is a part of the Osteoarthritis Initiative[34], and used in recent studies on patients with hip and knee OA[33, 35].

Chair rise performance was measured with the 30-second sit-to-stand test which is widely used as a functional performance measure in patients with OA and after total joint replacement[20, 32, 36-38].

Stair-climb performance is suggested and used when measuring functional performance in hip OA patients[39, 40] and after THR[14, 41, 42]. Participants ascended two sections of nine steps (16.5 cm high) as fast as possible without using the handrail.

Hand-held dynamometer (HHD) testing of lower extremity muscle strength is suggested as a valid measurement for evaluating orthopaedic patients[43] and has been applied in OA patients[44] and after total joint replacement surgery[15, 20]. Isometric strength in hip abduction and flexion was tested with the HHD Power Track II Commander (JTECH Medical, Salt Lake City, UT, USA). Standardised test procedures as described by Thorborg *et al*[45] were used. Additionally, we used a sound file with the verbal command to avoid that the voice and the accentuation of the tester would affect the test performance. The measurement in Newton was normalized for leg length and body weight and used as the data point.

HOOS 2.0 [46] was used to measure patient reported outcome in the following subscales; Symptoms, pain, activities of daily living (ADL), function in sport and recreation and hip related quality of life (QOL). HOOS is valid and reliable when evaluating patients undergoing THR[46]. Scores range from 0 to 100, where 100 represent the best possible score. HOOS was administered at two-, four-, six- and 10 weeks and at six- and 12 months. The subscale function in sport and recreation was not considered relevant at the earliest three measurements times after THR.

Deviations from the approved protocol and trial registration

Gait symmetry assessed by instrumented gait analysis was listed in the trial registration. These data have been collected in a subsample of patients in both treatment arms as an embedded mechanistic study, and will be reported later. Hip pain (0-100 mm VAS) and training load (kilograms lifted) has been recorded for all strength training exercises at every training session for the first four weeks in the IG only, but was not listed in the trial registration. These data were collected to indicate symptom exacerbation in the first weeks of PRT – which was not the case – and will be reported in detail later.

Sample size

Sample size calculation was based on earlier obtained leg extension power data from patients 3 months after THR (mean ± sd: 1.78 ± 0.49 Watt/kg). The expected difference in effect between intervention and control group was defined as 20% as suggested by Cochrane Musculoskeletal Group[47]. With a significance level of 0.05 and a power of 80%, the required sample size was 60. Based on an expected 15-20% drop out; 73 patients were included.

Statistical analysis

Normally distributed data are described by means and standard deviation (SD), and data not normally distributed by medians and interquartile range (IQR). The primary analysis used intention-to-treat principle including all randomised participants on the primary outcome; leg extension power. Data were analysed by a mixed model with a random person level and systematic effects of time, group and the interaction between time and group. The remaining group comparisons were extended per-protocol analysis using non-missing values only (no

imputations). Patients who discontinued the intervention were encouraged to participate in the follow up test anyway, and those who accepted were included in the analyses according to their original group assignment (see Figure 1). Groups were compared regarding changes over time using multivariate repeated measurement ANOVA with group and time as factors. The assumption of homogeneity in standard deviations and correlations was tested, and approximate test allowing for heterogeneity was used when appropriate. For model validation, histograms and probability plots of the data distribution at each measurement time and differences in each group were inspected and approved. The within-group changes between baseline and 10 week follow up were tested using Student's t-test (one-sample). Data were double entered and validated in EpiData 3.1 (Epidata association, Odense, Denmark). The statistical analyses were performed using STATA 12.1 (StataCorp, College Station, TX) software package. The significance level was set at 0.05.

Results

In the period September 2010 to November 2012, eligible patients were consecutively enrolled in the study. The participant flow is shown in Figure 1. In total, 73 patients were randomised to either IG (n=37) or CG (n=36). After randomisation, two patients in each group withdrew consent, and seven were excluded due to major events such as hip fracture. None of these events were associated with the rehabilitation (Figure 1).

INSERT Figure 1
INSERT Table 2

The baseline characteristics were comparable in the two groups, however three patients in the CG were hospitalized 3 days or more and none in the IG (Table 2). In 8 cases (=13%) the assessor-blinding failed, due to the patient revealing their group assignment during test.

Primary outcome measure

The intention-to-treat analysis on the primary outcome showed no statistically significant between-group difference at 10 week follow when adjusting for the baseline value (P = 0.79, Table 3). In both groups, statistically significant increases in leg extension power were achieved: mean

[95% CI] IG: 0.29 [0.13;0.45]and CG: 0.26 [0.10;0.42]W/kg, corresponding to relative improvements of 21% and 17%, respectively.

Secondary outcome measures

For the secondary outcomes, there were statistically significant effect of group over time in maximal walking speed (*P* = 0.008) and stair climb performance (p=0.04) in favor of the IG, and no difference in the remaining outcomes (Table 3). The relative improvements in the IG at 10 week follow up reached 18-26% in isometric muscle strength and 21-26% in the functional performance tests. The corresponding improvements in the CG were 4-12% and 11-20%. The scores on the HOOS subscales at each measurement time are presented in Table 4. There was no significant difference between groups over time in any of the subscales (*P*-value range: 0.31-0.90). Ceiling effect, defined as score= 100 in ≥ 20% of patients, was present in the pain subscale at 10 week follow up and in the other subscales at six month follow up, except from the subscale sport/recreation where ceiling effects appeared only at one year follow up. All secondary outcomes improved significantly from baseline to 10 week follow up in both groups except for hip flexion strength in the CG (Table 3 and 4).

Training compliance

The patients in the IG attended a median of 19 PRT sessions (IQR: 18;20). The resistance training was initiated median 5 (IQR: 5;6) days after surgery, postponed initiation was due to readmission for blood transfusion (n=1), wound oozing (n=1) and lack of energy (n=1). Home-based exercise was self-reportedly performed median 5 (IQR:4-7) days a week in the IG as prescribed and 6 (range: 4-7) days a week in the CG, where 7 days a week was prescribed.

Adverse effects

During PRT, five patients experienced adverse effects during or after training sessions. Two patients had discomfort and dizziness due to hypotension; regulation of their anti-hypertensive medication solved the symptoms. In one patient, an accumulation of blood burst during the third training session, the bandage was changed and no further complications were observed. One became nauseous and vomited after the training session; this was a well-known phenomenon for

her during physical exertion due to an earlier tumor in the brain, and led to discontinuation of the PRT. Knee pain in the contra-lateral leg also led to discontinuation of the PRT in one patient. In total, two patients discontinued the intervention due to adverse effects; they participated in follow up visits and are included in the analysis.

Discussion

Primary outcome: leg extension power

The main finding of the present study was no superior effect of 2 weekly sessions of supervised PRT in combination with 5 weekly sessions of unsupervised home-based exercise in improving leg-extension power of the operated leg 10 weeks after surgery, when compared to 7 weekly sessions of unsupervised home-based exercise in patients with THR, who had lower pre-operative function. Results from the intention-to-treat and extended per protocol analysis on leg extension power were similar, indicating no systematic bias due to drop outs.

The result is in contrast to earlier smaller studies that have reported substantial additional effect of supervised resistance training compared to control groups performing home-based exercise with no external resistance and weekly supervision for 12 weeks[14] or supervised exercises with low or no external resistance 3-5 times a week for 4 weeks[18] on muscle performance – but not on leg extension power, specifically[14, 18]. It may be explained by the implementation of fast-track THR surgery, involving early mobilization and enhanced recovery of patients included in the present study, as opposed to the patients included in the previous studies. This study demonstrated changes in muscle strength and power after PRT (18-26%) comparable to changes in isokinetic quadriceps strength after 12 weeks of PRT after THR (22-28%) [14]. In that study, as well as the study by Husby *et al*[18], the control group showed a reduction or no change in muscle strength during the intervention period. That is opposite to the CG in the present study, where muscle strength and power increased by 4-16%, reaching statistical significance in leg extension power and hip abduction strength (Table 3). Furthermore, recent studies that have not applied PRT indicates that hip strength does not improve from the preoperative level during the first two to three months after THR[1, 7]. Hence, the CG in the present study showed larger improvements in muscle power and strength during 10 weeks of home based exercises than expected based on the current

literature, despite the inclusion criteria of HOOS ADL ≤ 67 points. However, our results are in line with earlier findings of 21-23% improvement in hip abduction strength during 12 weeks of home based exercise after THR using fast-track procedures[15]. It is possible that faster improvements than those already obtained by fast-track surgery and home-based exercise are not conceivable or requires more comprehensive interventions. Another theoretical explanation of the lack of additional effect of PRT is surgery-induced inhibition of muscles close to the operated hip, preventing strength gains beyond that of the CG. Such arthrogenic muscle inhibition is well known after total knee replacements[48], and has been indicated after THA as well[49].

Secondary outcomes

All secondary outcomes improved significantly from baseline to 10 week follow up in both groups, except from hip flexion muscle strength in the CG (Table 3 and 4). There was a statistical significant difference between groups over time in maximum walking speed (P = 0.008) and stair climb performance (*P* = 0.04) (Table 3). We question the clinical relevance of these findings, due to the small differences and the diminishing of the effect after six months (Table 3). The functional performance improvements after PRT in the present study (21-26%) correspond well with the findings from Suetta *et al*[14] of 28-30% improvements in functional performance after 12 weeks of PRT. The increase in maximum walking speed (IG: 21%, CG: 12%) is comparable to results from a recent study with preoperative neuromuscular training and outpatient physiotherapy post discharge (18%) [33]. Likewise, HOOS ADL scores showed slightly larger improvement in the present study at 10 week follow up (IG: 40, CG:37 points) than their 3 months follow up (~30 points) with comparable baseline values[33]. There were no significant between-group differences on the HOOS subscales in the present study (Table 4). The HOOS results indicate a rapid and substantial recovery in both groups in the present study, comparable with intervention groups in other studies[33, 50]. However, ceiling effect was observed for all HOOS subscales from the six months follow up and forward.

Strength and limitations

The qualities of this study encompass the assessor-blinded, randomised controlled design, the exclusion of the preoperative best functioning patients and the controlled, well-described

intensity and execution of the exercises. PRT as used in this study is simple to apply and is based on identified muscle deficits documented in the existing literature. We excluded the patients reporting least disability preoperative as an attempt to address the intervention to the patients with greatest rehabilitation needs (stratified medicine), as advocated in previous studies[13, 22]. A very high compliance to the PRT in combination with one-to-one supervision verifies that the intended exercise intervention was implemented.

The limitations of this study encompass potential selection bias and risk of attention bias. We possibly included motivated patients with a positive attitude towards training as they had to be willing to attend 2 -weekly training sessions which might weaken the external validity of the trial. We aimed at including patients with lower pre-operative function, but the cut-off level (75th percentile) might have been too high to actually reflect the patients with low function only. However this was deemed necessary for completion of the trial, since non-consenters tend to be more disabled than those participating in clinical studies[51]. To comply with the possible risk of attention bias it would have been optimal to perform supervised placebo training in the CG, but this was not deemed feasible. The results must be interpreted with this potential attention bias in mind.

Implications

The findings from this study suggest no clinically relevant additional effect of PRT compared to home-based exercise after fast-track THR. These findings do not claim being exhaustive, but needs to be confirmed or contradicted in future research. There might be a subgroup of patients profiting from PRT and maybe different timing and dosage could change the conclusions. Considering the rapid and substantial improvements in this study (despite of group assignment) the persisting deficits stated in the literature needs to be further studied in patients following a fast-track course of treatment and compared to healthy peers as well. It is required to identify patients needing supervised rehabilitation and those recovering well by unsupervised home-based rehabilitation. Today, there is a large variation between rehabilitation procedures after THR, ranging from no supervised physiotherapy after discharge to all patients being referred to outpatient physiotherapy or even rehabilitation unit stay. This emphasizes the need for further knowledge to achieve optimal allocation of health care resources.

Conclusions

In this trial, supervised PRT twice a week in addition to 5 weekly sessions of unsupervised exercise for 10 weeks was not superior to 7 weekly sessions of unsupervised home-based exercise for 10 weeks in improving the primary outcome, leg-extension power of the operated leg, at the primary endpoint 10 weeks after surgery in THR patients with lower pre-operative function.
However, it is currently unknown whether PRT is effective in other subgroups of patients, at higher training dosage (e.g. increased longevity of the training), different timing or on different outcomes.

Acknowledgements

We would like to acknowledge all the physiotherapists and patients participating in this study.

Contributions

LRM, KS, TB, AKP and IM all contributed to the conception and design of the study. LRM, LBJ and SM contributed to data acquisition. LRM was responsible for analysis and interpretation of data and drafting the article with all co-authors contributing with critical revision for important intellectual content. All authors approved the final version to be submitted. First and last authors take responsibility for the integrity of the work as a whole, from inception to finished article. E-mail last author: annempte@rm.dk.

Role of the funding source

The study was supported by grants from The Health Research Fund of Central Denmark Region, The Danish Rheumatism Association, The Association of Danish Physiotherapists, The Health Foundation and Aase and Ejnar Danielsens Foundation. The study sponsors had no role in the study design, collection, analysis and interpretation of data; nor in the writing of the manuscript or the decision to submit the manuscript for publication.

Competing interest statement

All authors declare that they have no competing interest

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Figure 1. Participant flow throughout the study

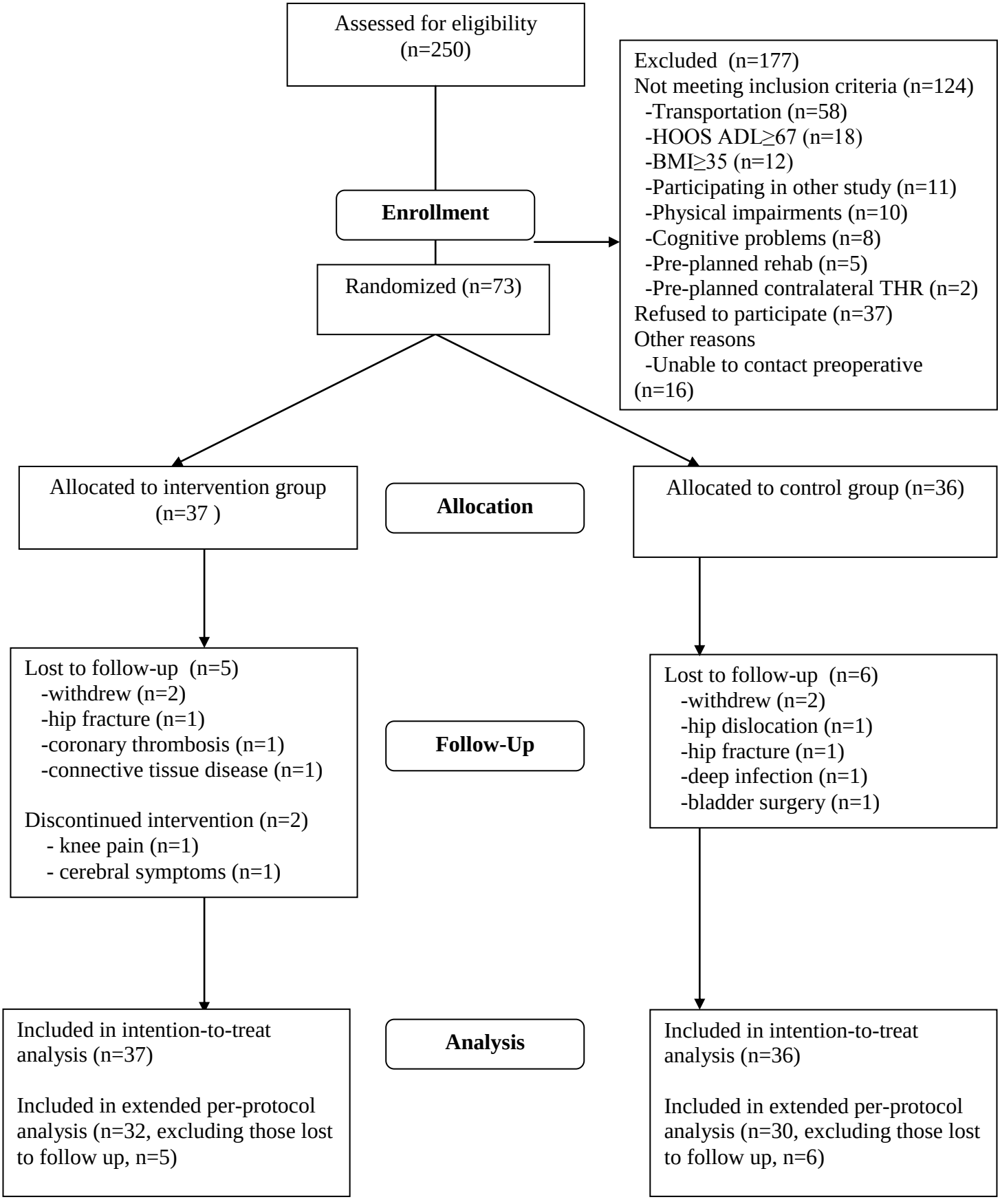

Table 1. Strength training descriptors of the exercises performed in the intervention group

Load	12 RM (week 1), 10 RM (week 2-5), 8 RM (week 6-10)
Repetitions	10-12 (week 1), 10 (week 2-5), 8 (week 6-10)
Set per session	3 sets
Rest between sets	60 seconds
Sessions per week	2 per week
Duration of training period	10 weeks
Contraction modes	3 seconds concentric, 1 second isometric, 3 seconds eccentric
Rest between repetitions	0 sec
Time under tension	210 sec / exercise / session
Contraction failure in each set	Yes
Range of motion	Maximum possible
Rest between training sessions	≥48 hours
Anatomical definition of the exercises	Yes

Table 2. Baseline characteristics of patients allocated to intervention or control group

	Intervention (n=32)	Control (n=30)
Female gender, n (%)	14 (44)	12 (40)
Age, mean (SD)	64.8 (8)	65.1 (10)
BMI, kg/m^2, mean (SD)	27.5 (4)	25.4 (4)
Physical status* (2 missings)		
ASA I	15 (47)	15 (50)
ASA II	15 (47)	14 (47)
ASA III	1 (3)	0 (0)
Prosthesis type		
Cementless	29 (91)	28 (93)
Cemented/Hybrid	3 (9)	2 (7)
Contralateral hip		
Hip Replacement	8 (25)	7 (23)
Osteoarthritis	5 (16)	4 (13)
Postoperative days in hospital		
1 day	22 (69)	20 (67)
2 days	10 (31)	7 (23)
≥3 days	0	3 (10)

BMI: Body Mass Index, THA: Total hip replacement

*American Society of Anesthesiologists physical status classification: I-Healthy patient, II-Patient with mild systemic disease, III+IV-Patient with severe systemic disease.

Table 3. Results from the physical outcome measures in the intervention group and control group at all measurement times. Values are mean (SD), change scores are mean [95% CI].

Primary outcome	**Baseline**		**10 week**		**6 month**		**Change baseline-10 week**		**Difference**	**P-value**
	IG	**CG**	**IG**	**CG**	**IG**	**CG**	**IG**	**CG**		
Leg extension power (W/kg)[§]										
Intention-to-treat analysis (IG: n=37, CG: n=36)	1.41(0.6)	1.50(0.7)	1.72(0.6)*	1.78(0.6)*	2.04(0.7)	1.97(0.6)	0.29 [0.13;0.45]	0.26 [0.10;0.42]	0.03 [-0.20;0.26]	0.79[#]
Extended per-protocol analysis (IG: n=32, CG: n=30)	1.44(0.6)	1.55(0.7)	1.72(0.6)*	1.78(0.6)*	2.04(0.7)	1.97(0.6)	0.28 [0.12;0.44]	0.25 [0.02;0.48]	0.03 [-0.24;0.31]	0.23†

Secondary outcomes (IG: n=32, CG: n=30)	**Baseline**		**4 week**		**10 week**		**6 month**		**Change baseline-10 week**		**P-value†**
	IG	**CG**	**IG**	**CG**	**IG**	**CG**	**IG**	**CG**	**IG**	**CG**	
Maximum walking speed (seconds)	14.02(4.8)	13.57(3.5)	13.85(3.7)	13.72(3.0)	11.08(2.4)*	11.99(2.6)*	10.81(2.8)	11.02(2.6)	2.94 [1.8;4.1]	1.58 [0.7;2.4]	0.008[a]
Hip abduction strength (Nm/kg)	0.82(0.3)	0.92(0.4)	0.87(0.3)	0.90(0.3)	1.03(0.3)*	1.03(0.3)*	1.08(0.3)	1.15(0.3)	0.21 [0.1;0.3]	0.11 [0.0;0.2]	0.26[a]
Hip flexion strength (Nm/kg)	1.07(0.3)	1.27(0.4)	1.11(0.3)	1.21(0.3)	1.25(0.3)*	1.32(0.4)	1.33(0.3)	1.41(0.4)	0.19 [0.1;0.3]	0.05 [-0.1;0.2]	0.29
Sit-to-stand test (repetitions)[§]	11.56(3.9)	11.90(4.6)	Not measured		14.41(3.9)*	13.13(4.3)*	15.47(4.5)	15.07(5.1)	2.84 [1.8;3.9]	1.34 [0.2;2.5]	0.12
Stair climb test (seconds)	12.83(7.9)	13.12(7.2)	Not measured		9.49(3.2)*	10.54(4.0)*	9.07(3.0)	9.03(2.8)	3.32 [1.0;5.7]	2.58 [0.6;4.6]	0.04[a]

Abbreviations: THR: Total hip replacement, diff: difference, W/kg: Watt/kilogram bodyweight, Nm/kg: Newton*meter/kilogram bodyweight,
[§]1 missing at baseline, the patient was not able to perform the test due to pain, [#] Mixed effect model comparing between-group changes with adjustment for baseline values †Multivariate repeated measurement analysis, testing the difference between groups over time, *Significant within group difference from baseline to 10 week follow up ($P < 0.05$), [a]Approximate test, allowing for heterogeneity.

Table 4. Results from the questionnaire: Hip osteoarthritis outcome scale (HOOS) in the intervention group (IG, n=32) and control group (CG, n=30). Values are mean (SD)

Measure-ment time		HOOS subscale				
		Symptoms	**Pain**	**ADL**	**Sport/rec**	**QOL**
Baseline	**IG**	43.0 (13)	46.3 (8)[1]	49.6 (10)	29.5 (16)	32.6 (13)
	CG	43.7 (15)	48.1 (17)	49.9 (17)	32.8 (21)	37.5 (16)
2 week	**IG**	62.9 (16)[4]	68.2 (15)[4]	63.8 (11)[4]		51.8 (16)[4]
	CG	64.6 (16)[2]	67.7 (15)[2]	65.8 (16)[3]	Not	55.1 (16)[3]
4 week	**IG**	72.8 (12)	74.9 (13)	74.9 (11)	measured	61.9 (16)[1]
	CG	73.3 (16)	78.8 (15)[1]	76.5 (14)		62.3 (18)[1]
6 week	**IG**	76.2 (14)[2]	82.5 (15)[2]	81.1 (13)[2]	62.6 (25)[3]	67.6 (21)[3]
	CG	74.6 (17)[5]	81.9 (15)[5]	82.0 (14)[5]	69.5 (24)[5]	69.5 (21)[5]
10 week	**IG**	82.9 (12)[1]*	88.7 (12) [1]*	89.1 (10)[1]*	77.0 (18)[1]*	79.0 (16)[1]*
	CG	80.3 (17)*	86.3 (16) [1]*	86.5 (13)*	74.4 (21)[1]*	75.6 (20)[1]*
6 month	**IG**	85.0 (15)	91.7 (10)[1]	90.4 (11)	80.1 (17)	83.8 (18)
	CG	86.2 (13)	91.4 (13)[1]	91.7 (10)	83.7 (17)	86.7 (17)
12 month	**IG**	90.7 (11)[1]	94.0 (8)[1]	93.4 (8)[1]	81.9 (20)[1]	86.7 (16)[1]
	CG	90.0 (14)	92.2 (14)	92.1 (12)	82.8 (19)	86.0 (20)
***P* value†**		0.90[a]	0.31[a]	0.82[a]	0.39	0.47[a]

Subscale abbreviations: ADL: Activities of daily living, Sport/rec: Function in sport/recreation, QOL: Hip-related quality of life. Superscript numbers indicate the number of missing values, †Multivariate repeated measurement analysis, testing the difference between groups over time, *Significant within group difference from baseline to 10 week follow up ($P < 0.05$), [a]Approximate test, allowing for heterogeneity.

Appendix 4

List of theses from the orthopaedic research group

THESES FROM THE ORTHOPAEDIC RESEARCH GROUP

PhD and Doctoral Theses from the Orthopaedic Research Group, www.OrthoResearch.dk, University Hospital of Aarhus, Denmark

PhD Theses

1. In vivo and vitro stimulation of bone formation with local growth factors
   Martin Lind, January 1996
   www.OrthoResearch.dk

2. Gene delivery to articular cartilage
   Michael Ulrich-Vinther, September 2002
   www.OrthoResearch.dk

3. The influence of hydroxyapatite coating on the peri-implant migration of polyethylene particles
   Ole Rahbek, October 2002
   www.OrthoResearch.dk

4. Surgical technique's influence on femoral fracture risk and implant fixation. Compaction versus conventional bone removing techniques
   Søren Kold, January 2003
   www.OrthoResearch.dk

5. Stimulation and substitution of bone allograft around non-cemented implants
   Thomas Bo Jensen, October 2003
   www.OrthoResearch.dk

6. The influence of RGD peptide surface modification on the fixation of orthopaedic implants
   Brian Elmengaard, December 2004
   www.OrthoResearch.dk

7. Biological response to wear debris after total hip arthroplasty using different bearing materials
   Marianne Nygaard, June 2005
   www.OrthoResearch.dk

8. DEXA-scanning in description of bone remodeling and osteolysis around cementless acetabular cups
   Mogens Berg Laursen, November 2005
   www.OrthoResearch.dk

9. Studies based on the Danish Hip Arthroplasty Registry
   Alma B. Pedersen, 2006
   www.OrthoResearch.dk

10. Reaming procedure and migration of the uncemented acetabular component in total hip replacement
    Thomas Baad-Hansen, February 2007
    www.OrthoResearch.dk

11. On the longevity of cemented hip prosthesis and the influence on implant design
    Mette Ørskov Sjøland, April 2007
    www.OrthoResearch.dk

12. Combination of TGF-β1 and IGF-1 in a biodegradable coating. The effect on implant fixation and osseointegration and designing a new in vivo model for testing the osteogenic effect of micro-structures in vivo
    Anders Lamberg, June 2007
    www.OrthoResearch.dk

13. Evaluation of Bernese periacetabular osteotomy; Prospective studies examining projected load-bearing area, bone density, cartilage thickness and migration
    Inger Mechlenburg, August 2007
    Acta Orthopaedica (Suppl 329) 2008;79

14. Rehabilitation of patients aged over 65 years after total hip replacement - based on patients' health status
    Britta Hørdam, February 2008
    www.OrthoResearch.dk

15. Efficacy, effectiveness, and efficiency of accelerated perioperative care and rehabilitation intervention after hip and knee arthroplasty
    Kristian Larsen, May 2008
    www.OrthoResearch.dk

16. Rehabilitation outcome after total hip replacement; prospective randomized studies evaluating two different postoperative regimes and two different types of implants
    Mette Krintel Petersen, June 2008
    www.OrthoResearch.dk

17. CoCrMo alloy, *in vitro* and *in vivo* studies
    Stig Storgaard Jakobsen, June 2008
    www.OrthoResearch.dk

18. Adjuvant therapies of bone graft around non-cemented experimental orthopaedic implants. Stereological methods and experiments in dogs
    Jørgen Baas, July 2008
    Acta Orthopaedica (Suppl 330) 2008;79

19. The Influence of Local Bisphosphonate Treatment on Implant Fixation
    Thomas Vestergaard Jakobsen, December 2008
    www.OrthoResearch.dk

20. Surgical Advances in Periacetabular Osteotomy for Treatment of Hip Dysplasia in Adults
    Anders Troelsen, March 2009
    Acta Orthopaedica (Suppl 332) 2009;80

21. Polyethylene Wear Analysis. Experimental and Clinical Studies in Total Hip Arthroplasty.
    Maiken Stilling, June 2009
    Acta Orthopaedica (Suppl 337) 2009;80

22. Step-by-step development of a novel orthopaedic biomaterial: A nanotechnological approach.
    Thomas H.L. Jensen, September 2009
    www.OrthoResearch.dk

23. Osteoclastic bone resorption in chronic osteomyelitis
    Kirill Gromov, November 2009
    www.OrthoResearch.dk

24. Use of medications and the risk of revision after primary total hip arthroplasty
    Theis Thillemann, December 2009
    www.OrthoResearch.dk

25. Different fixation methods in anterior cruciate ligament reconstruction
    Ole Gade Sørensen, February 2010
    www.OrthoResearch.dk

26. Postoperative pain relief after total hip and knee replacement; prospective randomized studies evaluating two different peri- and postoperative regimes
    Karen V. Andersen, June 2010
    www.OrthoResearch.dk

27. A comparison of two types of osteosynthesis for distal radius fractures using validated Danish outcome measures
    Jesper O. Schønnemann, September 2010
    www.OrthoResearch.dk

28. Optimizing the cementation of femoral component in hip arthroplasty
    Juozas Petruskevicius, September 2010
    www.OrthoResearch.dk

29. The influence of parathyroid hormone treatment on implant fixation
    Henrik Daugaard, December 2010
    www.OrthoResearch.dk

30. Strontium in the bone-implant interface
    Marianne Toft Vestermark, January 2011
    www.OrthoResearch.dk

31. The applicability of metallic gold as orthopaedic implant surfaces – experimental animal studies
    Kasra Zainali, April 2011
    www.OrthoResearch.dk

32. Gene transfer for bone healing using immobilized freeze-dried adeno-associated viral vectors
    Mette Juul Koefoed, June 2011
    www.OrthoResearch.dk

33. Mobile or fixed bearing articulation in TKA? A randomized evaluation of gait analysis, implant migration, and bone mineral density
    Michael Tjørnild, December 2011
    www.OrthoResearch.dk

34. Hip resurfacing arthroplasty. Failures and complications investigated by a meta-analysis of the existing literature, and clinically by microdialysis, laser doppler flowmetry, RSA, DXA and MRI
    Nina Dyrberg Lorenzen, March 2012
    www.OrthoResearch.dk

35. Manipulation of the mevalonate pathway in the bone-implant interface
    Mette Sørensen, September 2012
    www.OrthoResearch.dk

36. Bone allograft and implant fixation tested under influence of bio-burden reduction, periosteal augmentation and topical antibiotics
    Jeppe Barckman, January 2013
    www.OrthoResearch.dk

37. Sternal healing characteristics. Animal and clinical experimental investigation
    Rikke Vestergaard, March 2013
    www.OrthoResearch.dk

38. Assessment of factors influencing the surgical outcome of periacetabular osteotomy for treatment of hip dysplasia in adults
    Charlotte Hartig-Andreasen, June 2013
    www.OrthoResearch.dk

39. Stem cells derived from adipose tissue and umbilical cord blood for cartilage tissue engineering in scaffold cultures
Samir Munir, December 2013
www.OrthoResearch.dk

40. Flexor tendon adhesions – a mouse model of flexor tendon injury and repair
Sys Hasslund Svensson, 2014
www.OrthoResearch.dk

41. The association between obesity and the effect of total knee – and hip arthroplasty
Anette Liljensøe, 2014
www.OrthoResearch.dk

Doctoral Theses

1. Hydroxyapatite ceramic coating for bone implant fixation. Mechanical and histological studies in dogs
Kjeld Søballe, 1993
Acta Orthop Scand (Suppl 255) 1993;54

2. Growth factor stimulation of bone healing. Effects on osteoblasts, osteomies, and implants fixation
Martin Lind, October 1998
Acta Orthop Scand (Suppl 283) 1998;69

3. Calcium phosphate coatings for fixation of bone implants. Evaluated mechanically and histologically by stereological methods
Søren Overgaard, 2000
Acta Orthop Scand (Suppl 297) 2000;71

4. Adult hip dysplasia and osteoarthritis. Studies in radiology and clinical epidemiology
Steffen Jacobsen, December 2006
Acta Orthopaedica (Suppl 324) 2006;77

5. Gene therapy methods in bone and joint disorders. Evaluation of the adeno-associated virus vector in experimental models of articular cartilage disorders, periprosthetic osteolysis and bone healing
Michael Ulrich-Vinther, March 2007
Acta Orthopaedica (Suppl 325) 2007;78

6. Assessment of adult hip dysplasia and the outcome of surgical treatment
Anders Troelsen, February 2012
www.OrthoResearch.dk