

The anterior approach in total hip arthroplasty

*Assessment of the approach and comparison to
other approaches*

Thesis by

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**“He who laughs most, learns best”
— John Cleese**

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Abbreviations

6MWD	6-Minute Walk Distance
95% CI	95 % Confidence interval
CDH	Congenital Dislocation of the Hip
CK	Creatine Kinase
CRP	C-Reactive Protein
EQ-5D	Five-dimensional scale of EuroQol
EQ-VAS	Visual analogue scale of EuroQol
FNP	Femoral Nerve Palsy
HHS	Harris Hip Score
MCID	Minimum Clinically Important Difference
ME	Morphine equivalents
MIS	Minimally Invasive Surgery
n	Number
NAR	Norwegian Arthroplasty Register
OHS	Oxford Hip Score
RR	Relative risk
THA	Total Hip Arthroplasty

Summary and publications

Total hip arthroplasty (THA) is a well-established and reliable treatment in restoring function and relieving pain in end-stage osteoarthritis of the hip. Different surgical approaches can be used for the procedure. The most used are the posterior approach, where the external rotators of the hip are released, and the direct lateral approach where the gluteus minimus and the anterior part of the gluteus medius are released. The direct anterior approach has increasing popularity. The approach utilizes a muscle and nerve neutral interval and is advertised as “minimally invasive surgery (MIS)”. The aim of this thesis was to evaluate the anterior approach and compare it to other approaches.

Paper 1

Mjaaland KE, Kivle K, Svenningsen S, Pripp AH, Nordsletten L.

Comparison of markers for muscle damage, inflammation, and pain using minimally invasive direct anterior versus direct lateral approach in total hip arthroplasty: A prospective, randomized, controlled trial. Journal of Orthopaedic Research 2015;33(9):1305-10.

We hypothesised that the direct anterior approach would cause less muscle damage and inflammation as measured by Creatine Kinase (CK) and C-Reactive Protein (CRP), respectively, and consequently cause less pain than the direct lateral approach.

164 patients with end-stage coxarthrosis were randomised to receive a THA through either the anterior (n=84) or the direct lateral approach (n=80). In all patient, an uncemented stem (Corail), cemented cup (Marathon) and a 32 mm in diameter ceramic head (Biolox forte) were used.

Patients operated with the anterior approach had higher levels of CK than those operated with the direct lateral approach at all postoperative measures, though only statistically significant directly postoperative and on day four. CRP were equal in both groups. The patients operated with the anterior approach required less pain medication on the day of surgery and had clinically significantly lower pain levels before and after physiotherapy on postoperative days one through four, than the direct lateral group.

We concluded that the use of CK to measure “invasiveness” might not be appropriate and warrants further studies and that clinically the anterior was less invasive in that it caused less pain than the direct lateral approach.

Paper 2

Mjaaland KE, Svenningsen S, Fenstad AM, Havelin LI, Furnes O, Nordsletten L.

Implant Survival After Minimally Invasive Anterior or Anterolateral Vs. Conventional Posterior or Direct Lateral Approach: An Analysis of 21,860 Total Hip Arthroplasties from the Norwegian Arthroplasty Register (2008 to 2013). The Journal of Bone and Joint Surgery American volume. 2017;99(10):840-7.

Since 2008, the use of MIS anterior and anterolateral approaches has increased in Norway as well as the rest of the world. We wanted to compare the revision rates and risk of revision using these approaches to the conventional posterior and direct lateral approaches.

THAs with uncemented stems implanted between 2008 and 2013 were identified in the Norwegian Arthroplasty Register (NAR). 2,017 were operated through the anterior, 2,087 through the anterolateral, 5,961 through the posterior and 11,795 through the direct lateral approach.

No difference was found in 2 and 5-year implant survival between the approaches. Relative risk (RR) of revision for any cause was not different. The RR of revision due to infection was double for the direct lateral approach compared to the anterior and anterolateral approaches (RR = 0.53, 95% CI= 0.36 to 0.80, p = 0.002) and the posterior approach (RR = 0.57, 95% CI = 0.40 to 0.80, p= 0.001). The posterior approach had double risk of revision due to dislocation compared to the direct lateral (RR = 2.1, 95% CI = 1.5 to 3.1, p < 0.001), the risk was not different when comparing the direct lateral and the anterior and anterolateral approaches (RR = 0.71, 95% CI = 0.40 to 1.3, p = 0.25).

We concluded that the anterior and anterolateral approaches were not associated with increased revision rates or increased risk of revision compared to the posterior or the direct lateral approaches.

Paper 3

Mjaaland KE, Kivle K, Svenningsen S, Nordsletten L.

Do Postoperative Results Differ in a Randomized Trial Between a Direct Anterior and a Direct Lateral Approach in THA? Clinical Orthopaedics and Related Research. 2019;477(1):145-55.

The 164 patients from **paper 1** randomised to THA through the anterior or the direct lateral approach were followed prospectively at 3, 6 12 and 24 months. At each control a physiotherapist blinded to approach recorded the Harris Hip Score (HHS), the 6-Minute Walk Distance (6MWD) and directly after the walk test, performed the Trendelenburg test. The patients completed the Oxford Hip Score (OHS) and the EQ-5D. 94 percent of the patients completed the 2-year follow-up, five patients in each group were lost to follow up.

No clinically important differences were found between the groups at any time point in HHS, 6MWD, OHS or EQ-5D. The Trendelenburg test was positive in a significantly higher number of patients in the direct lateral group at all time points and remained so at 24 months (16% [12 of 75] versus 1% [one of 79]; odds ratio 15; $p = 0.001$). Patients with positive Trendelenburg, irrespective of approach used, had clinically significant worse HHS, OHS and EQ-5D at all controls compared to those with negative test.

Three patients in the direct anterior group had transient femoral nerve injury and one had permanent damage to the tibial nerve. Four patients in the direct lateral group were reoperated due to detachment of the gluteus minimus and released part of the gluteus medius.

We concluded that both approaches yield comparable results except for the increase in Trendelenburg test positive patients using the direct lateral approach and that care should be taken to ensure good abductor function.

Norsk sammendrag

Total hofteprotese er en veletablert og pålitelig behandling for å gjenvinne funksjon og fjerne smerte ved endestadium hofteleddsartrose. Flere kirurgiske tilganger kan benyttes. De mest brukte er bakre tilgang, hvor man kutter over hoftens utadrotatorer, og direkte laterale tilgang hvor man løsner ut gluteus minimus og fremre del av gluteus medius. Fremre tilgang blir stadig mer populær. Tilgangen bruker et muskel- og nervenøytralt intervall og blir ofte omtalt som «miniinvasiv». Målet med denne avhandlingen var å evaluere den fremre tilgangen og sammenligne den med andre tilganger.

I **artikkel 1** var hypotesen at fremre tilgang ville gi mindre muskelskade målt med Kreatin kinase (CK) og inflammasjon målt med C-reaktivt protein (CRP) og dermed mindre postoperativ smerte enn den direkte laterale tilgangen.

164 pasienter med endestadium hofteleddsartrose ble randomisert til å få hofteprotese via enten fremre (n=84) eller direkte lateral tilgang (n=80). Alle fikk innsatt usementert stamme (Corail), sementert kopp (Marathon) og et 32 mm keramisk hode (Bilolox forte).

Pasienter operert med fremre tilgang hadde høyere CK-verdier enn pasienter operert med direkte lateral tilgang, men forskjellen var statistisk signifikant kun straks postoperativt og på dag 4. Det var ingen forskjell i CRP-verdier mellom gruppene. Pasienter operert med fremre tilgang trengte mindre smertestillende på operasjonsdagen og hadde klinisk signifikant mindre smerter de fire første postoperative dager enn pasienter operert med direkte lateral tilgang.

Vi konkluderte med at CK-målinger kanskje ikke er egnet for å vurdere «invasivitet» at det er behov for ytterligere studier på området, og at fremre tilgang var mindre invasiv da den gav mindre smerter enn den direkte laterale tilgangen.

Siden 2008 har bruken av miniinvasiv fremre og anterolateral tilgang økt, både i Norge og resten av verden. I **artikkel 2** sammenlignet vi revisjonsrater og risiko mellom disse tilgangene og konvensjonelle bakre og direkte lateral tilgang.

Totale hofteproteser operert med usementert stamme mellom 2008 og 2013 ble identifisert i Nasjonalt Register for Leddproteser. 2,017 var operert med fremre tilgang, 2,087 med anterolateral, 5,961 med bakre og 11,795 med direkte lateral tilgang.

Ingen forskjell ble funnet på 2- og 5-års overlevelse av implantat mellom tilgangene. Relativ risiko (RR) for revisjon av alle årsaker var ikke forskjellig. RR for revisjon grunnet infeksjon var dobbel for direkte lateral tilgang sammenlignet med fremre og anterolateral tilgang (RR = 0.53, 95% CI= 0.36 to 0.80, p = 0.002) og bakre tilgang (RR = 0.57, 95% CI = 0.40 to 0.80, p= 0.001). Bakre tilgang hadde dobbel risiko for revisjon grunnet luksasjon sammenlignet med direkte lateral tilgang (RR = 2.1, 95% CI = 1.5 to 3.1, p < 0.001) mens det ikke var forskjell mellom fremre og anterolateral og direkte lateral.

Vi konkludere med at fremre og anterolateral tilgang ikke var assosiert med økt revisjonsrate eller økt risiko for revisjon sammenlignet med bakre eller direkte lateral tilgang.

I **artikkel 3** fulgte vi de 164 pasientene fra **artikkel 1** randomisert til fremre eller direkte lateral tilgang prospektivt med kontroller 3, 6, 12 og 24 måneder etter total hofteproteseoperasjonen. Ved hver kontroll vurderte en fysioterapeut blindet for hvilken tilgang som var brukt Harris Hip Score (HHS), 6 minutters gangtest (6MWD) og Trendelenburg test, sistnevnte rett etter gangtesten. Pasientene fylte ut Oxford Hip Score (OHS) og EQ-5D. 94 prosent av pasientene fullførte 2-års oppfølging, fem pasienter i hver gruppe falt fra.

Ingen klinisk vesentlig forskjell ble funnet mellom gruppene på noe tidspunkt vurdert med HHS, 6MWD, OHS eller EQ-5D. Trendelenburg test var positiv hos signifikant flere pasienter i gruppen operert med direkte lateral tilgang på alle måletidspunktene og dette varte ved til 24 måneder (16% [12 av 75] versus 1% [en av 79]; odds ratio 15; p = 0.001). Uavhengig av tilgang hadde pasienter med positiv Trendelenburg test dårligere HHS, OHS og EQ-5D på alle kontroller sammenlignet med pasienter med negativ test.

Tre pasienter operert med fremre tilgang hadde forbigående skade på femoralisnerven og en fikk permanent skade på tibialnerven. Fire pasienter operert med direkte lateral tilgang ble reoperert grunnet løsning av gluteus minimus og den løsnede delen av gluteus medius.

Vi konkluderte med at begge tilganger gav sammenlignbare resultater med unntak av økt antall pasienter med positiv Trendelenburg test hos pasienter operert med direkte lateral tilgang og at man må tilstrebe god adduktor funksjon etter total hofteproteseoperasjon.

Introduction

Total hip arthroplasty



Figure 1. X-ray of a total hip arthroplasty

Total hip arthroplasty (THA) (Figure 1), synonymous with total hip replacement, is where the articulating surface of the acetabulum is replaced by an implant and the femoral head is resected and replaced by a femoral stem. Both the acetabular and femoral component can be fixed to the bone by use of polymethyl methacrylate (PMMA), commonly referred to as bone cement(1). The recommended fixation is based on age and sex. Younger patients do well with uncemented implants, whereas older patients and especially older women, do better with cemented implants(2, 3).

The most common indication for THA is primary osteoarthritis, the most common joint disease worldwide(4). Other indications include fracture of femoral neck, rheumatoid arthritis, congenital dysplasia of the hip and sequela of epiphysiolysis or Calvé-Legg-Perthes disease(5) (Table 1).

Year	Primary osteoarthritis	Rheumatoid arthritis	Sequela after hip fracture	Congenital dysplasia	Cong. dysplasia with dislocation	Epiphysiol./Perthes' disease	Spondyloarthropathy	Acute fracture of the femoral neck	Avascular necrosis of the femoral head	Sequela after acetabular fracture	Other	Missing information
2018	7572	98	296	651	24	111	21	568	267	22	275	27
2017	7301	108	299	679	19	105	26	404	270	34	282	13
2016	7108	138	355	685	11	107	19	343	229	33	247	9
2015	6796	108	332	587	11	106	21	322	181	26	200	19
2014	6414	115	356	648	18	86	28	288	250	22	176	19
2013	6415	125	351	611	10	115	31	288	172	29	192	30
2012	6220	157	366	615	12	92	45	206	186	16	203	14
2011	5787	132	373	573	24	96	26	189	138	21	187	30
2010	5734	130	355	594	36	88	20	161	151	16	191	50
2009	5515	131	390	560	26	127	24	151	174	11	165	32
2008	5359	144	443	498	25	99	21	149	145	19	144	6
2007	5166	146	475	457	21	80	22	159	174	22	110	15
2006	4819	147	486	445	17	83	24	131	172	19	126	13
2005	5097	166	550	437	29	87	22	102	143	14	107	14
2000-04	23329	823	2768	2176	124	399	134	356	395	62	460	131
1995-99	18268	887	3169	1851	170	340	123	146	236	70	542	241
1987-94	23126	1297	4508	2768	518	453	154	93	115	116	623	318
Total	150026	4852	15872	14835	1095	2574	761	4056	3398	552	4230	981

Diseases are not mutually exclusive. More than one reason for operation is possible

Table 1. Indication for primary total hip arthroplasty. Table from the Norwegian Arthroplasty Register report 2019.

The hip and surrounding structures

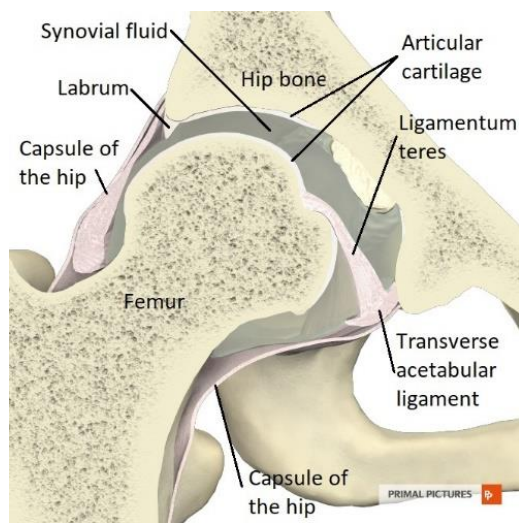


Figure 2. Coronal section of the hip joint.
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The hip is a ball-and-socket joint between the acetabulum and the head of the femur. The spherical femoral head is covered by hyaline cartilage, extending past the equator of the head, covering 60-70%. The acetabulum is covered with cartilage in its entirety with the exception of the acetabular fossa(6). Around the periphery of the acetabulum, the labrum is attached. This is horse-shoe shaped, connected inferiorly by the transverse acetabular ligament and adds stability to the joint(7). Encapsulating the joint is the capsule, arising from the outer margin of the

acetabulum and the labrum and attaching to the intertrochanteric line on the femur(6) (Figure 2).

21 muscles cross the hip joint, contributing both to movement and stability(8). Different groupings of the muscle have been described, based on anatomic location(6), layers(9) or function(7, 8, 10). In surgery, the division in layers is perhaps the most useful. The superficial muscles surrounding the hip from ventral to lateral/dorsal is the sartorius, the tensor fascia latae inserting into the iliotibial tract and the gluteus maximus(11) (Figure 3,4)

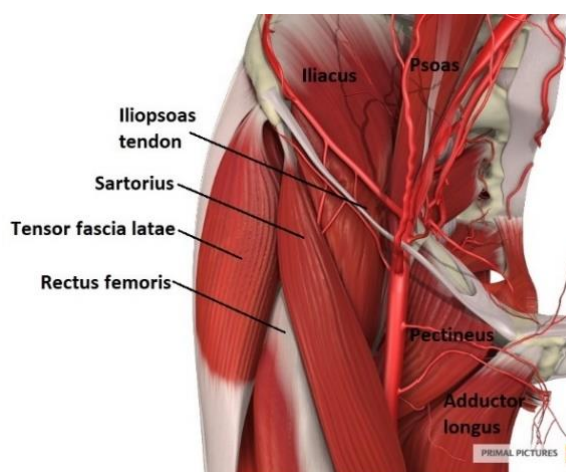


Figure 3. Anterior view of the hip.
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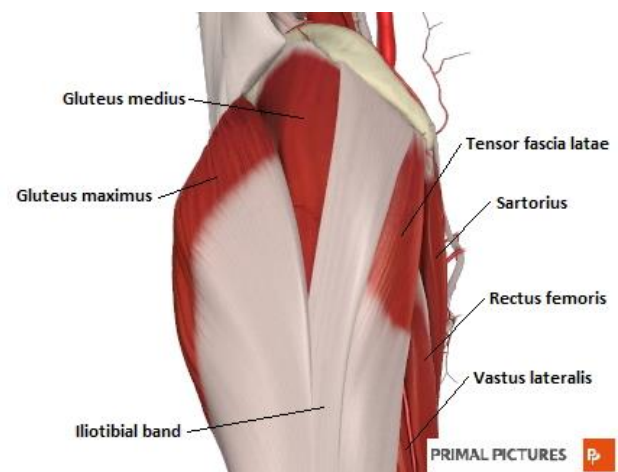


Figure 4. Lateral view of the hip.
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The deeper layers consists of, from ventral to lateral/dorsal, the rectus femoris, vastus lateralis, the gluteus medius and minimus and the short external rotators(9) (Figure 5,6).

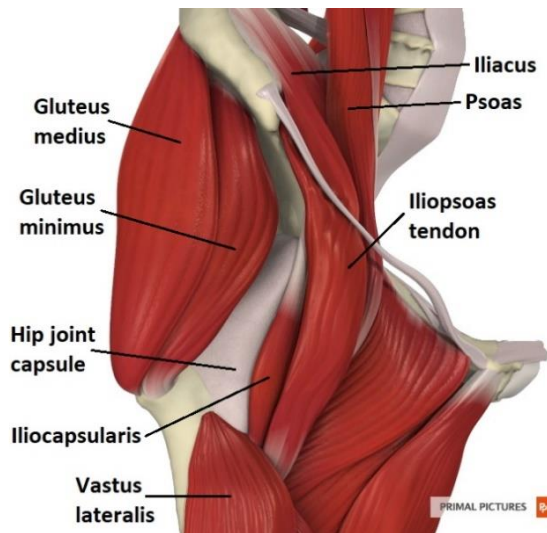


Figure 5. Anterior view of the hip with the sartorius, tensor fascia late and rectus femoris muscles removed.

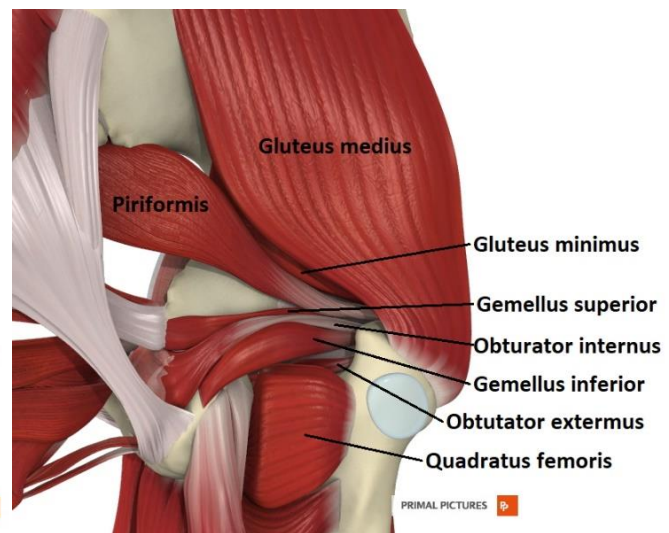


Figure 6. Posterior view of the hip with the gluteus maximus muscle removed.

The sartorius, rectus femoris and the vastus lateralis muscle are innervated by the femoral nerve arising from the lumbar plexus (L2 to L4)(10). The superior gluteal nerve arises from the sacral plexus (L4 to S1) and innervates the gluteus medius, minimus and the tensor fascia latae muscles. The gluteus maximus is innervated by the inferior gluteal nerve, also arising from the sacral plexus (L5 to S2). The short external rotators are innervated by nerves derived directly from the sacral plexus, the piriformis from S1 to S2, the obturator externus and superior gemellus from L5 to S2 and the quadratus femoris and the inferior gemellus from L4 to S1(12).

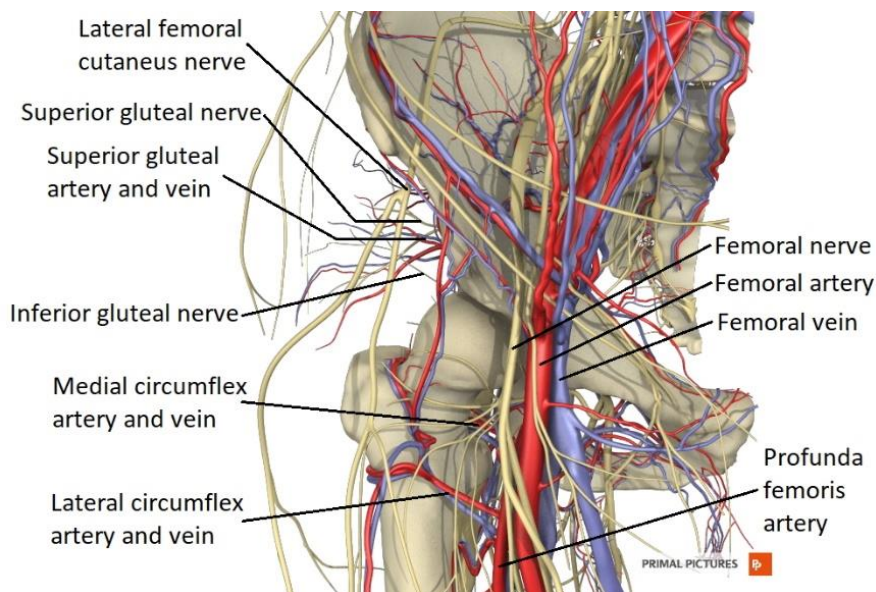


Figure 7. Anterior view of nerves and vessels surrounding the hip.
Copyright Primal Pictures Ltd.

The hip joint (i.e. the femoral head) receives its blood supply mainly by the medial circumflex femoral artery, but also from the lateral circumflex femoral artery(13). Both the circumflex arteries are most commonly

branches of the profunda femoris artery, but can be direct branches of the femoral artery(14). The profunda

femoris artery is a branch of the femoral artery usually branching of between 3 to 6 cm below the inguinal ligament(15). The femoral artery with its branches supplies the muscles of the thigh(14-16).

The gluteus maximus receives its blood supply from the superior and inferior gluteal arteries, both branches of the internal iliac artery(12). The superior gluteal artery also supplies the gluteus medius and minimus muscles, as well as the tensor fascia latae. In addition to the gluteus maximus, the inferior gluteal artery supplies the piriformis, internal obturator, gemellus superior and inferior and quadratus femoris muscles(12, 14, 17) (Figure 7).

The history of approaches to the hip

Total hip replacement has been deemed “the operation of the century”(18) and is now by far the most commonly performed operation on the hip joint(19). To gain access to the hip joint and provide sufficient visualisation, several approaches are currently in use(5), mainly the posterior, anterior, anterolateral and direct lateral approaches(11, 20). Though now used for total hip arthroplasty, several of the approaches were developed for different indications than hip replacement and by well-known surgeons (Figure 8).

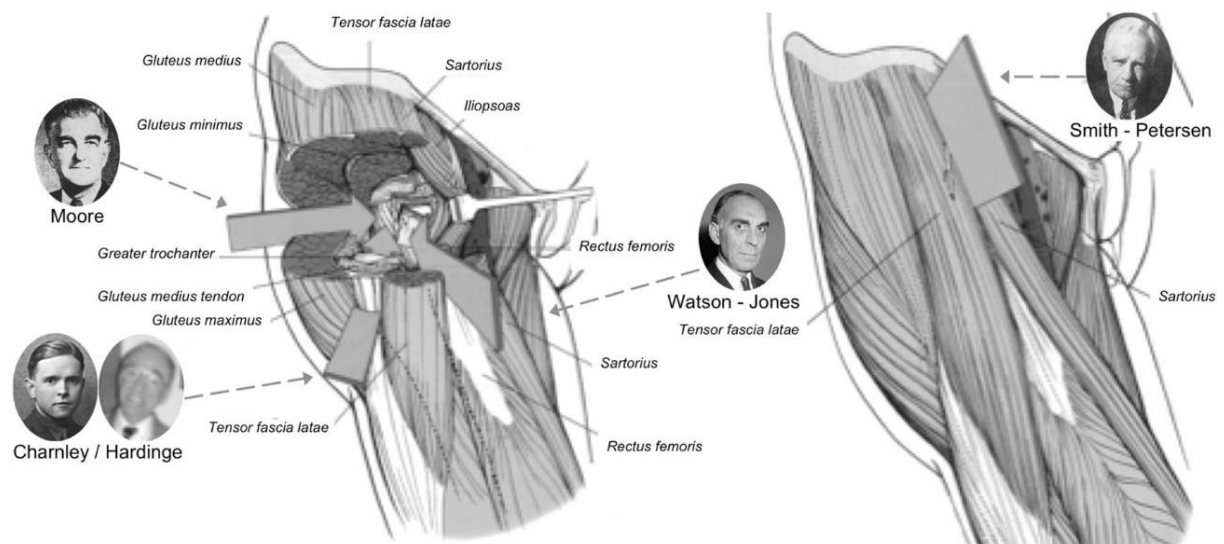


Figure 8. Approaches to the hip and the surgeon(s) affiliated with them. Reprinted with permission from Springer Nature.

The posterior approach

The first description of what would be developed into the now called the posterior approach dates back to 1867 and the publication by Bernhard von Langenbeck titled “Ueber die Schussfracturen der Gelenke und ihre Behandlung”(21).

Von Langenbeck (1810-1887) was born in Padingsbüttel, Germany. He studied medicine at the University of Göttingen and received his doctorate in 1834(22). His academic career spanned nearly fifty years, serving as a lecturer and professor in Göttingen and later as Professor of Surgery at the University of Kiel and at the University of Berlin(21).

Rising to the grade of lieutenant general, von Langenbeck served in the army in several wars(23). This might have inspired his creation of a posterior approach as he used it primarily for infection and war wounds affecting the hip. The incision passed from “above the ischiatic notch to the middle of the greater trochanter, reaching the joint by passing between the bundles of the gluteal muscles”(21). He would resect the femoral head, add postoperative traction and drain, indicating that a posterior approach would improve wound drainage in a supine patient.

Langenbeck’s approach was modified by Theodor Kocher (1841-1917), published in the book “Chirurgische Operationslehre” in 1892. In this publication he not only describes the modification on Langenbeck’s approach, but also discuss the anterior approach as first described by Hueter. However, he only regarded the anterior approach indicated in partial excisions or for operation on congenital dislocation of the hip(24).

Born in Bern, Switzerland, Kocher graduated from the University of Bern. After visits to Berlin, London, Paris and Vienna, he returned to Bern to take up a position in the surgical clinic. In 1871 he applied for and eventually got the post of Professor of Surgery, a position he held for 45 years(24). Deemed “the greatest Swiss surgeon of all time”, Kocher’s work touched nearly all disciplines of surgery and his work on the thyroid gland earned him the Nobel Prize in Medicine in 1909(25).

Kocher extended Langenbeck’s approach caudally, describing an angular incision from the base of the greater trochanter, curving at its superior angle and continuing obliquely in the direction of the gluteus maximus. The gluteus maximus tendon was divided and the short external rotators was detached after internal rotation of the hip(21). His use of the approach was primarily for resection of the hip due to tuberculosis.

The fact that Kocher applied for postgraduate training at Langenbeck’s clinic in Berlin, but was denied due to his Swiss nationality(24), is slightly ironic given that their hyphenated approach now titled the Kocher-Langenbeck approach, is still widely used today(26).

Further advancements in the posterior approach was made by the Scottish surgeon Alexander Gibson (1883-1956). Born in Edinburgh he graduated with a medical degree from the university of his hometown. In 1913 he was made Chair of Anatomy in the Medical School of the University of Manitoba at Winnipeg, Canada(27). His paper “Posterior exposure of the hip joint”(28) starts by stating that due to the popularity of the anterior approach, the posterior approach was ignored and unfamiliar to many surgeons. He described dividing the fascia latae in front of the gluteus maximus and dividing the attachment of gluteus medius and minimus on the greater trochanter to gain access to the joint. The hip was dislocated forward after anterolateral opening of the capsule.



Figure 9. Austin Talley Moore. Reprinted with permission from Springer Nature.

Austin Talley Moore (1899-1963)(Figure 9) is credited with developing and describing the posterior approach as it is used today(29), though calling it the “Southern approach”. He was born in Ridgeway, South Carolina, USA. Moore graduated from Medical College of South Carolina in 1924 and after his internship in Columbia, South Carolina, he started working at the University of Pennsylvania(30). He returned to practice orthopaedic surgery in Columbia in 1927 and founded the Moore Clinic in 1939(29).

In the publication “The Self-Locking Metal Hip Prosthesis”(31) he described the first known case of an intramedullary metal hip implant(32). The prosthesis was made of the cobalt chrome molybdenum alloy Vitallium and was first implanted in 1942 replacing the upper femur of a patient with a giant cell tumour. The patient, weighing an excess of 110 kilograms, regained acceptable function and survived for two years before dying of a condition unrelated to the hip(32). This gave an alternative in the form of a functioning hemi arthroplasty to those suffering from “the unsolved problem” of femoral neck fractures, in the cases where internal fixation and/or immobilisation was not an option. The first Austin Moore hip prosthesis were implanted through the anterior approach. According to Moore’s own statement, this was very difficult(31), making him develop an approach so the prosthesis could be implanted with greater ease. The approach described blunt dissection of the fibres of the gluteus maximus, but no release of the abductor muscles. The short external rotators were released, capsulotomy performed and the hip dislocated by internal rotation.

The anterior approach

The German surgeon Carl Hueter (1838-1882) is attributed with the first written description of the anterior approach(33). He was born in Marburg and started studying medicine at the age of sixteen, graduating at the age of twenty. After graduating, he received further training in Berlin and on educational journeys to Vienna, England, Scotland and Paris. In 1865 he studied under Langenbeck,(34). Hueter became full professor of surgery in Rostock, Germany at the age of 29 and later moved to Greifswald where he published numerous works.

Hueter described the anterior approach in his “Der Grundriss der Chirurgie” published in 1881(35). The incision was similar to that used today but was described for resection of the hip. Hueter recommended a skin incision of 10-15 cm in adults. Further dissection utilized the interval that now bears his name, the Hueter interval, between the sartorius and tensor fascia lata muscles(33, 35).

The spread of the anterior approach in the English-speaking world is credited to Marius Nygaard Smith-Petersen (1886-1953) (Figure 10) and the approach is commonly referred to as the Smith-Petersen approach(33).

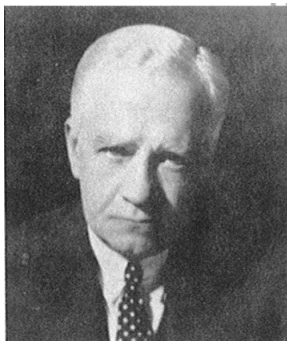


Figure 10. Marius Nygaard Smith-Petersen. Reprinted with permission from Springer Nature.

Smith-Petersen was born in Grimstad, in Aust-Agder County, Norway. After the death of his father, Smith-Petersen emigrated with his mother to Milwaukee, Wisconsin, USA. Arriving in the United States at the age of sixteen unable to speak English, he quickly adapted and eventually graduated from Harvard Medical School in 1914(36). He served his surgical internship at Peter Bent Brigham in Boston under the supervision of doctor Harvey Cushing and after finishing he started orthopaedic internship at the Massachusetts General Hospital in 1916(37).

There, he assisted in an open reduction of a congenital dislocation of a hip, exposed through a Kocher incision. The patient survived by a very narrow margin and in Smith-Petersen’s own words: “It was bloody; it was brutal”. Shocked, he asked his senior dr. Roy Abbott if there was another way of exposing the hip. He answered: “Why don’t you figure one out?”, and so he did(37). Inspired by the subperiosteal muscle flaps used in cerebellum exposure, he combined the anterior approach through the Hueter interval with periosteal reflection of the muscles from the lateral aspect of the ilium(38). From 1923 until his death, he was

instructor, assistant clinical professor and clinical professor at Harvard, and in 1929 he was appointed chief of orthopaedic surgery at Massachusetts General Hospital(36).



Figure 11. A Smith-Petersen mould arthroplasty revised 48 years after implantation. Photo courtesy of Torbjørn Tyri Fagerberg.

Interested in fractures of the neck of the femur, Smith-Petersen designed a triflange nail to be driven from the lateral surface of the trochanter, through the neck and fracture and into the head of the femur(39). Previous attempts at internal fixation of these fractures had been abandoned due to providing only partial and temporary fixation and these fractures were commonly followed by non-union. The triflange nail proved successful, and by making pin fixation of hip fractures accepted, greatly reduced the non-union rates(40). Smith-Petersen advocated open reduction and fixation, utilizing his described approach(39).

In addition to his approach, Smith-Petersen is also known for his mould arthroplasty(37), introduced in 1923 (Figure 11). Originally the mould arthroplasty consisted of a hollow hemisphere of glass placed over the head of the femur to stimulate cartilage regeneration. The glass functioned as a smooth surface providing encouraging results but could not endure the stress of walking causing failure. After experimenting with other materials, eventually Vitallium(36), satisfactory results were achieved(37) and again the Smith-Peterson approach was used and recommended(41).

The anterolateral approach

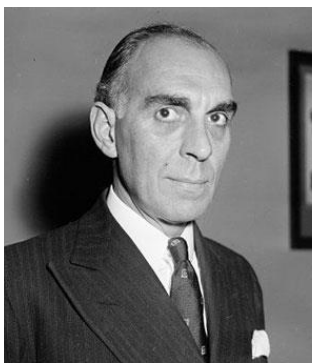


Figure 12. Sir Reginald Watson-Jones. Reprinted with permission from Springer Nature.

The anterolateral approach is often referred to as the Watson-Jones approach after the man who first described it, Sir Reginald Watson-Jones (1902-1972) (Figure 12). Born in Brighton, Sussex he was raised and studied medicine in Liverpool(29). Though from birth “just” Jones, he hyphenated his name with his mother’s maiden name to distinguish himself from the other Jones’ in Liverpool(42), among others his mentor sir Robert Jones, the surgeon who established orthopaedics as a speciality(42).

After finishing his training in 1926, Watson-Jones started a private clinic and was senior surgical registrar at the Liverpool Royal Infirmary and in 1935 he joined the honorary staff. During the Second World War he was a civil orthopaedic consultant to the Royal Air Force. From 1943 he was the director of the orthopaedic and accident department at the London hospital and he was orthopaedic surgeon to both King George VI and the Queen of England(43).

He published his first paper in the early 1930's and subsequently published more than three manuscripts a year. His textbook "Fractures and Joint Injuries"(44) published just before WWII was the first text comprehensively dealing with fractures and remained the "bible" in fracture management for decades. It has been translated to several languages and reprinted numerous times(42).

Watson-Jones described the approach bearing his name in 1936 in the publication "Fractures of the neck of the femur". In it he praised the Smith-Petersen's triflange nail, but held that Smith-Petersen's approach was not suited to control the insertion of the nail(45). Instead, he advocated a lateral approach exposing the femur in the interval between the gluteus medius and tensor fascia latae which after opening the capsule offered "a wonderfully clear view of the whole line of the neck of the femur"(45).

The direct lateral approach

The origin of the direct lateral approach is often credited to McFarland and Osborne as they state in their paper "Approach to the hip: A suggested improvement on Kocher's Method" published in 1954 that the approach was "essentially lateral"(46).

John Bryan McFarland (1930-2013) studied medicine in Liverpool, qualifying in 1954. Though spending most of his professional life in Liverpool, he spent time in Kenya during his service in the Royal Army Medical Corps, mainly working as an anaesthetist(47).

Geoffrey Vaughan Osborne (1918-2005) was born in North Wales but began his medical training at the age of 16 at Liverpool Medical School. Graduating in 1940, he initially considered radiology. The need for surgeons during the war however made him become a surgeon, practicing in Liverpool for most of his career(48).

The McFarland-Osborne approach was based on the notion that the gluteus medius and vastus lateralis were in direct functional continuity through the periosteum covering the

greater trochanter(46). The trochanteric attachment of gluteus medius was peeled off transferring forward the sheet of the combined gluteus medius and vastus lateralis muscles(46, 49). The gluteus minimus was split, divided and retracted upward to expose the capsule. To close, the capsule and gluteus minimus were sutured in one before returning the gluteus medius and vastus lateralis to their original position and sutured in place(46).



Figure 13. Sir John Charnley. Reprinted with permission from Springer Nature.

The further development of the direct lateral approach was strongly influenced by Sir John Charnley (1911-1982)(Figure 13), the surgeon and inventor who influenced the development of hip replacement more than any other(50).

Sir John was born In Bury, Lancashire, UK. He studied medicine at the Victoria University of Manchester graduating in 1935. As the youngest surgeon to receive the honour he became a Fellow of the Royal College of Surgeons at Guy's Hospital in London at the age of twenty-five(51). After brief stints at Salford Royal Hospitals in Wiltshire and King's College in London, he returned to Manchester in 1939 becoming resident casualty officer at the Manchester Royal Infirmary(51).

During WWII, Charnley volunteered to join the Royal Army Medical Corps and his postings included Northern Ireland, the Middle East and Dover, England. After the war he spent six months working at the Robert Jones and Agnes Hunt Orthopaedic Hospital in Shropshire, England, later returning to Manchester before developing a hip centre at Wrightington Hospital in Wigan near Manchester(51).

After some trial and error, Charnley eventually developed the first functioning total hip arthroplasty, the “low friction arthroplasty”(52). This involved an Ultra High Molecular Weight Polyethylene (UHMWP) cup in the acetabulum and metal stem in the femur, both fixed to the bone by acrylic cement(1). The principals of this method is still used in today's hip arthroplasties(5).

Charnley used a lateral approach with a trochanteric osteotomy when performing his arthroplasties(53, 54). This was not only for access as he believed that the optimal biomechanics were obtained by medializing the femur and lateralizing the trochanter, reducing the stress on the implant while at the same time increasing the lever arm of the abductors(55, 56).

The low friction arthroplasty was widely applauded and adopted by an increasing number of orthopaedic surgeons, but the trochanter osteotomy for many caused problems and the need was questioned(29, 56). This led to the development of the direct lateral approach which facilitated the Charnley low friction arthroplasty without the trochanteric osteotomy, published by Hardinge in 1982 titled “the direct lateral approach to the hip” (57).



Figure 14. Kevin Hardinge.
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from Springer Nature.

Kevin Hardinge (1939-) (Figure 14) was born in Douglas on the Isle of Man. He studied medicine at Liverpool University starting in 1957. Qualifying as an orthopaedic surgeon in 1969, he worked at Manchester Royal Infirmary before starting at the Centre for Hip Surgery at Wrightington Hospital in 1976(29). He there worked with Sir John and learned how to perform the low friction arthroplasty.

Instead of performing a trochanteric osteotomy, Hardinge released the anterior portion of the gluteus medius and the gluteus minimus to reach the hip capsule, the muscles reattached after the work on the hip was done. Charnley originally thought it sacrilege to perform a hip replacement without a trochanteric osteotomy, but after seeing that Hardinge’s patients performed as well as those with the osteotomy, he accepted the use of the approach, though not changing his own practice(56).

Though different variations of the direct lateral approach exists (58), it is still commonly referred to as the Hardinge approach and is used far more than Charnley’s approach with trochanteric osteotomy(19) in primary THA.

Changes in approach used for total hip arthroplasty in Norway

During the first period in the Norwegian Arthroplasty Register from 1987-94, the most used approach was the direct lateral, with 67% of the operations. The posterior approach was used in 26% in the same period. Trochanteric osteotomy was reported in 18% of the operations. Similar division between the direct lateral and the posterior approach was reported for consecutive years until 2009, with the use of trochanteric osteotomy dropping to 6% in the period between 1995-99, 1.1-2.6% between 2000-2007 and used in less than 1% since(59).

From 2009 there was an increase in the use of the anterior approach and later the anterolateral approach, the anterior approach stabilising at around 8 % and the anterolateral at around 13 % from 2016 onwards. There has been a great reduction in the direct lateral approach, only used in 5% in 2018. The posterior approach has increased, in 2018 the approach was used in 71% of all primary THAs in Norway(5) (Figure 15).

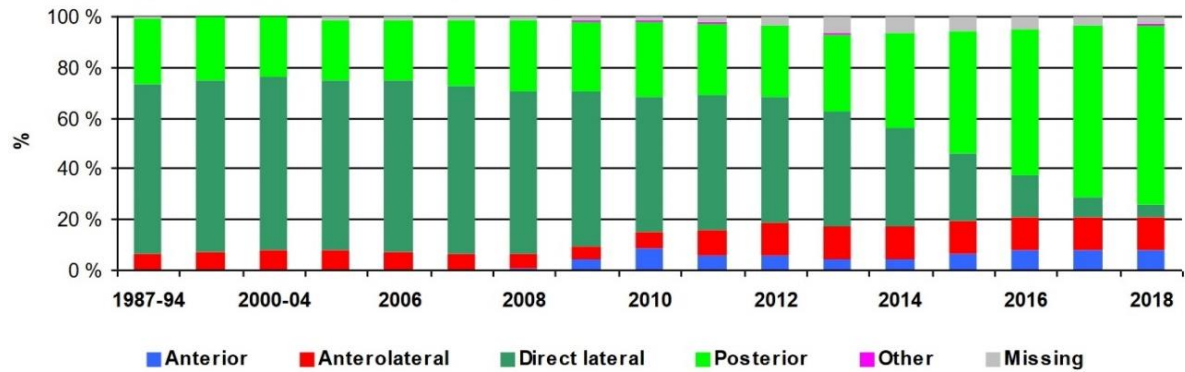


Figure 15. Approaches used in primary total hip arthroplasty. Table from the Norwegian Arthroplasty Register report 2019.

The reported use of minimally invasive surgery has increased from 1% in 2008 to over 20% since 2016, consistent with the increase in the use of the anterior and anterolateral approaches (Table 2).

Year	Yes	No	Missing	Total
2018	2 068 (21,6%)	7 080 (74,1%)	405 (4,2%)	9 553
2017	1 943 (21,2%)	6 881 (75,0%)	350 (3,8%)	9 174
2016	1 818 (20,3%)	6 897 (77,0%)	238 (2,7%)	8 953
2015	1 594 (18,9%)	6 543 (77,4%)	314 (3,7%)	8 451
2014	1 337 (16,4%)	6 531 (80,2%)	273 (3,4%)	8 141
2013	1 409 (17,4%)	6 321 (78,0%)	374 (4,6%)	8 104
2012	1 328 (16,9%)	5 862 (74,7%)	659 (8,4%)	7 849
2011	1 000 (13,6%)	6 005 (81,6%)	355 (4,8%)	7 360
2010	934 (12,7%)	6 171 (84,2%)	225 (3,1%)	7 330
2009	398 (5,6%)	6 671 (93,8%)	46 (0,6%)	7 115
2008	65 (0,9%)	6 755 (98,6%)	28 (0,4%)	6 848
2007	4 (0,1%)	6 567 (98,6%)	89 (1,3%)	6 660
2006	58 (0,9%)	6 006 (95,0%)	255 (4,0%)	6 319
2005	144 (2,2%)	5 814 (88,1%)	639 (9,7%)	6 597

Table 2. Mini invasive surgery in primary total hip arthroplasty. Table from the Norwegian Arthroplasty Register report 2019.

The Norwegian Arthroplasty Register



Figure 16. The logo of the Norwegian Arthroplasty Register depicting a Christiansen stem.

The Norwegian Arthroplasty Register (NAR) was started by the Norwegian Orthopaedic Association in September 1987(60). The inferior results of the Christiansen stem, and the extended period it took to reveal the high failure rate(61), showed the need for a register to detect inferior implants. Initially the register was only for hip arthroplasties, all joint replacements in Norway was included in January 1994(62). It was approved as a national quality register in 2009.

The primary surgery is registered and linked with subsequent revision using the 11-digit identity number assigned to all of Norway's inhabitants. The one-page form used for both primary surgery and revisions is filled in by the operating surgeon, usually directly after surgery(63).

In addition to patient identification, date of surgery, indication, affected side, approach and implant used are reported, as well as duration of surgery. Adjuvant treatment, such as antibiotics, thrombosis prophylaxis etc. are also reported. From 2005 the form includes information on the use of minimally invasive surgery (MIS)(64).

The NAR has been validated (65) and has a high level of registration completeness, both for primary surgery and revision(5, 66).

Approaches as now used in total hip arthroplasty

The anterior approach

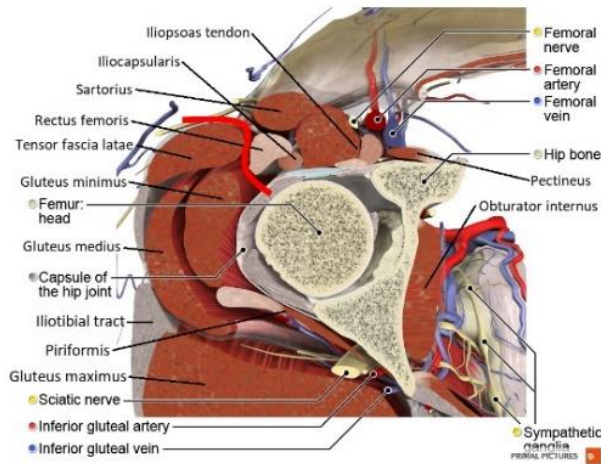


Figure 17. Axial view of the hip with the anterior approach indicated with red line.

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The anterior approach (Figure 17) in THA is now mostly used as a “minimally invasive approach”. The patient is usually placed in the supine position, either on an orthopaedic table(67) or on a standard table(68). Various skin incisions are used(69). The hip capsule is reached through the interval between the sartorius and tensor fascia latae superficially and deeper between the rectus femoris and the gluteus medius/minimus. The anterior

approach is muscle and nerve neutral, but the ascending branches of the lateral circumflex femoral artery cross the surgical field and must be cauterized. After capsulectomy, osteotomy and removal of the femoral head, the acetabulum is accessible for preparation. Before preparation of the femur, capsule release is performed to lift the femur(70) and placing it in external rotation and adduction(20).

The anterolateral approach

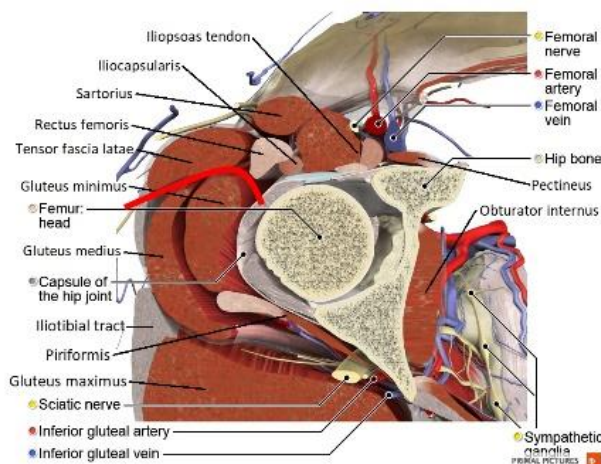


Figure 18. Axial view of the hip with the anterolateral approach indicated with red line.

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The anterolateral approach (Figure 18) is now also mostly used as a “minimally invasive approach”. The patient is usually placed in the supine position, but lateral decubitus position is also used(71). Various skin incisions are also used in this approach(72). After incising the fascia, the interval between the tensor fascia latae and the gluteus medius is palpated and opened to reach the capsule. Some branches of the lateral

circumflex artery may need cauterization. The femoral head is released after capsulectomy and osteotomy. After preparation of the acetabulum, capsular release is performed to gain access to the proximal femur.

The direct lateral approach

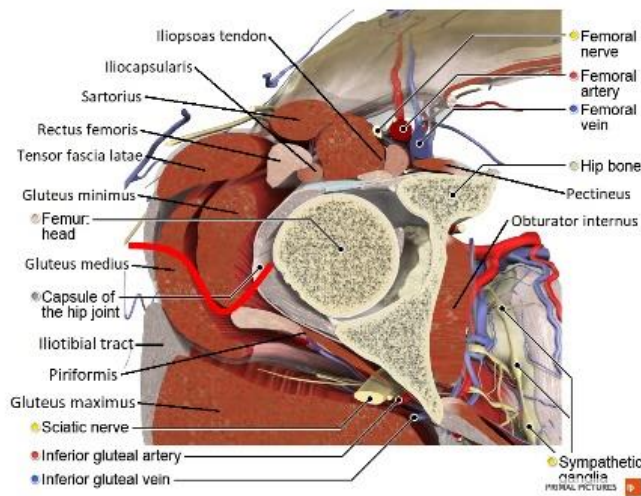


Figure 19. Axial view of the hip with the direct lateral approach indicated with red line.
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Though originally described with the patient in the supine position(57), the direct lateral approach (Figure 19) is now most commonly performed with the patient in the lateral decubitus position(58). The skin incision is centred over the greater trochanter, either as a straight incision or slightly curved. The fascia latae is incised in line with the skin incision. The anterior third or half of the gluteus medius and the whole gluteus

minimus is released from the greater trochanter to expose the capsule(73). After capsulotomy, the hip is dislocated by external rotation and osteotomy performed. After preparation and implantation of the prosthesis, the gluteus medius and minimus is reattached to the trochanter major, usually by osteosutures(58).

The posterior approach

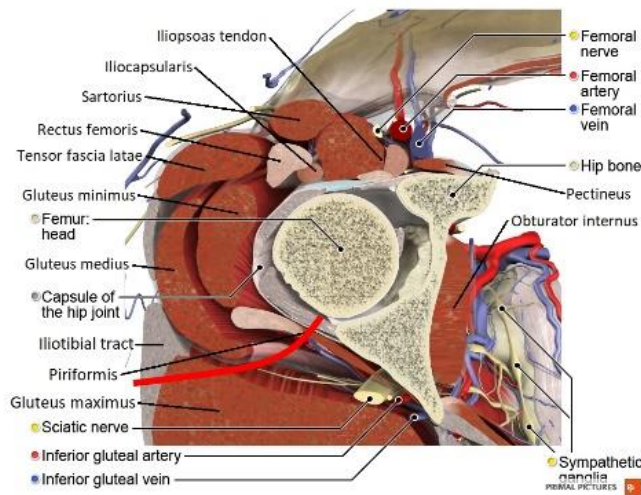


Figure 20. Axial view of the hip with the posterior approach indicated with red line.
Copyright Primal Pictures Ltd.

The posterior approach (Figure 20) is most commonly performed with the patient in the lateral decubitus position. The skin incision is centred over the greater trochanter, curving backwards in line with the fibres of the gluteus maximus superior to the trochanter(73). The fibres of the gluteus maximus are bluntly divided superiorly and the fascia is split distally. The hip is placed in internal rotation and the short external rotators

are cut along with the capsule(74). The hip is dislocated with internal rotation, osteotomy performed before acetabular and femoral preparation. After implantation of the prosthesis, the obturator internus, piriformis and the posterior capsule are reattached to the femur.

Aim of the studies

The overall aim of this thesis was to evaluate the anterior approach and compare it to other approaches, mainly the direct lateral approach, by:

Paper 1: Comparing the postoperative levels of CK, CRP and pain after THA through either the anterior or the direct lateral approach.

Paper 2: Comparing implant survival and relative risk of revision between the anterior, anterolateral, posterior and direct lateral approaches.

Paper 3: Comparing postoperative clinical and patient reported outcome measures after THA through either the anterior or the direct lateral approach with two-year follow-up.

Recording complications after THA through either the anterior or the direct lateral approach.

Methods

Ethics

The Declaration of Helsinki(75) developed by the World Medical Association include 37 items as statement of ethical principles for medical research involving human subjects. Issues covered include evaluation by an ethical committee, confidentiality, risk minimizing, informed consent, proper methodology and more.

The randomized trial in **paper 1 and 3** was approved by the Regional Ethics Committee prior to inclusion of patients. A randomized trial between a “new” and “old” approach could pose an ethical challenge. However, if one accepts the null hypothesis that the two approaches will provide equal result, the ethical challenge is limited. In addition, both the anterior and the direct lateral approaches were established and in use in our department prior to the start of the study. All patients were scheduled for THA prior to being approached for study inclusion.

Signed, informed consent was given by all participating patients. Patients were attempted blinded to approach used. Any blinding of patients is ethically challenging given the ideal of informed consent. It is however likely that, after discharge, all patients figured out which approach was used based on the localization of the scar.

Additional blood tests were drawn from the patients because of participating in the study and additional tests were performed, for instance the 6-minute walk distance (6MWD). The patients also had to fill in several forms like Oxford Hip Score (OHS) and Eq-5D. This is ethically challenging as it was of no direct benefit to the patients, but the added discomfort for the patients seems reasonable as it was of no direct harm.

The register study in **paper 2** offers few ethical challenges. The data on all THAs performed are recorded in the NAR irrespective of planned studies. Patients sign informed consent for their operation to be registered, but the recording is done by the operating surgeon. All data collection done by the NAR is approved the Norwegian Data Inspectorate.

Patients

Paper 1 and 3 – A randomised controlled trial

The 164 patients included in the prospective, randomized trial in **paper 1 and 3** were recruited from the outpatient clinic at Sørlandet Hospital Arendal between January 2012 to June 2013. Patients aged between 20 and 80 with clinical and radiographic end-stage osteoarthritis were considered candidates. Patients with previous hip surgery on the included hip, BMI >35 kg/m², mental illness or inadequate language skills preventing follow-up were excluded. Patients with an explicit request regarding approach was also excluded. During the inclusion period, 379 THAs were performed at our institution. 201 patients were excluded, mainly due to requesting a particular approach (n=114), age over 80 (n=43) or due to previous surgery of the hip (n=27). 14 patients declined to participate. Written consent was obtained from all participating patients. One patient withdrew prior to surgery due to being diagnosed with cancer. Randomization was done using sealed envelopes, allocating 84 patients to THA performed through the anterior approach and 80 through the direct lateral.

After discharge, patients were evaluated at three, six, 12 and 24 months postoperatively. Five patients from each group were lost to follow-up, while all others attended all postoperative controls.

Paper 2 – A register study

The 21,860 THAs included in **paper 2** were primary THAs registered in the NAR between 2008 and 2013. Only uncemented stems were included due to very few cemented stems being implanted using the anterior or anterolateral approach during the study period.

2,017 THAs were operated using the anterior approach, 2,087 using the anterolateral, 5,961 the posterior and 11,795 the direct lateral. Follow-up ended on December 31st 2015.

Treatment

All patients in **paper 1 and 3** were operated with a cemented cup (Marathon©, DePuy, Warsaw, Indiana, USA), uncemented stem (Corail©, DePuy) and ceramic 32 mm head (Biolog forte©, Ceramtec, Plochingen, Germany) (Figure 21). Spinal anaesthesia combined



Figure 21. Marathon cup, Biolox forte head and Corail stem.

with local infiltration anaesthesia was used. 2 grams of Cefalotin i.v. was given prior to surgery and a further three doses were given after surgery. 500 mg of Tranexamic acid was administered at the onset of surgery and at closure. The surgical procedures are described in detail in **paper 3**. Five surgeons with experience in both approaches performed all operations. Full weight bearing was allowed as tolerated immediately after surgery. The postoperative regime was the same for all patients.

Patients in **paper 2** were reported to the NAR due to having had a primary THA. Subsequent revisions were also reported.

Outcome measures

The aim of **Paper 1** was to compare the rise in CK and CRP between patients receiving a THA through the anterior and direct lateral approach as well as comparing pain levels and use of pain medications. The use of pain medication was compared by converting all pain medication to morphine equivalent (ME)(76).

The outcome in **Paper 2** was revision, defined as any exchange, addition or removal of any or all parts of the implant.

In **Paper 3**, the aim was to compare postoperative results with two-year follow-up between patients receiving THAs via the anterior and direct lateral approach. The main outcome was the Harris Hip Score (HHS). Also compared were the 6MWD, OHS, Eq-5D and the Trendelenburg test. Complications, both surgical(77) and general, were recorded.

Creatine Kinase

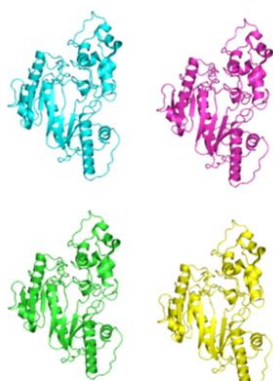


Figure 22. Crystal structure of human Creatine kinase.

Source: rcsb.org

Creatine kinase (Figure 22(78)) reversibly catalyses the conversion of creatine and ADP to phosphocreatine and ATP. ATP is the principal energy storing and transferring molecule in cells(79) and CK is therefore important in high energy demanding tissue(80).

The enzyme is a large protein composed of two distinct polypeptide subunits, M and B(81) making three isoenzymes found in human tissue. CK-MM is found predominantly in skeletal muscle, CK-MB in cardiac muscle and CK-BB in the brain. 99% of CK activity in

adult human skeletal muscle is CK-MM(82). Increase in CK values in serum occur both after reversible and irreversible muscle damage(83).

CK measurement in serum is regarded as the best and most sensitive marker for of skeletal muscle damage(84-86). Damage of skeletal muscle during surgery causes a rise in CK levels in serum(87-89) and studies indicate greater increase after major surgery than after minor(82, 90). The half-life of CK is 1.5 days(85).

C-reactive protein

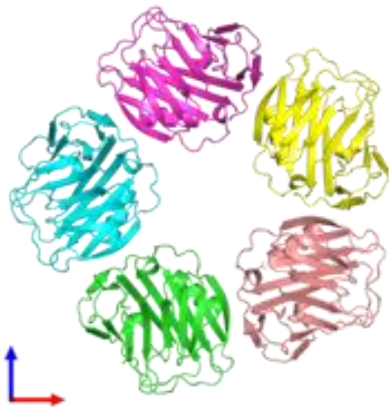


Figure 23. Crystal structure of human C-reactive protein. Source: rcsb.org

CRP (Figure 23(78)) was first described in 1930 by Tillett and Francis(91). Originally designated Fraction C, the name C-reactive protein arose due to its binding to pneumococcal somatic C-polysaccharide(92). CRP is an acute phase protein(93, 94) and present only in low amounts in healthy individuals (95, 96). In response to tissue injury, inflammation and infection(97), the protein is secreted by the liver(98). CRP binds to phosphatidyl choline expressed the surface of dead or dying cells and microbial capsule tagging them for destruction (opsonization)(99). Levels of CRP is used both to diagnose infections and to monitor the effect of treatment(100, 101). The level also increases as a normal response to surgery(102-104). The half-life of CRP in plasma is 19 hours(105).

Visual analogue scale (VAS) pain

Visual analogue scales have been used for several years measuring different aspects in medicine(106-109) and are commonly used to assess pain levels in clinical studies(107, 110, 111). Patients are asked to place their level of pain between 0, indicating no pain, and 10, indicating the worst pain imaginable(112). VAS is easily applied with minimal instruction(113) and the results do not differ based on sex or age(114).The minimum clinically important difference (MCID) in VAS pain score is determined to be between 0.9 and 1.5(114-118).

Harris Hip Score

The score was described by William H. Harris in 1969 as a method of assessing the result after hip surgery(119). Though the article was on “Traumatic Arthritis of the Hip after Dislocation and Acetabular Fractures: Treatment by Mold Arthroplasty”, the score was

according to Harris “designed to be applicable to different hip problems and different methods of treatment”. HHS is widely used in assessing symptoms of osteoarthritis and results after THA(120-123). Four domains are covered: Pain (0-44 points), function (0-47 points), absence of deformity (0-4 points) and range of motion (0-5 points)(124). A score of 100 indicates best possible outcome. The score is responsive to change, has high reliability(125) and is a valid measure of outcome after THA(126), though some concerns have been about ceiling effect when using the score(127). The MCID is not well established(128), values stated varying from 4 to 18 points (126, 129-131).

6-minute walk distance

The 6MWD was originally devised as a measure of exercise capacity in patients with chronic heart failure(132), but is now also used in the evaluation of several other medical conditions (133-139). The test has high reliability in evaluating patients before and after THA(140), is responsive in detecting change in function of these patients(141) and is often used in evaluating the results after THA(142-147). The MCID is 79 meters(145).

Oxford Hip Score

The OHS was described in 1996(148) as a measure of patients’ perception of their outcome after THA(148). It has both high reliability(149) and validity(150). The score is a patient reported outcome measure (PROM) and consists of 12 items. Each item has five possible responses. Originally the score ranged from 12 to 60, 12 being the best score. After revision, each item ranges from 0 (worst) to 4 (best), resulting in total score from 0 to 48 (worst to best)(151). In addition to its use in clinical studies, the OHS is also used by several arthroplasty registers(152-154). The MCID is 5 points(155).

EQ-5D

The Eq-5D is a generic health-related quality of life measurement published by the EuroQol Group in 1990(156). The first part of the EQ-5D is a described part consisting of five items: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The EQ-5D-3L version used in **paper 3** has three possible responses to each item (no problem, some or moderate problems or extreme problems). From these, the EQ-5D index is calculated using value sets produced for specific countries or regions, generated using either time trade-off (TTO) or VAS valuation technique(157). The European VAS-based value set was used in **paper 3**(157). A score of 1 indicates best imaginable health state, 0 indicating death and negative value indicating a state worse than death. The MCID for EQ-5D index is

0.074(158). The second part is the EQ-VAS consisting of a 20-cm visual scale ranging from zero to 100, 100 indicating best health imaginable. It is intended as the individual respondents' quantitative measure of health(159). The EQ-5D is used to evaluate health in general populations, in clinical studies, economic health studies and is also used by several national arthroplasty registers(160-168).

Trendelenburg test

Professor Friedrich Trendelenburg (1844-1924) described the test bearing his name (Figure 24) in 1895. He offered evidence that the “swaying gate” seen in patients with congenital dislocation of the hip (CDH) or progressive muscular atrophy was due to abnormal abductor function. The accepted explanation at the time was that the gate was caused by the femoral head sliding up the ilium, but Trendelenburg attributed it to reduction in the size of the gluteus medius and altered work distance and angle for the glutei(169).

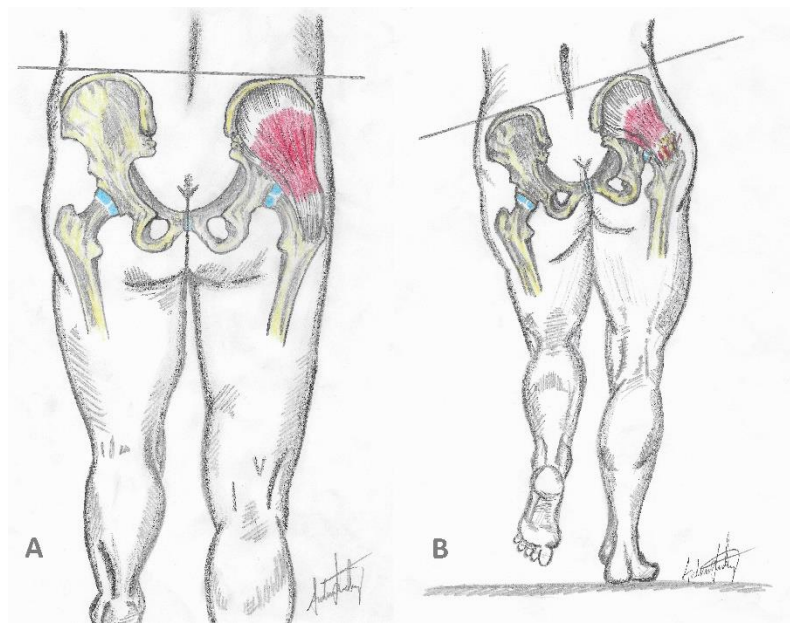


Figure 24A. Negative Trendelenburg test. B. Positive Trendelenburg test. Illustration by Andreas Lødrup.

Though initially describing patients with CDH and progressive muscular atrophy, the test has been used to assess general hip function and often to assess the result after THA(170, 171). It tests the abductor function of the hip, but does not differ between damage to the glutei, nerve damage or altered leg length or offset(171-173). Originally,

the test was described by Trendelenburg as negative if the patient could stand on the treated leg and raise the buttock of the other side up to or above the horizontal line(169). The test has later been performed and interpreted in different ways but was “redefined” by Hardcastle and Nade in 1985(171). They defined that the test was positive if the described position could not be held for at least 30 seconds. In **paper 3** the period was set to at least 5 seconds due to all patients performing the 6-minute walk test directly before the Trendelenburg test.

Statistics

In **paper 1 and 3**, mean and standard deviation (SD) were presented for continuous variables and percentages for categorical variables. Mean difference with 95% confidence interval (CI) was calculated and tested using an independent sample t-test for group comparison. Chi-square test was used for categorical variables. For the HHS and OHS the ceiling effect was calculated. The significance level was set at $p \leq 0.05$. Statistical analysis was performed using various versions of SPSS (IBM SPSS, Chicago, IL, USA).

In **paper 2**, 2 and 5-year implant survival was calculated using Kaplan-Meier survival analysis. Log-rank test was used to compare the groups. Cox proportional hazard model analysis adjusted for age, sex, primary diagnosis, ASA grade, size of femoral head component, cup fixation, type of articulation and duration of surgery was used with revision as end point based on different causes. Sensitivity analysis was performed to look for case-mix bias. Two and 5-year implant survival rates and the relative risk (RR) with 95% confidence interval (CI) were presented. The significance level was set at $p \leq 0.05$. Analyses were performed using IBM SPSS Statistics, version 23, and the statistical program RStudio, version 2.15.032(174).

Power calculation

The primary study outcome in **paper 3** was the HHS at 2 years. Power calculations was based on a MCID of 10 and SD of 15. With a standardized difference of 0.66, according to Altman's monogram(175), 70 patients in each group were needed to provide 80% power with a significance level of 5%(176). To account for loss of follow-up, it was decided to include at least 80 patients in each group.

Results

Demographics

Baseline demographic data on the patients included in the randomized trial in **paper 1** and **paper 3** (Table 3) showed comparable groups.

	Anterior Approach	Direct Lateral Approach
Number of patients	84	80
Age (yrs)	67.2 ± 8.6	65.6 ± 8.6
Sex (M/F)	25/59	30/50
Body mass index (kg/m ²)*	27.7 ± 3.6	27.6 ± 3.9
ASA grade*†	1.9 ± 0.7	1.8 ± 0.7
Charnley Category*‡	1.6 ± 0.7	1.7 ± 0.7
*Values are given as mean and standard deviation. †ASA = American Society of Anesthesiologists ‡Category 1/A denotes patients with only one affected hip, 2/B both hips affected and 3/C systemic factors affecting locomotion		

Table 3. Demographic data on the patients included in in the randomized trial comparing the anterior and the direct lateral approach in THA.

In **paper 2**, demographic data revealed differences between the groups in age distribution, cup fixation and diagnosis leading to THA (Table 4). A larger proportion of patients operated via the direct lateral approach had heads smaller than 32 mm. The articulation differed between the approaches. Ceramic on cross-linked polyethylene was the most used articulation with the anterior (67%) and the direct lateral (41%) approaches. With the anterolateral approach, the most used articulation was metal on cross-linked polyethylene (65%). Ceramics on cross-linked polyethylene (36%) and metal on cross-linked polyethylene (34%) was used in almost equal amounts with the posterior approach.

The longest duration of surgery was with the anterior approach with mean 90 minutes (95% CI = 89 to 91) and shortest for the posterior approach with 77 minutes (95% CI = 76 to 78). The mean for the anterolateral approach was 83 minutes (95% CI = 82 to 84) and for the direct lateral 85 minutes (95% CI = 84 to 85).

	Anterior approach n (%)	Anterolateral approach n (%)	Posterior approach n (%)	Direct lateral approach n (%)	All n (%)	P-values
Total	2017 (9.2)	2087 (9.5)	5961 (27.3)	11795 (54.0)	21860 (100)	
Sex						
Male	675 (33.5)	762 (36.5)	2106 (35.3)	4564 (38.7)	8107 (37.1)	<0.001†
Female	1342 (66.5)	1325 (63.5)	3855 (64.7)	7231 (61.3)	13753 (62.9)	
Age, years						
Mean (SD)	67 (11)	67 (11)	65 (12)	64 (12)	65 (12)	<0.001‡
<55	271 (13.4)	262 (12.6)	1079 (18.1)	2171(18.4)	3783 (17.3)	<0.001†
55-64	571 (28.3)	499 (23.9)	1777 (29.8)	3799 (32.2)	6646 (30.4)	
65-74	686 (34.0)	800 (38.4)	1925 (32.3)	3664 (31.0)	7075 (32.4)	
>75	489 (24.2)	526 (25.2)	1180 (19.8)	2161 (18.3)	4357 (19.9)	
ASA* grade						
ASA 1	491 (24.4)	360 (17.2)	1323 (22.2)	3007 (25.5)	5181 (23.7)	<0.001†
ASA 2	1245 (61.8)	1378 (66.1)	3704 (62.1)	6691 (56.8)	13018 (59.6)	
ASA 3	263 (13.1)	321 (14.4)	863 (14.5)	1931 (16.3)	3378 (15.5)	
ASA 4	1 (0.0)	2 (0.1)	18 (0.3)	26 (0.2)	47 (0.2)	
Missing	17 (0.8)	26 (1.2)	53 (0.9)	140 (1.2)	236 (1.1)	
Deaths						
	111 (5.5)	79 (3.8)	269 (4.5)	745 (6.3)	1204 (5.5)	<0.001‡
Cup Fixation						
Uncemented	907 (45.0)	107 (5.1)	4015 (67.3)	4140 (35.1)	9169 (41.9)	<0.001†
Cemented	1088 (53.9)	1978 (94.8)	1894 (31.8)	7536(63.9)	12496 (57.2)	
Missing	22 (1.1)	2 (0.1)	52 (0.9)	119 (1.0)	195 (0.9)	
Diagnosis						
Osteoarthritis	1756 (87.1)	1831 (87.7)	4175 (70.0)	8533 (72.3)	16295 (74.5)	<0.001†
Other	258 (12.8)	251 (12.0)	1756 (29.5)	3215 (27.3)	5480 (25.1)	
Missing	3 (0.1)	5 (0.2)	30 (0.5)	47 (0.4)	85 (0.4)	
*American Society of Anaesthesiologists †Chi-square test ‡Student T-test						

Table 4. Demographic data on the patients included in in the register study comparing the anterior, anterolateral, posterior and the direct lateral approach in THA.

Paper 1

The aim of **paper 1** was to compare levels of muscle damage (CK), inflammation (CRP) and pain using either the anterior or the direct lateral approach in THA.

CK

In both groups the maximum level of CK was reached on the 3rd postoperative day. The level was higher in the anterior group on all postoperative measurements (Figure 25). Statistically significant difference was found immediately after surgery (mean difference 29.6, 95% CI 4.27 to 54.9, p=0.02) and on postoperative day 4 (mean difference 193, 95% CI 60.7 to 326, p=0.005).

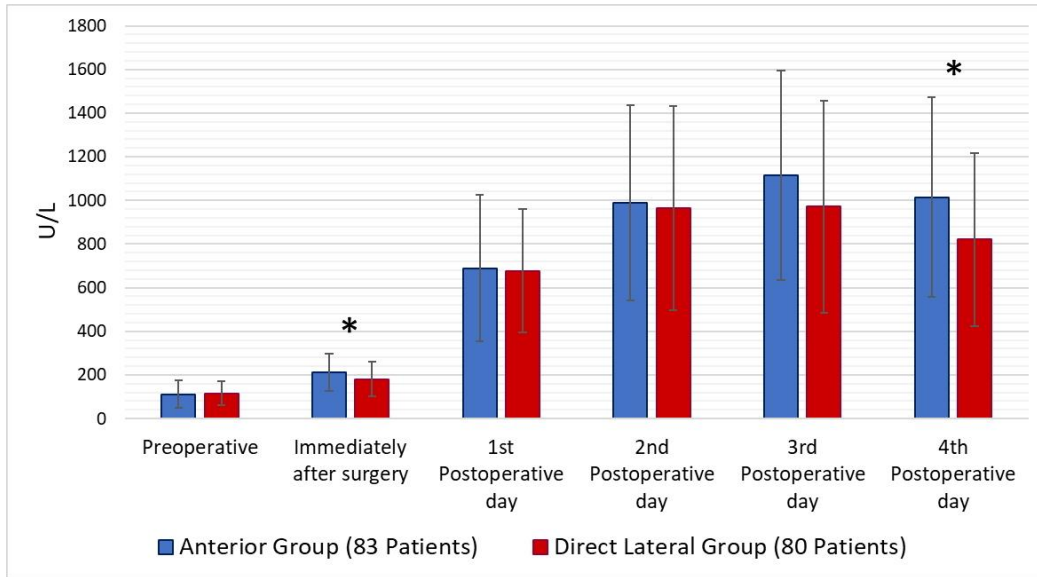


Figure 25. CK values comparing anterior and direct lateral approach. Chart indicate mean \pm SD.

* Indicates statistically significant difference.

CRP

No difference was found in CRP levels between the groups (Figure 26). Maximum levels, and maximum difference between the groups, were reached on the third postoperative day with mean level in the anterior group 48 mg/L and 52 mg/L in the direct lateral (mean difference 3.2, 95% CI -15 to 9.0, $p=0.6$).

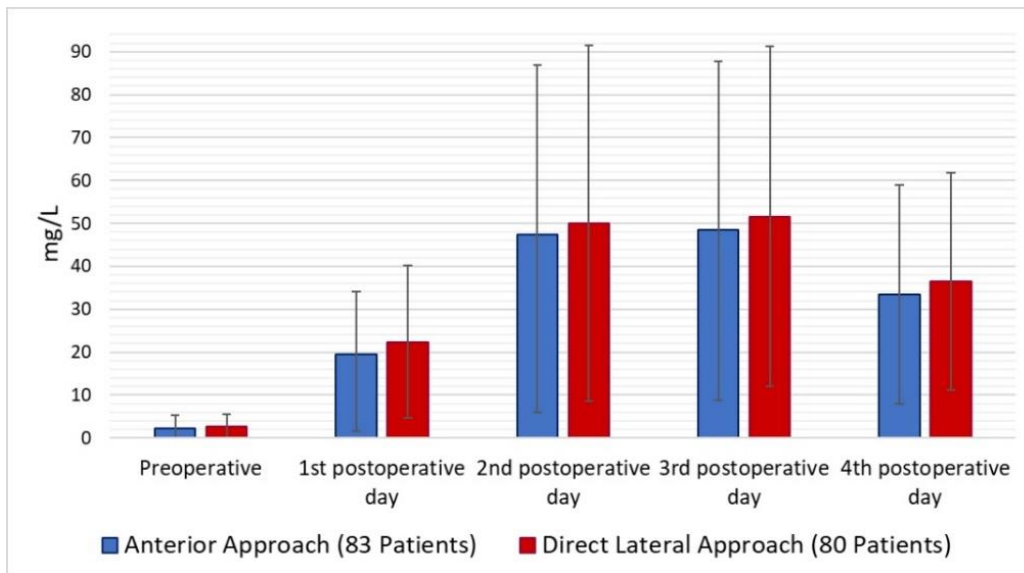


Figure 26. CRP values comparing anterior and direct lateral approach. Chart indicate mean \pm SD.

Pain

On the day of surgery, the direct lateral group had significantly higher analgesia use with 15.1 ME compared to 10.9 ME in the anterior group (mean difference 4.2, 95% CI 1.0-7.4, $p=0.01$). Postoperatively, the use of pain medication was higher with a mean difference from 0.6 to 1.2 ME in the direct lateral group compared to the anterior group (Figure 27).

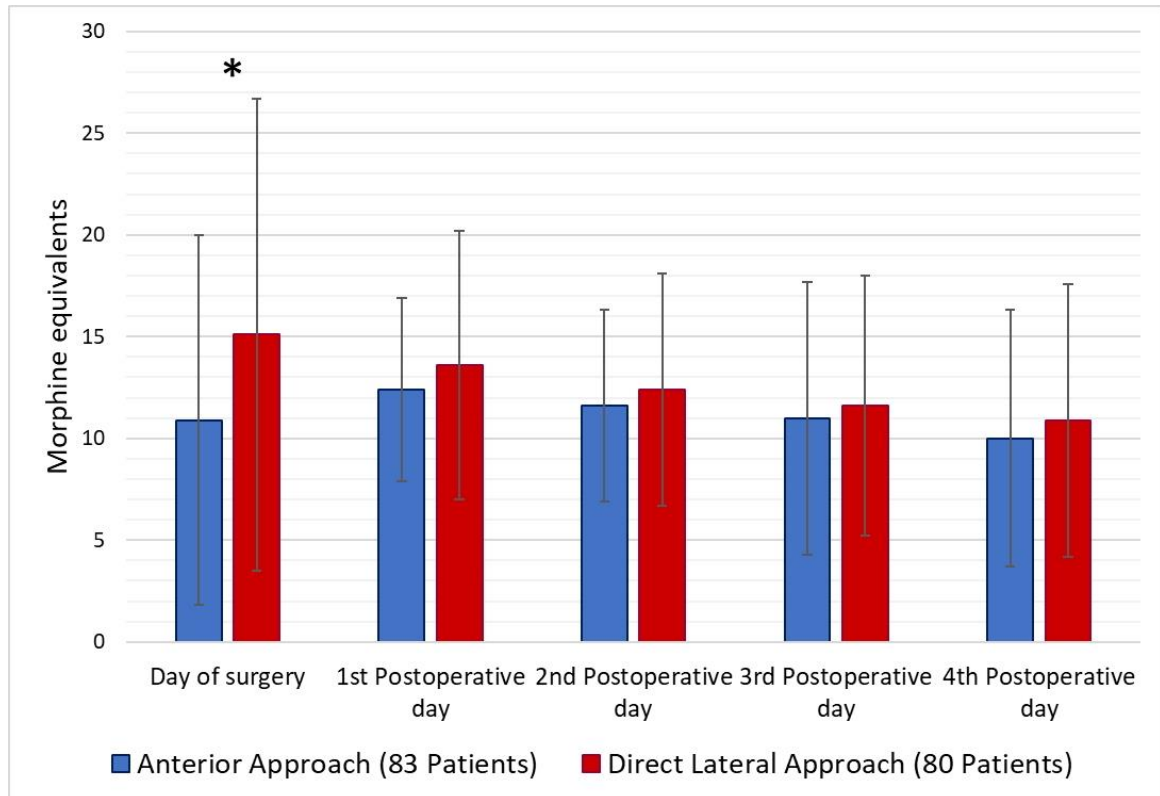


Figure 27. Analgesia consumption in morphine equivalents comparing anterior and direct lateral approach. Chart indicate mean \pm SD. * Indicates statistically significant difference.

Preoperative VAS pain score was 5.8 (SD \pm 1.9) in the anterior group and 5.7 (SD \pm 1.9) in the direct lateral. Pain levels (VAS) were lower in the anterior group compared to the direct lateral group on all postoperative measurements (Figure 28). The difference ranged from 0.78 to 1.4 before physiotherapy ($p<0.007$) and from 1.1 to 1.6 after physiotherapy ($p<0.001$).

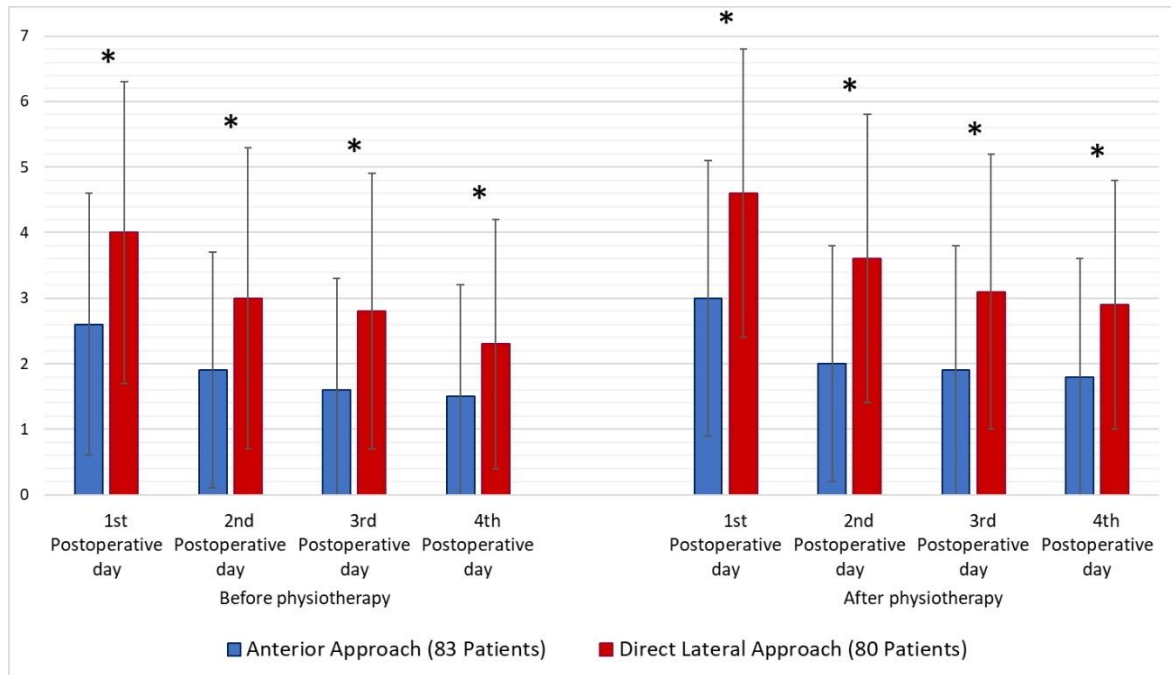


Figure 28. Pain levels measured by VAS comparing anterior and direct lateral approach. Chart indicate mean \pm SD. * Indicates statistically significant difference.

Paper 2

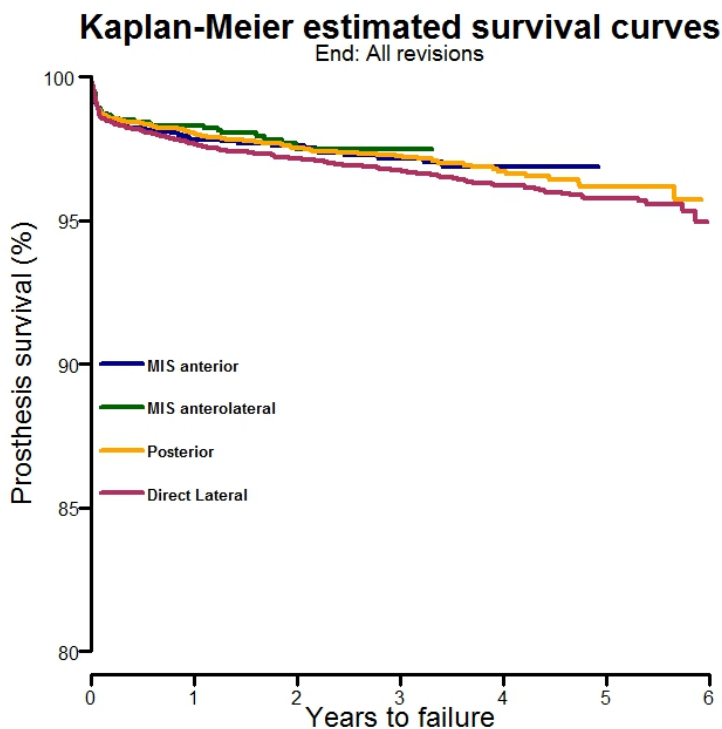


Figure 29. Kaplan-Meier survival curves comparing the different approaches with end point revision due to any cause.

The aim of **paper 2** was to compare implant survival of THAs operated via the anterior, anterolateral, posterior or direct lateral approach and to calculate relative risk of revision due to various causes of the different approaches.

Implant survival

No significant difference was found between the approaches for overall survival at 2 or 5 years (Figure 29, Table 5).

	Two-year survival (95% CI)	Five-year survival (95% CI)
Anterior	97.6 (97.0-98.2)	96.8 (96.0-97.6)
Anterolateral	97.5 (96.9-98.1)	96.5 (95.5-97.5)
Posterior	97.6 (97.2-98.0)	96.4 (95.8-97.0)
Direct lateral	97.2 (96.8-97.6)	96.0 (95.6-96.4)
p=0.187 (log-rank test)		

Table 5. 2 and 5-year survival comparing different approaches using Kaplan-Meier analysis.

Relative risk of revision

	Relative risk	95% CI	P-value
Revision, any cause (n=789)			
Direct lateral			
Anterior	0.90	0.68-1.2	0.47
Anterolateral	0.95	0.71-1.3	0.74
Posterior	0.90	0.75-1.1	0.25
Revision due to infection (n=244)			
Direct lateral			
Anterior/anterolateral	0.53	0.36-0.80	0.002
Posterior	0.57	0.40-0.80	0.001
Revision due to dislocation (n=154)			
Direct lateral			
Anterior/anterolateral	0.71	0.40-1.3	0.25
Posterior	2.1	1.5-3.1	<0.001

Table 6. Relative risk of revision comparing different approaches using Cox regression analysis

No differences were found in RR between the approaches for revision due to any cause or revision due to femoral fracture, aseptic loosening or other/unknown causes. The risk of revision due to infection was close to double for the direct lateral approach compared to the other approaches. The posterior approach had double the risk of revision due to dislocation compared to the anterior/anterolateral and direct lateral approaches (Table 6).

Paper 3

The aim of **paper 3** was to compare postoperative results after THA through the anterior and the direct lateral approach with outcome measures (HHS and 6MWD), patient-reported outcome measures (OHS and EQ-5D) and abductor function (Trendelenburg test).

Complications were also recorded. 10 patients, 5 in each group, were lost to follow-up (Figure 30).

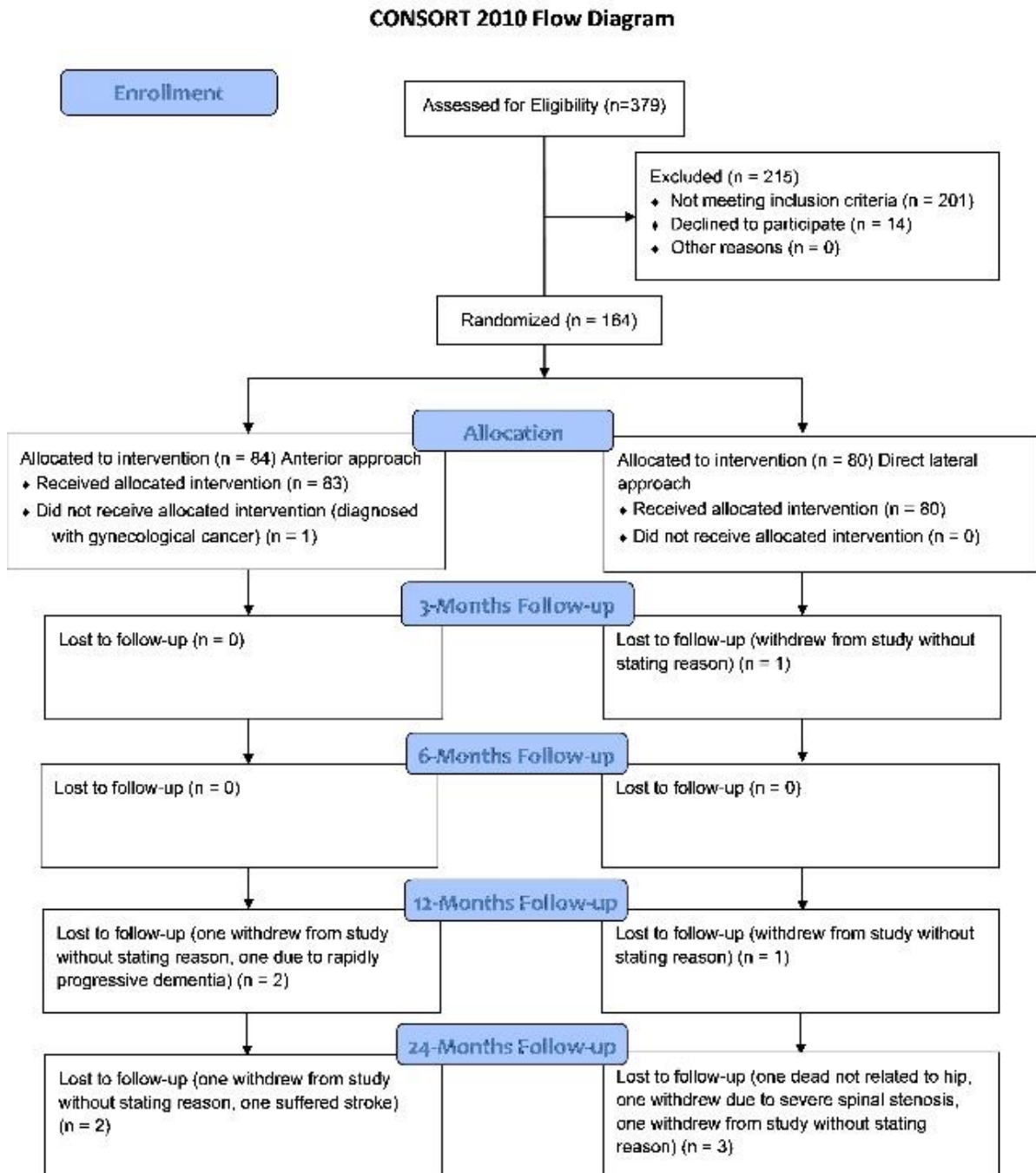


Figure 30. Consort flow chart.

Outcome measures

No significant differences were found between the anterior and the direct lateral group during follow-up in the Harris Hip Score (Figure 31) or the 6-minute walk distance (Figure 32).

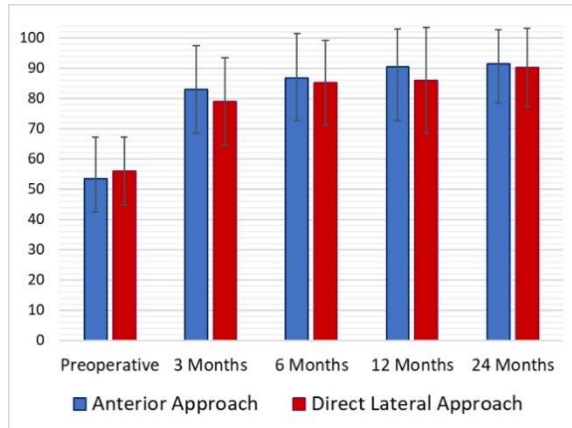


Figure 31. Harris Hip Score comparing the Anterior and the Direct Lateral approach. Chart indicate mean \pm SD.

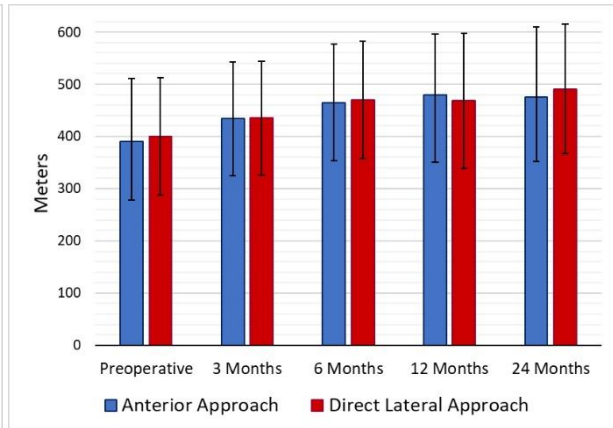


Figure 32. 6-minute walk distance comparing the Anterior and the Direct Lateral approach. Chart indicate mean \pm SD.

Patient reported outcome measures

The Oxford Hip score showed statistical difference at 3 months in favour of the anterior approach (mean difference 3, 95%CI 0.5-5, $p=0.02$), at other time points no difference (Figure 33).

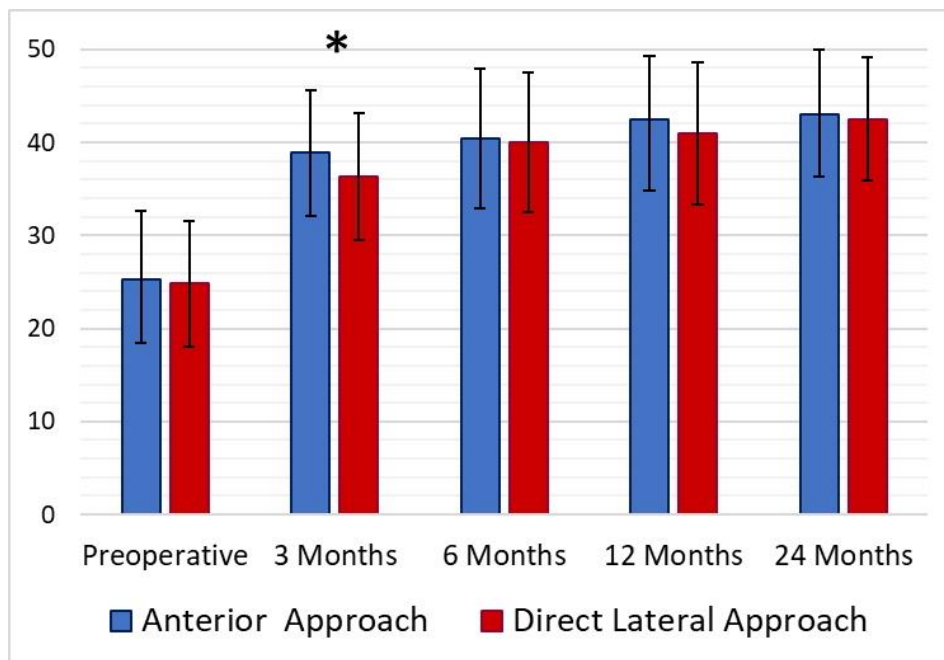


Figure 33. Oxford Hip Score comparing the Anterior and the Direct Lateral approach. Chart indicate mean \pm SD. * Indicates statistically significant difference.

The EQ-5D index showed no statistical difference except at 12 months in favour of the anterior approach (mean difference 0.062, 95% CI 0.0030-0.12, p=0.04) (Figure 34). The EQ-5D VAS showed no difference.

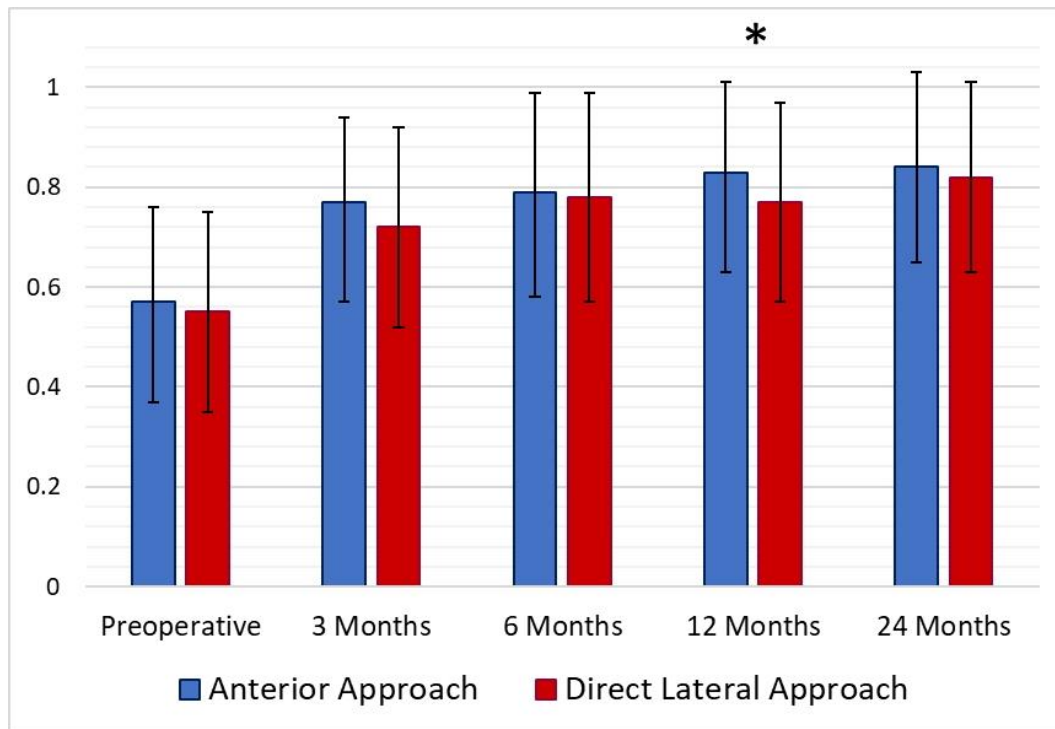


Figure 34. EQ-5D index comparing the Anterior and the Direct Lateral approach. Chart indicate mean \pm SD. * Indicates statistically significant difference.

Trendelenburg test

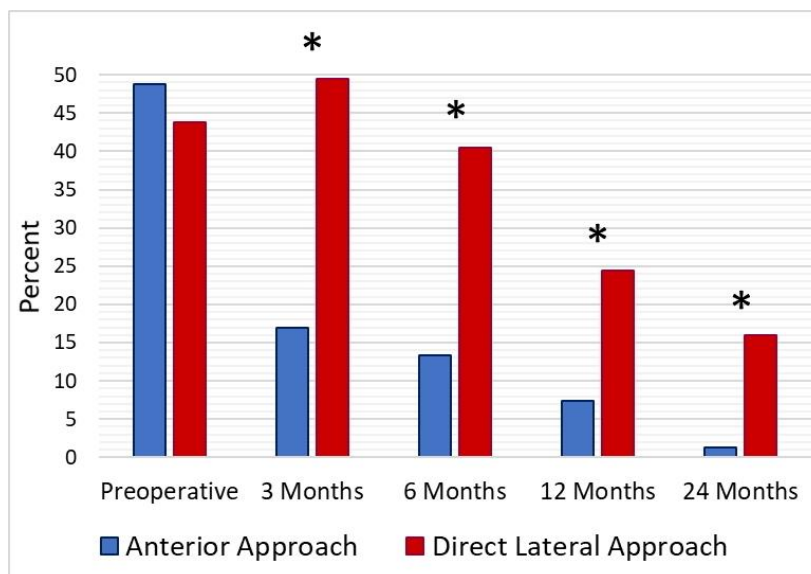


Figure 35. Percentage of Trendelenburg test positive patients comparing the anterior and the direct lateral approaches. * Indicates statistically significant difference.

The percentage of Trendelenburg test positive patients increased in the direct lateral group from preoperative to 3 months but decreased in the anterior group. At 3 months, 17% (14 of 83) were positive in the anterior group and 49% (39 of 79) in the direct lateral group (odds ratio 5, 95% CI 2-10, p<0.001).

13% (11 of 83) in the anterior and 41% (32 of 79) in the direct lateral group were positive at 6 months (odds ratio 5; 95% CI 2-10; $p < 0.001$). 7% (6 of 81) in the anterior group were positive at 12 months, 24% (19 of 79) in the direct lateral (odds ratio 4, 95% CI 2-11, $p = 0.003$). At 24 months 1% in the anterior group (1 of 79) and 16% (12 of 75) in the direct lateral group were Trendelenburg test positive (odds ratio 15, 95% CI 2-117, $p = 0.001$) (Figure 35).

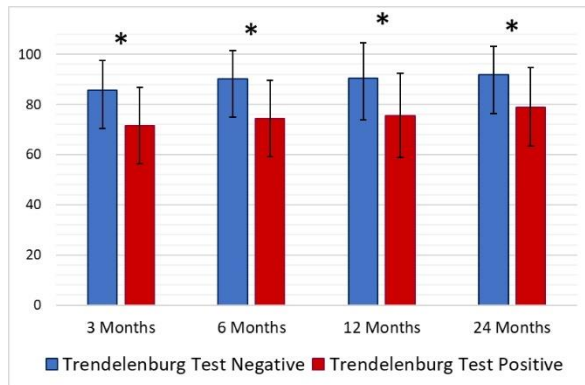


Figure 36. HHS comparing Trendelenburg test-negative and -positive patients irrespective of approach. Chart indicate mean \pm SD. P-value < 0.001 on all measurements. * Indicates statistically significant difference.

Patients with positive Trendelenburg test, irrespective of approach used, had worse mean postoperative HHS, OHS and EQ-5D index compared to those with negative test. The difference in HHS ranged from 13.0 (95% CI 6.36-19.6) to 15.8 (95% CI 11.4-20.2) (Figure 36). The difference in OHS ranged from 5.7 (95% CI 3.6-7.8) to 6.6 (3.6-9.5) (Figure 37) and in EQ-5D from 0.10 (-0.0059-0.21) to 0.18 (0.11-0.24) (Figure 38).

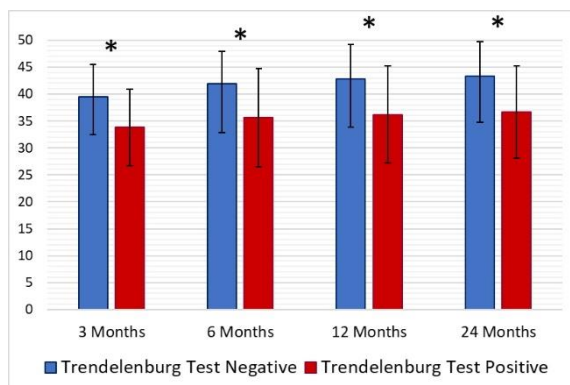


Figure 37. OHS comparing Trendelenburg test-negative and -positive patients irrespective of approach. Chart indicate mean \pm SD. P-value < 0.001 at 3, 6 and 12 months and 0.001 at 24 months. * Indicates statistically significant difference.

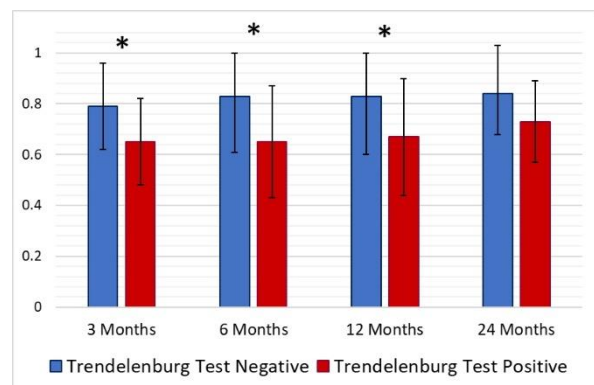


Figure 38. EQ-5D index comparing Trendelenburg test-negative and -positive patients irrespective of approach. Chart indicate mean \pm SD. P-value < 0.001 at 3, 6 and 12 months and 0.06 at 24 months. * Indicates statistically significant difference.

Complications

In the anterior approach group, three patients had transient femoral nerve palsy (FNP). All were female with a BMI ≤ 30 and were operated due to osteoarthritis. None of them had postoperative leg lengthening over 0.5 centimetres. One was incomplete with intact knee

extension but with reduced strength, completely resolved within the second postoperative day. The other two had no active knee extension postoperatively, both completely resolved at 3 months and all three patients reached HHS > 90 at 3 months. One patient suffered damage to the posterior tibial nerve with hyperesthesia and pain in the dermatome innervated by the nerve, but preserved motor function. The patient was female, had a BMI of 23 and was operated due to osteoarthritis. The leg was not lengthened. A further patient had permanent damage to the lateral femoral cutaneous nerve. No patients in the direct lateral group had any nerve damage.

Two patients in the direct lateral group had postoperative infections. One was superficial and was treated only with antibiotics for 14 days, the patients later showed no signs of infection and had no revision of the implant. The other had a deep infection leading to a one-stage revision performed 13 months after the primary surgery. The cause was assumed to be the removal of a painful exostosis from the greater trochanter nine months after the primary surgery. No patients in the anterior group had postoperative infection.

Detachment of the released part of the gluteus medius and minimus was found in four patients (in the direct lateral group), diagnosed by clinical examination and confirmed by MRI. All were reoperated with reinsertion of the muscles 2, 9 10 and 11 months after the primary surgery. Two of the patients improved reaching a HHS of 84 and 92, the other two did not benefit from the reoperation with highest recorded HHS of 52 and 41.

One patient in the anterior group had a suspected deep vein thrombosis 13 days after surgery, not confirmed by ultrasound or venography, treated with Warfarin (Marevan™; Takeda, Tokyo, Japan) for three months. The same treatment was given to a patient in the direct lateral group, who was diagnosed with a pulmonary embolus on CT angiography 30 days after surgery.

No patient dislocated during the 2-year follow-up.

Discussion

Methods

The aim of this thesis was to evaluate the anterior approach and compare it to other approaches, mainly the direct lateral. Due to continued improvements in perioperative management(177-179), comparing THAs from different time periods could potentially be biased in favour of the newest method, necessitating prospective randomized trials(180). At the same time, a randomized trial will likely be underpowered and with insufficient follow-up to evaluate differences in revision rates or risk of revision where a register study will be better suited(181, 182).

This thesis consists of both a randomized trial and a register study which complement each other in evaluating different aspects of THA. **Paper 1** was set up to compare the anterior and direct lateral approach in the immediate postoperative period, both with objective serum markers and use of pain medication as well as patient subjective with VAS pain. **Paper 3** was set up to evaluate postoperative results over two-year follow-up and complications. Outcome measures were chosen to cover different aspects of THA with an objective score (HHS), a patient reported hip specific score (OHS), a patient reported generic health score (EQ-5D), a functional test (6MWD) and assessment of the abductor function (Trendelenburg test). **Paper 2** was set up to compare revision rates and relative risk of revision between the anterior, anterolateral, posterior and direct lateral approach which the randomized trial in **paper 1** and **3** was not powered to evaluate.

Paper 1 and 3

Paper 1 and **3** report on a prospective, randomized, controlled trial. Both papers were rated as level of evidence 1(183, 184) by the journals, but would be rated level 2 using the Oxford Levels of Evidence(185, 186) since level 1 here is reserved for systematic reviews. Both papers adhere to the CONSORT 2010 statement on reporting randomized trials(187).

Randomized controlled trials are regarded as the gold standard in establishing a relationship between cause and effect between treatment and outcome (188). In eliminating selection bias, if properly conducted, the trial will have high internal validity(189). The results from a set sample of the population in question, in this case patients receiving a THA, is used to extrapolate the results valid for the whole population, the study's external validation. The external validity of a study will be affected by the inclusion and exclusion criteria(190).

In our study, 201 patients were excluded from inclusion based on the inclusion/exclusion criteria and a further 14 declined to participate. The majority of patients excluded, 114, were due to the patient expressing an explicit request as to which approach was to be used.

Including these patients would potentially introduce a bias in that they if, or ultimately when, they discovered which approach was used, could be more positive or negative based on whether their preferred approach was used. Also, in **paper 3**, demographic data of the patients with explicit request and the 14 patients who declined to participate was compared to the patients included in the study. Except for higher BMI (mean difference 2 kg/m²) in the included patients, no differences were found between the groups.

43 patients were excluded due to age above 80, constituting 11% of the patients receiving a THA during the inclusion period. This matches well with the proportion of patients receiving a THA at the age of 80 and above reported to the NAR of about 12%(5). Several studies indicate that pain reduction and increase in function after THA in patients above 80 are similar to those of younger patients(191-193), though the rate of complications are increased(194). Increasing the age limit in our study could therefore theoretically increase the level of complications but not alter the other results. Loss of follow-up could be a bigger problem with an older study population. We therefore believe that the age limit was reasonable.

The third most common reason for exclusion was previous hip surgery. Previous surgery on the hip before a THA is known to influence the result(195, 196) and including these patients in a study evaluating approaches could potentially have introduced a bias.

Power calculation

The power calculation for the randomized trial in **paper 1** and **3** was based on the HHS at 2 years, with an estimated 70 patients needed in each group. As mentioned, concerns over the ceiling effect when using the HHS have been raised. In our study, above the recommended 15% had the highest possible score (127) at 12 and 24 months follow-up raising the question if basing the power calculation on the HHS was a poor choice.

Basing the power calculation on the OHS, 69 patients in each group would be needed to obtain 90% power with 5% significance level(197). Though reported that ceiling effect is not a big issue when using the OHS(198), in our study the levels of patients with the highest score were above 15% in the anterior group from 6 months and in the direct lateral group after 12 months(199). Our study had few lost to follow-up with only 5 patients in each

group and over the recommended number of patients in each group, based on both the HHS and OHS, completed the two-year follow-up. We therefore believe that the study was sufficiently powered.

For the analysis in **paper 1**, no separate power calculation was performed. Bergin et al when comparing inflammation and muscle damage markers, calculated that to detect difference between two groups with 80% power and an alpha value of 0.05, 29 patients in each group were needed(200). Based on this the analysis in **paper 1** should be sufficiently powered.

Blinding

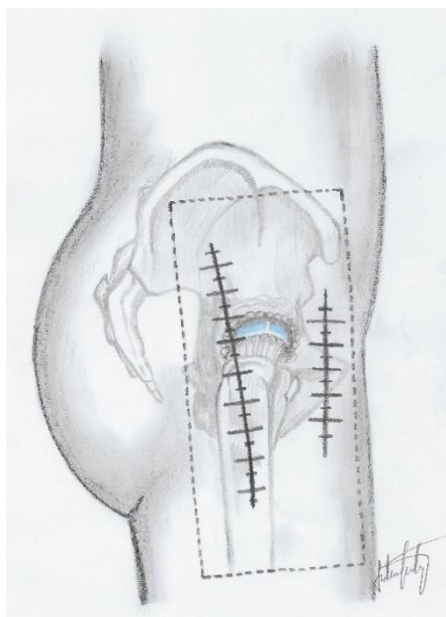


Figure 39. Lateral view indicating the incision for the direct lateral and anterior approach with dressing covering both indicated. Illustration by Andreas Lødrup.

In an ideal study, the patients would be blinded to approach used until follow-up was completed(180, 188, 201). In our study, attempts were made in that patients were not informed of which approach was used and large dressings covering both possible incisions were used (Figure 39). Despite this, one must assume that the patients figured out which approach was used, if not immediately than surely after discharge. This could influence the results if some, or all, of the patients believed one approach to be superior.

All personnel dealing with the patients during admission and, perhaps most important, all assessors, both during admission and follow-up, were blinded to approach used eliminating assessor bias.

Paper 2

Paper 2 was a register study, i.e. an observational cohort study. The evidence according to both the publishing journal and the Oxford Levels of Evidence was level 3(186).

A randomized trial powered to evaluate revision rates and risk of revision between different approaches in THA would be a time-consuming and expensive ordeal, whereas an observational cohort study provides a good option(202, 203).

Though including all THAs performed in Norway, there is still a potential selection bias when evaluating the surgical approaches. Some hospitals may have introduced the anterior

and anterolateral approach gradually, selecting “easy” cases while other approaches were used in more difficult cases. There could also be continued different indications within hospitals or between surgeons on the choice of approach introducing confounding by indication(204). When introducing a new approach in surgery, it is likely that a few, and the most experienced surgeons, in each hospital first adopt the method. In contrast, the direct lateral and posterior approaches, having been used for several years, may be used by several surgeons of varying level of experience.

In our study the analysis was redone excluding the 50 first THAs performed using the anterior or anterolateral approach in each hospital to account for a potential learning curve(205) influence when the approaches were introduced. We also did a sensitivity analysis(206) to check for selection bias. None of these analyses significantly altered the results.

As with other observational studies, small differences should not be overestimated due to confounding risk factors(207). The Cox regression analysis accounts for the known confounders based on the data collected by the NAR. Increased BMI has been shown to increase risk of component malpositioning(208), result in worse clinical outcome and increased risk of early revision(209) and increase the risk of complications(210). BMI could be both a confounder and represent selection bias if during the introduction of the anterior and anterolateral approaches the most obese patients were avoided or if surgeons have an upper BMI limit to use the approaches. The NAR does not record patients’ BMI, making it impossible to assess its influence on the analysis.

The end point used in our study, as in most register studies, was revision. The indication to do a revision is often not clear-cut. Could the indication be different based on the approach used? Could it be different as some surgeons might hesitate to revise through a new and unfamiliar approach leaving the hip unrevised, while the same case would be revised by a different surgeon using a different approach? This could represent a bias which is not detected by the NAR.

We used the Kaplan-Meier survival analysis(211) to calculate implant survival which is known to overestimate the probability of revision in the presence of competing risk such as death(212). This is however a bigger problem when the risk of death is high and, in those cases, cumulative incidence function is recommended. In our study, the risk of death was

low, 5.5% of the patients died during the study period suggesting that the Kaplan-Meier survival analysis could be used(213).

Results

Paper 1

In **paper 1** we found higher CK values in patients who had a THA via the anterior compared to the direct lateral approach, the difference statistically significant directly postoperatively and on postoperative day four. No difference was found between the groups in CRP levels. The anterior group used less pain medication on the day of surgery and reported significantly less pain than the direct lateral group.

CK/CRP

Other studies have compared levels of markers for muscle damage for different approaches after THA. In a review article by Ries(9) published in 2019 seven articles evaluating muscle damage was referred, but only two of them compared the anterior approach to the direct lateral, including **paper 1**. A different review article, by Tottas et al(214), also published in 2019, identified 21 studies evaluating markers for muscle damage. Of these, only one additional study compared the anterior and the direct lateral approach.

De Anta-Díaz et al(215) compared 40 patients receiving a THA through the anterior approach and 50 patients through the direct lateral in a prospective, randomized trial. They found statistically significant higher levels of CK at postoperative day 2 and 4 with the direct lateral group but considered the result clinically insignificant. The difference in U/L on day two was 184 and on day four 85. Differences in CRP levels between the groups were maximum 3 mg/L and as such not clinically relevant.

Nistor et al(216) compared 35 patients operated through the anterior approach to 35 operated through the direct lateral, also in a randomized, controlled trial. The first postoperative day, the difference 31 U/L was higher in the direct lateral group, while on postoperative day two through five, the anterior group had higher values. The difference ranging from 34 U/L on the 5th postoperative day to 112 U/L on the second, with no significance found at any time point.

In **paper 1**, we found higher levels of CK in the anterior group at all postoperative measurements, with statistical significance immediately after surgery and on postoperative day four. The difference in mean immediately after surgery was 30 U/L and on

postoperative day four 193 U/L. Whether these differences are clinically relevant, is not clear, but perhaps doubtful. To diagnose rhabdomyolysis, defined as the breakdown of skeletal muscle combined with myalgia, myoglobinuria and increase in serum CK, values should exceed 1000 U/L (217). Exercise can induce elevated CK-levels, after intensive exercise values above 5000 U/L are described without the individuals requiring specific treatment(218). The differences found in our study are small by comparison. Studies comparing CK levels between different approaches in THA also conclude that the results do not correlate with clinical results(219), as was the case in our study, also indicating that further studies are needed before CK values can be used to evaluate invasiveness in THA.

Several other studies support our finding that the postoperative level of CRP is not influenced by the approach used(219-221) indicating that the rise in CRP is dependent on the general trauma of the surgery, not the specific approach used.

Analgesia/pain

Use of pain medication was significantly lower on the day of surgery in the anterior group. Assumably, the day of surgery is the most painful. On the postoperative ward the pain medication given is dependent on the level of pain reported by the patient and intravenous injection are often used. On the orthopaedic ward, more standardized doses of medication are given and mostly restricted to oral medications. We did not record the VAS pain on the day of surgery, but it was lower in the anterior group both before and after physiotherapy on postoperative day one through four. The use of more pain medication suggests more pain in the direct lateral group leading to higher demand for pain medication when it was more readily available and higher levels of pain when the availability of pain medication was reduced.

Both groups had low levels of postoperative pain, the maximum VAS pain was 4.6 in the direct lateral group after physiotherapy on the first postoperative day. The difference in VAS pain between the groups ranged from 0.8 to 1.4 before physio and from 1.1 to 1.6 after physio. In addition to exceeding the MCID(114, 117, 118, 222) it represents lower VAS pain in the anterior group of 35%. This exceeds the value suggested by Jensen et al that a 33% decrease in pain represents a change in pain meaningful from a patients perspective(223). We therefore believe that these values in addition to being statistically significant are also clinically significant. The lower pain levels found with the anterior

approach in our study are supported by several other studies including several meta-analysis(224-226).

Paper 2

In **paper 2** we found no difference in 2 and 5-year implant survival or RR of revision due to any cause between the anterior, anterolateral, posterior and direct lateral approach. RR for revision due to infection was 0.53 for the anterior and anterolateral approach and 0.57 for the posterior compared to the direct lateral approach. The RR for revision due to dislocation was 2.1 using the posterior approach compared to the direct lateral with no difference between the anterior and anterolateral and the direct lateral.

Sheth et al(227) reported on 42,438 THAs from the Kaiser Permanente Total Joint Replacement Registry performed between April 2001 and December 2011. Their result were similar to ours as they found no difference in risk of revision between the anterior, anterolateral, posterior and direct lateral approach for revision due to aseptic loosening or infection, but reduced risk of revision due to dislocation using the anterior (adjusted HR 0.29) and anterolateral approach (adjusted HR 0.44) compared to the posterior approach.

From the Dutch Arthroplasty Register, Zijlstra et al(228) reported on 166,231 THAs performed between 2007 and 2015, evaluating the effect of femoral head size and surgical approach on revision for dislocation. They concluded that the anterior and anterolateral approach reduced the risk of revision due to dislocation but increased the risk of stem revision and other revision compared to the posterior approach. Angerame et al(229) reported similar findings in a retrospective study based on patients from a high-volume arthroplasty centre. In 6894 THA performed between 2007 and 2014, 2431 via the anterior approach and 4463 via the posterior, they found no difference in overall revision rates. Revision due to aseptic loosening was more common when the anterior approach was used while revision due to dislocation was associated with the posterior approach.

Eto et al(230) and Meneghini et al(231) have also reported increased risk of femoral revision using the anterior approach. These studies are however based on patients referred to special centres for revision. As such they did not evaluate the revision rate or risk of revision using the anterior approach but rather the cause of revision in the THAs inserted via the anterior approach referred for revision. The most common cause of revision was aseptic femoral loosening.

While several studies report on increased risk of revision due to dislocation using the posterior approach, the increased risk of revision due to infection using the direct lateral approach we found have not been reported in other studies. It should be interpreted with caution as it could be the result of selection bias or confounding factors.

Paper 3

In **paper 3** we found no clinical important difference in HHS, 6MWD, OHS or EQ-5D between the anterior and direct lateral approach with two-year follow-up. Significantly more patients were Trendelenburg test negative in the anterior group at all postoperative measurements compared to the direct lateral group. Irrespective of approach used, patients who were Trendelenburg test positive had significantly worse HHS, OHS and EQ-5D than those who were negative. Complications were of different nature, transient femoral nerve palsy (FNP) was the most common complication in the anterior group while detachment of the released glutei was the most common in the direct lateral.

In our study, patients were first evaluated 3 months after the operation. Several studies, both individual and meta-analysis have indicated that the anterior approach yields better short-term results, but that the results even out by six to twelve weeks, or have shown no difference between different approaches(225, 226, 232-234). If we had had a checkpoint earlier, a difference might have been found, but this remains a speculation.

When no significant difference is found in an RCT, there is always the question if the study was underpowered. When comparing the groups, their mean values were very similar with fairly narrow confidence intervals. A study with more patients might therefore give statistically significant differences, but whether it would yield any clinically significant differences is doubtful.

At all postoperative evaluations, the direct lateral group had a significantly higher percentage of Trendelenburg test positive patients, and 16 percent remained positive throughout follow-up compared to 1 percent in the anterior. A positive Trendelenburg test status after THA through the direct lateral approach is not pathognomonic of detachment of the released glutei(235) as it could be the result of both damage to the superior gluteal nerve or failure to restore offset and/or leg length(236). Component placement, leg length and offset restoration in our study have been published(237), and no difference was found between the groups. This indicates that the difference in Trendelenburg test status between the groups was not due to differences in component placement, leg length or offset

restoration between the groups. The differentiation of damage to the superior gluteal nerve from detachment of the glutei is not straight forward. Nerve damage can both be asymptomatic and transient(238) which could explain why the abductor function improves over time. Svensson et al(239) added markers to measure the integrity of the insertion of the gluteus medius after THA via DLA and found that the degree of separation did not correlate with poor abductor function.

Irrespective of the precise cause, several studies support our findings and report limping and/or positive Trendelenburg test after THA through the direct lateral approach, the percentage vary but up to 30% are reported(170, 221, 238, 240-242). This indicates that the approach has an inherent risk of abductor failure which in our study was not present with the anterior approach.

The difference in HHS, OHS and EQ-5D between Trendelenburg positive and negative patients in **paper 3** was significant, both statistically and clinically. Amlie et al (243) found that patients operated with the direct lateral approach reported worse outcome 1-3 years after THA compared to the anterior and posterior. Limping was twice as common in patients operated via the direct lateral approach compared to the anterior and posterior. Also, when adjusting for limping, the differences between the approaches were almost eliminated. This suggest that it is most important to avoid limping/Trendelenburg positive patients after THA, irrespective of approach, but that this is easier to accomplish with the anterior (or posterior) approach.

Complications

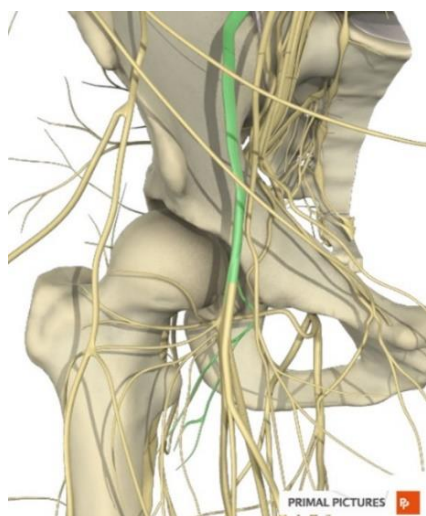


Figure 40. The femoral nerve (in green) crossing the acetabulum.
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When considering complications, it is important to acknowledge that the study in **paper 3** was not powered to evaluate complication rates. However, nerve injuries in the anterior group and detachment of the gluteus minimus and released part of gluteus medius in the direct lateral group stood out as “approach-specific complications”.

Only one patient operated via the anterior approach suffered damage to the lateral femoral cutaneous nerve with loss of sensation in the innervated skin area. In the literature, damage to the nerve in up to 81% of patients

are reported(244), but hip function is usually not affected(245).

Femoral nerve palsy (FNP) is a rare complication in THA but more frequent with the anterior approach than the posterior and direct lateral(246, 247). The incidence varies widely in the literature from 0.17 to 4.6% of patients(248, 249). Though the exact cause is often unknown, hematoma formation after aggressive anticoagulation and excessive leg lengthening are reported risk factors(250), as is female sex, cementless fixation, hip dysplasia and post-traumatic arthritis(247). Except for female sex and cementless fixation of the femur, none of our affected patients had any of these risk factor.

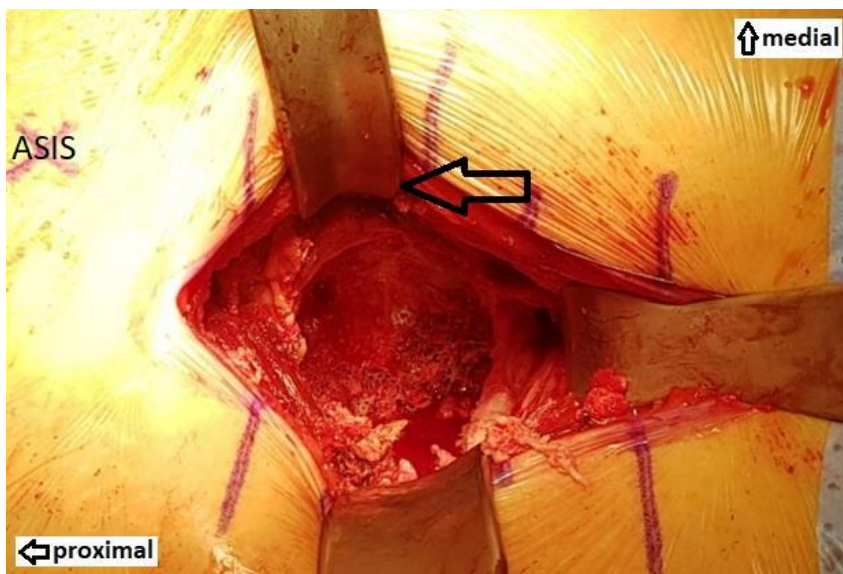


Figure 41. Perioperative image showing the reamed acetabulum of a right hip with retractor over the anterior wall (arrow). ASIS = anterior superior iliac spina.

The femoral nerve (Figure 40) lies on the iliopsoas muscle in close proximity to the anterior wall and rim of the acetabulum(251), the distance shorter in women than in men(252). When using the anterior approach, a retractor is placed on the anterior wall of the acetabulum (Figure 41).

Misplacement or excessive manipulation of the retractor is a common cited cause of FPN(251, 253, 254) and in the absence of other obvious causes must be suspected in our patients. All affected patients in our study were obese which could have been a factor, but again, the study was not sufficiently powered to evaluate this.

The sciatic nerve is the most commonly damaged nerve during THA(249), but when the anterior approach is used, the incidence of FNP is over 4 higher than for damage to the sciatic nerve(255). The risk of damage is higher for the peroneal division than for the tibial(250). In our patient, no clear cause was found for the nerve damage. Excessive manipulation of the extremity or misplaced retractors are potential causes. The prognosis for recovery after damage to the sciatic nerve is poorer than after damage to the femoral

nerve(246) and in contrast to the patients with FNP, the patient did not fully recover during the study period.

Four patients were reoperated due to symptomatic detachment of the gluteus minimus and released part of the gluteus medius. While abductor deficiencies are reported in up to 22% of patients after THA(240), no consensus exists on the indication for surgical reattachment(242). Svensson et al(239) used metal markers placed on each side of the attachment site of the abductors and separation of these were seen in up to 50% of cases, but even with separation >3 cm, only 6% were symptomatic. Hypertrophy of the tensor fasciae latae muscle can compensate for ruptures of the gluteus medius and minimus(256) indicating that repair is not always necessary.

All our patients had an MRI which indicated detachment of the released muscles as well as abductor weakness and severe pain. Conservative treatment was attempted, with physiotherapy and pain medications, but did not improve the condition. The indication for surgery therefore seems just.

Two of the patients improved after reattachment surgery while two did not, in concordance with other studies also indicating inconsistent results(242, 257). Successful repair is dependent on muscles without chronic degeneration(257), so time from primary surgery to repair could influence the final result. Lübbecke et al(258) found better outcome after early repair compared to late, defining early repair between one and 14 months and late after 20 months, while Weber and Berry(259) found no correlation between outcome and time to repair. All our patients had their abductor repair done before 12 months after their THA.

Other operative treatment strategies, like transfer of the gluteus maximus and tensor fasciae latae(260, 261) have been described and might have been an option in the two patients with no improvement, but that is beyond the scope of this thesis.

Conclusion and clinical implications

Paper 1

THA implanted via the anterior approach caused less postoperative pain than the direct lateral approach.

Patients operated via the anterior approach used less pain medication on the day of surgery compared to those operated via the direct lateral.

Postoperative CK levels were higher in patients operated via the anterior approach compared to the those operated via the direct lateral approach which was in contrast with clinical results (levels of pain).

Postoperative CK values as a measure of invasiveness may not be a valid method.

Postoperative CRP levels were similar in both approaches.

Paper 2

Revision rates and risk of revision were not different when comparing the anterior, anterolateral, posterior and direct lateral approach in primary THA.

Relative risk of revision due to infection was approximately double for the direct lateral approach compared to the anterior, anterolateral and posterior approaches.

Relative risk of revision due to dislocation was approximately double for the posterior approach compared to the anterior, anterolateral and direct lateral approaches.

Paper 3

When comparing results after THA via the anterior or the direct lateral approach with two-year follow-up, no differences were found between the approaches in HHS, 6MWD, OHS or the EQ-5D.

The direct lateral group had a significantly higher number of postoperative Trendelenburg test positive patients compared to the anterior group.

Trendelenburg positive patients, irrespective of approach, had significantly worse HHS, OHS and EQ-5D than Trendelenburg negative patients emphasising the importance of ensuring good abductor function after THA.

The groups differed in complication characteristics, nerve damage (transient and permanent) were only seen in the anterior group. Detachment of the released glutei needing reoperation were as expected only seen in the direct lateral group.

Suggestions for future research

Most published randomized trials comparing the anterior approach to other approaches have follow-up of two year or less. There is a need for studies with longer follow-up. The patients

from **paper 1** and **3** (and from other randomized trials on the subject) should be recalled, perhaps at regular intervals to evaluate long term results.

The register study from **paper 2** should be repeated as it would now include more patients and specifically more operated via the anterior and anterolateral approaches. All implants, both cemented and uncemented, should be included.

The aim of deciding “the best approach for THA” should perhaps be abandoned and the idea of “patient-specific approach” should be studied. Different approaches might provide better result based on patient’s activity level, BMI or other (and perhaps unknown) factors.

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Comparison of Markers for Muscle Damage, Inflammation, and Pain Using Minimally Invasive Direct Anterior Versus Direct Lateral Approach in Total Hip Arthroplasty: A Prospective, Randomized, Controlled Trial

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ABSTRACT: It is proposed that the use of biochemical markers for muscle damage and inflammation provides an objective measure on invasiveness in total hip arthroplasty. We analyzed levels of creatine kinase and C-reactive protein (CRP) after total hip arthroplasty in patients randomized to minimally invasive direct anterior approach or direct lateral approach, also recording consumption of pain medication and levels of pain postoperatively. Eighty-three patients were operated by the use of anterior approach and eighty using lateral. Creatine kinase and CRP levels were measured preoperatively, creatine kinase directly after surgery, and both creatine kinase and CRP on postoperative day 1 through 4. The use of pain medication and levels of pain were recorded. Creatine kinase were higher in the anterior group compared to the lateral group, reaching statistical significance directly postoperative and on day 4. Levels of CRP did not differ, reaching a maximum of mean 52 mg/L on day 3. The use of pain medication was higher in the lateral group on the day of surgery ($p = 0.011$), and pain levels were higher on all days in the lateral group ($p < 0.007$). In conclusion, the use of minimally invasive anterior approach caused less pain, but higher postoperative levels of CK, than the use of direct lateral approach. © 2015 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. *J Orthop Res* 33:1305–1310, 2015.

Keywords: THA; creatine kinase; approach

Total hip arthroplasty is a well-established and successful treatment for end-stage osteoarthritis.^{1,2} In Norway, the most commonly used approach is the direct lateral approach (DLA). There is, however, an increased interest in and increased use of minimally invasive approaches, both the direct anterior (Smith–Petersen) and anterolateral (Watson–Jones).³

Minimally invasive direct anterior (MIDA) utilizes a nervous and muscle neutral plane and the theoretical advantages include less trauma to muscle and tendons, less pain, and increased functional outcome.^{4–8} There is, however, a continuous debate whether these advantages also apply in a clinical setting. Few studies have shown lasting better functional results compared to those using traditional approaches.⁹ Other authors have reported increased level of complications^{9,10} and a long learning curve using this approach.¹¹

The DLA with release of the anterior part of gluteus medius and gluteus minimus offers good exposure,¹² but carries the risk of gluteal insufficiency and pain postoperatively.^{13,14}

In our hospital, we used the direct lateral approach for several years before introducing the MIDA in November 2009. Five surgeons started using the approach and after we collectively felt beyond the initial “learning curve,” combined having performed more than 200 procedures, we wanted to do a

prospective randomized trial to see if our new approach led to better clinical results.

It has been suggested that the use of serum markers of muscle damage and inflammation offers an objective measure of the invasiveness of the procedure. The postoperative rise in serum creatine kinase (CK) should indicate the level of muscle damage,^{15,16} and the rise in C-reactive protein (CRP) indicating the level of inflammation.¹⁷ We wanted to compare the rise in CK and CRP postoperatively using either minimally invasive anterior approach or direct lateral approach. We recorded the use of opioids and pain level during the admission to see if the patients operated with the MIDA had less pain than those operated with the DLA.

Our hypothesis was that the use of minimally invasive anterior approach would cause a lower rise in CK and CRP and cause less pain, and consequently lower opioid use, than the use of direct lateral approach.

METHODS

The regional ethics committee (REK) approved this level I, prospectively, randomized, controlled study (id 2011/2581 D) and it was registered on Clinical Trials (ClinicalTrials.gov identifier: NCT01578746).

Patients with end-stage clinical osteoarthritis of the hip, verified on plain radiograms, were considered candidates. Further inclusion criteria were age between 20 and 80 years and willingness to offer written consent to participate in the study. Exclusion criteria was previous surgery of the hip, BMI > 35 kg/m², and dementia/psychiatric illness preventing follow-up, as was an explicit request regarding approach.

Conflict of interest: None.

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During the inclusion period (January 2012–June 2013), 379 primary total hip arthroplasties were performed at our hospital. One hundred and forty-four patients had an explicit request regarding approach, 43 were over the age of 80, 27 had had previous surgery in the hip, 8 had a BMI over 35 kg/m², and 5 required custom-made implants. Two patients were excluded due to not understanding Norwegian, and two due to psychiatric illness/dementia, leaving 201 excluded based on these criteria. One hundred and eight patients were asked to participate in the study, 14 declined, giving 164 patients eligible for randomization. Randomization was performed using sealed envelopes. Eighty-four were randomized to minimally invasive anterior approach and 80 to direct lateral approach. One patient from the anterior group withdrew before surgery due to being diagnosed with cancer, resulting in 83 patients operated using the anterior approach and 80 using the direct lateral approach.

Five surgeons with experience with both approaches operated the patients. They considered themselves to be beyond the initial “learning curve” using the direct anterior approach. The patients were not told which approach was used and further blinding was attempted using a large dressing covering both possible incisions.

Prior to surgery, we recorded baseline demographic data including age, sex, body-mass-index (BMI), American Society of Anesthesiologists (ASA) grade, and Charnley category¹⁸ (Table 1). Preoperative levels of CK, CRP, hemoglobin (Hb), and creatinine were measured and preoperative pain was recorded using a visual analog scale (VAS) ranging from 0 to 10. Harris hip score and Oxford hip score were recorded (Table 2). Physiotherapists blinded to the planned approach recorded Harris hip score.

Surgery was performed using spinal anesthesia and local infiltration analgesia (LIA) with Ropivacain (NaropinTM) 300 mg, Ketorolac (ToradolTM) 30 mg, Triamcinolon (Leder-spanTM) 40 mg, and adrenaline 0.5 mg in saline solution to a volume of 150 ml. All patients were given Cefalotin 2 g i.v. prior to surgery and further three doses after surgery. Tranexamic acid of 500 mg were given intravenously at the onset of surgery and 500 mg at the time of closure. In all patients, a cemented cup (Marathon, DePuy, Warsaw, IN), unsemented stem (Corail, DePuy), and ceramic head with a diameter of 32 mm (BioloX forte, Ceramtec, Plochingen Germany)¹⁹ were used.

Direct anterior approach was performed with the patient supine. No traction was used. Direct lateral approach was

performed with the patient in lateral decubitus. Patients started physiotherapy on the first postoperative day allowing full weight bearing.

We recorded duration of surgery and length of skin incision. Immediately after surgery, within 1 h after closure, we measured CK. On postoperative day 1 through 4, CK, CRP, and hemoglobin were measured. Blood loss was calculated by subtracting the lowest measured hemoglobin level from the preoperative value.

Postoperative pain-regime included for all patients a daily dose of paracetamol of 4 g for the duration of admission and a total dose of ibuprofen of 4 g with a daily dose of 1200 mg. Tramadol was used from the first postoperative day in range of 200–400 mg daily. If needed, patients were given oxycodone or ketobemidone. All analgesic use was recorded and converted to morphine equivalents (ME).²⁰

On postoperative day 1 through 4, all patients were asked to state their level of pain using a visual analog scale ranging from 0 to 10, 0 indicating no pain and 10 the worst pain imaginable. Patients were asked prior to physiotherapy and directly after. A physiotherapist recorded the score.

All personnel involved with the study-patients during admission, including the nursing staff and physiotherapists, were blinded to approach used.

Statistics

Mean and standard deviation were calculated. For group comparison, the mean difference with 95% confidence interval were calculated and tested using independent sample *t*-test. Statistical analysis was performed using SPSS version 21 (IBM SPSS, Chicago, IL). *p*-Values less than 0.05 was considered statistically significant.

RESULTS

The incision length was on average 4 cm longer (95% CI; 3.7–4.3) in the direct lateral group ($p < 0.0001$), ranging from 8 to 13 cm in the direct anterior approach (mean 9.5) and 11 to 16 cm in the direct lateral (mean 13.5).

Average time of surgery was 15 min longer (95% CI; 11–19) using direct anterior approach ($p < 0.0001$), with a range of 52–136 min using anterior approach (mean 77) and 47–90 min using direct lateral approach (mean 62).

Hemoglobin levels were significantly lower in the MIDA group on all postoperative days ($p = 0.008–0.03$), the lowest value in both groups reached on postoperative day 2 (Table 3). Blood loss was estimated to mean 3.2 g/dl (SD 1.0) in the anterior group and 3.1 g/dl (SD 1.0) in the lateral group ($p = 0.368$).

Three patients in the MIDA group and four patients in the DLA group were given blood transfusion, 9 U of blood given in the MIDA group and 7 U in the DLA.

CK levels reached maximum levels on the third postoperative day, being mean 1,113 (SD 480) U/L in the direct anterior group and 972 (SD 486) U/L in the direct lateral group. All postoperative CK values were higher in the direct anterior group, statistical significant directly postoperative ($p = 0.022$) and day 4 ($p = 0.005$) (Table 4).

Table 1. Demographic Data on the Patients

	Minimally Invasive Anterior Approach	Direct Lateral Approach
Number of patients	84	80
Age (yr)	67.2 ± 8.6	65.6 ± 8.6
Gender (M/F)	25/59	30/50
Body mass index ^a	27.7 ± 3.6	27.6 ± 3.9
ASA grade ^a	1.9 ± 0.7	1.8 ± 0.7
Charnley category % (A/B/C)	51.2/38.1/10.7	45.0/41.3/13.7

ASA, American Society of Anaesthesiologists.

^aThe values are given as the mean and the standard deviation.

Table 2. Preoperative Pain^a, Functional Scores, and Serology

	Minimally Invasive Anterior Approach	Direct Lateral Approach
VAS pain	5.9 ± 1.8	5.7 ± 1.9
Harris hip score	53.6 ± 13.7	56.0 ± 11.2
Oxford hip score ^b	25.2 ± 7.5	24.8 ± 6.8
CK (U/L)	111.5 ± 61.5	114.9 ± 55.7
CRP (mg/L)	2.3 ± 3.0	2.6 ± 3.0
Hemoglobin (g/dl)	13.7 ± 1.2	14.1 ± 1.3
Creatinine (µmol/L)	76.8 ± 21.9	76.2 ± 26.4

Values are given as the mean and the standard deviation. ^aPain reported using a visual analog scale ranging from 0 to 10. ^bScore running from 0 to 48 with 48 being best outcome.

CRP reached maximum levels on the third postoperative day with mean 48 (SD 39) mg/L in the direct anterior group and 52 (SD 40) mg/L in the lateral group (*p* = 0.61) (Table 3).

Four patients had a preoperative diagnosis of rheumatoid arthritis. In the MIDA group, three patients all with preoperative CRP less than 2. One patient in the DLA group had RA, with a preoperative CRP of 11. No patient had a preoperative CRP-value above 12 and the mean was 2.4. No patients suffered from HIV, Chron's disease, or other active inflammatory diseases excluding them from the analysis.

The analgesia consumption was slightly higher in the direct lateral group on postoperative day 1 through 4, mean difference ranging from 0.6 ME to 1.2 ME. There was higher analgesia use on the day of surgery in the direct lateral group with mean 15.1 ME compared to 10.9 ME (mean difference 4.2, 95%CI; 1.0–7.4) in the direct anterior group (*p* = 0.011) (Table 5).

General levels of pain postoperatively were low in both groups. There were lower pain scores (VAS) in

the anterior group on all recorded days (*p* < 0.007), both before and after physiotherapy (Table 6).

DISCUSSION

Minimally invasive direct anterior approach gave higher CK levels postoperatively than the direct lateral approach in this study. On the other hand, pain and analgesic consumption was lower in the direct anterior group.

Bergin et al.¹⁷ compared levels of CK postoperatively in a non-randomized study of minimally invasive direct anterior versus posterior approach. The posterior approach gave higher levels of CK postoperatively. No difference was found regarding CRP. Landgraeber et al.²¹ compared minimally invasive anterolateral (Watson–Jones) to conventional lateral approach showing no significant differences in the two groups regarding postoperative CK levels. The values were higher in the minimally invasive group, so this could be a type 2 error due to relative low number of patients in each group (36 in the minimally invasive group and 39 in the conventional group). Again, no difference was found in postoperative CRP levels. In both studies, the duration of surgery were longer in the group with the highest postoperative CK levels.

Our study have some limitations. Locher et al.²² stated that blood loss is lower if patients are operated in lateral compared to supine position. We do not know if the postoperative levels of CK are affected by patient position during surgery.

The average duration of surgery in the DLA group was 62 min, in the MIDA group the average time was 77 min. These values are similar to the duration of surgery reported in other studies, also studies assessing postoperative CK values. Only six operations in the MIDA lasted longer than 100 min (one lasting 101 min), leaving 77 operations with duration between 52 and 100 min. However, the variation is obviously influenced by multiple surgeons, some surgeons operate fast and some slow, but since all surgeons performed both approaches in similar amount, this would not be a bias towards one

Table 3. Postoperative Levels of Hemoglobin (g/dl) and CRP (mg/L)

	Anterior Group ^a (83 Patients)	Lateral Group ^a (80 Patients)	Difference in Means (95%CI)	<i>p</i> -Value
Hemoglobin				
1st Postoperative day	11.1 ± 1.2	11.6 ± 1.3	0.5 (–0.9 to –0.1)	0.01
2nd Postoperative day	10.9 ± 1.3	11.3 ± 1.2	0.4 (–0.8 to –0.06)	0.03
3rd Postoperative day	10.9 ± 1.2	11.4 ± 1.3	0.5 (–0.9 to –0.09)	0.02
4th Postoperative day	11.0 ± 1.3	11.6 ± 1.4	0.6 (–1.0 to –0.2)	0.008
CRP				
1st Postoperative day	19.4 ± 14.8	22.4 ± 17.7	3.0 (–8.0–2.1)	0.25
2nd Postoperative day	47.5 ± 39.3	50.0 ± 41.5	2.5 (–15.0–10.0)	0.69
3rd Postoperative day	48.4 ± 39.3	51.6 ± 39.6	3.2 (–15.4–9.0)	0.61
4th Postoperative day	33.4 ± 25.6	36.5 ± 25.4	3.1 (–11.0–4.8)	0.44

p-values < 0.05 were considered significant. ^aThe values are given as the mean and the standard deviation.

Table 4. Postoperative Levels of CK (U/L)

	Anterior Group ^a (83 Patients)	Lateral Group ^a (80 Patients)	Difference in Means (95%CI)	<i>p</i> -Value
Immediately after surgery	209.9 ± 85.2	180.4 ± 78.1	29.5 (4.3–54.9)	0.022
1st Postoperative day	688.2 ± 335.0	677.2 ± 281.1	11.0 (–84.9 to 106.8)	0.82
2nd Postoperative day	989.5 ± 446.7	965.8 ± 467.8	23.7 (–117.7 to 165.2)	0.74
3rd Postoperative day	1113.1 ± 479.8	971.7 ± 486.3	141.4 (–8.0 to 290.9)	0.063
4th Postoperative day	1013.4 ± 458.0	820.1 ± 395.9	193.3 (60.7–325.9)	0.005

p-values <0.05 were considered significant.

^aThe values are given as the mean and the standard deviation.

approach. The same could apply to levels of CK. Surgeons “style” or soft-tissue-handling would affect postoperative CK levels, but again, since all surgeons performed both approaches, this should not be biased toward one approach.

The time of measuring the CK levels directly after surgery was similar in both groups, within 1 h after closure. However, if CK levels start to rise at the onset of surgery and rise in a linear fashion, the longer duration of surgery in the MIDA group could be related to the higher levels of CK in the MIDA group directly after surgery. This, however, would not explain the difference on postoperative days 3 and 4.

In our study, and in those of Bergin et al. and Landgraeber et al., duration of surgery was longer for the approach that gave the higher levels of CK postoperatively. The duration of surgery could be a factor in the different CK values postoperatively. However, stating that the levels would be similar if the duration of surgery was similar seems a theoretical exercise, given that the use of minimally invasive approaches inherently leads to longer duration of surgery.

We believe it was an advantage that the same five surgeons used both approaches. Thus, any bias due to the surgeon’s skills would be minimized. Involved staff was blinded to approach used as well as attempted blinding of the patients (even though this was difficult to achieve). All patients got the same implant and had the same pre, peri, and postoperative regime.

We found higher postoperative levels of CK in the MIDA group with no differences in CRP levels or blood loss. The use of pain medication consumed in the

different groups on the day of surgery was on average 4.2 morphine equivalents (i.e., 4.2 mg morphine administered intravenously) higher in the DLA group and the reported levels of pain was 10–15% lower in the MIDA group compared with the DLA group. Studies of VAS used for pain measurement^{23–26} report minimum clinically significant difference in VAS pain scores to be between 0.9 and 1.3 (i.e., 9–13%). Both groups in our study have relatively low levels of pain. The difference in VAS between the groups was between 33 and 44%. Jensen et al.²⁷ state that a difference in pain levels of 33% is clinically significant. We therefore find these differences clinically relevant.

Similar levels of CRP postoperatively would indicate that the general trauma of the arthroplasty (i.e., inflammation) is more connected to removal of bone and insertion of the implant than the release of soft tissues.^{17,21}

The direct lateral approach releases parts of the abductor muscles from the bone and splits the gluteus medius along the length of the muscle fibers.¹² The resulting damage and subsequent loss of function (i.e., positive Trendelenburg sign), might be due to failure of the reinsertion of the muscle or damage to the superior gluteal nerve, innervating the muscle. This could lead to damage to the abductor muscle as a functional unit, but might not cause a high rise in CK levels due to individual muscle fibers not being damaged.

Using the minimally invasive anterior approach, the muscles are retracted, but not released from the bone. A part of the muscle might suffer damage from the retractors, which could lead to higher rise in CK

Table 5. Postoperative Analgesic Consumption in Morphine Equivalents

	Anterior Group ^a (83 Patients)	Lateral Group ^a (80 Patients)	Difference in Means (95%CI)	<i>p</i> -Value
Day of surgery	10.9 ± 9.1	15.1 ± 11.6	4.2 (1.0–7.4)	0.011
1st Postoperative day	12.4 ± 4.5	13.6 ± 6.6	1.2 (–0.5 to 3.0)	0.16
2nd Postoperative day	11.6 ± 4.7	12.4 ± 5.7	0.8 (–0.8 to 2.4)	0.33
3rd Postoperative day	11.0 ± 6.7	11.6 ± 6.4	0.6 (–1.4 to 2.6)	0.54
4th Postoperative day	10.0 ± 6.3	10.9 ± 6.7	0.9 (–1.1 to 2.9)	0.38

p-values <0.05 were considered significant.

^aThe values are given as the mean and the standard deviation.

Table 6. Postoperative Levels of Pain*

	Anterior Group ^a (83 Patients)	Lateral Group ^a (80 Patients)	Difference in Means (95%CI)	<i>p</i> -Value
Before physiotherapy				
1st Postoperative day	2.6 ± 2.0	4.0 ± 2.3	1.4 (0.8–2.1)	<0.001
2nd Postoperative day	1.9 ± 1.8	3.0 ± 2.3	1.1 (0.5–1.8)	0.001
3rd Postoperative day	1.6 ± 1.7	2.8 ± 2.1	1.2 (0.6–1.8)	<0.001
4th Postoperative day	1.5 ± 1.7	2.3 ± 1.9	0.8 (0.2–1.3)	0.006
After physiotherapy				
1st Postoperative day	3.0 ± 2.1	4.6 ± 2.2	1.6 (0.9–2.2)	<0.001
2nd Postoperative day	2.0 ± 1.8	3.6 ± 2.2	1.6 (1.0–2.2)	<0.001
3rd Postoperative day	1.9 ± 1.9	3.1 ± 2.1	1.2 (0.6–1.8)	<0.001
4th Postoperative day	1.8 ± 1.8	2.9 ± 1.9	1.1 (0.5–1.7)	<0.001

p-values <0.05 were considered significant.

*Pain recorded on a visual analogue scale ranging from 1 to 10, 1 indicating no pain and 10 indicating worst possible pain.^aThe values are given as the mean and the standard deviation.

levels, but better function of the muscle as a unit might be possible postoperatively.

The higher levels of pain and use of pain medication in the DLA group could suggest that there were more damage to the soft tissues (i.e., muscles) compared to the MIDA, but it could also be that the release of the muscle from the bone in itself is a significant cause of pain. The reinsertion could cause pain, especially during mobilization when the reinsertion is put under strain, where in the MIDA no muscle attachments are affected.

There is no consensus on the definition of a “minimally invasive” total hip arthroplasty. Some relates this to the length of the skin incision^{28,29} while other relate the term to the level of dissection of soft tissue. Using markers for muscle damage and inflammation should theoretically offer an objective measure on the level of injury to the muscles surrounding the hip. Based solely on the postoperative CK levels in our study, the MIDA is more invasive than the DLA, which contrast to lower levels of pain and use of pain medications. We have continued the use of the minimally invasive anterior approach as our main approach for primary total hip arthroplasty, believing that less pain is more important than postoperative CK values. As stated by other authors, the clinical importance of postoperative CK values warrants further studies including other markers for surgical trauma and oxidative stress.

Perhaps the term “minimally invasive approach” is a misnomer, and that the term “muscle sparing” would be more accurate, signifying the attempt to spare the muscle as a unit without releasing any muscle attachments.

AUTHORS' CONTRIBUTIONS

Knut Erik Mjaaland: set up the study, recruited patients, performed surgeries, collected data, wrote the paper. Kjetil Kivle and Svein Svenningsen: substantial contribution to study design, recruited

patients, performed surgeries, critically revised paper. Are Hugo Pripp: statistical analyses, critically revised paper. Lars Nordsletten: substantial contribution to study design, critically revised paper. All authors have read and approved the submitted paper.

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