Outcomes of different bearings in total hip arthroplasty - implant survival, revision causes, and patient-reported outcome

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THIS THESIS IS BASED ON THE FOLLOWING THREE PAPERS:

Study I: Varnum C, Pedersen AB, Kjærsgaard-Andersen P, Overgaard S. Comparison of the risk of revision in cementless total hip arthroplasty with ceramic-on-ceramic and metal-on-polyethylene bearings. Acta Orthop. 2015;86(4):477-84.

Study II: Varnum C, Pedersen AB, Makela K, Eskelinen A, Havelin LI, Furnes O, Karrholm J, Garellick G, Overgaard S. Increased risk of revision of cementless stemmed total hip arthroplasty with metal-on-metal bearings. Acta Orthop. 2015;86(4):469-76.

Study III: Varnum C, Pedersen AB, Kjærsgaard-Andersen P, Overgaard S. Do different types of bearings and noise from total hip arthroplasty influence hip-related pain, function, and quality of life postoperatively? Acta Orthop. 2016 Dec;87(6):567-574.

INTRODUCTION

Total hip arthroplasty

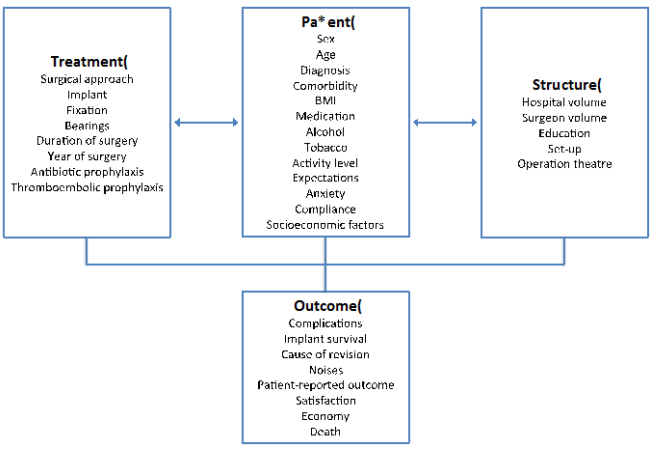
Total hip arthroplasty (THA) is a common and successful treatment of patients suffering from severe osteoarthritis (OA) that significantly reduces pain and improves hip function and quality of life (QoL). It has been proclaimed that THA is the operation of the century.[2] Historically in 1923, Smith-Petersen created a mould arthroplasty made of glass to be inserted between the reshaped articulating surfaces of the head of the femur and the acetabulum. It was thought that the moulded glass would guide nature's repair of the defects in the cartilage. Due to the fragility of the material used, the results were not encouraging, and in 1938 the first vitallium mould arthroplasty was performed.[3] During the 1950-60s, Sir John Charnley introduced the modern low torque friction arthroplasty, which included the use of acrylic cement to fix components to bone, high-density polyethylene as bearing material, and monoblock stem of metal.[2,4] Studies have reported remarkable durability with 77%[5] and 81%[6] survivorship of these THAs at 25-year follow-up with any revision as endpoint, and the concept is still the gold standard.

Outcome of total hip arthroplasty

Traditionally, the outcome of THA (Figure 1) has been evaluated from the surgeon's perspective. The surgeon-based outcome may be assessed in morbidity including peri- and postoperative complications. Surgical complications count bleeding, prosthetic joint infection (PJI), damage to anatomical structures including involvement of the sciatic nerve, dislocation, anisomelia, and periprosthetic fracture, whereas medical complications include pneumonia, deep venous thrombosis, and pulmonary embolism. Also biomechanical reconstruction, range of motion, prosthetic survival, causes of revision, and mortality are outcomes assessed by the surgeon.

Furthermore, noises from the THA[7] and persistent hip-related pain have been used as outcome measures after THA. Studies have shown, that persisting hip-related pain was seen in 28.1% of patients 12 to 18 months after primary THA[8], and that 7% of patients were dissatisfied or highly dissatisfied one year after primary THA[9]. By including measures of pain, disability and satisfaction into the definition of failure, a more balanced assessment of outcome can be made, as patients and orthopaedic surgeons may assess outcome after THA differently. Therefore,

Figure 1. Prognostic factors for the outcome of total hip arthroplasty



patient-reported outcome measure (PROM), which can be disease-specific or generic, is recognized as a very important tool for evaluating the outcome after THA.[10,11] The US Food and Drug Administration (FDA) have defined a patient-reported outcome (PRO) as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else".[12] FDA strongly recommends the use of PROs in clinical trials, and PROMs have been implemented in national hip arthroplasty registries.[10,13,14] Additionally, the economic outcome of THA may be assessed.[15]

The outcome after THA may be influenced by a number of prognostic factors, which may be related to the patient, treatment, and structure (Figure 1). Prognostic factors may be categorised into non-modifiable, e.g. sex and age, and modifiable, e.g. alcohol consumption, smoking habits, and activity level. Previous literature has shown that the patient-related factors sex, age, diagnosis, comorbitity, and use of medication influence the outcome of THA.[16-23] The outcome may also be affected by the surgical approach, implant design, fixation, type of bearings, and femoral head size.[21,24-31] Furthermore, hospital volume and fast-track set-up may be of importance for the outcome of THA.[32,33] Among all these determinants of the outcome of THA, the focus of this thesis is different types of bearings.

Types of bearings

Metal-on-polyethylene bearings

Metal-on-polyethylene (MoP), a femoral head of stainless steel articulating on a polyethylene acetabular liner, are by far the most commonly used bearings in THA and are therefore considered the "standard" bearings. The major concern related to the use of MoP bearings is wear and generation of polyethylene wear particles which potentially can lead to osteolysis and aseptic loosening of the implant. Aseptic loosening is the most prevalent cause of revision accounting for 51.8% of registered revisions in the Danish Hip Arthroplasty Registry (DHR).[16]

Generation of polyethylene wear particles can primarily result from three different processes: Abrasion (a harder surface make grooves in a softer material), adhesion (formation of a transfer film occurring when a softer material is smeared onto a harder surface), and fatigue (generation of particles resulting from subsurface cracks).[34] Wear particles can be found in periprosthetic osteolytic lesions embedded in a membrane also containing macrophages which release pro-inflammatory mediators when having phagocytized ultrahigh-molecular-weight polyethylene (UHMWPE) wear particles. Consequently, osteoclasts are activated to resorb the bone at the bone-implant interface that can result in painful loosening of the implant.[35-40] Previous research has stated that linear polyethylene wear exceeding 0.2 mm/year or volumetric wear surpassing 150 mm3/year predisposes to periprosthetic osteolysis.[41]

In cementless MoP THA, the polyethylene liner is inserted into a metal acetabular shell leading to both frontside and backside wear. Ex vivo, however, linear and volumetric wear from the articulating side were at least three orders of magnitude higher than the wear estimates at the backside. This variation was mainly explained by the difference in maximum sliding distance at the articulating surfaces (measured in mm) compared to the back surface (measured in μm).[42]

In order to reduce abrasive/adhesive and fatigue wear, much effort has been made to improve the tribological properties of polyethylene during the last decades. Charnley introduced the polytetrafluorethylene (Teflon) as material for the acetabular component but due to poor wear resistance, this material was abandoned in favour of high molecular weight polyethylene.[4,43] Charnley recommended the use of gamma sterilization for polyethylene components, a technique that is still used.[44] In hip simulators, wear rates decreased by a factor of more than 30 when the molecular weight of polyethylene increased from $5x10^5$ to $2x10^6$, and a single dose of gamma irradiation at 2.5-5.0 Mrad (1 Mrad=10 kGy) progressively improved the wear resistance in UHMWPE.[45] A drawback of gamma irradiation in air is, that it leads to long-lived free radicals which react with oxygen resulting in progressive oxidation and deterioration of the mechanical properties of the polymer.[46] In order to reduce oxidative degradation, some manufacturers started to gas-sterilize by ethylene oxide or gas plasma but in contrast to gamma irradiation, these alternative gas-sterilization methods did not cross-link the polyethylene.[47] In a radiographic wear study, higher wear rates was found for uncross-linked, gas-sterilized components when compared with gamma-sterilized controls.[48] Furthermore it was confirmed that, in hip simulator testing, elevated doses of irradiation cross-linking reduced wear rates, and thermal processing after irradiation influenced the mechanical properties and oxidative resistance. Irradiation cross-linking, whether by gamma or electron irradiation, when combined with annealing and remelting thermal treatments resulted, in the late 1990s, in the first generation of highly cross-linked polyethylene (HXLPE).[44,49,50]

Starting around 2005, the newer generations of HXLPE were developed by the use of different methods to stabilize the polymer: Sequential irradiation and annealing process whereby the polyethylene receives a high dosage of radiation cumulatively instead of during one event (X3 material)[51]; solid-state, hydrostatic extrusion that modify the physical and mechanical properties of HXLPE by induction of plastic deformation and orientation of the molecules (ArCom XL material)[52]; and incorporation of vitamin E (α-Tocopherol), which react with peroxy free radicals on lipid chains and arrest the oxidation reactions resulting in increased oxidative stability[53].

Ceramic-on-ceramic bearings

Ceramic-on-ceramic (CoC) bearings were introduced to reduce wear debris. In 1970, Boutin implanted the first THA with all-alumina bearings in France.[54] Today's ceramic bearings consist of aluminium oxide (alumina, Al_2O_3), zirconium oxide (zirconia, ZrO_2) or composites and have been changed in order to reduce fracture risk. The first generation alumina had low density and a very coarse microstructure, whereas the newer third generation had a higher purity and a finer grain structure and was hot isostatic pressed, laser engraved, and proof tested.[55] Alumina has been used for CoC bearings.[56-58] The safety of a ceramic component is correlated to its mechanical strength, and efforts for improving this strength have been made by developing different manufacturing processes.

Zirconia ceramic is used in the form of yttria stabalized tetragonal zirconia polycrystals (Y-TZP) to impede the hydrothermal degradation of zirconia. Y-TZP has a higher density and finer grain size than alumina, providing about double its fracture toughness and flexural strength. There is clear experimental evidence that the wear rate of zirconia-on-zirconia bearings is too high to use in prosthetic joints, and zirconia is traditionally used for the femoral head in combination with an UHMWPE acetabular liner.[59,60]

Two different composites can be made from alumina and zirconia: A zirconia matrix reinforced with alumina particles (alumina-toughened zirconia) or an alumina matrix reinforced with zirconia particles (zirconia-toughened alumina, ZTA). The hardness

of ZTA composites is greater resulting in higher wear resistance. With new processing techniques, it is possible to obtain high-density ZTA nanocomposites with a very homogeneous microstructure, nearly the same hardness as alumina, a higher fracture toughness, high hydrothermal stability, and high crack-resistance.[61,62]

The most frequently used ceramic materials today in THA are the third generation hot isostatic pressed alumina commercially known as BIOLOX forte and the fourth generation commercially known as BIOLOX delta, which is an alumina matrix composite comprised of 75% alumina, 24% zirconia, and 1% elongated oxides of chromium and strontium.[63] Some of the advantages with the use of CoC bearings are the low wear rates both ex vivo and in vivo.[63-66] In addition, wear debris produced from CoC bearings are less biologically active than metal or polyethylene debris.[67,68] The major concerns related to the use of CoC bearings are fracture of the ceramic components[69-73] and squeaking and other noises[7,74,75]. Also, the sandwich design for ceramic inserts have been reported to have problems in terms of dislodging of the ceramic insert.[76,77]

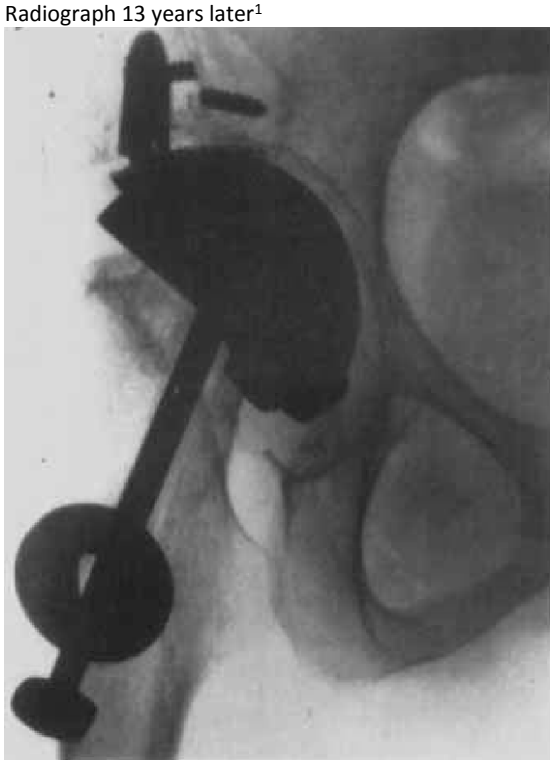
Metal-on-metal bearings

In 1938, Wiles performed the first THA consisting of pre-formed acetabulum and femoral head made of stainless steel attaching it to bone with bolts and screws.[1] During the beginning of the 1960s, McKee and Watson-Farrar implanted THAs with metal-on-metal (MoM) bearings. The components were constructed of chromium-cobalt alloy and fixed to the bone by methylmethracrylate.[78] In the same period, Ring developed a screw fixated cup to be used with the Moore's prosthesis.[79] By mid-1970s, MoM articulations were abandoned in favour of Charnley's technique.[80] Modified alloys marked a new era for MoM bearings, and in 1988 Weber implanted the first MoM THA with Metasul bearings manufactured from carbon rich cobalt chromium molybdenum alloy[81,82], and the Metasul bearings are still used today. The current MoM implants are made of a Cobalt-28 Chromium-6 Molybdenum Alloy (ASTM (American Society for Testing and Materials) F75 or ASTM F1537) and have a high carbon content above 0.20% which has the purpose of decreasing wear[83].

With the reintroduction of MoM bearings it was possible to use large-diameter-heads (LDHs) which were shown to reduce wear ex vivo.[84] Ex vivo, LDHs have been shown to improve range of motion (ROM) and, due to increased jump distance (the distance a femoral head requires for displacement from the acetabular cup before dislocation), decrease the component-to-component impingement and hereby the potential risk of dislocation.[85] However, a randomised clinical trial have shown no difference in total ROM for patients with LDH and hip resurfacing arthroplasty compared to patients having 28-mm femoral head.[86] In a study from the Finnish Hip Arthroplasty Register, a decreased risk of revision due to dislocation was found, when comparing 32-36 mm and femoral heads larger than 36 mm to 28 mm heads.[29]

The most important predictor of the wear rate in MoM bearings is edge-loading[87], and the chromium and cobalt wear particles may result in different periprosthetic soft-tissue lesions: metallosis[88], aseptic lymphocytic vasculitis-associated lesions (ALVAL)[89], pseudotumours[90] and adverse reaction to metal debris (ARMD)[91]. Metallosis is the gross staining of the periprosthetic soft tissue as a result of metal deposition and is seen at revision surgery. ALVAL is characterized by a diffuse and perivascular infiltrate of T- and B-lymphocytes and plasma cells, high endothelial venules, massive fibrin exudation, accumulation of macrophages, infiltrates of eosinophils, and necrosis and was found in periprosthetic tissues from patients with failed MoM

Figure 2. A ball-and-cup arthroplasty performed in 1938. Radiograph 13 years later[1]



bearings.[89] Pseudotumours are symptomatic reactive periprosthetic soft tissue changes demonstrated on magnetic resonance imaging (MRI) as thin- or thick-walled cysts or solid masses, and their histology resembles that of ALVAL, but a more diffuse lymphocytic infiltrate as well as extensive connective tissue necrosis characterise pseudotumours.[90,92] ARMD is used as an umbrella term and describes joint failures associated with pain, large sterile effusions of the hip and/or macroscopic metallosis/necrosis, thus including metallosis, ALVAL and pseudotumours.[91]

Apart from the local reactions, also systemic effects might be seen. Systemic cobalt toxicity have been described following revision of fractured ceramic bearings and in patients with failed MoM implants, and possible symptoms include impairment of vision and hearing, hypothyroidism, peripheral neuropathy, cardiomyopathy, depression, anxiety, tinnitus, fatigue, and anorexia.[93-99] There is dissemination of cobalt and chromium to sites distant to the orthopaedic implant.[100] It has been found, that patients having THA have a significant increase of chromosomal damage in peripheral blood lymphocytes, and that the changes may depend in part on the type of prosthesis.[101] However, the incidence of cancer after THA is low predicted from the normal population, and the overall risk of cancer is not higher for MoM than for any other type of bearings. The low risk of cancer must be read with caution, as the follow-up is relatively short (maximum 7-11 years).[102,103]

Motivation

In order to improve the outcome after THA, this PhD study was initiated. Although improvements of the polyethylene in MoP bearings, alternative bearings such as CoC and MoM have been used in THA, which may result in better implant survival and PRO. Only a few registry-based studies on CoC and stemmed MoM THA have been published.[28,104-107] These studies may be hampered by the lack of information on completeness of data, of examination of

implant types, and of causes of revision and may be limited by the short follow-up and the used statistical methods including lack of adjustments for confounders. Moreover, the existing literature on implant survival and PRO including information on hip-related noises from patients having MoP, CoC or MoM THA represents smaller series of patients involving one to few hospitals and clinics.[7,24,27,108-112] These studies are limited by the small sample size, and results from a single institution may reduce the generalizability of the findings. Furthermore, the results may be biased, as some authors have been involved in the development of the implant. To overcome these issues, we decided to perform nation-wide, population-based studies, which can take patient- and surgery-related characteristics into account, in order to provide patients the optimal type of bearings in THA.

AIMS OF THE THESIS

The aims of this thesis were:

Study I: To examine the revision risk and to investigate the causes of revision of cementless CoC THAs comparing them to those of "standard" MoP THAs.

Study II: To compare the six-year revision risk for MoM bearings with that for MoP bearings in cementless stemmed THA, and further to study the revision risk for different designs of stemmed MoM THAs and the causes of revision.

Study III: To examine the association between CoC, MoM, and MoP bearings and both generic and disease-specific PROMs, and furthermore to examine the incidence and types of noises from the three types of bearings and identify the effect of noises on PROM scores.

METHODOLOGICAL CONSIDERATIONS

Literature search

The literature search was not based on a systematic review. It was conducted throughout the study period with a final search in January 2016. PubMed was the main database for literature search, and the medical subject heading (MeSH) "Total hip replacement" was combined with the following keywords: "ceramic-on-ceramic", "alumina bearings", "metal-on-metal", "polyethylene", "HOOS", "EQ-5D", "UCLA", and "satisfaction". Also the reference lists of relevant articles and annual reports from national hip arthroplasty registries were reviewed. Furthermore, the Web of Science database was used to search for specific articles. The literature search was limited to articles in English or Danish and mainly to articles published from 2005 and onwards, although some key articles from before 2005 have been included due to historical interest.

Data sources

The Civil Registration System (study I-III)

Since the establishment in 1968, the Civil Registration System (CRS) has contained individual information on the unique 10-digit identification number issued to all Danish citizens at birth. This personal identification number encodes for date of birth and sex and allows for individual-level linkage between Danish data sources. Moreover, the CRS contains information on address, protection against inquiry from researchers, and continuously updated information on migration and vital status including date of death. The CRS is virtually complete, since the prevalence of disappeared persons is around 0.3%. This ensures complete follow-up in Danish cohort studies when using CRS data for censoring.[113]

The Danish Hip Arthroplasty Registry (study I-III)

The DHR was established January 1, 1995 with the aim of registering and improving the results after THA in Denmark.[114] During 1995 to 2014, approximately 140,000 primary THAs and 22,000 revisions have been reported to the DHR. The coverage is very high and in 2014, 28 orthopaedic departments and 16 private clinics reported to the DHR, and the completeness has been about 95% for both primary procedures and revisions during the last many years compared to the Danish National Patient Registry (DNPR).[16] The authorities reimburse the orthopaedic departments when reporting to the DNPR; therefore, reporting to the DNPR is considered the gold standard. Clinical data on primary THAs, revisions, and at follow-up examinations are prospectively collected. Preoperative data include the unique personal identification number, hospital code, laterality of the affected hip, previous surgery in the same hip, function of walking according to Charnley's groups A, B, and C[115], and diagnosis. In addition, it is possible to register the preoperative Harris Hip Score (HHS)[116], but this is not compulsory. The perioperative data registered in the DHR include the date of surgery; antibiotic and thromboembolic prophylaxis; type of anaesthesia; duration of surgery; type of acetabular and femoral component and their fixation; complications in the acetabulum and the femur; and type, size, and material of the prosthetic femoral head and the acetabular liner. For revisions, defined as a new surgical procedure including complete or partial exchange or removal of the prosthetic components, the following is registered: Indication, prosthetic status before revision, extent of revision, number of earlier revisions, and classification of acetabular and femoral bone loss. Data collected at follow-up include the laterality of the hip, date of the latest surgery, date of follow-up examination, postoperative complications, the patient's assessment of satisfaction with the primary or revision THA, and possibly the HHS. As there are no national guidelines for postoperative follow-up after primary THA or revisions, postoperative follow-up data is registered at different time points for the different departments.

The completeness for both primary THAs and revisions is validated yearly in the annual reports, and data on diagnosis for primary THA and postoperative complications[117] and on deep PJI as cause of revision[118] has been validated. But no validation of the data on prosthetic components including material of the acetabular liner and the femoral head has been made.

The Nordic Arthroplasty Register Association (study II)

To obtain a larger study population, data from the Nordic Arthroplasty Register Association[119] (NARA) was used in study II. Hip arthroplasty registries were established in Sweden in 1979, in Finland in 1980, and in Norway in 1987.[120-122] In 2007, selected individual data on each THA registered in the arthroplasty registries in Denmark, Norway, and Sweden were merged into the NARA database, and Finland were able to deliver data in 2010.[123] Data in the four registries were not fully compatible as there were some differences in variables and in the definition of these. Therefore, a common dataset including data that all registries were able to deliver were defined, and consensus has been made according to definition of several variables. In each national registry, the selected data were anonymised, including deletion of the national civil registration number, before merging into the common NARA database.[124] Thus, identification of patients at an individual level was not possible. As a consequence, the completeness and quality of data in the NARA database depend on the completeness and quality of data in each of the four national registries. Although the healthcare systems, patient populations, and treatment traditions in the Nordic countries are rather

homogenous, there is no consensus regarding indication for neither primary THA nor revision procedures.

The Danish National Patient Registry (study I and III)
The DNRP was established in 1977 and contains data linked to the unique personal identification number on all admissions and discharges from somatic hospitals in Denmark, including dates of admissions and discharges, surgical procedures performed, and up to twenty diagnoses for every discharge. From 1977 to 1993, diagnoses were classified according to the Danish version of the International Classification of Diseases, eighth edition, and since 1994 according to the tenth edition. From 1995 and onwards, data on psychiatric hospitalisation and all outpatients and emergency visits have been included into the registry. The physician who discharges the patient assigns all discharge diagnoses.[125] Data from the DNRP was used to determine the Charlson comorbidity index (CCI) score.[126] Although the positive predictive value (PPV) for diagnosis and treatment vary substantially in the DNPR[125], the overall PPV for the 19 Charlson conditions was 98.0%[127].

Design and study population
Randomised clinical trials (RCTs) may be considered the gold standard when studying THA as an intervention. However, RCTs are labour-demanding and relatively costly, which may limit their use when examining rare outcomes. In such situations, observational cohort studies based on national registries are suitable as large study populations can be obtained.

Study I and II were designed as population-based cohort studies. As registration of the femoral head and acetabular liner material in the DHR started in 2002, patients operated before 2002 were not included in the studies. In study I, a data extract from 2010 including raw data on all primary THAs operated from 2002 to 2009 (n=58,731) revealed that 55,212 (94%) had registered the material of the femoral head, whereas 46,386 (79%) had registered the material of the acetabular liner. When combining the femoral head and liner material for determination of the couple of bearings, it was found that 14,537 (25%) primary THAs had missing data on bearings. This problem was in part redressed both retrospectively and prospectively by changes in the software (Klinisk Målesystem) used to report data on THA procedures to the DHR. In a new data extract from 2012 including primary THAs from the same time period, the proportion of THAs registered with missing data on couple of bearings was reduced to 5% (2,942 of 59,431). The latter data extract from the DHR was used in study I. The eligible number of cementless THA in patients diagnosed with primary OA of the hip, inflammatory arthritis, femoral head osteonecrosis, and childhood hip disorder was 25,656. Of these, 11,096 THAs with either CoC (n=1,773) or MoP (n=9,323) bearings were included. In study II, the eligible number of cementless THA was 85,371 and of these, 32,678 THAs having MoM (n=11,567) and MoP (n=21,111) bearings were included.

Study III was initially designed as a cross-sectional case-comparison cohort study. One case having CoC THA was randomly matched on sex, year of birth, and year of surgery to one patient with MoM and one patient with MoP THA. Matching was performed in order to eliminate the confounding effect of sex, age, and follow-up. After matching, 2,025 CoC, 1,280 MoM, and 1,821 MoP THAs were identified and clearly, it was not possible to find a unique match to each case. Furthermore, a large number of patients with MoM and MoP THA were matched to more than one CoC THA (Table 1), and in some cases and matched patients operated bilaterally both THAs were included (Table 2). Even though patients with MoM and MoP THA were matched to more than one CoC THA, these patients should only receive one questionnaire. Moreover, only the first THA was included in case of bilateral THA. Thus, 1,803 patients with CoC THA, 834 patients with MoM THA, and 1,584 patients with MoP THA were included. Another limitation related to the matching was non-responders, i.e. patients who did not return a fulfilled questionnaire. If the matched case-comparison cohort design should be maintained, the corresponding case and matched patients should be omitted, when one of the three was a non-responder. This would have resulted in a significant reduction of the study population, which then only would have consisted of 621 patients. Therefore, the case-comparison cohort design was abandoned in favour of a cohort study design and instead, adjustments for sex, age, and year of surgery were made when performing the regression analyses.

Table 1. A number of MoM and MoP THAs were controls for more than one CoC THA, e.g. 202 MoM and 180 MoP THAs were each controls for 2 CoC THAs (study III)

Number CoC THA being controls for	MoM n=1,280	MoP n=1,821
1	857	1,606
2	202	180
3	81	26
4	44	8
5	28	1
6	25	0
7	17	0
8	11	0
9	9	0
10	5	0
11	1	0

Table 2. Number of patients with unilateral and bilateral THA (study III)

	CoC n=2,025	MoM n=857	MoP n=1,606
Unilateral THA	1,803	834	1,584
Also contralateral THA	222	23	22

Inclusion/exclusion criteria
In study I-III, patients having implanted hip resurfacing arthroplasties or dual mobility acetabular systems (Table 3) were excluded due to the different prosthetic concept and design with specific risks and complications, e.g. femoral neck fracture, for hip resurfacing arthroplasties, and specific patient selection, e.g. mentally disabled patients, for dual mobility acetabular systems. Thus, only patients having stemmed THA with a standard cup were included. Further, patients diagnosed with acute or sequelae from traumatic hip disorder were excluded from the study populations, because these patients have a specific risk profile including comorbidity influencing the outcome of THA. Also patients diagnosed with "other" diagnoses (than OA, femoral head osteonecrosis, inflammatory arthritis, and sequelae from childhood hip disorder), which includes patients having a specific risk profile due to, for instance, primary tumour or metastases, were excluded. As fixation is a well-known confounder and the vast majority of CoC (97.1%) and MoM THAs (86.5%) had cementless fixation, only cementless THAs were included in study I

Table 3. Designs and manufacturers of dual mobility acetabular systems checked for and excluded from the study populations

Brand	Manufacturer
Acorn Double Mobility Cup	Permedica
Avantage	Biomet
Collegia	Cremascoli-Wright
Dual Mobility Cup	Tornier
EOL	Norton-Ceramconcept
Evora	Science et Médecine
Gyros	DePuy
Modular Dual Mobility	Stryker
Novae-1	Serf
Novae-E	Serf
Novae Sunfit	Serf
Polarcup	Smith & Nephew
Restoration Anatomic Dual Mobility	Stryker
Saturne	Wright
Saturne Reconstruction	Wright
seleXys DS	Mathys
seleXys DS Revision	Mathys
Stafit	Zimmer
Tregor	Aston
Versafitcup Double Mobility	Medacta

and II. In study III, all fixation methods were included and adjusted for in the analyses.

Questionnaires (study III)

The set of questionnaires was supplemented by questions concerning the current height and weight. Patients were also asked to indicate by "yes" or "no", if they had undergone any reoperation in the specified hip with removal or exchange of the whole or any parts of the implant since primary surgery.

HOOS

The disease-specific hip disability and osteoarthritis outcome score (*HOOS*)[128] was constructed by adding dimensions concerning sport and recreation function and hip-related QoL to the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[129]. In study III, HOOS was chosen as it is well validated and widely used, but other disease-specific questionnaires, e.g. the Oxford Hip Score[130], which is translated into Danish and validated in a Danish registry setting[131,132], could also have been used. In contrast, the HHS is not self-administered and therefore not suitable for a questionnaire survey.

The HOOS is constituted of five subscales (dimensions): pain (HOOS Pain), other symptoms (HOOS Symptoms), activities of daily living (HOOS ADL), sport and recreation function (HOOS Sport), and hip related QoL (HOOS QoL). The validation of the instrument includes assessment of content and construct validity, responsiveness, minimal clinically important improvement (MCII), and patient-acceptable symptom state (PASS).[128,133,134] HOOS is recommended for evaluation of patients diagnosed with OA of the hip treated non-surgically or with THA.[135] For each subscale, a score from 0 to 100 is computed: A score of 100 indicates no problems and 0 indicates extreme problems. If at least 50% of items in the subscale have been answered, the subscale score can be calculated (HOOS scoring instructions available at http://www.koos.nu/index.html). Translation and cross-cultural adaptation of the original Swedish version of HOOS into Danish has been done using existing guidelines[136] although no testing of validity, reliability, and responsiveness in a Danish population has been performed. As the Danish and Swedish cultures are very similar, it is reasonable to assume, that there is no difference on validity, reliability, and responsiveness in the two cultures.

EQ-5D

The EuroQol EQ-5D-3L is a generic, reliable and validated instrument used for measure of QoL and is applicable to a wide range of health conditions and treatments including hip OA, THA, and revision hip arthroplasty.[137-140] The EQ-5D-3L was chosen as the generic questionnaire, as it is used in the Swedish Hip Arthroplasty Register (SHAR) and the National Joint Registry for England, Wales, Northern Ireland and Isle of Man (NJR).[10,14] Furthermore, the ED-5D-3L was used in a Danish registry setting[132], and it takes only a few minutes to fill in. Other relevant generic questionnaires that could have been used is the Short-Form 12[141].

The EQ-5D index describes the health-related QoL from a social perspective and the EQ visual analogue scale (VAS) from the patient's perspective. The EQ-5D index is determined from five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each with three levels (no problems, some/moderate problems, and extreme problems/unable to) resulting in 3^5=243 possible health states. The EQ-5D is translated into Danish, and based on the time trade-off method[142], a value set ranging from -0.624 to 1, where 1 describes full health, 0 represents being dead, and a negative value represents a health state worse than being dead, constitutes the Danish culture-adjusted EQ-5D index[143]. The EQ VAS is determined when the patients rate their current state of health on a thermometer scale ranging from 0 ("worst imaginable") to 100 ("best imaginable"). A newer version of the EQ-5D (EQ-5D-5L) with five levels (no problems, slight problems, moderate problems, severe problems, and extreme problems/unable to) for each of the five dimensions has been developed in order to improve the sensitivity and to reduce floor and ceiling effects.[144,145] The EQ-5D-5L was compared to the EQ-5D-3L in patients with hip and knee OA referred to total joint replacement and provided stronger evidence of validity specifically for the dimensions mobility, usual activities, and pain/discomfort that are particularly relevant for OA patients.[146]

UCLA activity score

University of California, Los Angeles (UCLA) activity score was first described in 1984, is disease-specific, and has 10 descriptive activity levels ranging from wholly inactive and dependent on others (level 1), to moderate activities such as unlimited housework and shopping (level 6), to regular participation in impact sports such as jogging or tennis (level 10). Regardless of frequency or intensity of participation, the UCLA activity score is based on the highest-rated activity.[147] The UCLA activity score, which includes different types of sporting activities, was included in the questionnaire to supplement the Sport subscale in the HOOS. The activity score is found to correlate well to pedometer data in a population but for individual patients with the same UCLA activity score, the difference in the average steps per day could vary by up to a factor of 15.[148] The UCLA activity score was compared to the International Physical Activity Questionnaire as gold standard and was found to be the most appropriate scale for assessment of physical activity levels in patients undergoing total joint replacement, as it had high reliability and completion rate and showed no floor effects.[149] A validated Danish version of the UCLA activity score, although not published yet, was used.

Questionnaire about noises

Owen et al. defined noises as any audible sound that the patient perceived as originating from the THA.[150] Other authors have defined a squeaking as a squeaking, clicking, or grating sound with origin from the THA during movement[151], thus classifying different qualities of noises as squeaking, whereas noises from THA also have been described as "pops", "snaps", and "grinds" by other authors[7]. In 2010, Swanson et al. proposed a scale for grading the frequency and the intensity of the noise, and the authors defined "problem squeaking" as any squeak always audible to others and occurring at least once per week.[152] Furthermore, the Melbourne Orthopaedic Noise Assessment, including questions about noise frequency, noise type, and audibility of the noise to others, was published in 2013.[112] For aim III, a questionnaire to collect information on noises from THA was created based on the literature.[7,152] All patients were asked if they had experienced noises from the THA. If confirmed, they were asked to characterise the noises as squeaking, creaking, grating, clicking, or other. Furthermore, patients were asked to answer questions about onset (number of months after surgery at which the noises started), frequency (at least once a day, at least once a week, more seldom than once a week), audibility (only audible to the patient, from time to time audible to others, always audible to others), activities triggering the noises (rising from a chair, sitting down, bending, walking, walking up or down the steps, climbing a high step, or other activity), and what degree noises led to reduced physical function and hindered the patient being together with other people ("no", "slight", "moderate", "severe", or "extreme"). Among all authors, consensus was obtained regarding phrasing of the questions. Subsequently, the questions about noises were slightly adjusted through a test phase based on 18 patients randomly selected among patients admitted to Department of Orthopaedic Surgery, Vejle Hospital, Denmark for primary THA surgery. Furthermore, three patients who had undergone revision at the same department of their CoC THA due to noises tested the questions and found these relevant and meaningful. Although the questions about noises do not result in an overall score, a major drawback is that the questions are not properly evaluated in relation to content and construct validity, and no test-retest in a smaller proportion of the patients have been performed. Further, no objective assessment has been made to validate the self-reported noises. However, in the literature no thorough validation of questions on noises from THA has been made, and the definition of "problem squeaking" was made by Swanson et al. without knowing if this definition was meaningful for the patients with squeaking THA.[152]

Choice of PROM

Since 2002, PROMs have been included stepwise in the SHAR in order to increase the sensitivity of the registry. Patients undergoing primary THA are asked to complete a self-administered questionnaire, including Charnley's functional categories, a VAS for pain and satisfaction, and the EQ-5D. This is done preoperatively (except for satisfaction) and at one, six, and ten years postoperatively unless the patient has undergone revision surgery.[10] A study comparing collection of PROM data with either pen-and-paper or internet questionnaires found that the response rates for pen-and-paper and internet questionnaires were 49% and 92%, respectively.[153] This is in contrast to a small series study that reported very high correlation of scores from HHS, WOMAC, Short Form-36, EQ-5D, and UCLA activity score obtained with the paper, touch screen, and web-based modes.[154] However, the use of pen-and-paper questionnaire is costly and laborious due to postage and double manual data entry. With the use of HOOS and EQ-5D-3L questionnaires, Paulsen et al. performed a comparison between automated forms processing and double manual data entry for highly structured forms containing only check boxes, numerical codes and no dates, and no differences in the proportion of errors were found.[155] Moreover, HOOS and EQ-5D-3L were found appropriate for administration in a hip arthroplasty registry.[132] To compare symptoms, function, activity, and QoL before and after primary THA, both a generic and a disease-specific questionnaire can be administered via the Internet with supplement of pen-and-paper questionnaire prepared for automated forms processing.

Several factors may be taken into account when interpreting the PROMs. Patients' preoperative expectations to THA may vary considerably, and Judge et al. reported that greater numbers of preoperative expectations were associated with younger age, women, increasing body mass index (BMI), and more education. Patients were more likely to improve after surgery the more preoperative expectations they had.[156] However, other authors report, that there was no association between the level of preoperative expectations and fulfilment of expectations or outcome. Furthermore, there was no relation between depression and expectations.[157] Otherwise, patients with anxiety or depression preoperatively had lower PROM scores after THA than patients without these mental disorders.[158] In a study from the SHAR, changes in EQ-5D index, EQ VAS, and pain VAS increased with higher educational level[159], and other authors reported higher likelihood of less than excellent or good HHS and thigh pain ≥3 on a VAS for patients with less than a high school education.[160] In another study, Short From-36 was used to compare QoL, and completed level of schooling had no effect on the improvement in QoL after THA[161], which indicates that differences may appear due to different PROMs, study designs, follow-up, and cultures. None of these factors were treated separately in study III.

Statistics

In all studies, the exposure was THA with different types of bearings: CoC and MoP in study I; MoM and MoP in study II; and CoC, MoM, and MoP in study III. In study I and II, the primary outcome was time to revision for any cause, whereas time to revision for aseptic loosening, dislocation, and other causes were secondary outcomes. In study III, the outcome was generic and disease-specific PROMs.

Traditionally, time-to-event or survival analysis has been performed with the Cox regression, but competing risk cannot be addressed properly with this method[162]. The Kaplan-Meier estimator used in Cox regression overestimates the risk of revision when the risk of death is high[163], and THA is most common in older patients having higher risk of death compared to younger patients. In study I and II, we therefore chose to perform the survival analysis with regression with the pseudo-value approach taking the competing risk of death into account. Pseudo-values are calculated at prespecified time points. The pseudo-observation is a transformation of the time-to-event data in which each time-to-event observation is represented by the amount of information it contains when the observation is deleted from the dataset. Subsequently, a model for relative risk (RR) for the uncensored data is applied via a generalised estimating equation obtained in a generalised linear model for the pseudo-values with normal distribution and robust variance estimation.[164,165] The pseudo-value method relies on, as any time-to-event analysis, the censoring being independent. In the current context independent censoring is satisfied since the risk of revision was assumed to be constant over calendar time. The measure of association of Cox

regression is the hazard ratio (HR), which may be a little difficult to interpret and may often be interpreted as a measure of the RR. One assumption when performing the Cox regression is proportional hazards meaning that the HR is constant over time, and this assumption was not fulfilled in study I and II. When using regression with the pseudo-value approach, there is no assumption of proportional hazards to be satisfied. Another advantage is, that the measure of association of regression with the pseudo-value approach is a real RR, which may ease the interpretation of the results. However, a drawback with this method, and contrary to the Cox regression, is that it is not possible to have survival curves adjusted for confounders.

In study III, multivariate linear regression has been performed to determine adjusted mean differences of PROM scores between the types of bearings. For the HOOS subscales, EQ-5D index, and EQ VAS the resulting scores are continuous. For the UCLA activity score, the resulting score is between one and ten, but each individual score corresponds to one activity statement, and the difference in activity level between score two and three is not the same as, for instance, between score seven and eight. Therefore, one could argue that the appropriate analysis would have been one for ordered categorical outcome, e.g. ordinal logistic regression. One of the drawbacks with the use of such a model is, that the outcome is an odds ratio, which is more difficult to **!Uventet afslutning på formel**to analyse the UCLA activity score in study III knowing full well that the results may be interpreted with caution as the UCLA activity score had been treated as a continuous variable.

Bias and confounding

Several factors may influence the validity of our results. The association observed could have several explanations that have to be considered before inferring a causal association. These factors include selection problems potentially leading to selection bias, information problems potentially leading to information bias, chance, and confounding (Figure 3).

Selection bias

In general, selection problems in a cohort study can occur due to lost to follow-up. However, in study I and II we have complete follow-up of all patients included in the study population. Thus, selection bias is not likely. In contrast, selection bias may influence the results in study III, as patients who did not answer the questionnaire (non-responders) were lost to follow-up. Non-responders had a greater proportion of patients younger than 50 years and smaller proportion of patients aged 70 years or older, which may result in lower activity scores in study III, as younger patients are more active than older. Among non-responders, a smaller proportion was diagnosed with OA and a greater proportion with other diagnoses, which corresponds well with differences in the age groups. Furthermore, there was a smaller proportion without comorbidity and a greater proportion with high comorbidity, which may give higher PROM scores in the study. Among non-responders there was a smaller proportion with CoC bearings, and a greater proportion of patients with MoP bearings than responders, which may be explained by the greater proportion of patients with high comorbidity that are more likely to be treated with MoP THA.

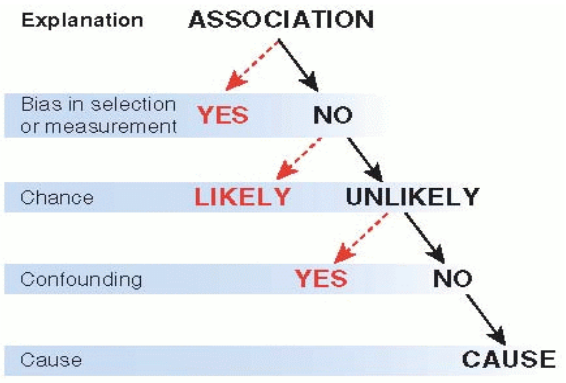
In study I, another selection problem can occur because the use of CoC bearings may be reserved for young and active patients as recommended by some authors[167], or some departments may have CoC as their "standard" bearings, whereas other departments may reserve these bearings for only very rare cases, e.g. very young patients suffering from childhood hip disorders[168]. In study II, there is a greater proportion of males, a greater proportion diagnosed with OA, and a smaller proportion diagnosed with childhood hip disorders operated with MoM compared to MoP bearings. Furthermore, in Denmark not all orthopaedic departments have used MoM bearing in THA, and within the Nordic countries there is a huge variation in the use of MoM THA: In study II, 72% of patients were operated in Finland, 23% in Denmark, and 5% in Sweden and Norway. These differences may reflect surgeons' preferences, the "culture" for using alternative/new implants, and socioeconomic circumstances and may result in better outcome for patients treated in countries, in hospitals, and by surgeons with greater experience with the specific bearings.

Information bias

In registry-based cohort studies, information problems can occur due to misclassification of exposure or outcome. However, only if misclassification of exposure is dependent of misclassification of outcome (hence, when misclassification is differential), the results may be influenced by information bias. We may have misclassification of both exposure and outcome, but if these were independent of each other (non-differential misclassification), the RR estimates would go towards the null hypothesis.

In studies I-III, misclassification of bearings can occur, if data are missing or registered incorrectly. The lack of validation of data, e.g. bearings, implant design, femoral head size, and causes of revision, in the DHR and the NARA database may give rise to concerns related to the quality of these data. In study I and II, misclassification is obviously related to the unambiguous registration of a couple of bearings. However, the misclassification of causes of revision was unlikely to be related to the registration of the type of bearings for primary THAs due to the prospective registration of data in DHR and the NARA dataset. The resulting non-differential misclassification may produce bias towards the null hypothesis. Moreover, the two worst-case scenarios that all patients registered with missing bearings had either CoC or MoP (study I) and MoM or MoP (study II) have been calculated. In neither of the studies, the RR for revision of any cause was significantly changed in any of these scenarios. Although the proportion of missing data in study III was low, non-differential misclassification may be present, as there was no difference in missing subscale scores between bearing groups. Misclassification

Figure 3. Bias, chance, and confounding should be excluded before concluding that a causal association is likely. From Fletcher RH, Fletcher SW, Fletcher GS. Clinical Epidemiology: The Essentials. 5th edition. Lippincott Williams & Wilkins 2015



was minimised by using well validated questionnaires (HOOS, EQ-5D-3L, and UCLA activity score) and relevant questions about noises from the THA. Five to nine answer categories on a scale have been proposed to be ideal in most circumstances[169] and in 43 of 68 items, five steps were present in the response scale. Furthermore, no evident external interests were present. The resulting high response rate (85%) reduces the misclassification.

Recall bias may be a problem for retrospective items. Thus in study III, in question no. 7 about onset of noises from the THA, 50-52% of patients with noises from the THA indicated that the onset of noises was "unknown", which illustrates the probable recall bias.

Chance

Chance, or random error, is inherent in all observations. The statistical precision of an estimate is expressed as a confidence interval (CI) that represents the range of values that is likely to include the true value. Statistical precision increases with the statistical power of the study, which is dependent of the sample size. We have performed large cohort studies resulting in increased precision of the estimates, but sample size calculation has not been performed.

Confounding

Three conditions must be present for confounding to occur:

1. The confounding factor must be associated with both the exposure and the outcome.
2. The confounding factor must be distributed unequally among the groups being compared.
3. A confounder cannot be an intermediary step in the causal pathway from exposure to outcome.

In a study by Johnsen et al. from the DHR, males had a 20% higher RR of any revision compared to females, and patients younger than 60 years had increased RR of revision after 0.5-year follow-up. Diagnosis was found to be a time-dependent predictor, although no difference in RR of revision was found for any diagnosis after 0.5-year follow-up, whereas high CCI predicted higher RR of revision.[18] For sex, age, diagnosis, and comorbidity,the definition of confounding is fulfilled, and adjustments were made for these four patient-related confounders in order to eliminate the confounding effect on the results (Table 4). Adjustment for comorbidity has not been performed in study II, as the NARA database do not contain any information allowing for determination of the CCI score or other evaluation of the comorbidity. BMI and THA due to OA may be associated[170], and BMI >35 kg/m^2 has been found to be a predictor for revision due to PJI: RR=2.1 (95% CI: 1.1–4.3) for BMI 35–39.9 and RR=4.2 (95% CI: 1.8–9.7) for BMI ≥40.[171] In study III, mean BMI varied between the three bearing groups indicating that BMI is a confounder. But information on height and weight is not registered in the DHR or in the NARA database, which explains that BMI is not adjusted for in study I and II. This may result in an underestimated RR of revision for MoM compared to MoP THA, if patients having MoM THA have lower BMI as found in study III. In contrast, BMI have been adjusted for in study III. Among the surgery-related factors, the fixation technique has been shown to influence the risk of revision.[16,19] The confounding effect of fixation is eliminated in study I and II, because only cementless THAs have been included, whereas adjustments have been made in study III. Larger femoral head sizes increase the jump distance[85] and decrease risk of revision due to dislocation (RR=0.09 (95% CI: 0.05–0.17) for femoral head sizes >36 mm compared to head size of 28 mm)[29]. In study II, 92% of MoM THAs had femoral head sizes ≥38 mm and 97% of MoP THAs had head sizes <38 mm. Therefore, femoral head size was considered a proxy for the bearings and was not adjusted for. Duration of surgery, which may reflect the surgeon's skills and the complexity of the patient case, was found to be a predictor for revision due to PJI after primary THA (RR=2.0 (95% CI: 1.5–2.8) for duration of surgery longer than two hours compared to less than one hour)[172], and the confounding effect of duration of surgery was reduced by adjustments in study I, but duration of surgery was not registered in the NARA database and therefore not adjusted for. The confounding effect of year of surgery may be related to the introduction of new implants or bearings during recent years, e.g. BIOLOX Delta or incorporation of vitamin E in HXLPE, and surgeons may have been better to register data in the DHR resulting in higher completeness. Also the confounding effect of year of surgery was reduced by adjustments.

Table 4. Confounders adjusted for in study I-III

Confounders	Study I	Study II	Study III
Patient-related			
Sex	X	X	X
Age	X	X	X
Diagnosis	X	X	X
Comorbidity	X		X
BMI			X
Surgery-related			
Fixation			X
Femoral head size	X		X
Duration of surgery	X		
Year of surgery	X		X

Although adjusting for many patient- and treatment-related confounders, unmeasured confounding may be due to patient-related prognostic factors including medication (postoperative use of statin was associated with lower RR of revision)[23]; alcohol use (associated with non-traumatic osteonecrosis of the femoral head, and this diagnosis has a higher RR of revision)[173,174]; smoking habits (a strong association between smoking and risk of revision of MoM THA has been found)[175]; physical activity before and after primary surgery (some predictors of high activity at 5 years after surgery were younger age, male sex, and lower BMI)[166]; patients' expectations (the more preoperative expectations the patients had, the more likely they were to improve after surgery)[156]; anxiety (preoperative depressive symptoms predicted smaller changes in HOOS subscale scores and patients were less satisfied 12 months postoperatively)[158,176]; socioeconomic factors including education (high educational level was associated with higher health-related QoL and less pain)[159]. Treatment-related prognostic factors potentially leading to confounding include surgical approach (worse scores on HOOS and EQ-5D were reported after lateral approach than after posterior approach, and lateral approach was shown to increase the risk of revision du to aseptic loosening and decrease the risk of revision due to dislocation)[31,177,178]; type of polyethylene as both cross-linked and highly cross-linked polyethylene have been included (the use of highly cross-linked polyethylene reduces polyethylene wear substantially)[179]; antibiotic and thromboembolic prophylaxis[180-182]. The structure-related prognostic factors, which may result in confounding, include hospital volume (hospitals operating ≤50 procedures per year had an increased risk of revision after two-,

five-, 10-, and 15-year follow-up)[32]; set-up including fast-track[33]; surgeon's skills including learning-curve and positioning of components[183-185]; operation theatre (airflow, plastic adhesive draping, separate skin and deep knives)[186]. Furthermore, information from any radiological examinations including MRI and blood concentrations of chromium and cobalt may also be prognostic factors. Except from blood concentrations of chromium and cobalt and results of MRIs and ultrasound examinations, which have been included in the DHR since 2013 for MoM THA, none of these prognostic factors are registered in the used hip arthroplasty registries.

MAIN RESULTS

Study I

Risk of any revision

11,096 patients having cementless THA with CoC (n=1,773 (16%)) and MoP (n=9,323 (84%)) bearings were included. The median follow-up was 5.0 (interquartile range (IQR): 3.1-6.5) years for CoC and 3.9 (IQR: 2.0-5.9) years for MoP bearings (p<0.001 based on a Wilcoxon rank-sum test). The entire study population had 444 revisions (4.0%): 4.0% (71 of 1,773) for CoC THA and 4.0% (373 of 9,323) for MoP THA. At 8.7-year follow-up, the cumulative incidence for any revision was 5.4% (95% CI: 4.0-7.1) for CoC THA and 5.3% (95% CI: 4.7-5.9) for MoP THA. No significant difference in the RR of revision for any cause was found for CoC THA compared to MoP THA at two-, four-, six-, and 8.7-year follow-up (Table 5).

Table 5. Crude and adjusted[a] RR of revision for any cause, with 95% CIs, in THA with CoC and MoP bearings

	Patients in the beginning of the period (n)	Revisions performed within the period (%)	Crude RR (95% CI)	Adjusted[a] RR (95% CI)
At 2-year follow-up (0 to 2 years postoperatively)				
CoC	1,773	48 (2.7)	0.91 (0.67-1.24)	1.18 (0.65-2.13)
MoP	9,323	274 (2.9)	1 (ref.)	1 (ref.)
At 4-year follow-up (2 to 4 years postoperatively)				
CoC	1,519	15 (1.0)	0.95 (0.72-1.26)	1.12 (0.70-1.81)
MoP	7,065	62 (0.9)	1 (ref.)	1 (ref.)
At 6-year follow-up (4 to 6 years postoperatively)				
CoC	1,135	4 (0.4)	0.91 (0.68-1.21)	1.03 (0.60-1.77)
MoP	4,501	26 (0.6)	1 (ref.)	1 (ref.)
At 8.7-year follow-up (6 to 8.7 years postoperatively)				
CoC	543	4 (0.8)	1.02 (0.74-1.39)	1.33 (0.72-2.43)
MoP	2,230	11 (0.5)	1 (ref.)	1 (ref.)

[a]Adjustments were made for sex, age, diagnosis of primary THA, comorbidity, year of surgery, femoral head size, and duration of surgery

Causes of revision

Eight CoC THAs were revised due to component failure. The proportion of revision due to component failure was higher for CoC than for MoP bearings (p<0.001 based on a chi-square test) (Table 6). Of the eight patients registered with component failure as revision cause, six (0.34%) patients had ceramic fracture and two (0.11%) patients had impingement between the stem-neck and the rim of the liner. No statistically significant difference in the risk of revision due to aseptic loosening (adjusted RR 0.84, 95% CI: 0.21-3.4), dislocation (adjusted RR 1.2, 95% CI: 0.29-5.3), and all other revision causes (adjusted RR 1.1, 95% CI: 0.14-8.8) was found for CoC compared to MoP bearings.

Table 6. Main indications for THA revision registered in the DHR. For CoC and MoP bearings, the number and percentage (%) for the specific cause of revision is given

	CoC n=71 (%)	MoP n=373 (%)	p-value
Aseptic loosening	10 (0.6)	43 (0.5)	0.6
Osteolysis without loosening	0 (0.0)	3 (0.0)	0.5
Deep infection	6 (0.3)	61 (0.7)	0.1
Femoral bone fracture	9 (0.5)	56 (0.6)	0.6
Dislocation	22 (1.2)	156 (1.7)	0.2
Component failure	8 (0.5)	6 (0.1)	<0.001
Pain	9 (0.5)	26 (0.3)	0.1

Table 7. Crude and adjusted[a] RR of revision for any cause, with 95% CIs, in THA with MoM and MoP bearings

	Patients in the beginning of the year (n)	Revisions performed within the year (%)	Crude RR (95% CI)	Adjusted[a] RR (95% CI)
At 1-year follow-up (0 to 1 year postoperatively)				
MoM	11,567	198 (1.7)	0.81 (0.68-0.95)	0.83 (0.70-1.00)
MoP	21,111	448 (2.1)	1 (ref.)	1 (ref.)
At 2-year follow-up (1 to 2 years postoperatively)				
MoM	11,295	91 (0.8)	0.92 (0.80-1.06)	0.94 (0.81-1.09)
MoP	20,495	123 (0.6)	1 (ref.)	1 (ref.)
At 3-year follow-up (2 to 3 years postoperatively)				
MoM	9,640	66 (0.7)	1.01 (0.89-1.15)	1.02 (0.89-1.18)
MoP	15,653	72 (0.5)	1 (ref.)	1 (ref.)
At 4-year follow-up (3 to 4 years postoperatively)				
MoM	7,251	44 (0.6)	1.09 (0.96-1.23)	1.10 (0.96-1.26)
MoP	11,976	45 (0.4)	1 (ref.)	1 (ref.)
At 5-year follow-up (4 to 5 years postoperatively)				
MoM	4,638	49 (1.1)	1.32 (1.17-1.50)	1.37 (1.19-1.57)
MoP	9,137	22 (0.2)	1 (ref.)	1 (ref.)
At 6-year follow-up (5 to 6 years postoperatively)				
MoM	2,466	18 (0.7)	1.44 (1.27-1.63)	1.49 (1.30-1.71)
MoP	6,811	19 (0.3)	1 (ref.)	1 (ref.)

[a]Adjustments were made for sex, age, and diagnosis of primary THA

Study II

Risk of any revision

The study population included 32,678 patients having cementless stemmed THA with MoM (n=11,567 (35%)) and MoP (n=21,111 (65%)) THAs. The median follow-up was 3.6 (IQR: 2.4-4.8) years for

MoM and 3.4 (IQR: 2.0-5.8) years for MoP bearings (p<0.001 based on a Wilcoxon rank-sum test). 1,236 (3.8% of 32,678 patients) first time revisions following primary THA were registered during the study period: 4.1% (470 of 11,567 patients) for MoM and 3.6% (766 of 21,111 patients) for MoP bearings. The cumulative incidence of any revision was 7.0% (95% CI: 6.0-8.1) for MoM and 5.1% (95% CI: 4.7-5.6) for MoP at eight-year follow-up. The RR of any revision was statistically significantly increased for MoM after five- and six-year follow-up (Table 7).

Stratified analyses and causes of revision

The MoM cup/stem combinations of Articular Surface Replacement (ASR)/Summit, ASR/Corail, and "other" had statistically significantly higher RR of revision for any reason compared to MoP THAs (Table 8). The cementless MoM THAs had higher proportion of revisions due to aseptic loosening (p<0.001 based on a chi-square test) and "other" causes (p=0.03 based on a chi-square test). A lower frequency of revisions due to dislocation (p<0.001 based on a chi-square test) was found for MoM THA regardless of femoral head size compared to MoP THAs. At six-year follow-up, the RR of revision due to dislocation was lower (0.27, 95% CI: 0.19-0.39) for MoM than for MoP bearings, but the RR of revision due to aseptic loosening (5.5, 95% CI: 3.8-7.9) and all other revision causes (1.2, 95% CI: 1.0-1.5) was higher when

Table 8. Median follow-up for combination of acetabular and femoral components in MoM THA. Crude and adjusted[a] RR of revision for any cause at six-year follow-up with, 95% CIs, compared to MoP THA.

	n=32,678 (%)	Median follow-up (IQR)	Any revision (n)	Crude RR (95% CI)	Adjusted[a] RR (95% CI)
All MoP THAs	21,111 (65)	3.4 (2.0-5.8)	766	1 (ref.)	1 (ref.)
Recap/Bi-Metric	4,990 (15)	3.2 (2.2-4.4)	138	0.90 (0.76-1.06)	0.96 (0.80-1.15)
M^{2}a/Bi-Metric	2,407 (7)	4.8 (3.0-6.1)	95	1.16 (0.87-1.53)	1.25 (0.93-1.67)
Pinnacle/Corail	910 (3)	2.9 (2.0-3.9)	31	1.21 (0.89-1.65)	1.25 (0.90-1.74)
Conserve Plus/Profemur	418 (1)	3.2 (2.7-3.9)	18	1.53 (1.00-2.33)	1.47 (0.95-2.27)
ASR/Summit	401 (1)	3.9 (2.8-4.8)	56	6.35 (4.74-8.49)	7.27 (5.18-10.2)
Birmingham/Synergy	369 (1)	4.2 (3.4-5.1)	10	1.07 (0.51-2.24)	1.26 (0.56-2.84)
ASR/Corail	307 (1)	3.7 (2.7-4.5)	35	5.00 (3.54-7.07)	5.17 (3.53-7.56)
Others	1,765 (6)	3.7 (2.5-4.9)	87	1.77 (1.39-2.26)	1.75 (1.29-2.36)

[a]Adjustments were made for sex, age, and diagnosis of primary THA

Table 9. Association between experience of noise from THA with CoC, MoM, and MoP bearings and mean differences of PROM subscales with 95% Cis comparing MoM to MoP bearings.

		Noisy CoC (95% CI)	Noisy MoM (95% CI)	Noisy MoP (95% CI)	Silent MoP (95% CI)
HOOS Symptoms					
Mean difference	Crude	-12.9 (-14.9 to -10.8)	-11.4 (-15.2 to -7.65)	-16.8 (-20.6 to -13.0)	0 (ref.)
	Adjusted	-13.6 (-15.8 to -11.4)	-12.0 (-16.2 to -7.83)	-16.1 (-20.0 to -12.2)	0 (ref.)
HOOS Pain					
Mean difference	Crude	-7.33 (-9.21 to -5.45)	-5.11 (-8.31 to -1.90)	-14.0 (-18.1 to -9.97)	0 (ref.)
	Adjusted	-7.79 (-10.0 to -5.59)	-5.11 (-8.56 to -1.67)	-13.4 (-17.5 to -9.37)	0 (ref.)
HOOS ADL					
Mean difference	Crude	-7.29 (-9.63 to -4.95)	-5.52 (-9.19 to -1.84)	-14.2 (-18.3 to -10.1)	0 (ref.)
	Adjusted	-8.53 (-11.2 to -5.89)	-7.58 (-11.8 to -3.40)	-13.6 (-17.9 to -9.27)	0 (ref.)
HOOS Sport					
Mean difference	Crude	-9.45 (-13.0 to -5.94)	-7.16 (-11.8 to -2.47)	-21.2 (-26.9 to -15.5)	0 (ref.)
	Adjusted	-11.3 (-15.6 to -7.13)	-11.6 (-17.8 to -5.44)	-19.7 (-25.4 to -13.9)	0 (ref.)
HOOS QoL					
Mean difference	Crude	-12.1 (-15.0 to -9.24)	-12.3 (-16.8 to -7.76)	-20.1 (-24.6 to -15.5)	0 (ref.)
	Adjusted	-11.8 (-14.7 to -8.94)	-12.2 (-17.3 to -7.10)	-19.1 (-24.0 to -14.3)	0 (ref.)
EQ-5D index					
Mean difference	Crude	-0.059 (-0.085 to -0.032)	-0.067 (-0.100 to -0.034)	-0.113 (-0.144 to -0.081)	0 (ref.)
	Adjusted	-0.061 (-0.088 to -0.035)	-0.073 (-0.117 to -0.030)	-0.108 (-0.137 to -0.079)	0 (ref.)
EQ VAS					
Mean difference	Crude	-3.07 (-5.80 to –0.38)	-2.81 (-6.63 to 1.01)	-9.99 (-14.5 to -5.51)	0 (ref.)

	Adjusted	-4.56 (-7.20 to -1.92)	-6.29 (-9.72 to -2.87)	-9.44 (-13.5 to -5.38)	0 (ref.)
UCLA activity score					
Mean difference	Crude	0.08 (-0.20 to 0.35)	0.16 (-0.16 to 0.47)	-0.53 (-0.89 to -0.17)	0 (ref.)
	Adjusted	-0.12 (-0.38 to 0.15)	-0.44 (-0.88 to 0.00)	-0.56 (-0.88 to -0.25)	0 (ref.)

Study III

Comparison between bearing groups

The response rate was 85% (3,089 of 3,625). In the study population (n=3,089), 45% received CoC, 17% MoM, and 38% MoP THA. There was similar distribution of sex within the three bearing groups: 44-46% were females, and 54-56% were males (p=0.68 based on a chi-square test). Mean age difference was -1.6 (95% CI: -2.3 to -1.0) years for CoC and -1.9 (95% CI: -2.7 to -1.0) years for MoM THA compared to patients with MoP THA. Mean follow-up was 6.9 years for CoC and MoP THA and 5.1 years for MoM THA. For HOOS Symptoms, the adjusted mean score was significantly lower for the CoC group compared to the MoP group (adjusted mean difference (aMD) -2.3 (95% CI, -4.1 to -0.5)). No other statistical significant adjusted differences were found for the other HOOS subscales, EQ-5D index, EQ-5D VAS, or UCLA activity score when comparing the CoC and MoM groups to the MoP group.

Noises

27% of patients with CoC, 29% of patients with MoM, and 12% of patients with MoP bearings had experienced noises from the THA. Stratified analyses for the three types of bearings with and without noises showed significantly lower adjusted mean scores of all HOOS subscales, EQ-5D index, and EQ-5D VAS for patients experiencing noises from the CoC, MoM or MoP THA compared to patients having MoP THA without noises. For all subscales, the aMD was largest for MoP THA with noises. Only for the ULCA activity score, no difference was found for CoC and MoM THA with noises compared to MoP THA without noises (Table 9).

DISCUSSION

Discussion of bearings

When the surgeon together with the patients shall choose the couple of bearings, pros and cons may be weighted. MoP bearings were introduced in the Charnley era and are still the most commonly used bearings. Hence, the clinical experience with these bearings is very long, and MoP THA may be considered a safe treatment. The most prominent challenge with MoP bearings has been wear and generation of polyethylene wear particles possibly resulting in osteolysis and aseptic loosening of the implant, if wear rate is too high. However, the newer generations of polyethylene have shown promising durability as regards wear.[179,187] From CoC bearings, there are fewer wear particles generated and these are supposed to be more bioinert than polyethylene wear particles, which may reduce the problem with aseptic loosening. On the other hand, the risk with CoC bearings is fracture of the head or insert which is a serious complication. In study I, the prevalence of revision due to ceramic fracture was 0.34%, which is in accordance with a study by Traina et al., who reported a prevalence of ceramic fracture of 0.5%[188]. Ceramic fracture is a serious complication because there is a high risk of more than one revision following ceramic fracture.[189] There exist no consensus about the best strategy for revision surgery in patients with ceramic fracture[73] although it has been recommended to implant CoC or ceramic-on-polyethylene (CoP) bearings.[188] A high complication rate was seen by Lee et al. when using MoP bearings during revision for ceramic fracture.[190] Another drawback to take into account in relation to CoC bearings is noises. Noises have been described particularly from CoC bearings[152,191,192], but in study III it is revealed, that the prevalence of self-reported noises from both CoC and MoM THA is high (27-29%), whereas noises from MoP THA were prevalent in 12%. The reported high frequency of noises question, what the patient in fact report as a noise. But it seems to bother the patients reporting noises, as noisy THAs resulted in lower PROM scores compared to silent MoP THAs in study III, thus indicating that noises from the THA may be of clinical significance. CoC bearings are recommended by some authors to be used in young and active patients[167], and as found in study I, patients with CoC were younger than patients with MoP demonstrating that patients are selected to this bearing. This had, however, no influence on the activity level, which was similar for patients with CoC and MoP bearings after mean follow-up of 6.9 years (study III). Some surgeons may reserve CoC bearings to a highly selected group of very young patients suffering from childhood hip disorder. Hannouche et al. published a series of 105 CoC THAs in patients younger than 20 years at the time of primary THA, and the 10-year survival rate with aseptic loosening as endpoint was 90.3% (95% CI: 82.4%–98.9%).[168]

Since 2012 the use of MoM bearings has been abandoned in Denmark because of the concerns for the long-term prognosis. The higher risk of revision of MoM compared to MoP THA was confirmed in study II. However, PROM scores from patients having MoM THA were similar to PROM scores from patients having MoP THAs, which may be due to revision of the unsuccessful MoM THA (study III).

Another thing to account for when choosing the bearings for the patient is the cost-effectiveness, as CoC and MoM bearings in general are more expensive than MoP bearings. However, Pulikottil-Jacob et al. reported that the differences in quality-adjusted life-years between different bearings and fixation methods were extremely small. It was recommended that the choice of prosthesis should be determined by the rate of revision, local costs and the preferences of the surgeon and patient.[15]

MoP are still considered “standard” bearings by most surgeons.[193,194] CoC bearings may be recommended in younger patients, whereas the use of MoM bearings is not recommended, before population-based studies with long-term follow-up have shown similar survival as for CoC and MoP bearings. In addition, CoP bearings were found to have lower 13-year HR=0.80 (95% CI: 0.74-0.88) for any revision compared to MoP THA[16], but population-based studies are lacking.

Choice of outcome

This thesis has focused on the association between bearings and the risk of revision and PROs but in relation to THA, several outcomes may be of relevance: Radiological findings, metal-ion levels, second revision, economy, and mortality. When asking a scientific question, the chosen outcome shall be appropriate to give an answer. In study I and II, the outcome was firstly revision for any and secondly for specific causes. Studies on implant survival or annual reports from hip arthroplasty registries answer the question: “What is the longevity of the implant?”, but from these studies it is not possible to answer: “What is the QoL after

THA?" However, survival studies are very important to identify any early failure of a new implants, as the lost survival will never be regained with longer follow-up. This is illustrated in study II and other studies reporting lower survival rates for MoM THA[105,107]. If THA is only defined as a failure, when the implant is revised, the patient with a poor outcome and no awaiting revision surgery will not be captured, which results in an overestimation of the success of the THA.[11] Therefore, PROMs shall be used in combination with survival in order to give a more balanced and real measure of the success after THA.

In study III, the outcome was disease-specific and generic PROM scores and noises from the THA, as the aim was to examine if type of bearings was a prognostic factor for PROM scores and noises. Only a few studies have reported the influence of type of bearings on PROM scores[111,195], but one could argue that PROMs are too coarse to possibly answer, if there might be difference in the patients' perception of THA with different types of bearings.

Results compared to other studies

Ceramic-on-ceramic total hip arthroplasty

The main concerns of CoC are fracture of the components whereas reduced wear is an advantage. This may in the long-term run result in fewer revisions compared to MoP bearings. NJR is the registry with the largest number of CoC THA registered, and the cumulative incidence of revision of any cause was 4.22% (95% CI: 3.85-4.62) at 10-year follow-up. This was lower than in study I, where we found a cumulative incidence of revision of 5.4% (95% CI: 4.0–7.1) for CoC at 8.7-year follow-up. When comparing the HR for revision of any cause, the HR for CoC compared to MoP THA was 0.81 (95% CI: 0.70-0.94) after 13-year follow-up in the DHR[16], whereas the HR for CoC compared to metal-on-highly cross-linked polyethylene (MoHXLPE) in the Australian Orthopaedic Association National Joint Replacement Registry (AOA NJRR) was 1.08 (95% CI: 1.02-1.14) after 14-year follow-up[193]. The differences in HR from these two registries may be due to inclusion of both conventional and highly cross-linked polyethylene in the analyses from the DHR. These findings are in contrast to those in study I, where no difference in RR of revision was found for CoC compared to MoP THA. This might be due to shorter follow-up and better adjustments for confounding in our study. In another study based on data from six national and regional registries, cementless CoC THA with femoral head sizes >28 mm had similar risk of revision as MoHXLPE THA after nine-year follow-up, but CoC THA with femoral head ≤28 mm had increased risk of revision (HR=1.36 (95% CI: 1.09-1.68)).[106] This was in contrast to study I, where no difference in RR of any revision was found for any femoral head size ≤28 mm or >28 mm. Furthermore, a meta-analysis including 18 randomised clinical trials having a minimum two-year follow-up and an average age younger than 65 years in the included studies found no difference in risk ratio for revision of CoC THA when compared to MoHXLPE.[196] Hence, these results are in accordance with study I.

The risk of revision due to dislocation later than one year after index surgery after median follow-up of seven (range: 1-13) years was examined in a study from the New Zealand Joint Registry including 8,177 CoC THAs. In patients younger than 65 years having 28 mm femoral heads, more revisions for late dislocation was found for CoC THAs compared to MoM THAs (p=0.014), whereas no other statistically significant differences were found for CoC THAs when stratified by age and head size.[197] In study I, no difference in RR of revision due to dislocation was found for CoC compared to MoP THA, but no stratification for femoral head size was made. Furthermore, other differences in causes of revision were examined in study I, and we found a higher frequency of revision due to component failure for CoC than for MoP bearings (p<0.001).

The weakness of the current knowledge of CoC bearings is the relatively short follow-up. A difference in revision rate between MoP and CoC may first become evident after 15 to 20 years due to the very low wear in the new generations of polyethylene. Thus, patients who may benefit from CoC THA may be relatively young with a life expectancy longer than 15 to 20 years.

Metal-on-metal total hip arthroplasty

MoM bearings in THA were reintroduced as alternative bearings to MoP. Although one advantage is the possibility to use large head sizes and the following reduced the risk of dislocation, there major concern is related to increased risk of revision. In the NJR, the cumulative incidence of revision was 12.7% (12.3-13.2) at seven-year and 20.2% (95% CI: 19.2-21.2) at 10-year follow-up.[194] These cumulative incidences are higher than that of 7.0% (95% CI: 6.0–8.1) for MoM at eight years found in study II, and these differences may be caused by the use of different component designs. In the AOA NJRR, the HR of any revision was 1.36 (95% CI: 1.21-1.54) after 14 years.[193] This is in accordance with results in study II where the RR of revision was 1.49 (95% CI: 1.30–1.71), although the follow-up was only six years. Furnes et al. published a study with seven-year follow-up including data from six national and regional registries, and a significantly increased HR=2.15 (95% CI: 1.63-2.83) was found for MoM THA with femoral head size >36 mm compared to MoHXLPE in patients aged from 45-64 years.[28] Furnes et al. had excluded patients with the ASR acetabular component. When patients having the ASR acetabular component were excluded in study II, no difference in RR for any revision was found for MoM compared to MoP THA at six-year follow-up. In study II, both cross-linked and highly cross-linked polyethylene was included. As revision rates for metal-on-conventional polyethylene are higher than that for MoHXLPE[193], the revision rate for MoP THA in study II may be higher than in the study by Furnes et al., who only included MoHXLPE and therefore, the resulting RR of revision for MoM THA in study II may be smaller than in the study by Furnes et al.

The causes of revision were examined in study II, and MoM had a higher RR of revision due to aseptic loosening than MoP THA. This confirmed the findings in the study based on data from the NJR by Smith et al.[107] Lombardi et al. published a study from a single institution including 1,440 MoM THAs with mean follow-up of seven years. The 12-year survival rate was 87% (95% CI: 84-90), and the two most common indications for revision were ARMD (48%; 47 of 108 hips revised) and aseptic loosening or failure of ingrowth (31%; 34 of 108).[198] According to the NJR, the highest patient-time incidence-rates for specific causes of revision was found for MoM THA revised for adverse soft tissue reaction to particulate debris.[194] However, in the NARA database it was not possible to register the cause of revision as due to adverse soft tissue reaction to particulate debris or metal-related pathology.

The discrepancies between registries may reflect national variations in the use of or reluctance to use MoM bearings, indications for primary surgery and revisions, different implant designs, and selection of patients.

Patient-reported outcomes

PROs may be influenced by a number of factors. Preoperative selection of patients for specific bearings may be, among other

factors, related to the activity level. Differences in PROs may therefore possibly reflect this selection. In a study from the NJR including 4,596 PROMs-linked primary THAs with a mean follow-up of seven months, there was no difference in change (postoperative compared to preoperative) for EQ-5D index score between patients having MoP, CoP, or CoC bearings, but there were statistically significant differences in median postoperative EQ-5D index scores with CoC having the highest and CoP THA the lowest score.[195] However, the differences in postoperative EQ-5D index scores between bearings are small (maximum 0.052) and may be without clinical significance, as MCII in a Danish registry setting was determined to be 0.31 one year after primary THA[134]. Similar findings after longer follow-up are reported in study III, although patients having MoM and not CoP were included. In a series including 208 consecutive, large-diameter CoC THAs from a single institution, there were 143 silent hips (69%), 22 (11%) with noises other than squeaking, 17 (8%) with unreproducible squeaking and 26 (13%) with reproducible squeaking. The HOOS subscales and UCLA activity scores were compared for patients with silent and noisy THAs, and no statistically significant difference was found for the UCLA activity score, HOOS Pain, HOOS ADL, and HOOS QoL. However, patients with noisy THA had lower scores for HOOS Symptoms and HOOS Sport.[112] In study III, similar prevalence of noises from CoC THA was found but except from the UCLA activity score, significant lower scores for all subscales were found when comparing noisy CoC to silent MoP THAs.

CONCLUSION

The main conclusions of the thesis are:

Study I: At 8.7 years of follow-up, CoC THA had a 33% higher risk of revision for any reason than MoP THA, but this was not statistically significant. CoC THA had a significantly higher incidence of revision due to component failure. The incidences of ceramic head and liner fracture were 0.28% and 0.17%, respectively.

Study II: A higher RR of revision for any reason at six-year follow-up was found for MoM THA than for MoP THA, but after exclusion of patients with the ASR acetabular component, the risk of revision was similar between the two groups of bearings. At six-year follow-up, there was a much higher risk of revision with prosthetic design combinations of ASR/Summit and ASR/Corail than for MoP THA, whereas the risk of revision was similar for the Recap/Bi-Metric combination and for MoP THA.

Study III: No significant difference in mean scores in the five HOOS subscales, EQ-5D index, EQ VAS, or UCLA activity score was found between patients with CoC, MoM, and MoP THA after mean follow-up of 6.9, 5.1, and 6.9 years, respectively. There were significantly lower mean subscale scores for all types of bearings and subscales when comparing noisy THA to silent MoP THA, except for patients having noisy CoC and MoM THA who had similar mean UCLA activity scores as patients with silent MoP THA.

FUTURE PERSPECTIVES

The DHR has a very high coverage and completeness and contains well validated data on diagnosis for primary THA.[16,117] However, a number of prognostic factors for the outcome of THA have not been validated, thus further studies may be performed in order to validate data on, for instance, implant design, types of bearings, and coating with/without hydroxyapatite. Since PJI is the only revision cause that has been validated[118], future studies may be conducted to validate other revision causes.

CoC and MoM bearings were introduced in order to reduce problems related to aseptic loosening of MoP THA. As aseptic loosening most commonly occurs with longer follow-up, there is a continuing need for large population-based studies comparing survival of THA with different types of bearings - including CoP. There are several prognostic factors for outcome in relation to bearings that are of interest and deserve further investigation: As CoC THA are recommended for young and active patients by some authors[167], the association between CoC bearings and activity level before and after surgery should be examined in more detail in a cohort study. For MoM THA, the association of results of chromium and cobalt ion measurements, ultrasound examinations, and MRIs may now be assessed in nationwide population-based cohort studies, as these variables are contained in the DHR since 2013.

When younger patients are treated with THA, the risk of more than one revision is increased. Ceramic fracture is a specific revision cause only related to the use of CoC bearings and in study II, revision due to aseptic loosening was more frequently for MoM

Table 10. Abbrevaitions

ALVAL	Aseptic lymphocytic vasculitis-associated lesions
AOA NJRR	Australian Orthopaedic Association National Joint Replacement Registry
ARMD	Adverse reaction to metal debris
ASR	Articular Surface Replacement
ASTM	American Society for Testing and Materials
BMI	Body mass index
CCI	Charlson comorbidity index
CI	Confidence interval
CoC	Ceramic-on-ceramic
CoP	Ceramic-on-polyethylene
CRS	Civil Registration System
CT	Computed tomography
DHR	Danish Hip Arthroplasty Registry
DNPR	Danish National Patient Registry
FDA	Food and Drug Administration
HHS	Harris Hip Score
HOOS	Hip disability and osteoarthritis outcome score
HR	Hazard ratio
HXLPE	Highly cross-linked polyethylene
IQR	Inter-quartile range
LDH	Large-diameter-head
MCII	Minimal clinically important improvement
MeSH	Medical subject heading
MoHXLPE	Metal-on-highly cross-linked polyethylene
MoM	Metal-on-metal
MoP	Metal-on-polyethylene
MRI	Magnetic resonance imaging
NARA	Nordic Arthroplasty Register Association
NJR	National Joint Registry for England, Wales, Northern Ireland and Isle of Man
OA	Osteoarthritis
PASS	Patient-acceptable symptom state
PJI	Prosthetic joint infection
PPV	Positive predictive value
PRO	Patient-reported outcome
PROM	Patient-reported outcome
QoL	Quality of life

RCT	Randomized clinical trial
ROM	Range of motion
RR	Relative risk
SHAR	Swedish Hip Arthroplasty Register
THA	Total hip arthroplasty
UCLA	University of California, Los Angeles
UHMWPE	Ultrahigh-molecular-weight polyethylene
VAS	Visual analogue scale
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index
Y-TZP	Yttria stabalized tetragonal zirconia polycrystals
ZTA	Zirconia-toughened alumina

bearings. Therefore, the types of bearings may be a prognostic factor also for the second revision, which may call for further investigation.

Although the treatment with THA is successful, not all patients will have their expectations fulfilled or be satisfied after THA. Therefore, patient selection for surgery is very important and may be influenced by many factors, which together result in a patient's risk profile in relation to the outcome after THA. PROMs may be very useful to identify this risk profile, and PROMs should be incorporated more systematically in the DHR.

SUMMARY

Total hip arthroplasty (THA) is a common and successful treatment of patients suffering from severe osteoarthritis that significantly reduces pain and improves hip function and quality of life. Traditionally, the outcome of THA has been evaluated by orthopaedic surgeons and assessed in morbidity and mortality rates, and implant survival. As patients and surgeons may assess outcome after THA differently, patient-reported outcomes (PROs) have gained much more interest and are today recognized as very important tools for evaluating the outcome and satisfaction after THA. One of the prognostic factors for the outcome of THA is the type of bearings. This PhD thesis focuses on the influence of different types of bearings on implant survival, revision causes, PROs, and noises from THA.

The aims of the thesis were:

Study I: To examine the revision risk and to investigate the causes of revision of cementless ceramic-on-ceramic (CoC) THAs comparing them to those of "standard" metal-on-polyethylene (MoP) THAs.

Study II: To compare the six-year revision risk for metal-on-metal (MoM) with that for MoP bearings in cementless stemmed THA, and further to study the revision risk for different designs of stemmed MoM THAs and the causes of revision.

Study III: To examine the association between CoC, MoM, and MoP bearings and both generic and disease-specific PROMs, and furthermore to examine the incidence and types of noises from the three types of bearings and identify the effect of noises on PROM scores.

In study I and III, we used data from the Danish Hip Arthroplasty Registry combined with data from the Civil Registration System and the Danish National Patient Registry. In study II, data from the Nordic Arthroplasty Register Association, containing data from hip arthroplasty registries in Denmark, Norway, Sweden, and Finland, was used.

In study I, 11,096 patients operated from 2002 through 2009 with cementless THA were included. Of these, 16% had CoC THA and 84% had MoP THA. At 8.7-year follow-up, no difference in RR of revision for any cause was found for CoC compared to MoP THA. One cause of revision related only to CoC THA is ceramic fracture. Medical records were reviewed for patients who had revision surgery due to component failure, and six patients (0,34%) had been revised due to ceramic fracture. No other difference in prevalence of causes of revision was found when comparing CoC to MoP THA.

Study II included 32,678 patients who were operated from 2002 through 2010 with cementless stemmed THA with either MoM bearings (11,567 patients, 35%) or MoP bearings (21,111 patients, 65%). At six-year follow-up, the RR of revision for any cause was significantly higher for MoM compared to MoP THA. When comparing different combinations of cup/stem with MoM to MoP bearings, there was an increased RR of revision for any cause for the ASR/Summit, ASR/Corail, and "other" combinations. There was a higher prevalence of revision due to aseptic loosening for MoM compared to MoP THA. In contrast, the prevalence of revision due to dislocation was lower for MoM THA.

In study III, a set of questionnaires including HOOS, EQ-5D, UCLA activity score, and a questionnaire about noises from the THA was send to patients having THA with CoC, MoM, or MoP bearings. The response rate was 85% and among the 3,089 patients responding, 45% received CoC, 17% MoM, and 38% MoP THA. No differences in mean subscale scores were found for CoC and MoM compared to MoP THA, except for CoC THA that had a lower mean HOOS Symptoms score than MoP THA. 27% of patients with CoC, 29% of patients with MoM, and 12% of patients with MoP bearings had experienced noises from the THA. For the three types of bearings, PROM scores from patients with noisy THA were significantly lower when compared to silent MoP THA, except for noisy CoC and MoM THA that had the same mean UCLA activity score as silent MoP THA.

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