The press-fit acetabular component: fixation and bearing surfaces

Justin van Loon

Propositions belonging to this thesis

The press-fit acetabular component: fixation and bearing surfaces

1. Dynamic trial fitting can help to achieve sufficient press-fit for the definitive implant, without affecting its primary stability. *(This thesis)*

2. Dynamic trial fitting holds the potential to replace traditional trial cups by more precise assessment of the reamed acetabulum and could thereby prevent both early and long-term revision in press-fit THA. *(This thesis)*

3. CoHXLPE outstands CoPE on the outcomes regarding wear rates and conventional PE should therefore be avoided whenever possible. *(This thesis)*

4. The high early aseptic loosening rate of the seleXys TH+ cup could be partially attributed to the influence of CoC on osseointegration during the transition of primary to definitive stability. *(This thesis)*

5. Press-fit THAs with CoC bearing has a higher two-years cup revision rate compared to CoPE, with cup loosening as the only significant reason for revision and seen more often in CoC and mostly aseptic. *(This thesis)*

6. CoC could be a potential key factor for the multifactorial problem of early migration and potential resulting aseptic loosening in press-fit total hip arthroplasty. *(This thesis)*

7. CoC could be considered more often in younger patients due to the wear advantages, but should be restricted to cases in which no impaired bone quality is expected or in which gaining primary stability intraoperatively is not troublesome. *(This thesis)*

8. "Opportunities don't happen, you create them." — *Chris Grosser*

9. "Als wielrennen mij iets geleerd heeft, is het dat als je iets bereikt zonder moeite, het niets waard is." — *Greg Lemond*

10. "Kujbeheriepe?" — *Een Zeeuw (na het lezen van dit proefschrift)*

14. "Je kunt beter ten onder gaan met je eigen visie, dan met de visie van een ander." — *Johan Cruijff*

Justin van Loon
Amsterdam, July 6th 2023

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van Loon, J.
The press-fit acetabular component: fixation and bearing surfaces
PhD dissertation, University of Amsterdam, The Netherlands

This research was initiated by Xpert Clinics Orthopedie.

The research in this thesis was embedded in Amsterdam Movement Sciences Research Institute, at the department of Orthopaedic Surgery, Amsterdam UMC, University of Amsterdam, the Netherlands

ISBN: 978-94-93315-51-8
Cover: Laurent Muller, www.laurentmuller.com
Lay-out and printed by: Proefschrift All In One (AIO)

Printing of this thesis was financially supported by: Xpert Clinics Orthopedie, Medichanical Engineering ApS, Amsterdam UMC Department of Orthopaedic Surgery, Leuk Orthopedie B.V., George In Der Maur, Bauerfeind Benelux B.V., BAP Medical, Tromp Medical B.V., Implantcast GmbH, Noord Negentig accountants en belastingadviseurs, ABN AMRO, Mathys Orthopaedics a company of Enovis, Bauerfeind Benelux B.V., Chipsoft B.V., Nederlandse Orthopaedische Vereniging, Anna Fonds.

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ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Universiteit van Amsterdam
op gezag van de Rector Magnificus
prof. dr. ir. P.P.C.C. Verbeek
ten overstaan van een door het College voor Promoties ingestelde commissie,
in het openbaar te verdedigen in de Agnietenkapel
op donderdag 6 juli 2023, te 13:00uur

door Justin van Loon
geboren te Vlissingen

Promotiecommissie

Promotor:	Prof. dr. G.M.M.J. Kerkhoffs	AMC-UvA
Copromotores:	Dr. D. Haverkamp	Xpert Clinics Orthopedie
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Chapter 1

General introduction

GENERAL INTRODUCTION

Osteoarthritis (OA) is a serious problem and the prevalence is increasing worldwide. This condition affects both the individual, by pain, disability, potential costs and loss of income, as well as society as burden on the health-care systems and associated socioeconomic costs. [1] New treatment modalities, like immunotherapy to induce regeneration or decrease the process of degeneration of the articular cartilage, are widely investigated but no part of routine treatment. For early OA the focus is on joint saving and conservative therapy. Nevertheless, after failed conservative treatment and for end-stage hip OA a total hip arthroplasty (THA) is still considered the most effective treatment. [2] Due to rising life expectancy worldwide from 66.8 years in 2000 to 73.4 years in 2019 and increasing prevalence of obesity which tripled between 1975 and 2016 to 13% worldwide in 2016, OA is becoming more prevalent and THAs are performed more often. [3-5] In the Netherlands, 31,514 THAs were implanted in 2021, which reflects a growth of 34.4% compared to 2010. [6] An additional explanation for the increase in THA implantations in the Netherlands is the rising number of THAs performed in younger patients compared to the past. All these reasons ask for a prolonged longevity of the THA, which is an ongoing important topic in orthopedic research and is therefore the focus of this thesis.

Osteoarthritis of the hip

Prevalence, etiology, and risk factors of hip osteoarthritis

In the Netherlands, approximately 175,300 men and 301,600 women were diagnosed with hip OA by their general practitioner in 2020. [7] The definition of OA is described as: 'a disorder involving movable joints characterized by cell stress and extracellular matrix degradation initiated by micro- and macro-injury that activates maladaptive repair responses including pro-inflammatory pathways of innate immunity'. [8] Joint degeneration can arise from underlying conditions such as (avascular) osteonecrosis, prior trauma to the hip joint, prior septic arthritis, Paget disease or inflammatory diseases such as rheumatoid arthritis. Moreover, anatomical disorders, like developmental dysplasia of the hip (DDH), slipped capital femoral epiphysis (SCFE) or femoroacetabular impingement (FAI) are predisposing factors for OA. When any of these problems are present in hip OA, the condition is defined as secondary OA. In case no underlying disease or anatomical disorder is identified, the process is called idiopathic or primary OA. Accordingly, it is possible to define risk factors for OA instead of pathophysiological processes, which influence both primary and secondary OA. [9-11] Risk factors at the joint level, which may be considered as an etiological basis for the development of hip OA, are conditions affecting joint morphology, shape and muscular function (e.g. DDH, SCFE, FAI); (avascular) osteonecrosis; joint injury; labral tears;

and muscular dysfunction. [9-11] At an individual level, identified risk factors which contribute to the development of hip OA are increasing age, female gender, increased BMI, genetic predisposition, ethnicity (higher prevalence in African-American compared to Caucasian, and even lower in Asian), diet (e.g. antioxidant vitamins like C and D to prevent progression of OA), medicine use (e.g. corticosteroids), metabolic diseases and high-impact physical activity (in daily life, occupation, and sports). [9-11]

Clinical symptoms and physical examination

Despite the multifactorial cause of hip OA, patients often present with the same symptoms of progressive joint pain (typically located in the groin), limited and painful joint motion (especially internal rotation), morning stiffness, pain at rest, stiffness after resting, pain at night and restricted mobility. [12] Hip OA is usually diagnosed based on the aforementioned clinical symptoms. [13, 14] However, in the non-OA hip groin pain and limited motion can be caused by numerous underlying conditions, well described in '*the Layer Concept*', which is a systematic approach for determining which structures of the hip are the pathological source, which generate the pain and how to implement this concept in treatment. [15] Reaching from layer 1 at the osteochondral level, layer 2 the inert tissue layer including the labrum and capsule, layer 3 the contractile layer, containing the muscles surrounding the hip and layer 4 the neuromechanical layer, comprising neural and mechanical causes outside the hip joint. [15]

Radiological examination

Severe OA on radiographs correlates strongly to hip pain if present. Notably, hip pain is not always present in radiographic OA cases and radiographic severity of OA does not always correlate with cases presenting with severe OA pain. [16, 17] This emphasizes the need to combine clinical presentation and radiographic assessment in the diagnostic process. Radiographic assessment of the hip is graded by the Kellgren and Lawrence scale. [18] This classification is based on the main characteristics of OA present at radiographs, which are cartilage loss resulting in narrowing of the joint space, osteophytes, subchondral sclerosis, cyst formation and deformity of bone ends. [19]

Conservative treatment

Since there is no cure for OA and disease-modifying treatment of hip OA is still only used in the research setting, conservative treatment is focused on reduction of complaints. [20-22] Interventions in daily practice are focused on physical overload reduction by modification of daily activities, weight reduction and muscle strengthening therapy under supervision of a physical therapist. In addition, pain reduction can be achieved by using pain medication like paracetamol, non-steroid anti-inflammatory drugs (NSAID) or in more severe cases opioids. The last and maybe most important factor of

conservative treatment is psychological education for the patients about the diagnosis of OA, to allow insight and expectation management in order to better cope with hip OA in daily life. Conservative interventions can be useful to postpone surgical intervention. [23] Intra-articular injection under fluoroscopic guidance can be used both for diagnostic and therapeutic purposes. Diagnostic by the use of local anesthesia to confirm an intra-articular origin of hip pain and therapeutic with the aim to (temporarily) relieve pain by the use of corticosteroids, hyaluronic acid, platelet rich plasma or other agents. [24, 25] If the conservative treatment for hip OA is insufficient, a THA is considered the next step in the management of OA.

Total hip arthroplasty

History of THA

The current concept of THA is a result of development of this procedure over time during the 19th and 20th century. The first attempts to replace femoral heads by ivory during the late 19th century, were performed by professor Themistocles Glück. [26] During this same time period experiments were performed with interpositional arthroplasty using fascia lata, skin, pig bladders and submucosa to mobilize ankylosed joints. [27] The development went further, and a mold arthroplasty was invented by Marius Smith-Petersen in 1925 to fit over the OA affected head. Although this material shattered due to weight-bearing forces, Smith-Petersen experimented with other materials for mold arthroplasty like Vitallium, together with Philip Wiles. [28] This development resulted in the use of stainless steel to create the first 'hip replacement' like surgery in 1938, with an acetabular stainless steel implant and steel femoral head attached to a lateral femoral plate (**Figure 1**). [29]

George McKee was the first to use a metal-on-metal prosthesis in 1953, using a cemented hemi-arthroplasty together with a cup of cobalt-chrome inserted in the acetabulum. [27] In 1957 the Swiss professor Maurice Muller developed a banana-shaped stem and 32mm head made of cobalt-chromium in combination with a plastic acetabular cup. [30] Further development of this idea, was also performed by Sir John Charnley. [27] This low friction arthroplasty design was based on the use of three parts: a polyethylene (PE) acetabular implant, a femoral stem made of metal and acrylic bone cement to fix the components (**Figure 2**). [31]

Professor Bernhard Weber further developed the banana-shaped stem to the nowadays widely used concept of the anatomical stem. The shape of this stem is designed to follow the shape of the intramedullary canal. [32] In 1972 ceramic heads and inlays made of alumina oxide were developed and introduced by Heinz Mittelmeier as a different and more wear resistant bearing. The current concept of modern THA is still based on the

same principles of the low friction arthroplasty design, using a separate stem, cup, inlay and head. Nevertheless, a lot of improvement is seen on tribology and fixation methods of the implants ever since, like the introduction of press-fit fixation. Substantial progress is also made in surgical techniques and improvement of surgical instruments. However, innovation is still needed to continue the search for the perfect implant, bearing and surgical technique for THA.

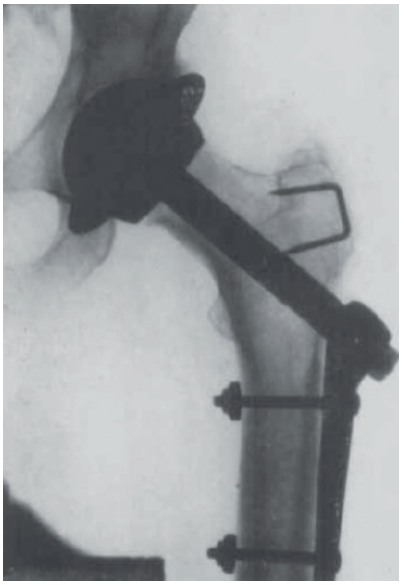

Figure 1. The first hip replacement like surgery, performed by Philip Wiles: 'A ball-and-cup arthroplasty after 1 year. The stem is sliding outwards showing that the neck is being absorbed. (A posterolateral approach was used with a staple to re-attach the smaller gluteal muscles.)' (*Reprinted from The British Journal of Surgery, vol 45 (193), P. Wiles, The Surgery of the Osteo-arthritic Hip, 488-497, Copyright (1958), with permission from Wiley*) [29]

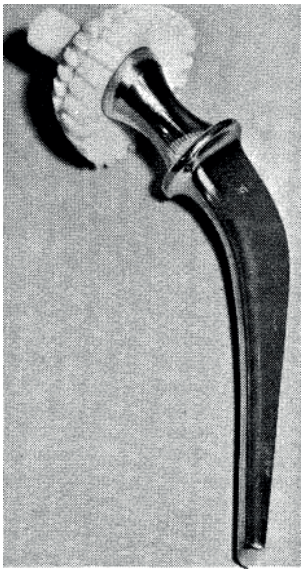

Figure 2. Example of the low-friction arthroplasty design, as performed by Sir John Charnley: 'Final pattern of low-friction arthroplasty. Note thick socket with deep external serrations and small femoral-head prosthesis' *(Reprinted from The Lancet, vol. 277 (7187), John Charnley, ARTHROPLASTY OF THE HIP A New Operation, 1129-1132, Copyright (1961), with permission from Elsevier)* [31]

Indications for THA

As registered in the Dutch Arthroplasty Register (LROI) in 2021, 86.1% of the THAs were performed for primary OA. [33] Other indications include femoral neck fracture (FNF) (5.8%), primary treatment for osteonecrosis (2.6%), late post-traumatic (2.2%), primary treatment for DDH (1.3%), Post-Perthes disease (0.2%), tumor of the hip joint (0.4%) and other remaining indications (1%).

Operation technique

Several surgical approaches for total hip arthroplasty are described, whereas direct anterior, direct lateral and posterior approaches remain the most used. [34] Each surgical approach has its specific advantages and disadvantages and could thereby affect both clinical outcome and incidence of complication rates. [35-37] Therefore, the choice of surgical approach is determined by the patient's medical history and anatomy, and the surgeon's experience and preference. Depending on the approach, the patient is placed in supine or lateral decubitus position. Standard antibiotics prophylaxis is given prior to incision, according to the indicator of the Health and Youth Care Inspectorate of the Ministry of Health, Welfare and Sports and Dutch Orthopedic Association 'Total Hip Prosthesis' guidelines. [38, 39] After approaching the hip joint, a capsulectomy or capsulotomy is performed, the femoral head is luxated and a femoral neck osteotomy is performed. The exact sequence of these three steps depends on the approach and preference of the orthopaedic surgeon. Next, the acetabular exposure is sufficient to perform preparation of the acetabulum by reaming. Testing of the aimed size of the cup and the obtained press-fit in case of press-fit fixation is traditionally performed by use of trial cups. As the next step, a cup is implanted in the reamed acetabular cavity and in case of a modular cup (instead of a monoblock), the liner is inserted. Positioning of the cup is usually aimed at 15 (± 10) degrees of anteversion and 40 (± 10 degrees) of inclination. Malposition of the cup can lead to dislocation, increased wear, poor biomechanics, and squeaking (in ceramic-on-ceramic (CoC) bearing). [40, 41] Reaming of the femoral shaft is now performed for placement of the femur component. Before placement of the definitive femur component, testing of stability of the hip joint and the positioning of the implant is performed. Femoral offset and leg length are aimed to be identical to the other side. Afterwards, the definitive femoral implant is inserted, a femoral head is placed on the femoral component, in case a modular stem in used, and the hip joint is relocated and again tested for stability and positioning. At last, layered closure of the hip capsule (if not resected), muscles, fascia, subcutis and skin is performed depending on the approach. The following postoperative rehabilitation protocol depends on both the surgeon's preference and the approach related restrictions, but usually consists of immediate full weightbearing with crutches for (two to) six weeks.

Fixation

Fixation of both components can be obtained by either a press-fit principle or using bone cement. Hybrid THA is recognized as cementless press-fit acetabular component fixation with a cemented femoral stem, whereas reverse hybrid THA is performed using a cemented cup and cementless press-fit femoral component. Bone cement is based on polymethylmethacrylate (PMMA) and functions a grout, which results in a mechanical interlocking fit between the prosthesis and the cancellous bone. [42, 43] Uncemented fixation is based on the press-fit principle, in which the definitive prosthesis is larger than the last used reamer and trial implant. Hereby the definitive component is placed in a slightly underreamed bone cavity, generating a circumferential compressive situation. The implant needs to be initially stable to prevent micromotion which is the most important factor for sufficient subsequent osseointegration and thereby survival of the implant on long-term. [44-47] Trial cups used to choose the size of the definitive implant, never mimic the size of the definitive implant. This makes achieving sufficient primary stability of the definitive implant challenging, by making it a subjective feeling obtained by experience. Therefore, in revision cases or in cases performed by less experienced surgeons or residents, achieving sufficient primary stability might be even harder. If primary cup stability is insufficient, additional reaming might be necessary or screws can be used, or a decision can be made to switch to a cemented THA. [48] Following transition to secondary or so-called definitive stability of the implant in press-fit fixation, is achieved by osseointegration, which is achieved fully in two to three years postoperatively. [49-51] Uncemented prosthesis designs promote osseointegration by several techniques. At first, the biocompatibility of the prosthesis can be increased by use of porous titanium material which promotes tridimensional in-growth of bone. [52-54] Second, the microscopic structure of the implant can be blasted with grit and sprayed with a special coating, for example hydroxyapatite, to improve on-growth of bone on the prosthesis. [55, 56] At last, the macroscopic texture can be modified by use of rims, tetrahedrons, spikes or other designs to increase the contact surface and hereby improve the primary stability. Although a better short-term clinical outcome, particularly improved pain score, is seen in cemented THA, no difference in mortality or postoperative complication rates was observed. [57] Therefore, more long-term and clinical outcome data is needed to confirm the best choice of fixation. As a result, the choice of fixation method is usually based on the indication, the surgeon's preference, the patient and its bone quality. Worldwide, national joint registries show an increase in popularity of uncemented THA and hereby the majority of the THAs is placed uncemented. [33, 58-61]

Bearing choice

The use of metal-on-polyethylene (MoPE) bearing, as introduced by Sir John Charnley and professor Muller, showed promising results, but the main long-term problem was wear of PE. [62] The role of PE wear and resulting loss of bone stock was first described by Revell et al. and Mirra et al. in respectively 1978 and 1982. [63, 64] PE debris particles deposit in the tissue surrounding the prosthesis. The resulting biological local reaction and accompanying immune response are characterized by a foreign body reaction with granulomatous chronic inflammation, which initiates the process of periprosthetic osteolysis and can result eventually in loosening of the implant. [65-67] Although this reaction is still an important research topic, it is assumed that several molecular pathways induce osteoclastogenesis and stimulate osteoclast differentiation, activation, and survival. [65] The cytokines involved in this process, synergize the osteoclastic reaction, but maintain to mediate proinflammatory response on themselves as well. [65] Research focused on medical interventions preventing osteolysis is increasing, but no treatment against osteolysis has been found so far. The best way to overcome osteolysis is prevention. Since wear rates are a valuable predictor for osteolysis in press-fit acetabular components, choosing a bearing that does not show wear-induced osteolysis or a bearing with lower wear rates of PE are worthwhile. [68] Radiostereometric analysis (RSA) or radiostereometry is a radiological technique in which biplanar X-rays are simultaneously taken through a calibration cage, during both baseline and follow-up to measure the three-dimensional position of orthopedic implants, compared to embedded markers in the periprosthetic bone, implanted during surgery. This is an accurate technique for the measurement of wear, migration and (micro)motion of implants over time.

The first option to reduce PE wear is improvement of the PE using gamma-irradiation and heating, forming free-radicals that create cross-links in the PE, forming so-called cross-linked PE (XLPE). [69]. By annealing or remelting the PE, free radicals that did not react were eliminated, realizing the better wear resistant highly cross-linked PE (HXLPE). [70, 71] This inlay is mostly used in combination with a ceramic or metal head, or less often with an Oxinium (ceramicized metal) head. Nevertheless, these different materials show a difference in wear of HXLPE as well. Literature is inconclusive about the use of either a ceramic or metal head, but short-term RSA showed no wear difference and at long-term ceramic heads showed less wear compared to metal heads in PE. [72-74] Focused on Oxinium, there is no advantage over metal heads on wear and in combination with a higher cost of Oxinium, its use is not routinely recommended. [75, 76] The second option to overcome wear of PE as seen in hard-on-soft bearings, is the use of hard-on-hard bearings like metal-on-metal (MoM) and CoC. MoM bearings have the potential of low wear rates, but their popularity and use decreased to almost nil due to the concern of metal ion generation and pseudotumor formation. [77, 78] CoC bearings have the advantage

of the lowest rate of wear compared to all other bearings, high resistance to mechanical damage, the possibility to use a bigger head size and hereby decreasing the chance of dislocation, high chemical stability and good lubrication. [74] However, disadvantages of CoC are component related noise, like squeaking, and concern about fracture of the ceramic components. [79, 80]

Influence of bearing on primary stability in press-fit THA

After implantation of the cup, the obtained press-fit and hereby the overall stability decreases for a short period. Subsequent osseointegration improves the overall stability and results in the definitive stability of the implant. [51] If there is a lack of primary press-fit or osseointegration, the implant can be at risk for loosening. In the 1980's it was already observed that excessive implant movement relative to the bone, results in a fibrous tissue connection instead of osseointegration. [81] In literature, hard-on-hard bearings like CoC are mentioned as a potential reason to hamper osseointegration as well. [82-85] Since the total stiffness of an implant is increased by a ceramic insert, the normal weightbearing forces might get less absorbed by the coupling and implant compared to the PE inlay. Hereby, the forces can get transferred to the interface between the bone and implant, jeopardizing press-fit stability and osseointegration as mentioned above. Nevertheless, research focused on this theory, about the influence of CoC on the primary stability and osseointegration of press-fit THA, is still limited.

CLINICAL RELEVANCE, AIMS AND OUTLINE OF THIS THESIS

Initial stability obtained by press-fit THA is important for long-term performance of the cup. In specific cases or in unexperienced hands this might proof challenging. Hence, the need to study options to ease achieving satisfactory primary stability of the cup remains. Since life expectancy is increasing, THAs are performed more often, the implant needs to prove itself for a longer period and in more active and younger people. [86] To improve long-term outcome of THA, tribology of the materials requires further improvement, especially PE wear induced osteolysis needs to be reduced since this is the main reason for long term revision. [87] As mentioned previously, this can be achieved using more wear-resistant bearings. Focused on the use of these bearings in the western national arthroplasty registries, ceramic-on (highly cross-linked)-polyethylene (Co(HXL)PE) is one of the used bearings in for example the Netherlands and Germany. [33, 61] Since CoHXLPE and CoC have the potential to improve longevity of press-fit THA, it is important to investigate potential flaws and complications of both bearings. Short-term studies focused on complication and revision rates and long-term studies focused on clinical performance and revision are still limited.

The first aim of this thesis is to gain insight in options to ease the estimate of the obtained press-fit by the definitive implant, by use of more objective measurement tools and to investigate their influence on primary stability. The second aim is to determine whether CoPE, CoHXLPE or CoC shows better outcomes in press-fit THA. The third aim is to investigate the potential influence of the aforementioned bearings on short-term revision and complication rates, specifically focusing on primary stability of the cup.

Part 1: Primary stability of the press-fit acetabular component

In **Chapter 2** the influence of a dynamic trial fitting tool called the X-pander® on primary stability of the definitive cup was investigated. A cadaveric randomized biomechanical study was performed, measuring lever-out forces of the acetabular implant after trial fitting with either traditional trial cups or the X-pander®, which mimics the obtained press-fit of the definitive implant. In **Chapter 3,** the clinical use of the X-pander® was explored by a questionnaire study among orthopaedic surgeons that used this device. The aim of the use of this device was to help objectify the decision of the expected primary stability obtained by the definitive implant.

Part 2: Bearing surfaces in total hip arthroplasty

Clinical performance of bearings such as CoPE and the more promising CoHXLPE and CoC are of major importance due to their wear reduction potential in THA. In **Chapter 4** we investigated wear and migration using RSA and clinical functioning between CoPE and CoHXLPE. In **Chapter 5** we present the long-term performance of CoPE and CoC, focused on clinical functioning and radiological performance, investigated in a prospective observational study. In addition, we performed a systematic review and meta-analysis describing the clinical functioning by investigating the revision rates of CoC versus CoPE in literature, which are presented in **Chapter 6.**

Part 3: Influence of bearing choice on the primary stability of the press-fit acetabular component

In search for the perfect implant and bearing in THA, focus on flaws and complications is at least as important as investigating the functional outcomes. Therefore, in **Chapter 7** the ten-years outcomes after retrospective screening of a cohort of CoC THAs with a high early failure rate due to loosening were presented. To examine the role of the bearing on early failure of the cup, the two-year cup revision rate of CoC versus CoPE in the LROI was investigated in **Chapter 8.** In **Chapter 9** we present a randomized controlled trial using RSA, comparing migration of the implants between CoC and CoPE bearing at five-years follow-up**.**

Discussion and future perspectives

In **Chapter 10** the findings of this thesis are discussed and compared with literature. The resulting clinical implications are mentioned, and future perspectives are presented. **Chapter 11** comprises an English and Dutch summary of this thesis.

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Part 1

Primary stability of the press-fit acetabular component

Chapter 2

Dynamic trial fitting by an expanding trial cup does not jeopardize primary acetabular component stability

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Clinical Biomechanics (2020) 78 ; 105077

Abstract

Background: Trial fitting of the acetabular component in uncemented total hip replacement is traditionally done by trial cups. Since trial cups do not resemble the real press-fit obtained by the definitive cup, a dynamic trial inserter, called the X-pander ®, was developed to mimic the real amount of press-fit. However, the concern is raised of losing the initial press-fit by using the X-pander® due to pre-expansion of the acetabulum. The purpose of this study was to assess if there is a difference in primary stability between both methods.

Methods: A biomechanical randomized study was performed with bovine calf acetabula, with randomization between either using the X-pander® or the traditional trial cups to assess primary stability. The primary outcome was the force needed to achieve lever out of the implanted cup (Anexys, Mathys or Trident, Stryker), measured in Newton meter (Nm) with a biomechanical testing set up.

Findings: In total, 54 cups (19 Anexys, 35 Trident) were inserted and tested after randomized trial fitting. Overall mean lever out was 45.1 Nm (SD 14.6) for the X-pander® group and 45.0 Nm (SD 14.5) for the trial cups group. After adjustment for potential confounders (cup size and type) mixed model analysis did not reveal a significant difference in lever out force between both testing devices (mean 1.0 Nm, 95%CI (-5.9; 8.0), p = 0.77).

Interpretation: Initial press-fit of the implanted cup is not lost by pre-expansion as done with dynamic trial fitting with the X-pander®.

INTRODUCTION

Primary stability of the uncemented acetabular component in total hip arthroplasty is the most important factor to ensure osseointegration and therefore long-term survival of the implant. [1-4] After reaming the acetabulum, a trial cup is inserted to get an impression of the press fit which can be achieved with the definitive cup. When a satisfactory press fit impression is obtained by using the trial cup, the definitive cup is inserted. In fear of losing press-fit and thereby primary stability of the definitive cup after impaction of an oversized trial cup, the trial cups never resemble the actual cup size, surface texture (scratch fit) and stability of the definitive cup.

The association between lack of primary stability and early failure has been described in the past. [5] Since achieving the perfect primary stability is a subjective feeling obtained by experience, an experienced orthopedic surgeon can generally judge this sufficiently. However, this can be more difficult in revision cases or in the hands of the unexperienced surgeon or resident. Therefore, the subjective feeling of primary stability and variation between different surgeons and implant brands can still not be overruled by an objective measurement. A new instrument is developed to overcome this problem.

The X-pander® is a universal trial inserter manufactured by Medichanical Engineering ApS, which is dynamic rather than static. This form of dynamic trial fitting cup, with a surface texture comparable to the definitive cup, helps to make a more objective decision about the expected primary stability achieved with the implanted acetabular component. During total hip replacement, a X-pander® measuring head can be fitted into the acetabulum and expanded until satisfactory fixation is achieved. This provides the experience of the real amount of press fit to be obtained with the final implant and replaces the well-educated guess using a trial cup. This can overcome both over-reaming and under-reaming. When a certain diameter reamer is used and the trial cup would not maintain sufficient primary stability, the orthopaedic surgeon might choose for a bigger reamer, which might jeopardize primary stability by over-reaming. However, when the X-pander® would be used and after expansion sufficient primary stability would be obtained, it would tell the orthopaedic surgeon that the use of a bigger reamer might not be necessary. Instead a better suitable implant size can be chosen, without getting in risk of over-reaming. Moreover, the X-pander® can overcome under-reaming as well. If a trial cup would achieve perfect primary stability, the definitive implant will always be oversized, since trial cups never mimic the definitive implant size. The danger of under-reaming and as a risk acetabular fractures, will not occur when using the X-pander®, since the orthopaedic surgeon can be more precise in choosing the implant size because of the opportunity of expanding the head of the X-pander®. Hereby the

choice of a smaller or better press-fit definitive implant can be made without being at risk of under-reaming.

Although the X-pander® seems to be a good device in total hip replacement to obtain primary stability, it might have some flaws as well. The most important issue with using an instrument like the X-pander® is that the primary press-fit is not lost by the pre-expansion of the dynamic measuring head and thereby the acetabulum.

In comparison to cortical and subchondral bone, spongious bone is flexible, the main reason why primary stability is obtained. Ladesteijn & Leslie showed deformation of the cup after insertion in stiff bone, making liner insertion problematic. [6] After cup implantation, relaxation of the bone occurred over time and resulted in reduction of the cup deformation. This principle of reduction of the deformation implies reduction of press-fit as well. Since stiffness of the bone will be better obtained when testing primary stability with the X-pander®, this problem can be overruled by additional reaming before placement of the cup. As a result of this, the deformation process seen in the study of Ladesteijn & Leslie will less likely occur when using the X-pander®, raising the suspicion that primary stability is jeopardized. [6] Another theoretical concern with the use of the X-pander® is that by simulating the final press-fit, some of the elasticity of the trabecular bone may be lost, resulting in less deformation and thereby adaption of the cup to the acetabulum. If this process occurs when using the X-pander® in trabecular bone, it might result in reduced primary stability of the final cup as well. This could have major consequences, since insufficient primary stability could cause both early and late failure of the acetabular component. [7] Since this problem apparently does not occur with the traditional trial cups, we considered this as the golden standard. Therefore, we used the traditional trial cups as control group when testing the X-pander®. Hereby we hope to tackle the biggest concern of the X-pander® among the many advantages of this device.

Our hypothesis was that there would be no difference in primary stability when using the X-pander® in comparison to the traditional trial cups.

METHODS

Study design

This is a biomechanical pilot study using bovine calf acetabula. The bovine calf acetabula were left-overs from the normal meat processing and obtained from a local butcher. According to this, no animals were hurt or sacrificed for this study and therefore the

regulation regarding animal studies does not apply to this project. The study was approved by the local ethics committee of Slotervaart Medical Center (P1738).

Study population and randomization

The properties of bovine bone and their acetabular size, approximately 52 mm, correspond well with human dimensions, therefore they are chosen for our biomechanical testing. [8] A total of nine bovine calf pelvises were used. One pelvis was used to test the experiment set-up, the other eight pelvises were used for the definitive testing. A total of 16 acetabula were randomized for starting trial fitting with a standard trial cup or the X-pander®. In every calf pelvis multiple tests were done, allowing comparison between the two methods in similar bone.

Surgical procedure

Both sides were prepared according to the standard principles of acetabular component placement. Reaming was performed in steps of two millimeter until cortical bone was exposed. Trial fitting was done with either the X-pander® (**Figure 1**) or classical trial cup. The measuring head is a single use device that is inserted in the acetabulum after reaming in the correct position and depth. By turning the knob of the handle, the head can expand its diameter up to three mm and is available in 10 individual sizes with two mm increments, covering the span from 48 mm – 69 mm. For instance, if a 54 mm reamer is used and the true size of the implant is 55.4 mm, then a 54 mm X-pander® can be inserted and expanded for 1.4 mm to mimic the true press fit of the definitive implant. When trial fitting was done with classical trial cups, two different types of cups were used; the Anexys from Mathys and the Trident from Stryker. Different types of cups were used to correct the results in our analysis for the type of cup, to overcome that outcomes would be influenced by the type of cup being used. Both cups have the same texture on the entire surface of the cup, except for additional peripheral rims for better peripheral grip, which are only present on the Anexys and not on the Trident. Every brand has its own difference in diameter between trial cup, reamer and definitive implant. When using trial cups, the diameter was 0.5mm bigger than the last used reamer in case of the Anexys and the same size as the last used reamer in case of the Trident. The definitive implant being used was 1.5mm bigger than the last used reamer in case of the Anexys and 1-2mm bigger in case of the Trident.

After primary stability was obtained by the orthopedic surgeon through trial fitting with the X-pander® or with the traditional trial cup, the acetabular component matching the measured size was implanted. The used cup sizes varied between ø 52mm and ø 60mm. The cup was inserted in the acetabulum according to the specific surgical instruction provided by the manufacturer. After implantation testing was done as mentioned below

until lever out of the cup. Thereafter, each acetabulum was reamed again with a two mm bigger reamer and prepared for placement of a following cup. Before the cup was inserted, trial fitting was done with the other one of the two testing devices, than the one used in the previous placed cup, namely the X-pander® or trial cups. Afterwards a two mm bigger cup size was inserted and testing until break out was performed again. This alternating kind of usage of X-pander® or trial cups was performed in each acetabulum. Testing was continued until no larger cup size was available or until the acetabulum was no longer regarded suitable for testing. Acetabula were regarded no longer suitable if fractures occurred or if not enough acetabular bone was left for adequate placement of the cup.

Biomechanical testing

After implantation of the cup a central pin was attached to the central screw hole perpendicular to the cup. (**Figure 2**) Biomechanical testing was performed by applying a traction force to the handle attached to the cup until the cup was levered out. The testing set up being used was the same as the study of Naher & O'Callaghan using a fixated angle of inclination of 10 degrees. [9] This ensures that only lever-out forces were measured with no pull-out action. Therefore, the fixation instrument that extended from the inserted cup implant, makes a resulting angle of 80 degrees with the cable applying the lever out force. A pulley and cable system were used to transfer the vertical force applied by the testing machine to a horizontal direction. The force applied to the handle was measured until loosening of the cup was documented. Loosening was defined at the instance where the testing equipment registered a sudden loss of measured resistance force and therefore loss of fixation. A Mecmesmin® MultiTest 2.5-dV and a Mecmesmin® AFG 2500 N were used for applying and measuring the force and traction applied to the cup.

The VectorPro™ MT Materials Testing Software was used to analyze the measurements. Before obtaining results for analysis, one pelvis will be used for testing the procedure and testing set-up.

Outcome

The primary outcome of this study was the lever out of the definitive cup expressed in Newton meter (Nm) when using the X-pander® in comparison to the traditional trial cups to assess the difference in primary stability of the definitive cup. This outcome was obtained by measuring the breakout force (N) and converting this to lever out (Nm).

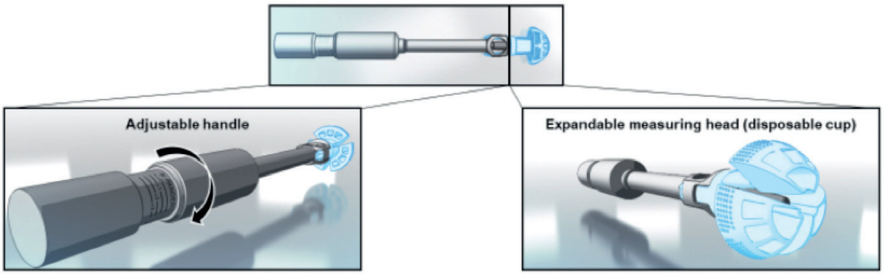

Figure 1. The X-pander®, by turning the handle the diameter of the X-pander® changes. The correct diameter can be read from the handle.

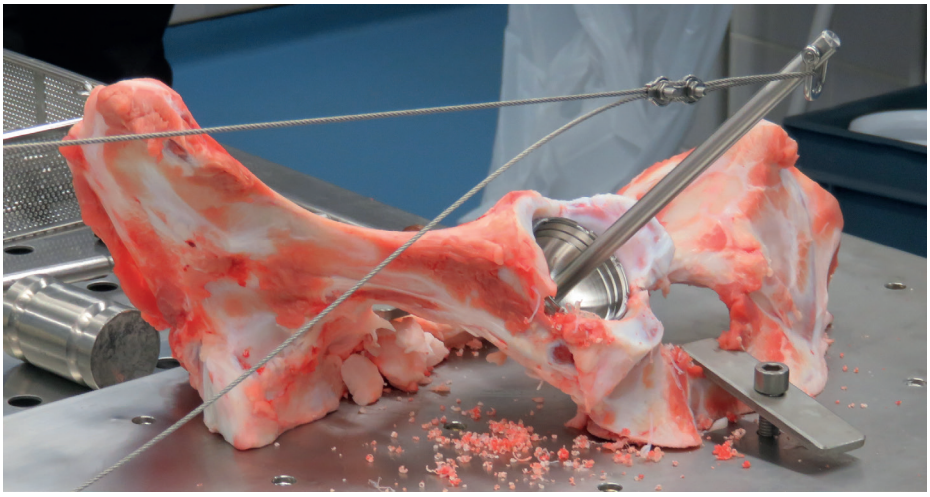

Figure 2. Picture of setup. Cup is placed and the lever out force is applied when in perfect position. The wire is connected to the described measuring device (Mecmesmin® MultiTest 2.5-dV and a Mecmesmin® AFG 2500 N).

Statistical analysis

All data were exported to Statistical Package for Social Sciences (SPSS)® version 24.0 (SPSS Inc. Chicago, IL) for statistical analysis. Results are described as numbers with accompanying percentages and in case of continuous variables as means with accompanying standard deviations (SD) or 95% confidence intervals (95%CI). Since the data was normally distributed after testing, the difference in lever out between the trial cups and the X-pander® was assessed. A multilevel analysis was performed by use of mixed model analysis to account for the correlation between the measurements. When necessary, adjustment for potential confounders (cup size, type of cup, reamer size) was performed. A p-value <0.05 was considered statistically significant.

RESULTS

A total of nine bovine calf pelvises were used. One pelvis was used to test the experiment set-up, the other eight pelvises were used for the definitive testing. A total of 16 acetabula were randomized for starting trial fitting with a standard trial cup or the X-pander®. A total of 55 cups were inserted by one orthopedic surgeon. First 35 Trident cups were implanted and tested, whereafter 35 Anexys cups should have been placed. However, at the time of placement of the 20th Anexys cup the screw thread of the shaft of the testing setup was damaged. Therefore, testing was stopped and 19 Anexys cups (10 of 56mm, 9 of 58mm) were included in further analysis, together with 35 Trident cups. Due to the fact that the testing results in the cases of a cup size of 60mm were not reliable, because of negative measured force, these results were not included in further analysis. In 26 (48.1%) cases the X-pander® was used. As a result, different amounts in sizes of cups were used in both groups. (**Table 1**) Overall mean lever-out was 45.1 Nm (SD 14.6) for the X-pander® group and 45.0 Nm (SD 14.5) for the control group. Differences in lever-out between cup sizes were seen in both the X-pander® and the control group. (**Table 2**) After adjustment for potential confounders no significant difference in lever-out between the use of a traditional trial cup and the X-pander® was observed (mean difference 1.0 Nm, 95%CI (-5.9; 8.0), p = 0.77).

Table 1. Overview of the number of inserted cups in mm between both groups, n (%).

Cup size	Trial cups	X-pander®	Total
52	4 (7.4%)	4 (7.4%)	8 (14.8%)
54	4 (7.4%)	4 (7.4%)	8 (14.8%)
56	9 (16.7%)	9 (16.7%)	18 (33.3%)
58	9 (16.7%)	7 (13.0%)	16 (29.6%)
60	2 (3.7%)	2 (3.7%)	4 (7.4%)
Total	28 (51.9%)	26 (48.1%)	54 (100%)

Table 2. No significant difference in lever out force of the definitive cup in Nm between trial fitting with X-pander® and standard trial cups (mean with 95%CI).

Cup size	Trial cups	X-pander®
52	35.3 (95% CI, 18.8 to 51.7)	43.1 (95% CI, 20.1 to 66.1)
54	50.7 (95% CI, 33.8 to 67.5)	39.7 (95% CI, 20.9 to 58.5)
56	51.4 (95% CI, 43.6 to 59.1)	56.4 (95% CI, 48.4 to 64.4)
58	42.3 (95% CI, 27.2 to 57.3)	38.6 (95% CI, 26.5 to 50.8)

DISCUSSION

The main finding of this study is that no difference in lever out force of the definitive cup was observed when using the X-pander® for trial fitting, in comparison to the traditional trial cups. This means that no difference in primary stability was seen, and therefore no difference in initial press-fit of the implanted cup. Pre-expansion of the acetabular cavity prior to press-fit cup insertion does therefore not compromise primary cup stability.

Long-term survival and osseointegration of the acetabular implant depend on the primary stability which follows implantation. [4,10] This primary stability is provided by undersizing of the cavity after reaming in comparison to the implant size. [11,12] Furthermore, optimal stability is obtained by resulting circumferential tensile stresses in the bone acting as an elastic band on the inserted cup. [13] Therefore, the trial cups used in this study, such as the Mathys Trial Cup which is one mm undersized in comparison to the reamer size, do not mimic the definitive press-fit that is obtained by the oversized definitive implant. However, when using the X-pander® to simulate the definitive press-fit feeling, the concern was raised that some of the aforementioned undersizing and elasticity leading to the optimal primary stability, would be lost. This study shows comparable lever out forces, and therefore optimal primary stability is not lost when using the X-pander®.

On the other hand, acetabular fractures occur more commonly when under-reaming the acetabular cavity in comparison to line to line reamed cup placement. [14] By using the X-pander® the definitive cup size becomes a more line to line kind of placement and can overcome the risk of too much undersizing of the cavity in comparison to the implant size. With this knowledge in mind, the expectation is that the incidence of intraoperative acetabular fractures can be decreased by using the X-pander® as well.

Focusing on the assessment of primary stability, literature shows that this assessment intra-operatively currently relies on the surgeon's ability to estimate proprioceptively the evolution of the cup position in the bone cavity with each impact. [13] The use of these empirical approaches is assumed to be not precise enough and may lead to insufficient primary stability or even bone fracture. Therefore, the need of a quantitative estimation of press-fit is discussed in literature before. [1] The X-pander® is helpful to better estimate the definitive cup size needed to implant per-operatively. As aforementioned, the traditional trial cup is always smaller than the definitive cup size. By the usage of the X-pander® the educated guess between the size of the trial cup and the chosen implant size is no longer needed. Besides, literature shows that the only remaining factor for success of press-fit fixation is primarily dependent on the surgeon. Even the impact of

patient characteristics or implant characteristics are insignificant when using a proper operating technique. [15] By replacing the feeling of primary stability obtained by the orthopedic surgeon with traditional trial cups with the measurement of the X-pander®, the operation technique might improve. Since no other studies have been done on this subject before, this device and the results of this study can help to improve the insights on the need for better reliable objective measurement of primary fixation. Nevertheless, by overcoming this limitation the success of press-fit fixation in hip arthroplasty will increase.

All tests were performed on bovine calf acetabula, which is widely used in other studies before for testing acetabular fixation. [4,16,1,2] Moreover, the study of Fletcher & Williams recently validated juvenile bovine long bones as a suitable specimen for biomechanical testing mimicking human bone, even in pullout testing. [8] Although the same biomechanical properties are not confirmed in acetabula, this research indicates that bovine bone is as a good specimen for this biomechanical study. Additionally, it allows to obtain variability on bone properties likely to the clinical situation. [7] To reduce the differences in bone properties between using the X-pander® and the traditional trial cups, both were used in the same acetabulum alternately and in the other half of the pelvis. Moreover, polyurethane foam is less reliable for the primary research question since it does not have the same deformation qualities after implantation and testing as biological material, resulting in different primary stability results as well. [4]

Several tests were performed in the same acetabulum. Thereby the concern was raised that several tests cannot be performed on the same cadaver, as the properties of bone changes due to compression during implantation of the cup. However, a new situation of testing was obtained by reaming the acetabulum again before placement of a new cup, providing optimal primary stability in each new test situation. If there would be any differences in the mechanical properties of the bone, the initial stability in the bigger diameter cups would be less than the smaller cups. This result wasn't seen in our study as well as in the study of Adler & Stuchin where more tests were executed on the same test sample as well. [11] Moreover, differences in relaxation time were almost nil and will have minimally influenced the mechanical properties of the acetabular bone, especially in randomized setting.

In literature, primary stability is influenced by the type of surface coating on the implanted acetabular cup as well. [17] Therefore, this study used different cups to overcome this variability and mixed model analysis was done with the cup size and cup type as potential confounders.

Finally, in this study all operations were performed by one orthopedic surgeon. The impact of the experience between different orthopedic surgeons on the press-fit by using the X-pander® was not able to be analyzed in this study. Michel & Bosc showed that the impact momentum significantly correlated to the pull-out force. [2] Therefore, another way to gain information about primary stability can be retrieved from impact analysis. However, by testing with one orthopedic surgeon as proceeded in this study, the variance in impact analysis and the resulting primary stability was minimized.

Implications for further research

Since this study shows that the X-pander® does not jeopardize primary stability it seems safe to use it in clinical practice, further investigation of the effect of the X-pander® should be done by different orthopedic surgeons in clinical setting. Furthermore, research needs to be done to obtain information between the amount of feeling initial press-fit with the X-pander® and the resulting primary stability measured by lever out forces. Nevertheless, the idea is raised that the incidence of intraoperative acetabular fractures can be decreased by using the X-pander®. Further research should be done to investigate this hypothesis.

CONCLUSIONS

Initial press-fit of the implanted cup is not lost by pre-expansion as done with dynamic trial fitting with a X-pander® device. Therefore, the X-pander® can be safely used in clinical practice.

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Chapter 3

Dynamic trial fitting of the cup in press-fit total hip arthroplasty, a feasibility study

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Acta Orthopaedica Belgica 2021 ;87(2):327-331

Abstract

Background: Trial fitting of the cup during total hip arthroplasty (THA) is done by trial cups, which do not resemble the real press-fit obtained by the definitive implant. Our goal is to judge feasibility of the X-pander® in clinical practice; a device developed to mimic the real press-fit obtained by the definitive cup, to ensure satisfactory press-fit.

Materials and methods: In this feasibility study 45 experienced orthopaedic surgeons from 7 European countries filled in a structured survey after 78 primary THA and 31 revision surgeries, using the X-pander® instead of traditional trial cups. Primary outcomes were decision change concerning cup size or further reaming and increased confidence regarding cup insertion and size. Additionally, potential association between the primary outcomes and procedure (primary or revision), bone quality and experience of the surgeon were evaluated.

Results: In 33.3% of the primary and 32.2% of the revision cases the X-pander® measurement changed the decision and further reaming or change of cup size was decided. In 61.5% and 58.1% of respectively the primary and revision THAs the X-pander® was judged to give fairly to much more reliable information than traditional trial cups. The X-pander® could lead to less additional screw fixation, as stated in 37.2% of the primary and 25.8% of the revision cases and to better cup insertion in respectively 50.0% and 51.6%.

Conclusions: This study validates that the X-pander® may be a suitable option for accurate sizing and assessment of the reamed acetabulum and could replace traditional trial cups in THA.

INTRODUCTION

When placing a pressfit acetabular component during total hip arthroplasty (THA) it is important to ensure primary stability in order to secure transition to secondary stability by bone-ingrowth. [1] For most of the designs of acetabular components this principle is well proven. [2, 3] However, every implant has a specific learning curve, since the achieved press-fit is estimated on trial cups which do not have the same size as the implant and differ between brands of implants. [4] Therefore, experience of the surgeon and familiarity with the implant is an important factor. The role of primary stability on outcome of THA is well documented and not an issue of debate. [1,5] However, the exact amount of sufficient press-fit is not clear and is currently based on the experience of the surgeon. [3] Achieving the ideal primary stability remains a well-educated guess, especially since the actual press-fit is not exactly mimicked by the current design of trial cups.

In case of revision surgery of the acetabular component primary press-fit is equally relevant. [6, 7] However, assessment of initial press-fit by trial cups is more difficult and requires more surgical experience due to variations in bone geometry and mechanical properties. Especially in case of large defects or poor bone quality. The decision whether press-fit can be obtained with an uncemented acetabular component can be difficult to make and often results in the choice to use a cemented cup. Despite the discussion which revision implant is superior, it would be helpful for the orthopaedic surgeon to have a more tactile feedback of the achieved press-fit with the uncemented implant, especially if this was his first choice for the selected case.

A recently developed tool to provide tactile feedback of initial press-fit is the X-pander®. This tool is designed as a form of dynamic press-fit in which a trial fit cup can be expanded to mimic the stability and real size of the definitive cup. [8] Moreover, the surface texture and shape are more comparable to the definitive cup than normal trial cups. After reaming during total hip replacement, a X-pander® measuring head is fitted in to the acetabulum and can be expanded up to 3mm until satisfactory fixation is achieved. This allows the surgeon to experience the real amount of press-fit to be obtained with the final implant. Hereby the surgeon can overcome both over- and under-reaming of the acetabulum and can make a more objective decision for the size of the definitive cup based on the feeling of primary stability when using the X-pander®.

The goal of this study is to investigate feasibility of the X-pander® in clinical practice in terms of decision-making during surgery, confidence, usefulness and safety, in the hands of experienced hip surgeons, acquainted with THA.

METHODS

Study design, setting and eligibility

Forty-five surgeons in 7 European countries (Denmark, The Netherlands, France, Germany, Norway, Switzerland and the UK) and 20 Hospitals were asked to participate in this initial feasibility study. The participating orthopaedic surgeons were asked to use the X-pander® in a series of primary and or revision cases and to fill in a carefully developed questionnaire after each procedure. The design and reporting were performed in accordance to the Strengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement.

Ethical approval

Since the X-pander® has been introduced on the Market and has a CE marking, no IRB approval was required for this surgeon's survey.

Surgical procedure using the X-pander®

The surgical approach was according to the preference of the orthopaedic surgeon and preparation of the acetabulum was according to the standard principles of acetabular cup placement. Trial fitting was done with the X-pander®, a device developed by Medichanical Engineering ApS. (**Figure 1**) The measuring head is a single use device that is inserted in the acetabulum and can by expanded up to three mm in diameter by turning the knob of the handle. This device is available in 10 individual sizes with two mm increments, covering a span from 48mm to 69mm. For instance, if a 54 mm reamer is used and the true size of the implant is 55.4 mm, then a 54 mm X-pander® can be inserted and expanded for 1.4 mm to mimic the true press-fit of the definitive implant. If necessary, additional reaming can be done afterwards and the acetabular component matching the measured size that provides sufficient primary stability can be implanted.

Questionnaire

Main questions of the survey concerned change of decision of the cup size, decision to ream further, and confidence regarding cup insertion and size. Supplementary questions regarding the use of the X-pander® were included: did a fracture occur, was the cup fully seated, and did you have any drawbacks while using the X-pander®? Patient specific data (age, indication, gender, BMI), experience of the surgeon and operative details (bone quality: soft, medium or hard; implant type; size of the implant; surgical approach; fixation methods of the cup) were also registered. The final questions consist of impression and opinions regarding usefulness of the X-pander®. The survey for revision procedures was identical to the primary procedure with additional specific

questions regarding bone stock/defects and bone grafting. Missing data were obtained by contacting the orthopaedic surgeon that filled in the questionnaire.

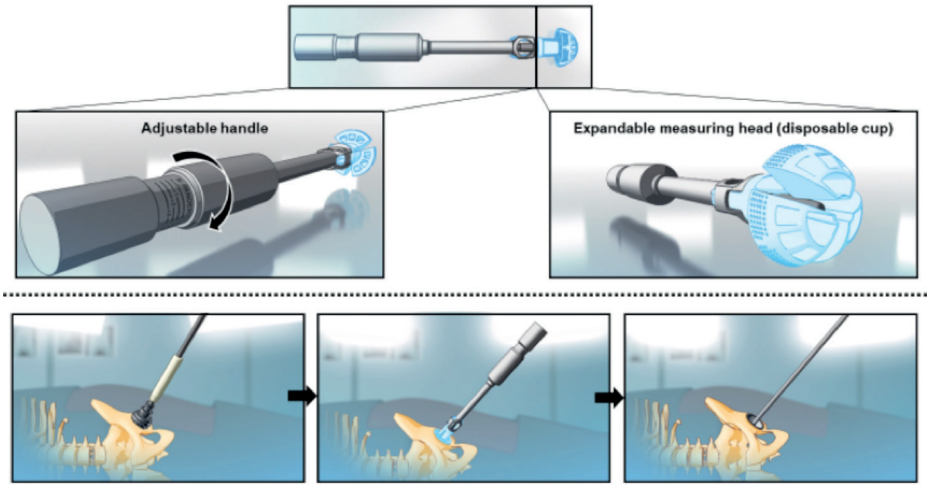

Figure 1. X-pander®, by turning the handle the diameter of the X-pander® changes. The correct diameter can be read from the handle. (small pictures: reaming, X-pander® testing and cup insertion).

Outcomes

The primary outcomes were 1) decision change concerning cup size, 2) decision for further reaming and 3) increased confidence regarding cup insertion and size. As secondary outcome potential association between the primary outcomes and procedure (primary or revision), bone quality (soft, medium, hard) and experience of the surgeon were evaluated.

Statistical analysis

Statistical analyses were performed with Statistical Package for Social Sciences (SPSS) version 26.0 (SPSS Inc. Chicago, IL). Distribution of continuous variables was assessed using the Shapiro-Wilk tests. Normally distributed variables are stated as means with standard deviations (SD). Categorical data are described as numbers with accompanying proportions. To assess the association between the primary outcomes and procedure (primary or revision), bone quality (soft, medium, hard) and experience of the surgeon, mixed logistic regression analyses were performed to account for the correlation between multiple surveys within observers. A p-value of <0.05 was considered statistically significant.

Source of funding
This study was financially supported by Medichanical Engineering ApS. They were not involved in the determination of the study design; in the collection, analysis and interpretation of the data; in writing of the report or in the decision to submit the article for publication.

RESULTS

In this study 45 orthopaedic surgeons (109 cases) filled out the survey. The surgeons performed 78 primary procedures and 31 revision surgeries. Patients undergoing primary THA were mainly female (62.8.%), had a mean age of 66.3 (SD 12.8), mean BMI of 28.1 (SD 6.0). The 31 revision cases were mainly female (58.1%), with a mean age of 72.1 (SD 11.8) and mean BMI of 27.3 (SD 5.1).

Primary outcome
In the primary cases (78 cases and 39 surgeons) the surgeon judged that the X-pander® yields fairly to much more reliable information than traditional trial cups in 89.7%. In 26 (33.3%) of the procedures further reaming or change of cup size was done because of the X-pander®. In 13 (16.6%) procedures this was a combination of further reaming and change of cup-size, in five (6.4%) procedures only additional reaming was done without change of cup size and in eight (10.3%) cases only the size of the definitive implant was changed based on the X-pander® measurement without additional reaming. In 50.0% (n=39) of the procedures the orthopaedic surgeons answered that using the X-pander® led to better cup insertion compared to trial cup fitting. In the remaining cases no difference to regular trial fitting was reported. In 37.2% of primary THA cases (n=29) the surgeons stated that use the X-pander® could lead to the use of less additional screw fixation. In 48 (61.5%) of cases the surgeon felt more confident in achieving press-fit by the use of the X-pander®. The X-pander® was not judged as time-saving in most of the cases, only 18 (23.1%) judged it as being potentially time-saving. In 50 cases (64.1%) the surgeon judged the X-pander® suitable for replacing the traditional trial cup.

In the revision cases (31 cases by 18 surgeons) the surgeon judged the X-pander® as giving fairly to much more reliable information than traditional trial cups in 78.9% of the procedures. In 10 cases (32.2%) the use of the X-pander® changed the decision about reaming intra operatively or the size of the definitive implant changed based on the X-pander® measurement. In four (12.9%) procedures this was a combination of further reaming and change of cup-size, in one (3.2%) procedures only additional reaming was done without change of cup size and in five (16.1%) cases only the size of the definitive

implant was changed based on the X-pander® measurement without additional reaming. The orthopaedic surgeons scored in 16 of the revision cases (51.6%) that using the X-pander® led to better cup insertion compared to trial cup fitting, in the other cases no to moderate difference compared to regular trial fitting was reported. In 25.8% of the revision cases (n=8) the surgeons stated that using the X-pander® could lead to the use of less additional screw fixation. In 18 (58.1%) of the cases the surgeon felt more confident in achieving press-fit by the use of the X-pander®. The X-pander® was not judged as time-saving in most of the cases, only in six procedures (19.4%) the orthopaedic surgeons judged it as being potentially time-saving. In 17 cases (54.8%) the surgeon judged the X-pander® suitable for replacing the traditional trial cup.

Secondary outcome

Mixed logistic regression analysis showed no significant association between procedure (primary of revision), bone quality and experience of the surgeon on decision change concerning cup size, reaming or confidence regarding cup insertion and size.

DISCUSSION

The results of this survey on initial experience by the X-pander® by orthopaedic surgeons show that this product may play a role in future hip surgery. Accordingly, surgeons stated that the X-pander® give fairly to much more reliable information than traditional trial cups in 89.7% and 78.9% of respectively the primary and revision cases. Even more important is the fact that in primary cases 33.3% the choice of implant size changed, or further reaming was done and for revision cases this was 32.2% based on the X-pander® measurement. Although no comparable literature is available about this device, it shows that the X-pander® is a feasible option to overcome problems regarding primary stability of the cup in THA.

Giving some surgeons the option to perform more procedures using the X-pander® and measure their experience, could introduce a bias. However, not every procedure was judged the same by these surgeons, since many factors for achieving press-fit are patient specific. [6] To avoid bias by differences in the number of procedures performed by each surgeon, only the first five procedures per surgeon were included for analysis.

Although the definitive cup size changed in 30 of the 109 cases overall (27.5%) when using the X-pander® as measuring device, accounting 21 primary and nine revision cases, this does not mean that the decision to change the cup size is per definition better, since when surgeons are doubting about primary stability and choosing a bigger implant, per

definition more press-fit is obtained by a larger cup. In this cases the X-pander® gave the information that a bigger size fits and the fear for fractures on inserting the cup is not higher. [9] Since many surgeons in this study used additional screws to ensure primary fixation it seems that in regular practice it remains a problem to achieve press-fit by the implant itself. Our outcomes that in 33.3% of the primary cases and 32.2% of the revision cases the surgeon decided to change the cup size after measuring with the X-pander®, show that the X-pander® can be a potential solution for the problem of achieving adequate press-fit without additional screw fixation. [10–12]

CONCLUSIONS

This study validates that the X-pander® may be a suitable option for accurate sizing and assessment of the reamed acetabulum and could replace traditional trial cups in THA.

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Part 2

Bearing surfaces in total hip arthroplasty

Chapter 4

Highly cross-linked versus conventional polyethylene inserts in total hip arthroplasty, a five-year Roentgen stereophotogrammetric analysis randomized controlled trial

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World Journal of Orthopedics (2020) 11(10) ; 442-452

Abstract

Background: Polyethylene (PE) particles produced by wear of the acetabular insert are thought to cause osteolysis and thereby aseptic loosening of the implant in total hip arthroplasty (THA). As highly cross-linked polyethylene (HXLPE) is presumed to give lower wear rates, in vivo studies are needed to confirm this.

Aim: To compare the wear of REXPOL, a HXPLE, with conventional PE within the first five years after implantation using Roentgen stereophotogrammetric analysis (RSA).

Methods: Patients were randomized to receive either a HXLPE (REXPOL) or a conventional PE insert during primary THA. RSA images were obtained directly postoperative and after 6 wk, 12 wk, 6 mo, 12 mo, 24 mo and five years. Functional outcomes were assessed using the Hip Injury and Osteoarthritis Outcome Score and Harris Hip Score at baseline and five years after surgery.

Results: The HXLPE (REXPOL) showed less wear in the latero-medial direction. Significant wear rates of conventional PE were seen in the latero-medial and center-proximal direction and in volume and corrected volume, whereas the REXPOL did not show these outcomes over time. Improvement from baseline in functional outcome did not significantly differ.

Conclusion: Total 3D wear is less in THAs inserted with a REXPOL inlay than a conventional PE inlay after five years. This study confirms, for the first, that the REXPOL HXLPE inlay is preferred to standard PE.

INTRODUCTION

Since the introduction of total hip arthroplasty (THA) in the 1960s, the incidence of this procedure has been increasing. Although THA is one of the most successful orthopaedic procedures, the main causes of late revisions are wear, and the resulting osteolysis causing aseptic loosening of the implant. [1]

Therefore, the search to minimise wear continues and several bearing couplings over time have been tried, of which polyethylene (PE) with a ceramic head still remains the best option. [2] However, wear still occurs due to existing friction, resulting in progressive loss of material and the presence of microparticles. These PE particles induce a foreign-body reaction, which results in osteolysis. [3] The number of wear particles produced, the material used, and its morphological form determine the severity of the aforementioned reaction. [4] In response to this problem of PE wear, a highly cross-linked PE (HXLPE) has been developed. Following irradiation, free-radicals are formed, creating cross-links in the PE, which are increased by heating and reduce wear. [5] Depending on the type and dose of irradiation and the type of PE used as the control group, wear can be decreased by 42%-100% compared to traditional PE. [6]

To determine the performance of an implant, a standardized and reliable method is required to measure wear. Stilling et al. demonstrated that wear in different directions combined with volume wear of acetabular inserts can be calculated accurately using Roentgen stereophotogrammetric analysis (RSA). [7] As wear is one of the most important reasons for revision in THA, and therefore an indicator of long-term survival, HXLPE could reduce the number of revisions needed in the future. To prove this, in vivo analyses with RSA are needed to confirm that the in vitro results are confirmed in the real setting.

The objective of this randomized controlled trial (RCT) was to compare the wear of two different inlays, the HXLPE (REXPOL) and conventional PE acetabular inserts with similar ceramic head articulation, within the first five years after implantation.

Our hypothesis was that total 3D wear after five years in the REXPOL group would be less than that in the conventional PE group.

MATERIALS AND METHODS

Ethical approval/registration

This single center RCT was granted ethical approval by the local ethics committee review board of the Slotervaart Medical Center (registration number: NL23524.048.08; Dutch trial register: NL5605). The design and reporting of this study were conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) principles.

Study design

This was a single center, double-blind RCT comparing HXLPE (REXPOL, Smith and Nephew) to standard PE acetabular inserts (Standard PE, Smith and Nephew) with similar ceramic head (Biolox, Smith and Nephew) articulation. Both the patients and investigators were blinded with regard to the group patients were assigned to. RSA analysis was performed in a blinded mode. Randomization was performed by the use of numbered opaque envelopes, containing the prescribed PE insert. The orthopaedic surgeon randomly received those envelopes and opened them prior to the procedure.

Eligibility

Between January 2011 and January 2014, patients undergoing THA in the Slotervaart Medical Center were included in this study after completing an informed consent if they met the inclusion criteria (**Table 1**).

Table 1. Inclusion and exclusion criteria.

Inclusion	**Exclusion**
Primary arthroplasty due to:	Patients who recently suffered:
Primary osteoarthritis	Post-operative osteoarthritis
Avascular necrosis	Charnley C osteoarthritis
Femoral neck fracture	Infection of the hip
Hip dysplasia	
Age between 60 - 75 yr at surgery	Prior osteotomy or arthroplasty of the affected hip
Willing to comply with the post-operative review program	Under treatment for osteoporosis
	Body mass index > 35 kg/m^2
	Requiring cortisone medication

Sample size

Previous RSA studies showed a high degree of sensitivity and accuracy of measurements of migration; relatively small patient groups showed a statistically significant outcome. [8] Standard PE has a linear wear rate of around 0.06-0.08 mm/year, whereas REXPOL is expected to show almost no wear over five years. A recent publication on five-year wear results in THA measured by RSA, revealed a mean 3D wear of 0.23 mm (95%CI: 0.17-0.29) for HXLPE vs 0.41 mm (95%CI: 0.32-0.50) for conventional PE. [9] Based on this difference in wear of 0.18 mm, a SD of 0.21 and a power of 80%, a sample size of 21 patients was required in each group, to identify a statistically significant difference at the 0.05 significance level.

Surgical procedure

All THAs were performed in the Slotervaart Medical Center in the standardized way using a straight lateral approach, according to the surgical technique described by the manufacturer of the implants. All patients received the same uncemented acetabular cup (EP-FIT PLUS, Smith and Nephew) and a titanium uncemented Zweymuller femoral stem implant (SL-PLUS, Smith and Nephew) with the same ceramic head articulation (Biolox, Smith and Nephew). As inclination of > 45˚ gives more wear, the navigated position of the cup is aimed to be between 40 and 45˚ of inclination and 15 to 25˚ of anteversion. [10,11] In these series, computer navigation was used to determine this position (CT free navigation Galileo, Plus Orthopedic AG, Switzerland). The liner used was either a HXLPE liner (REXPOL, Smith and Nephew) or a standard PE liner (Standard PE, Smith and Nephew). Leg length and femoral offset were aimed to be identical to the contralateral side. In addition to this procedure, at least five well-scattered tantalum markers were installed (ø 1.0 mm) with a specially designed insertion instrument into the bone around the stem component to obtain skeletal landmarks.

RSA outcomes

Patient demographics were recorded at baseline. RSA evaluations were performed postoperatively, after receiving the same standard rehabilitation program, within one week, at 6 wk, 3 mo, 6 mo, 12 mo, 24 mo and 60 mo after implantation. RSA measurements were performed as described in the guidelines of Valstar et al. in the supine position using a uniplanar calibration box (Medis CarbonBox nr. 011, Medis Specials, Leiden, Netherlands). [8] Analysis of the radiographic images was carried out with the model-based RSA Software, version 4.1 (RSAcore, Dept. of Orthopaedics, LUMC, Netherlands). The RSA system resulted in anteroposterior and lateral views of the hip simultaneously. The RSA at four to seven days postoperatively was used as a baseline. By using the implanted tantalum balls that were fixed in the bone around the implant, the position of the implant relative to the bone was accurately assessed using a model-based RSA

technique. (**Figure 1**) With this technique the 2D head penetration as a measure of linear wear was measured in millimetres by the proximal-distal migration (A-axis) and medial-lateral migration (B-axis). Using this penetration, the thickness of the inlay could be calculated in millimetres. Additionally, the anterior-posterior migration (C-axis) was measured to calculate 3D head penetration, to determine the volume. The volume of the PE inlay was determined (in mm3/year) to measure the number of millimetres of linear wear/year. Normally wear occurs in the upward direction, in a cylindrical shape. However, as the wear is not only in a neat upwards direction, but also in other angles or directions, a corrected volume was also calculated, according to the formula of Hashimoto. [12] This formula has been validated as the most accurate way to determine volume wear from linear wear. [13]

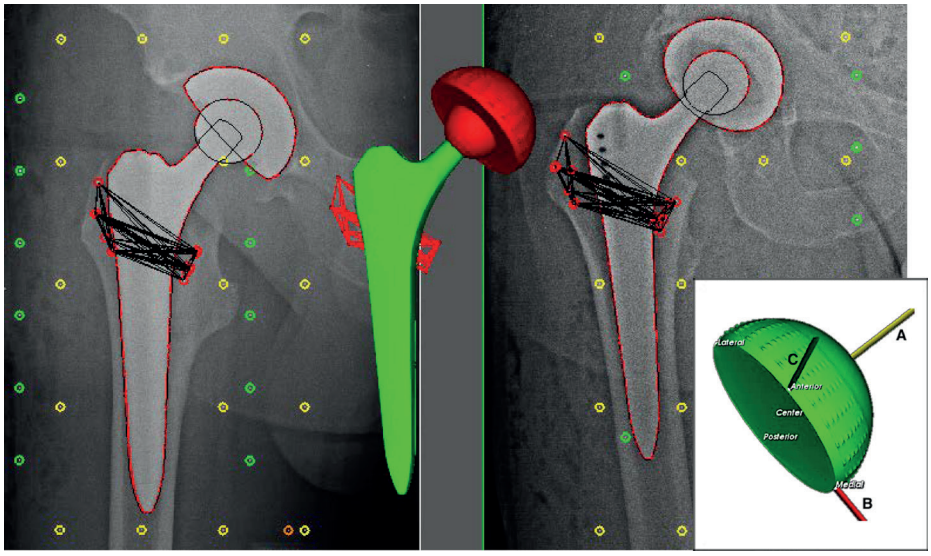

Figure 1. Model of Roentgen stereophotogrammetric analysis technique on right-sided acetabular component after insertion of tantalum markers, by measuring the penetration of the head in the proximal-distal (A-axis), medial-lateral (B-axis) and anterior-posterior migration (C-axis) direction.

Functional outcomes

The pain and activity of daily living (ADL) domains of the Hip Injury and Osteoarthritis Outcome Score (HOOS) were assessed pre-operatively, and after five years by a research nurse. [14] The HOOS was constructed to assess patient-relevant outcomes in five separate subscales: pain, symptoms, ADL, sport and recreation function and hip-related quality of life. The sum scores of the domains in this questionnaire are transformed into a zero to 100, worst to best scale. Another functional questionnaire assessed, was the Harris Hip Score (HHS). [15] This questionnaire was focused on pain and function,

completed by range of motion and deformity. The maximum of 100 points is the best possible outcome.

Statistical analysis

Statistical analyses were performed with IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, United States). After confirmation of normal distribution, continuous variables are presented as mean ± SD. Categorical data are described as numbers with accompanying proportions. A mixed model analysis was performed to evaluate the amount of wear between both groups during follow-up. The effect of the different inlay was considered as a model factor and interaction with the follow-up time was evaluated to assess the differences in progression of wear in both inlays. The difference in wear at final follow-up was assessed by the Student's t-test. To assess the differences of the PROMs between the inlay groups after five years, univariate as well as multivariate regression analyses were performed to adjust for potential confounders such as demographics. The differences were significant if the p-values were less than 0.05. All statistical methods in this study were performed by a biomedical statistical expert (Inger N Sierevelt).

RESULTS

A total of 51 consecutive patients were included in this study at baseline. **Figure 2** shows a flow chart of the patients during this study. Seven patients were excluded, and the remaining 44 patients were included in our analysis; 22 in the REXPOL and 22 in the Standard PE insert group. During follow-up, five patients in the REXPOL group and three in the Standard PE group were lost to follow-up. The patient demographics and baseline characteristics of both groups were comparable and are shown in **Table 2**. No significant differences were seen in cup sizes between the two groups and no revisions were needed during follow-up in either group.

RSA migration

The total wear of the inlay measured from baseline showed less wear in all directions in the REXPOL group, which was significant in the REXPOL group in the latero-medial direction. All results of total wear measured from baseline are shown in **Table 3**. Due to a significant interaction between cup type and follow-up time, the wear pattern during follow-up of the REXPOL and Standard PE inlay were analyzed separately. These wear patterns over the years showed greater wear in all directions in the conventional PE group, which is shown in **Figures 3-6**. The corresponding wear rates over this time period in **Table 4** show that in all directions and volumes calculated, conventional PE

had significant wear rates, whereas REXPOL did not show this outcome over time. The RSA images showed no signs of osteolysis.

Table 2. Patient and baseline characteristics.

	Conventional PE	REXPOL
Number of patients, *n* (%)	25 (49)	26 (51)
Gender, *n* (%)		
Male	10 (40)	10 (39)
Female	15 (60)	16 (59)
BMI, mean ± SD kg/m²	26.7 ± 2.9	27.2 ± 3.4
Age at operation in years, mean ± SD	68.5 ± 4.6	68.6 ± 5.1
HOOS pain, mean ± SD	46.5 ± 21.6	51.1 ± 17.7
HOOS ADL, mean ± SD	41.1 ± 16.6	46.0 ± 17.2
HHS, mean ± SD	50.6 ± 12.7	54.6 ± 10.9

PE: Polyethylene; BMI: Body mass index; HOOS: Hip injury and osteoarthritis outcome score; ADL: Activity of daily living; HHS: Harris hip score.

Table 3. Total wear in all directions at the five-year follow-up, presented as mean with ranges.

	Conventional PE	REXPOL	p-value
Medial (mm)	-0.128 (-0.202 to -0.054)	0.013 (-0.054 to 0.081)	0.006
Proximal (mm)	0.196 (0.054 to 0.338)	0.017 (-0.120 to 0.154)	0.07
Volume (mm³)	113.39 (-2.48 to 229.26)	-30.59 (-167.16 to 105.98)	0.10
Corrected volume (mm³)	121.6 (17.76 to 225.46)	-12.45 (-122.94; 98.03)	0.07

PE: Polyethylene.

Table 4. Mean wear rates per year, presented as mean with ranges.

	Conventional PE	p-value	REXPOL	p-value
Medial (mm/yr)	-0.021 (-0.028 to -0.015)	< 0.001	0.004 (-0.002 to 0.009)	0.21
Proximal (mm/yr)	0.033 (0.018 to 0.047)	< 0.001	0.003 (-0.011 to 0.017)	0.66
Volume (mm³/yr)	15.94 (2.729 to 29.15)	0.02	-5.545 (-20.36 to 9.269)	0.46
Corrected volume (mm³/yr)	18.53 (7.188 to 29.86)	0.002	-2.142 (-14.13 to 9.841)	0.72

PE: Polyethylene.

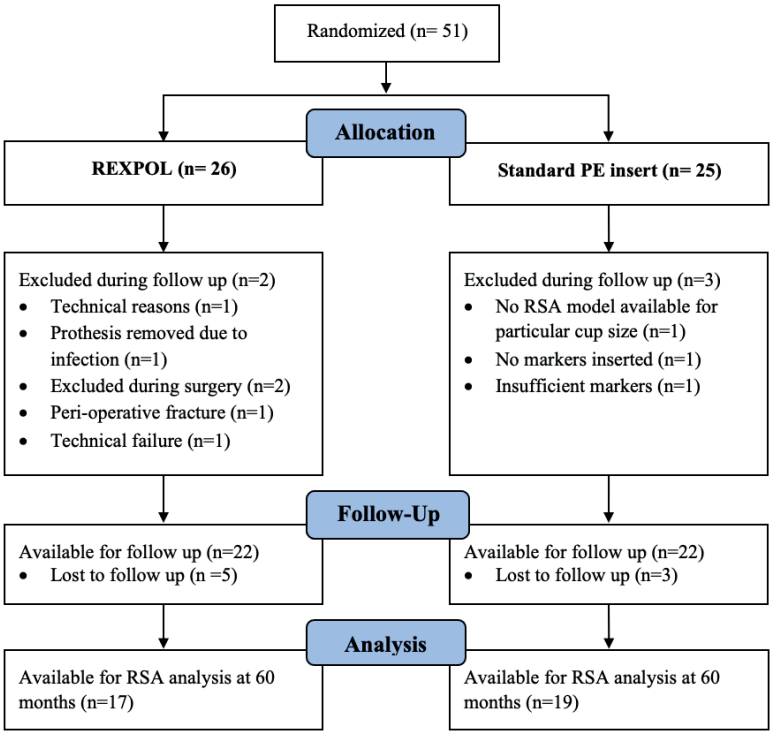

Figure 2. Flow chart of follow-up.
PE: Polyethylene; RSA: Roentgen stereophotogrammetric analysis.

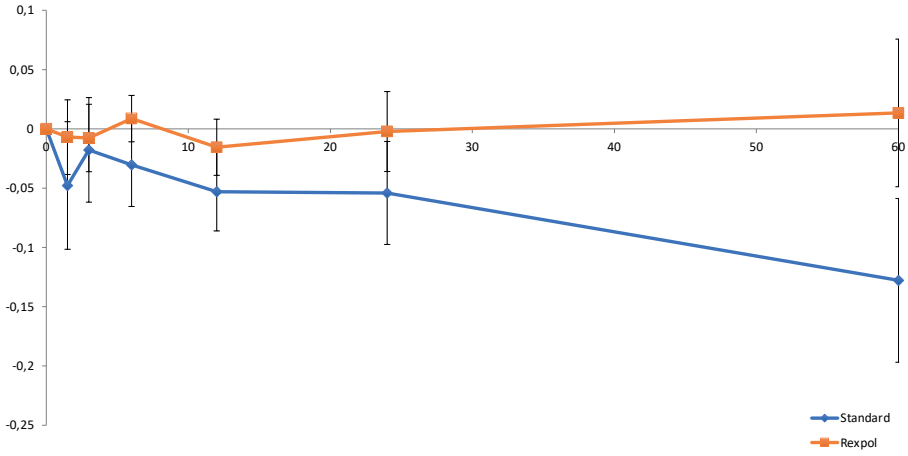

Figure 3. Wear of the inlay in the medial direction in mm over time (months).

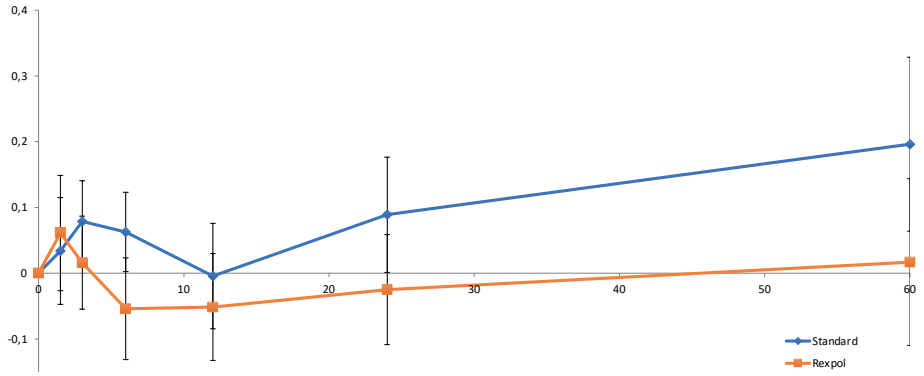

Figure 4. Wear of the inlay in the proximal direction in mm over time (months).

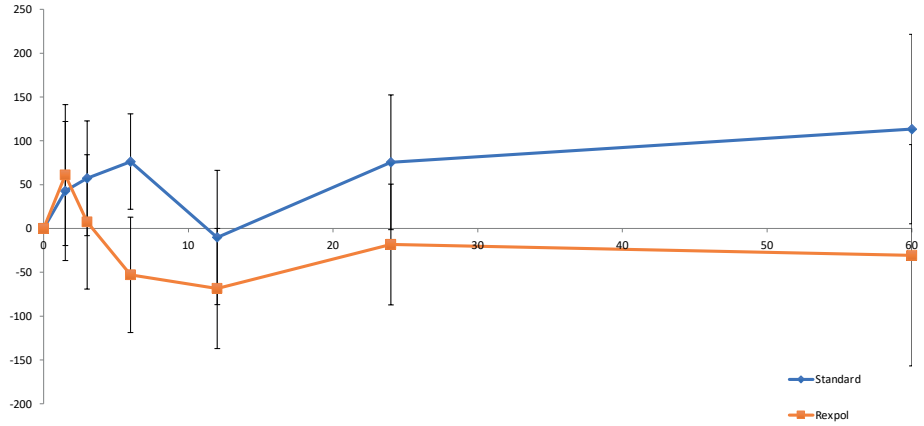

Figure 5. Volumetric wear of the inlay in mm3 over time (months).

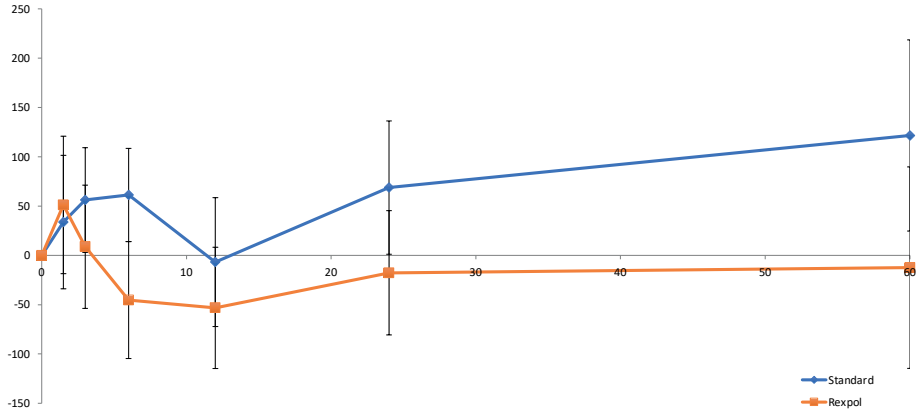

Figure 6. Corrected volumetric wear of the inlay in mm3 over time (months).

Functional outcomes

The functional questionnaires were obtained at five years, to detect potential differences in functional outcomes. These results are shown in **Table 5**, with no significant differences observed.

Table 5. Functional outcomes at the five-year follow-up, presented as mean with 95%CI.

	Univariate			Multivariate	
	Conventional PE (n = 17)	**REXPOL (n = 17)**	**p-value**	**Adjusted β-coefficient**	**p-value**
HOOS pain	93.8 (86.8; 100)	85.9 (77.1; 94.7)	0.15	-3.3 (-14.9; 8.3)	0.57
HOOS ADL	89.0 (81.2: 96.8)	77.6 (66.6; 88.5)	0.08	-8.6 (-23.3; 6.1)	0.24
HHS	89.7 (83.0; 96.4)	86.5 (78.8; 94.2)	0.51	0.15 (-10.1; 10.4)	0.98

PE: Polyethylene; HOOS: Hip injury and osteoarthritis outcome score; ADL: Activity of daily living; HHS: Harris hip score.

DISCUSSION

The main finding of this study is that total 3D wear was less in the REXPOL group than in the standard PE group, with significant less wear in the medial direction after five years. Moreover, the wear rates in the medial and proximal direction and in both volume and corrected volume were significant in the standard PE group, but not in the REXPOL group.

Several in vivo studies have shown that HXLPE can reduce wear in comparison with normal PE inlays in THA. [16] However, only one study investigated the results of REXPOL in vivo, without randomization and RSA analysis. [17] The outcomes in that study supported our findings of reduced wear in the REXPOL group, with approximately 70% less wear at the five-year follow-up. Therefore, this study is the first to present randomized clinical RSA data regarding the REXPOL liner.

In other in vivo studies using RSA, a systematic review performed by Callary et al. showed that only 12 cohorts comprising 260 THAs have compared the outcomes of HXLPE vs normal PE. [18] Their recommendations on standardization of reporting RSA outcomes are applied in our study. However, the studies included in their review assessed different inlays and not all of them were randomized. Thus, our study contributes to their statement that more longer-term standardized studies are needed to improve our understanding of the factors related to wear. Moreover, this will provide a better indication of the chance of osteolysis and as a result loosening of the cup and revision in the longer term.

A literature review by Dumbleton et al. showed that a threshold for wear of 0.05 mm/year would eliminate osteolysis. [19] Although both standard PE and REXPOL showed wear rates below this threshold in our study, the long-term wear of REXPOL is still unclear. Long-term results were reported in the study by Broomfield et al. using another brand of HXPLE with the same low wear rates at 12 years. [20] Rates of 0.03 mm/year were seen in the standard PE group and 0.003 mm/year in the HXLPE group, with higher wear rates in patients with osteolysis. Their long-term outcomes were supported by several studies showing ten-year or longer wear rates in favour of HXLPE. [21-23] Moreover, the study by Oparaugo et al. clarified the correlation between wear debris-induced osteolysis, volumetric wear-rates and revision. [24]

Despite this correlation, subsequent concern was raised that HXLPE microparticles would show increased bioactivity in vivo as this had been observed in in vitro studies, since these particles are smaller than conventional PE. [25-27] However, the in vivo study by Lachiewicz et al. showed that at 10 to 14 years, small osteolytic lesions were also seen with HXLPE. [28] Broomfield et al. supported this outcome and showed 50% osteolysis after 12-years with conventional PE vs 4% with HXPLE, which was statistically significant. [20] This shows that HXLPE wear particles are not more biologically active than conventional PE and may not elevate the risk of osteolysis.

As osteolysis is one of the main reasons for loosening of the cup, the aforementioned results on long-term reduction of osteolysis become even more clinically relevant if a reduction in revisions is seen over time. The study by Hanna et al. showed less wear in the HXLPE group and as a result no osteolysis or revisions at 13-years in the HXPLE group with an implant survival rate of 100% vs 86% in the conventional PE group. [29] De Steiger et al. also confirmed this in a large observational study and showed a 16-year cumulative revision rate of 11.7% with conventional PE vs 6.2% with HXLPE. [30] The aforementioned outcomes confirm that the lower wear rates of HXLPE as seen in our study can reduce the risk of osteolysis when compared to conventional PE and can also reduce revision rates in the longer term.

By measuring wear as the slope of the amount of penetration in the different directions, some negative results on wear are seen in this study. These negative wear rate outcomes have been reported in previous studies. [1,31-35] However, this may be due to lower wear rates of HXLPE being harder to accurately measure compared to conventional PE. Although RSA is considered the best way to measure wear of a prothesis, it has an accuracy range of 0.022 mm to 0.086 mm, depending on the direction of measurement. In the case of HXPLE with even lower wear rates, it becomes more challenging to determine small amounts of wear. [36] Therefore, it becomes more important to have

large cohorts to detect significant differences. As our study was carried out with small cohorts, the wear results should be interpreted while bearing this in mind. The expectation is that in the longer term these wear rates can be calculated more accurately for HXLPE, because they will be determined outwith the threshold. Since our RSA analysis was performed while in the supine position, another explanation of the negative wear rates is subluxation of the femoral head while lying. However, this was not confirmed by the review conducted by Callary et al. who showed no differences between the studies on supine or standing RSA. [18] To overcome problems of negative wear results, long-term results of HXLPE wear are needed.

According to the outcomes in favor of HXLPE, this study confirms that the use of inlays such as the REXPOL, is preferred in THAs.

Limitations

The clinical outcomes of our study were measured to assess any major drawbacks of standard PE or HXLPE at the five-year follow-up. As improvement from baseline was seen in both groups with no significant differences between the groups, no practical disadvantages were seen by preferring one inlay over the other. As the study was not powered by clinical outcomes, further research is needed to investigate these outcomes.

Implications for further research

This study showed, for the first time, that REXPOL resulted in less wear in the short-term in a randomized setting by RSA. Therefore, further investigation of wear over a longer period should be performed, to confirm that REXPOL can reduce the risk of osteolysis and consequently reduce revision rates in THA. Also, more research needs to be carried out to overcome problems of minimal differences in wear rates. In addition, research on other variables that influence wear such as activity, weight and surgical factors such as inclination of the acetabular component should be performed.

CONCLUSIONS

Total 3D wear is less with REXPOL inlay than with conventional PE inlay in THAs after five years. This study confirmed, for the first time, that the REXPOL HXLPE inlay is preferred to the standard PE inlay.

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Chapter 5

Ceramic-on-ceramic vs ceramic-on-polyethylene, a comparative study with 10-year follow-up

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Abstract

Background: In press-fit total hip arthroplasty (THA) ceramic-on-ceramic (CoC) bearings are a potential for overcoming the wear that is seen in ceramic-on-polyethylene (CoPE) bearings, and can lead to wear-induced osteolysis, resulting in loosening of the implant. However, CoC bearings show disadvantages as well, such as squeaking sounds and being more fragile, which can cause ceramic head or liner fracture. Because comparative long-term studies are limited, the objective of this study was to determine the long-term difference in wear, identify potential predictive factors for wear, investigate radiological findings such as osteolysis, and evaluate clinical functioning and complications between these bearings.

Aim: To determine 10-year differences in wear, predictive factors for wear, and investigate radiological findings and clinical functioning between CoC and CoPE.

Methods: This observational prospective single-center cohort study with a 10-year follow-up includes a documented series of elective THAs. Primary outcome was wear measured by anteroposterior (AP) radiographs. Secondary outcomes were potential predictive factors for wear, complications during follow-up, Harris hip score (HHS), and radiological findings such as presence of radiolucency, osteolysis, atrophy, and hypertrophy around the cup. Due to the absence of wear in the CoC group, stratified analysis to identify risk factors for wear was only performed in the CoPE group by use of univariate linear regression analysis. HHS was expressed as a change from baseline and the association with bearing type was assessed by use of multivariate linear regression analysis, adjusted for potential confounders.

Results: A total of 17 CoPE (63.0%) and 25 CoC (73.5%) cases were available for follow-up and showed a linear wear of respectively 0.130 mm/year (range 0.010; 0.350) and 0.000 mm/year (range 0.000; 0.005), which was significant ($P < 0.001$) between both groups. Wear always occurred in the cranial direction. Cup inclination was the only predictive factor for polyethylene (PE) wear. No dislocations, ceramic head, or liner fractures were seen. The HHS score showed a mean change from baseline of 37.1 points (SD 18.5) in the CoPE group and 43.9 (SD 17.0) in the CoC group. This crude difference of 6.8 (range -5.2; 18.7) in favor of the CoC group was not significant ($p = 0.26$) and was not significant when adjusted for age, gender, and diagnosis either ($p = 0.99$). No significant differences in complications and radiological findings were seen between groups.

Conclusion: CoC bearing shows lower wear rates compared to CoPE at 10-year follow-up with cup inclination as a predictive factor for wear and no differences in complications, HHS, and radiological findings.

INTRODUCTION

Total hip arthroplasty (THA) is considered the operation of the century, but the search for the ideal articulation is still a point of discussion. [1] Several bearing surfaces have been developed in the past to reduce causes for revision. Polyethylene (PE) or highly cross-linked PE (HXLPE) inlay combined with a ceramic head still remains the option of choice. [2] Therefore, the use of a ceramic-on-polyethylene (CoPE) articulation increased with almost 20% in the last decade up to 63.4% of all THAs as seen in the Dutch Arthroplasty Register in 2019. [3]

Wear rates of PE are widely investigated, since wear-induced osteolysis resulting in aseptic loosening still remains one of the main causes of late revision. [4,5] The threshold of 0.05 mm/year was eventually stated to eliminate osteolysis, but recent long-term results showed that even wear rates below this threshold in both PE and HXLPE are associated with osteolysis. [6,7] Ceramic-on-ceramic (CoC) bearings are a potential to overcome this problem, with lower wear rates and incidence of osteolysis than CoPE. [8] However, CoC bearings show disadvantages as well, such as a squeaking sound and being more fragile, which can cause fracture of both the head and the inlay and makes revision THA challenging. [9,10]

Comparative long-term studies are needed to confirm if the aforementioned disadvantages of both bearings will be reflected in accompanying revision rates, clinical functioning, and radiological findings over time. Recent systematic reviews have shown that more data and especially more research focused on long-term are required to clarify clinical advantages of both bearings. [11,12]

The objective of this study was to determine the long-term difference in wear, identify potential predictive factors for wear, investigate radiological findings such as osteolysis, and evaluate clinical functioning and complications between CoC bearing vs CoPE in THA when using the same implants with a 10-year follow-up.

Our hypotheses were that CoPE would show higher wear rates than CoC and no differences would be observed in radiological findings, clinical functioning and complications.

MATERIALS AND METHODS

Ethical approval/registration

No ethical approval was needed for this observational prospective cohort study because this documented series was part of the normal follow-up of elective THAs. Reporting was done in accordance with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement. This research was conducted according to the Declaration of Helsinki.

Study design

This observational prospective single center cohort study with 10-year follow-up included a documented series of elective THAs performed between December 2003 and December 2004 comparing the EP-FIT PLUS press-fit cup system with ceramic insert (BIOLOX delta, Smith and Nephew) to standard PE acetabular inserts (Standard REXPOL, Smith and Nephew) with similar ceramic head (BIOLOX delta, Smith and Nephew) articulation. No randomization was performed in this study. The choice between PE or ceramic insert depended on patient characteristics and the experienced orthopedic surgeons' preferences. All patients included were seen in a standard follow-up scheme with X-rays at baseline, 3, 12, 36, 60, and 120 months post-operatively. After surgery, a standard postoperative rehabilitation protocol under guidance of a physical therapist consisted of immediate weightbearing and crutches for 6 wk. All outcomes were analyzed by a reviewer and checked by a second researcher who were both not involved in the selection, surgery, and follow-up process.

Eligibility

All indications for THA included in this study were primary osteoarthritis (OA), degeneration due to rheumatoid arthritis or other inflammatory arthritis, avascular necrosis and hip dysplasia. Patients were included after completing verbal informed consent. Patients with secondary OA due to trauma, infection of the hip, osteoporosis or a prior osteotomy or arthroplasty were excluded from this study. No a priori power analysis was performed.

Surgical procedure

All THAs were performed at Slotervaart Medical Center by experienced orthopedic surgeons using a straight lateral approach under standard antibiotic prophylaxis. The surgical approach was according to the surgical technique described by the manufacturer of the implants. The same uncemented acetabular cup (EP-FIT PLUS, Smith and Nephew) was used in all patients. This cup is an equatorial flattened press-fit cup design with an open porous titanium vacuum plasma coating to increase roughness, with initial

fixation by 2%-3% oversizing. A non-cemented Zweymuller titanium rectangular tapered shape femoral stem (SL-PLUS, Smith and Nephew) was used as femur component in all cases in combination with a ceramic head articulation (BIOLOX delta, Smith and Nephew). A 32 mm and 28 mm head were respectively used in CoC and CoPE bearing. The liner being used was either a ceramic insert (BIOLOX delta, Smith and Nephew) or a standard PE acetabular insert (Standard PE, Smith and Nephew). Both the ceramic head and liner are made of a zirconia toughened alumina ceramic alloy, a fourth-generation ceramic material. The aimed leg length and femoral offset was measured accordingly to be identical to the contralateral side.

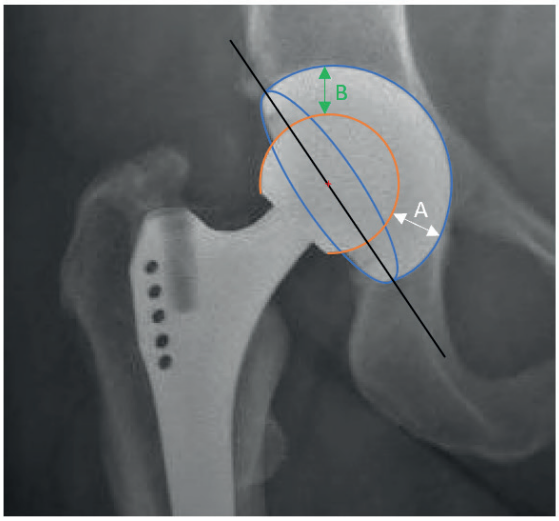

Figure 1. Method of wear measurement with center of rotation (red), boundaries of the cup (blue) and head (orange) and line for measurement of inclination angle (black). A: Widest distal part of inlay; B: Narrowest proximal part of the inlay.

Outcomes

Patient demographics were recorded at baseline, including age, gender, body mass index (BMI), indication for surgery (primary OA or other diagnosis), and operation side. Information regarding the operation was recorded as well including articulation, head size, and cup inclination in degrees on direct post-operative radiographs. Perioperative and complications during follow-up like ceramic articulation fractures, squeaking and dislocations were directly registered.

The primary outcome was wear in mm/year measured by an independent orthopedic surgeon, by consecutive radiography using standard weightbearing anterior-posterior radiographs. By using the penetration and the size of the head, the thickness of the inlay

was calculated. The method being used as demonstrated in **Figure 1**, is widely used and first described and validated by Charnley et al. [13] The width of the narrowest part of the inlay in the proximal weightbearing region (B) was subtracted from the widest part in the distal non-weightbearing area (A) and halved. With this formula, wear = (A – B)/2, wear was calculated as cranial migration in mm. These outcomes were used to calculate linear wear rates in mm/year. As an example, if no wear occurs, the thickness of the inlay is the same in all directions. Hereby the difference between the measurement of A and B is zero, meaning that there is no cranial migration and hereby no wear. If wear increases and more cranial migration is seen, the measurement of B will become lower and A will increase due to a wider distal part, resulting in a greater difference between both values (**Figure 1**). As a secondary outcome, potential predictive factors for wear such as gender, age, operation side, BMI, diagnosis (primary OA vs other), cup size, and cup inclination were determined. The Harris hip score (HHS) was used as a clinical questionnaire to measure patient reported outcomes. [14] Radiographs were evaluated by two researchers to determine presence of radiolucency, osteolysis, atrophy, and hypertrophy around the cup in Zones I-III according to DeLee et al. [15]

Statistical analysis

Statistical analyses were performed with Statistical Package for Social Sciences (SPSS) version 26.0 (IBM Corp., Armonk, New York, United States). Normally distributed continuous variables are stated as mean with standard deviation (SD) and tested by use of Student's t-test. In case of non-normality medians with interquartile ranges are presented and a Mann-Whitney U test was used to assess for significant differences between both groups. Categorical data were compared by use of chi-squared tests. Due to the absence of wear in the CoC group, stratified analysis to identify risk factors for wear was only performed in the CoPE group by use of univariate linear regression analyses. HHS was expressed as a change from baseline and the association with bearing type was assessed by use of multivariate linear regression analysis, adjusted for potential confounders (i.e. age, sex, and diagnosis). Differences were stated significant if p-values were less than 0.05. Complications and radiological findings were expressed as frequencies with percentage. All statistical methods in this study were done by a biomedical statistical expert (Inger N Sierevelt).

RESULTS

A total of 61 patients receiving THAs were included in this study at baseline (**Figure 2**). A significant difference in age and distribution of diagnosis (primary OA vs other) between both groups was observed (**Table 1**). A total of 17 CoPE (63.0%) and 25 CoC (73.5%) cases

were available for 10-year follow-up. Intra-operative trochanteric fracture occurred in one case (4%) in the CoPE group and two (6%) in the CoC group and were treated with a trochanteric wire. Delayed wound healing was seen in two (8%) and four (13%) patients in the CoPE and CoC group, respectively. Temporary peroneal nerve injury was observed in the CoPE group in two cases (7.4%). During follow-up, one periprosthetic joint infection (3%) was seen in the CoC group, which was initially treated with lavage and antibiotics; however, removal of the implant was done elsewhere after 3 years of follow-up. Femoral component loosening was the reason for one revision in both groups, treated by revision of the stem and inlay elsewhere in the CoC case and in our clinic in the CoPE patient. No dislocations, squeaking, and fracture of the ceramic liner were observed. A total of two revisions were planned in the CoPE group after the 10-year follow-up due to complaints combined with excessive wear. All complications showed no significant differences between both groups.

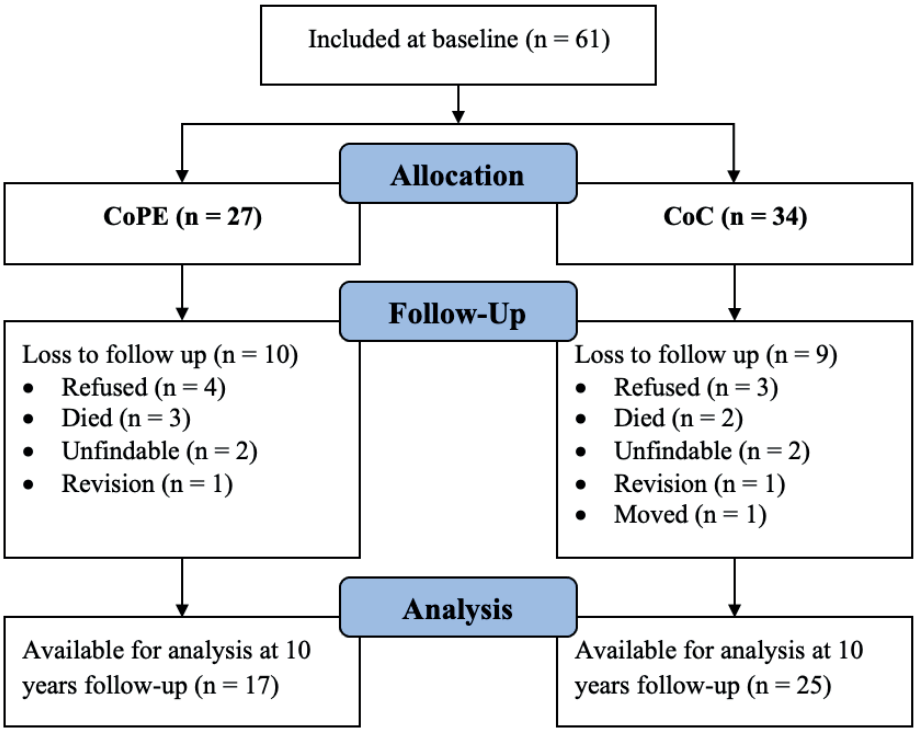

Figure 2. Flowchart of 10-year follow-up.

Primary outcome

After 10 years of follow-up, the median linear wear of CoPE and CoC bearing was 0.130 mm/year (range 0.010; 0.350) and 0.000 mm/year (range 0.000; 0.005), respectively. Wear always occurred in the cranial direction. In two patients in the CoC group, wear of 0.05 mm was measured, in all other cases, no wear was observed. The difference in wear between both groups was significant (P < 0.001).

Table 1. Baseline characteristics and operation information.

	CoPE, *n* = 27 (100%)	**CoC, *n* = 34 (100%)**	**p-value**
Female gender, *n* (%)	21 (78%)	22 (65%)	0.27
Right side, *n* (%)	19 (76%)	17 (50%)	0.11
Diagnosis, *n* (%)			0.01
Primary OA	23 (85%)	19 (56%)	
Other	4 (15%)	15 (44%)	
Age, in years, mean (SD)	64.2 (5.3)	55.7 (8.5)	< 0.001
BMI, in kg/m^2 mean (SD)	27.6 (4.1)	26.9 (4.1)	0.52
Cup size in mm, mean (SD)	52.1 (3.4)	53.6 (3.5)	0.10
Inclination cup in degrees, mean (SD)	46.8 (6.7)	44.6 (5.0)	0.22
HHS, mean (SD)	50.2 (13.3)	47.5 (13.4)	0.44

BMI: Body mass index; CoPE: Ceramic-on-polyethylene; CoC: Ceramic-on-ceramic; HHS: Harris hip score; OA: Osteoarthritis; SD: Standard deviation.

Secondary outcomes

The results of the stratified analysis to identify risk factors for wear in the CoPE group are shown in **Table 2**. Increased cup inclination was the only predictive factor for PE wear in CoPE bearing.

The HHS score showed a mean change from baseline of 37.1 points (SD 18.5) in the CoPE group and 43.9 (SD 17.0) in the CoC group. This crude difference of 6.8 (range -5.2; 18.7) in favor of the CoC group was not significant (p = 0.26). When adjusted for age, gender, and diagnosis (primary OA vs other), a mean difference of -0.02 (range -14.7; 14.7) was seen, which was not significant either (p = 0.99).

The radiological findings in the periacetabular cup zones are shown in **Table 3**. These outcomes showed no significant differences between both groups.

Table 2. Potential predictive values for polyethylene wear in beta-coefficient (range).

Potential predictive factors for PE wear	Beta-coefficient (95%CI)	p-value
Gender	0.06 (-1.18; 1.29)	0.93
Age	-0.01 (-0.10; 0.08)	0.82
Operation side	-0.40 (-1.53; 0.73)	0.46
BMI	-0.05 (-0.20; 0.10)	0.46
Diagnosis, primary OA *vs* other	1.10 (-0.42; 2.61)	0.14
Cup size	-0.06 (-0.23; 0.12)	0.52
Cup inclination	0.08 (0.02; 0.15)	0.02

BMI: Body mass index; CI: Confidence interval; OA: Osteoarthritis; PE: Polyethylene.

Table 3. Radiological findings in DeLee and Charnley zones I, II and III at 10-yr.

	CoPE, *n* = 17			CoC, *n* = 25		
Zones	**I**	**II**	**III**	**I**	**II**	**III**
Radiolucent lines	0	0	0	0	0	0
Osteolysis cup	0	1 (6%)	0	2 (8%)	3 (12%)	0
Atrophy	2 (12%)	3 (18%)	0	5 (19%)	5 (19%)	0
Hypertrophy	0	0	0	0	0	0

CoPE: Ceramic-on-polyethylene; CoC: Ceramic-on-ceramic.

DISCUSSION

The main finding of this observational prospective cohort study of 61 THAs with 17 CoPE and 25 CoC cases available for 10-year follow-up was a significantly different degree of wear between the CoPE and CoC, with values of 0.130 mm/year (range 0.010; 0.350) and 0.000 mm/year (range 0.000; 0.005), respectively in the cranial direction. Comparable significant differences in wear rates were seen in the literature in both the short and long-term. [8,16] Conventional PE inlays have been improved by cross-linking to improve wear rates, but CoC bearings still show the lowest wear rates. [17-19] Therefore, long-term follow-up is required to assess whether differences in wear will result in different survival rates. Although survival was not the focus of our study, to the best of our knowledge, the literature has only one comparative study with 12.6 years of follow-up showing no differences between CoC and CoHXLPE. [18] Studies that only focused on CoPE and CoHXLPE showed long-term survival rates of 86% and 100%,

respectively, at 13 years and 88.3% and 93.8%, respectively, at 16 years. [20,21] Long-term studies that focused only on CoC showed divergent survival rates, with a 15-year follow-up study showing a survival rate of 92%, whereas another 20 years of follow-up showed a survival rate of 99.7%. [22,23] Our wear rate results combined with the revision rates in the literature indicated a possible advantage of ceramic coupling over PE, which needs to be confirmed with longer follow-up studies of at least 20 years.

The low wear and revision rates of CoC in the longer term become highly relevant since a rise in prevalence of THA and a shift to younger age is seen over the last decades. [24] Moreover, our study shows that patients receiving CoC articulation were significantly younger. Since life expectancy is still increasing worldwide, further research is needed to show if CoC can improve the longevity of THAs. [25]

Our study showed that a higher inclination angle of the cup is a significant risk factor for wear. The same results are seen in the literature, with inclination angles above 45 degrees. [26-28] Since the mean angle of CoPE in our group was above this angle, it supports that acetabular positioning is highly important to reduce wear of CoPE.

In addition, inclination angles above 45 degrees are related to the higher incidence of squeaking in CoC. [29,30] In the literature, the incidence of squeaking is significantly higher in CoC than CoPE and varies between 0.5% and 20% and can influence the satisfaction of patients. [11,12,31] Although the mean angle of inclination in CoC in our study was just below the 45 degrees, no squeaking was reported.

Since the introduction of CoC, fracture of the ceramic, which was seen more often than in CoPE, was one of the greatest concerns against using this articulation. [11,12] A recent long-term meta-analysis showed that improvement of the ceramic over time led to lower fracture rates. [32] Additionally, in the literature, fourth-generation ceramic bearings showed no ceramic fracture when compared to third-generation CoC. [33] Since we used a fourth-generation ceramic bearing, this might be a reason that no head or liner fractures occurred in our study. [32,33]

Another complication that influences long-term outcomes is dislocation, which can be caused by wear and malpositioning. [34,35] In the literature, a trend is seen in favor to CoC over CoPE. [11,12] Although no dislocations were seen in our study, the higher wear rate and wider angles of inclination presented in CoPE can indicate an increased risk of dislocation, which might become significant in the longer term.

In our study, no differences in radiological findings such as osteolysis were seen, which was supported by recent systematic reviews comparing CoC and CoPE. [11,12] Longer follow-up is needed to see if differences in osteolysis will occur over time.

No significant differences in clinical outcomes on the HHS were seen in our study. Since comparable scores on the HHS were seen in systematic reviews, there is no preference for one of the bearings based on functioning. [11,12]

Finally, ceramic inserts are more expensive than PE, which might be an important issue in decision making in modern healthcare systems with an increasing focus on healthcare costs. Beaupre et al. stated that the costs of ceramic inserts were three times higher. [36] To the best of our knowledge, no cost-analyses are performed in the literature between CoC and Co(HXL)PE. Long-term analysis needs to clarify if differences in outcomes, complication, and revision rates are cost-effective to the costs of both bearings.

A strength of our study is that we provided comparative results of a fourth-generation ceramic bearing, which are limited in the literature including wear, clinical, and radiological results. A limitation of our study was that no randomization was performed, which can have consequences for the comparability of the groups and might give indication bias. Moreover, a high loss to follow-up was seen in this study. Wear measurements were done using standard AP radiographs, which is a valid method, but is subsidiary to radiostereometric analysis (RSA). [37] For example, we measured wear in two cases of CoC, which might be an error. Finally, no HXLPE was used, which is currently preferred when using a CoPE bearing.

CONCLUSIONS

In this study, higher wear rates were observed in CoPE compared to CoC bearing in THA at the 10-year follow-up, with cup inclination as a predictive factor for wear for CoPE bearing, and no differences in complications, HHS, and radiological findings. More long-term comparative studies are needed to confirm potential benefits of CoC bearing, which might be the preference in THA focused on wear and survival rates, especially in younger patients.

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Chapter 6

Revision in ceramic-on-ceramic and ceramic-on-polyethylene bearing in primary total hip arthroplasty with press-fit cups: a systematic review and meta-analysis of different methodological study designs

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Archives of Bone and Joint Surgery (2022) 10(11) ; 916-936

Abstract

Background: The influence of bearing on revision, especially in press-fit modular cup total hip arthroplasty (THA), remains underexposed.

Methods: A systematic literature review was conducted in PubMed, Embase, Cochrane Library, and ClinicalTrials.gov in line with the PRISMA guidelines. The primary outcome was overall revision between ceramic-on-ceramic (CoC) and all sorts of ceramic-on-polyethylene (CoPE) bearings. As secondary outcomes complications and reasons for revision were compared between bearings. Outcomes were presented in subgroups based on study design (randomized controlled trials (RCT), non-randomized comparative, and registry studies). The quality of evidence was assessed using the GRADE. The risk of bias was assessed using the Cochrane collaboration's tool and the MINORS criteria.

Results: This meta-analysis included twelve RCTs, three non-randomized comparative studies and two registry studies, including 38,772 THAs (10,909 CoPE and 27,863 CoC). Overall revision showed a lower risk in CoPE compared to CoC in the two registry studies (HR 0.71 (95%CI 0.53; 0.99)) (very low-quality GRADE evidence). In RCTs and non-randomized comparative studies, no difference was observed (low-quality GRADE evidence). Loosening, dislocation, infection, and postoperative periprosthetic fracture showed no significant differences in risk ratio for all designs.

Conclusion: The lower risk of overall revision in registry studies of primary THA with a press-fit modular cup using CoPE bearing compared to CoC should be considered preliminary since this outcome was just slightly significant, based on very low-quality GRADE evidence and based on only two studies with several limitations. Since no difference was observed in the other methodological designs and the separate reasons for revision showed no significant difference in all designs either, no preference for CoC or CoPE can be expressed, and therefore both seem suitable options based on the available literature. More comparative long-term studies are needed to confirm the potential advantages of wear-reduction of both bearings since the currently available literature is limited.

INTRODUCTION

In total hip arthroplasty (THA) various bearing surfaces have been investigated and developed. A polyethylene (PE) or highly cross-linked PE (HXLPE) inlay in combination with a ceramic head is still considered the option of choice. [1] The main reason for long-term revision is aseptic loosening caused by liner wear-induced osteolysis. [2] Hard-on-hard low-friction bearings like ceramic-on-ceramic (CoC) are one of the options to overcome liner wear. In CoC wear rates below 0.001 mm/year are observed, compared to 0.072 mm/year in conventional ceramic-on-polyethylene (CoPE) and 0.030mm/year in ceramic-on-highly cross-linked PE (CoHXLPE). [3] However, several CoC specific disadvantages are reported, such as squeaking and component fracture of both the head and inlay, which can complicate revision procedures. [4] Moreover, recent literature suggests higher short-term revision rates in CoC bearing due to aseptic loosening compared to CoPE. [5] In a stiffer bearing like CoC, loss of primary stability can occur due to micromotion, making the cup more vulnerable to loosening. Initial stability is also critical for long-term survival of the cup, which remains the weak component in THA. [6,7] The other main reasons for early revision are infection and dislocation, on which the influence of bearing on the short-term remains unclear. [8] In the long-term fewer infections are reported in CoC compared to CoPE at 15 years and fewer revisions due to dislocation in CoC at 9 years. [9,10] In summary, reasons, moments, and rates of revision widely differ between both bearings. Moreover, the incidence of THA with an uncemented cup has rapidly increased over the last years, with an incidence of 34.3% in Sweden, 69.6% in England, Wales, Northern Ireland, and the Isle of Man, 74.4% in The Netherlands and up to 97.1% in Australia. [11-14] Several studies have shown that, regardless of the bearing, uncemented THA decreases long-term aseptic loosening rates, but increases the short-term risk of dislocation, infection, and periprosthetic fracture. [15-17] Compared to the increasing number of press-fit cups placed with Co(HXL)PE and CoC in THA, the number of comparative studies on the aforementioned reasons for revision is still limited. In literature, several reviews have been performed comparing CoC and Co(HXL)PE, but never distinguished in fixation method. [18-21] This finding in combination with the potential influence of bearing on a revision due to loosening in press-fit THA is one of the reasons why we conducted this systematic review. The aim is to investigate if there is a difference in the revision rate of CoC and Co(HXL)PE bearing in THA with a press-fit modular acetabular implant and to investigate if reasons for revision differ between bearings.

MATERIALS AND METHODS

Search strategy

This systematic review was a priori registered in PROSPERO (registration number: CRD42020206779). During the registration in PROSPERO, we aimed to perform a review focused on (early) aseptic loosening only. Since we recognized that all reasons for revision in press-fit THA are not systematically reviewed, we changed the protocol of the review and included all reasons for the revision. The review was performed in accordance with the Cochrane library recommendations and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guideline. [22] The search was executed in PubMed (Medline), Embase (Ovid), Cochrane Library, and ClinicalTrials.gov. All studies until 29th July 2021 were included. The search was built with the aid of a clinical librarian and the search strategies are presented in **Appendix 1**. Additionally, reference lists of all included articles were screened for additional eligible articles.

Selection criteria

All comparative randomized and non-randomized, and (national) registry studies investigating CoC and Co(HXL)PE in primary total hip arthroplasty with a press-fit modular cup were included. When multiple bearings, cohorts, or fixations were compared in one study, only the data of press-fit cups with CoC and Co(HXL)PE bearings were included. When different sorts of PE or ceramic generation liners were used in one study, all were combined in respectively one CoPE group and one CoC group. The different sorts of liners included were registered. Studies were excluded if: the patients were younger than 18 years, prior arthroplasty of the affected hip was performed, the cup was cemented, and a screw cup or monobloc or sandwich cup was placed. Since screw fixation is optional in most cups and no difference in revision is reported in the literature between uncemented THA with and without screws, studies using optional additional screws were included as well. [23-25] Studies were excluded if the method of fixation was not mentioned. Systematic reviews, duplicates, and articles presenting data that were too scarce to calculate Hazard ratios for overall revision as the primary outcome were excluded as well. No limitation in publication date or language was enabled. The abstract and full-text screening were performed separately by two independent authors (JL and JG) and disagreements between the two authors were resolved by discussion with a third investigator (KO).

Data extraction

Data was extracted separately by two independent authors (JL and JG) using standardized forms and cross-checked afterward. Disagreements between the two reviewers were resolved by discussion with a third investigator (KO). Collected baseline

data included: age, gender, indication for THA (subdivided into primary osteoarthritis, secondary osteoarthritis (avascular necrosis of the femoral head, slipped upper femoral epiphysis, developmental dysplasia of the hip, Perthes disease, rheumatic arthritis, other inflammatory diseases, posttraumatic) or primary traumatic treatment), Body Mass Index (BMI), and follow-up time (in years). Collected surgical data included: cup implant type, cup size, head size, surgical approach, and complications during surgery and postoperative follow-up. Collected revision data included: the number of revision procedures, moments of revision, the different kinds of revision procedures performed, indications for revision, and complication rates of CoC and CoPE. The revision was defined as a procedure by which either the cup, the stem, or both were revised.

Outcomes

As the primary outcome, we will compare the total number of revisions of CoC and Co (HXL)PE bearing due to all reasons. As secondary outcomes, complication rates and different reasons for revision (loosening, dislocation, infection, postoperative periprosthetic fracture) will be analyzed. All outcomes will be presented and pooled in subgroups based on the study design.

Risk of bias assessment

The risk of bias assessment of the included studies was performed independently by two reviewers (JL and JG), using the Cochrane collaboration's tool for assessing the risk of bias for randomized controlled trials. [26] Studies were scored as having a high (red), unclear (orange), or low (green) risk of bias for the following domains: random sequence generation, allocation concealment, blinding of participants, blinding of the outcome, and attrition bias. For non-randomized cohort and registry studies, the methodological index for non-randomized studies (MINORS) criteria was used. [27] On 12 criteria studies were scored as 'not reported' scoring zero points, 'reported but inadequate' scoring one point, or 'reported and adequate' scoring two points, making the global ideal score 24 points for non-randomized comparative studies. The MINORS were also reported for the RCTs to compare the risk of bias between all studies. Disagreements between the two reviewers were resolved by discussion with a third investigator (KO).

Qualitative analysis

Assessment of the quality of evidence and the strength of the outcomes of all included studies were performed independently by two reviewers (JL and JG) using the Grades of Recommendation Assessment, Development, and Evaluation (GRADE). [28]

Statistical analysis

The study, patient, and clinical characteristics are reported using descriptive statistics. Weighted means with pooled standard deviations (SD) are calculated in the case of continuous variables, and categorical variables are presented as numbers with accompanying proportions. Concerning the primary outcome, crude Hazard Ratios (HR) for revision due to all reasons (CoPE vs CoC) were used to perform the meta-analysis. In case crude HRs were not reported, they were estimated using time-to-event data according to the method of Tierney et al. (2006) or using incidence density rates according to Bender and Beckman (2019), depending on the available data and comparability of observation time. [29,30] HRs were pooled using a random effect model with inverse variance weighting and stratified for study design (RCTs, non-randomized comparative cohort studies, and registry studies). Pooled HRs are presented with 95% confidence intervals (CI).

Additionally, for the studies reporting complications, Risk Ratio (RR) was calculated and pooled by use of a random effect model with inverse variance weighting. Stratification for study design was also performed. Pooled HRs and RRs were considered statistically significant if the 95%CI did not include 1.

Statistical heterogeneity was checked using the I2 value and Chi2 test. A $P>0.1$ and an $I2 \leq 50\%$ were interpreted as no statistical heterogeneity. [31] Statistical analyses were performed with R version 4.0.4 (R Foundation for Statistical Computing, Vienna, Austria) using a meta package for meta-analyses. [32] All statistical methods in this study were performed by a biomedical statistical expert. (IS)

RESULTS

Search results

We identified a total of 1109 articles. After title and abstract screening, a total of 128 studies remained. After full-text screening, we included 17 studies in a qualitative synthesis, including 12 randomized controlled trials, three non-randomized comparative studies, and two registry studies. [33-49] The flow chart of the article selection process, including reasons for exclusion based on full-text screening, is shown in **Figure 1**. Three included studies were written by the same author (Pitto et al.), but presented all different study cohorts. [44-46]

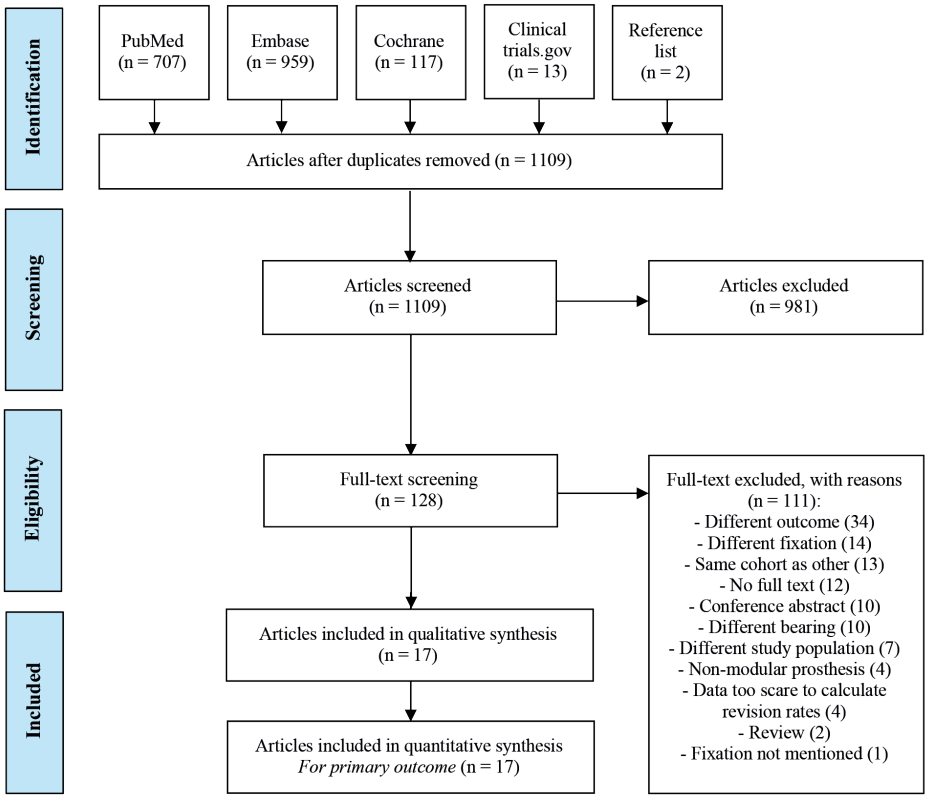

Figure 1. PRISMA flow chart of the article selection process

Study characteristics

All the selected studies were published between 2001 and 2021. The follow-up ranged from 1.0 to 16.5 years (weighted average of 5.52 years). A total of 38,772 primary THAs with a press-fit modular cup were included, 10,909 with a CoPE bearing (862 in RCTs, 134 in non-randomized comparative studies, 9,913 in registry studies) and 27,863 with a CoC bearing (984 in RCTs, 157 in non-randomized comparative studies, 26,722 in registry studies). The study characteristics of the included studies are shown in **Table 1**. A femoral head size of 28mm was used in all RCTs and cohort studies except two that combined 28mm and 32mm in both bearings. [33,35] The cup size was only reported in two studies: Kim et al. showed a mean cup size of 51.2mm (range, 48–54 mm) in both bearings and van Loon et al. showed a mean cup size of 52.1mm (SD 3.4) in CoPE and 53.6 (SD 3.5) in CoC. [41,49] Focusing on the sort of PE bearing, five (30%) studies used a conventional PE liner, one study (6%) a cross-linked liner, five studies (30%) a highly

cross-linked liner, five studies (30%) and ultra-high-molecular-weight liner, and one study (5%) used both conventional and highly cross-linked PE liners. A third-generation ceramic insert was used in eight studies (47%) and five studies (29%) used a fourth-generation ceramic insert. In four studies (24%) the generation and manufacturer of the ceramic insert were not mentioned.

A summary of all HRs and RRs of the primary and secondary outcomes is shown in **Table 1**.

Risk of bias

The results of the risk of bias assessment are shown in **Appendix 2** and **Appendix 3** from the perspective of the primary outcome. For the twelve RCTs included, the risk of bias was low in five studies, high in one study, and unclear in six studies. The high risk of bias in one study was due to a difference in the number of patients included in both groups after randomization and a high loss of follow-up. [33] The unclear risk of bias was mainly related to high loss to follow-up, selective reporting, and limited reporting of blinding and randomization methods. For the non-randomized comparative and registry studies, the main risk of bias was based on the lack of (reporting on) blinding, and not performing sample size calculation and for the registry studies, the high risk of indication bias was due to the methodological design of registry studies.

Qualitative analysis

The strength of evidence for the RCTs was low for the primary outcome and secondary outcomes loosening and infection, due to inconsistency and unclear risk of bias. For dislocation and postoperative periprosthetic fracture, the GRADE strength of evidence was moderate, due to the inconsistency of the included studies. For the non-randomized comparative studies group, the evidence for loosening, dislocation, and the postoperative periprosthetic fracture was very low due to their methodological design and selective reporting of these outcomes by only one study. The evidence of the registry studies was assessed as very low due to the high risk of bias and methodological design. The outcomes of the GRADE quality of evidence assessment are shown in **Table 2**.

Table 1. Characteristics of the included studies

Study	Bearing	Patients *n*	THAs *n*	Age *mean (SD)*	Female *n (%)*	BMI *mean (SD)*	Indication *n (%)*	Follow-up in years *mean (SD)*	Surgical approach *n (%)*	Manufacturer	Head size *n (%)*
RANDOMIZED CONTROLLED TRIALS											
Atrey (2018)	CoPE[a]	29	29	42.8 (6.9)	16 (55.2)	28.2 (5.2)	POA: 10 (34.5) SOA: 14 (48.3) PT: 5 (17.2)	16.5 (NR)	NR	Reflection, Smith&Nephew	28mm: 29 (100)
	CoC[h]	28	29	41.5 (8.9)	14 (50.0)	26.7 (6.6)	POA: 15 (51.7) SOA: 10 (34.5) PT: 4 (13.8)	16.8 (NR)	NR	Reflection, Smith&Nephew	28mm: 29 (100)
Beaupre (2015)	CoPE[b]	44	44	53.6 (6.5)	20 (45.5)	NR	POA: 10 (34.5)	10.0 (NR)	Post: 29 (65.9) Lat: 15 (34.1)	Secure Fit, Stryker	28mm: 40 (90.9) 32mm: 4 (9.1)
	CoC[h]	44	48	51.3 (6.9)	22 (45.8)	NR	POA: 10 (34.5)	10.0 (NR)	Post: 30 (62.5) Lat: 18 (17.5)	Secure Fit, Stryker	28mm: 9 (18.8)) 32mm: 39 (81.2)
Kim[#] (2013)	CoPE[c]	100	100	45.3 (NR)	34 (34.0)	23 (NR)	POA: 13 (13.0) SOA: 87 (87.0)	12.4 (NR)	Post: 100 (100)	Duraloc, DePuy	28mm: 100 (100)
	CoC[f]	100	100	45.3 (NR)	34 (34.0)	23 (NR)	POA: 13 (13.0) SOA: 87 (87.0)	12.4 (NR)	Post: 100 (100)	Duraloc, DePuy	28mm: 100 (100)
Cai (2012)	CoPE[d]	50	62	42.0 (10.6)	23 (46.0)	24.8 (4.1)	POA: 13 (21.0) SOA: 49 (79.0)	3.4 (NR)	Post: 62 (100)	T.O.P. press-fit porous-coated TiAl6V4	28mm: 62 (100)
	CoC[g]	43	51	42.1 (10.5)	18 (41.9)	24.6 (3.9)	POA: 11 (21.6) SOA: 40 (78.4)	3.4 (NR)	Post: 51 (100)	T.O.P. press-fit porous-coated TiAl6V4	36mm: 51 (100)
Amanatullah (2012)	CoPE[d]	146	161	54.7 (12.9)	62 (38.5)	28.0 (5.1)	POA or SOA (numbers NR)	5.0 (NR)	NR	Reflection, Smith&Nephew	28mm: 161 (100)
	CoC[h]	166	196	50.4 (12.8)	60 (36.1)	29.6 (12.4)	POA or SOA (numbers NR)	5.0 (NR)	NR	Reflection, Smith&Nephew	28mm: 61 (31.1) 32mm: 135 (68.9)

Table 1. Continued

Lewis (2010)	CoPE[d]	NR	26	42.8 (6.9)	NR	28.2 (5.2)	POA: 7 (26.9) SOA: 19 (73.1)	8.0 (NR)	Post: 26 (100)	Wright Medical Technology INC	28mm: 26 (100)
	CoC[h]	NR	30	41.5 (8.9)	NR	26.7 (6.6)	POA: 16 (53.3) SOA: 14 (46.7)	8.0 (NR)	Post: 30 (100)	Wright Medical Technology INC	28mm: 30 (100)
Hamilton (2010)	CoPE[c]	87	87	57.3 (NR)	40 (46.0)	NR	POA: 78 (89.7) SOA: 9 (10.3)	2.6 (NR)	Post: 87 (100)	Pinnacle, DePuy	28mm: 87 (100)
	CoC[g]	177	177	56.4 (NR)	87 (49.2)	NR	POA: 155 (87.6) SOA: 22 (12.4)	2.6 (NR)	Post: 177 (100)	Pinnacle, DePuy	28mm: 177 (100)
Pitto (2008)	CoPE[c]	20	20	66.1 (NR)	12 (60.0)	NR	POA: 20 (100)	1.0 (NR)	Lat: 20 (100)	Trilogy, Zimmer	28mm: 20 (100)
	CoC[f]	20	20	64.5 (NR)	13 (65.0)	NR	POA: 20 (100)	1.0 (NR)	Lat: 20 (100)	Trilogy, Zimmer	28mm: 20 (100)
Ochs* (2007)	CoPE[a]	31	31	69.2 (7.2)	NR (33.3)	NR	POA: NR (80.9) SOA: NR (19.1)	7.6 (6.5)	NR	Plasmacup press-fit cup, B.Braun-Aesculap	28mm: 31 (100)
	CoC[f]	35	35	56.0 (7.6)	NR (31.8)	NR	POA: NR (81.8) SOA: NR (18.2)	8.4 (7.2)	NR	Plasmacup press-fit cup, B.Braun-Aesculap	28mm: 35 (100)
Sonny Bal (2005)	CoPE[a]	241	250	60.9 (12.8)	133 (55.2)	NR	POA: 183 (73.2) SOA: 67 (26.8)	2.0 (NR)	NR	CeramTec AG, Plochingen, Germany	28mm: 250 (100)
	CoC[f]	238	250	55.0 (14.7)	112 (47.1)	NR	POA: 160 (64.0) SOA: 90 (36.0)	2.0 (NR)	NR	CeramTec AG, Plochingen, Germany	28mm: 250 (100)

Table 1. Continued

Pitto (2003)	CoPE[d]	27	27	NR	NR	NR	POA: 27 (100)	1.1 (NR)	NR	TiRC: Phönix, Brehm, Weisendorf, Germany	28mm: 27 (100)
	CoC[f]	23	23	NR	NR	NR	POA: 23 (100)	1.1 (NR)	NR	TiRC: Phönix, Brehm, Weisendorf, Germany	28mm: 23 (100)
Pitto (2001)	CoPE[a]	24	25	62 (4.5)	16 (66.7)	NR	POA: 25 (100)	5.0 (NR)	NR	TiRC: Phönix, Brehm, Weisendorf, Germany	28mm: 25 (100)
	CoC[f]	25	25	60 (5.5)	15 (60.0)	NR	POA: 25 (100)	5.0 (NR)	NR	TiRC: Phönix, Brehm, Weisendorf, Germany	28mm: 25 (100)
NON-RANDOMIZED COMPARATIVE											
van Loon[p] (2021)	CoPE[a]	27	27	64.2 (5.3)	21 (77.8)	27.6 (4.1)	POA: 23 (85.2) SOA: 4 (14.8)	10.0 (NR)	Lat: 27 (100)	EP-FIT PLUS, Smith&Nephew	28mm: 27 (100)
	CoC[g]	34	34	55.7 (8.5)	22 (64.7)	26.9 (4.1)	POA: 19 (55.9) SOA: 15 (44.1)	10.0 (NR)	Lat: 34 (100)	EP-FIT PLUS, Smith&Nephew	28mm: 34 (100)
Feng[r] (2019)	CoPE[c]	62	77	59 (NR)	33 (53.2)	23.2 (NR)	SOA: 77 (100) *all AVN*	7.2 (NR)	Post: 77 (100)	Pinnacle, DePuy	NR
	CoC[g]	71	93	51 (NR)	40 (56.3)	25.2 (NR)	SOA: 93 (100) *all AVN*	6.9 (NR)	Post: 93 (100)	Pinnacle, DePuy	NR
Schmidt[p] (2003)	CoPE[d]	30	30	60.0 (3.1)	18 (60.0)	25.1 (2.0)	POA, SOA and PT, numbers NR	5.6 (NR)	Lat: 30 (100)	TiRC: Phönix, Brehm, Weisendorf, Germany	28mm: 30 (100)
	CoC[f]	30	30	58.8 (3.3)	19 (63.3)	24.7 (2.3)	POA, SOA and PT, numbers NR	5.6 (NR)	Lat: 30 (100)	TiRC: Phönix, Brehm, Weisendorf, Germany	28mm: 30 (100)

Table 1. Continued

REGISTRY STUDIES											
Epinette (2016)	CoPE[c]	NR	5232	NR	NR	NR	NR	2.1 (NR)	NR	Trident, Stryker	</=32mm: 2521 (48.2) >32mm: 2711 (51.8)
	CoC[f]	NR	16182	NR	NR	NR	NR	3.8 (NR)	NR	Trident, Stryker	</=32mm: 13594 (84.0) >32mm: 2588 (16.0)
Jameson (2013)	CoPE[a,c]	NR	4681	NR	NR	NR	NR	5.0 (NR)	NR	Pinacle, DePuy	NR
	CoC[g]	NR	10540	NR	NR	NR	NR	5.0 (NR)	NR	Pinacle, DePuy	NR

Abbreviations: AVN: avascular necrosis; CoC: Ceramic-on-ceramic CoPE: Ceramic-on-Polyethylene; n = number; Lat: lateral; NR = not reported; POA = primary osteoarthritis; Post: posterior; PT = primary traumatic; SD = standard deviation; SOA = secondary osteoarthritis; THA = Total Hip Arthroplasty; TO = trochanteric osteotomy

** characteristics were reported at final follow-up instead of baseline*

 # Bilateral total hip arthroplasty

a: conventional PE liner, b: cross-linked PE liner, c: highly cross-linked PE liner, d: ultra-high-molecular-weight PE liner, e: sort of PE liner not specified, f: third generation ceramic bearing, g: fourth generation ceramic bearing, h: generation ceramic bearing not specified, p: prospective non-randomized comparative study, r: retrospective non-randomized comparative study

Note: numbers and percentages may not count up to total or 100% due to missing numbers

Table 2. Summary of Hazard Ratio for revision and Risk Ratios for complications of CoPE compared to CoC in modular primary total hip arthroplasty with a press-fit cup and qualitative analysis results

PRIMARY OUTCOME							
Complication	No. of studies	Study design	**Events CoPE** *n (%)*	**Events CoC** *n (%)*	**HR (95%CI)**	**Heterogeneity** I^2	**GRADE**
Revision	12	RCT	25 (2.9)	26 (2.6)	1.15 (0.71; 1.86)	0%	Low
	3	Non-randomized comp	4 (3.0)	2 (1.3)	1.79 (0.41; 7.79)	0%	Low
	2	Registry study	128 (1.3)	489 (1.82)	0.72 (0.53; 0.99)	61%	Very low
SECONDARY OUTCOMES*							
Complication	**No. of studies**	**Study design**	**Events CoPE** *n (%)*	**Events CoC** *n (%)*	**RR (95%CI)**	**Heterogeneity** I^2	**GRADE**
Loosening	6	RCT	5 (0.63)	7 (0.76)	0.78 (0.18; 3.32)	0%	Moderate
	1	Non-randomized comp	1 (0.75)	1 (0.64)	1.26 (0.08; 19.22)	Not applicable	Very low
Dislocation	7	RCT	31 (3.92)	28 (3.06)	1.37 (0.82; 2.29)	0%	Moderate
	1	Non-randomized comp	3 (2.24)	6 (3.82)	0.60 (0.16; 2.34)	Not applicable	Very low
Infection	5	RCT	5 (0.63)	9 (1.31)	0.68 (0.23; 1.97)	0%	Moderate
	2	Non-randomized comp	1 (0.75)	1 (0.64)	1.23(0.01; 129.56)	4%	Low
Postoperative periprosthetic fracture	3	RCT	2 (0.25)	9 (0.98)	0.29 (0.06; 1.31)	0%	Moderate
	1	Non-randomized comp	1 (0.75)	0 (0)	13.28 (0.02; 8452.09)	Not applicable	Very low

GRADE: High quality: Further research is very unlikely to change our confidence in the estimate of effect. There are sufficient data with narrow confidence intervals. There are no known or suspected reporting biases. Moderate quality: Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate; one of the domains is not met. Low quality: Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate; two of the domains are not met. Very low quality: Great uncertainty about the estimate; three of the domains are not met.
* Secondary outcomes were not reported separately per bearing by the included registry studies

Primary outcome: overall revision

The total number of revision procedures per study is shown in **Table 3**. The HR for revision of CoPE compared to CoC bearing, is shown in **Figure 2**. The pooled HR for revision was significant in registry studies, with a lower risk of revision in CoPE (HR 0.71 (95%CI 0.53; 0.99)). In RCTs and non-randomized comparative studies, the HR showed a non-significant lower risk of revision in CoC (respectively HR 1.15 (95%CI 0.71; 1.86) and HR 1.79 (95%CI 0.41; 7.79)).

Secondary outcomes: complications and reasons for revision

An overview of the surgical and postoperative complications and reasons for revision are shown in **Table 3** and **Appendix 4, Appendix 5, Appendix 6, and Appendix 7**. No registry studies mentioned the secondary outcomes separately per bearing and are therefore not reported for this study design. All outcomes (loosening, dislocation, infection postoperative periprosthetic fracture), showed no significant difference in the risk of revision. One study reported migration of components without loosening, with an incidence of 2.0% in CoC and 1.2% in CoPE. [33]

RCTs. [33,34] An incidence of PE wear of 13.8% and 0.6% respectively were observed, whereas the last-mentioned study also reported wear in 0.5% of the CoC THAs. One cohort study reported wear in CoPE with an incidence of 7.4%. [49] Fracture of the ceramic liner was reported during surgery in four RCTs with an incidence of respectively 2.0%, 1.0%, 0.6%, and 0.4%. [33,36,39,48] Fracture of ceramic components was seen in three RCTs. 33,34,39 One study showed an incidence of 3.4% in CoC of the ceramic head, one study showed an incidence of 0.6% of the ceramic liner, whereas the last study showed fractures of both the head and liner with an incidence of respectively 0.5% and 1.0% in CoC. [33,34,39] The last bearing-related complication was trunnionosis, which was seen in one RCT in CoC with an incidence of 3.4%. [34]

Bearing related complications or reasons for revision

The squeaking was described in three RCTs in CoC only with an incidence of respectively 13.0%, 3.9%, and 3.1%. [33,36,41] In one nonrandomized cohort study squeaking was reported with an incidence of 2.6% in CoPE and 8.6% in CoC. [38] Another component-related complication was wear, which was reported by two RCTs. [33,34] An incidence of PE wear of 13.8% and 0.6% respectively were observed, whereas the last-mentioned study also reported wear in 0.5% of the CoC THAs. One cohort study reported wear in CoPE with an incidence of 7.4%. [49] Fracture of the ceramic liner was reported during surgery in four RCTs with an incidence of respectively 2.0%, 1.0%, 0.6%, and 0.4%. [33,36,39,48] Fracture of ceramic components was seen in three RCTs. [33,34,39] One study showed an incidence of 3.4% in CoC of the ceramic head, one study showed an incidence of 0.6% of

the ceramic liner, whereas the last study showed fractures of both the head and liner with an incidence of respectively 0.5% and 1.0% in CoC. [33,34,39] The last bearing-related complication was trunnionosis, which was seen in one RCT in CoC with an incidence of 3.4%. [34]

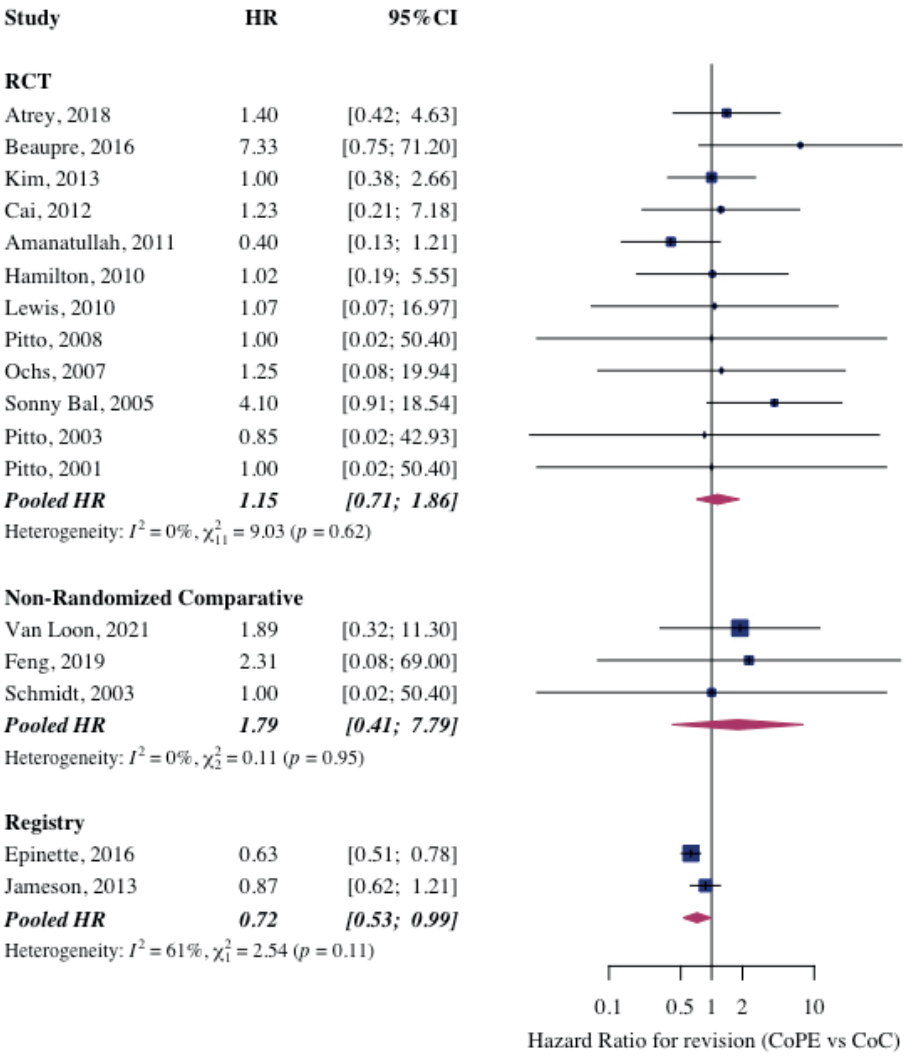

Figure 2. Hazard ratio (HR) for revision in modular primary total hip arthroplasty with a press-fit cup of CoPE compared to CoC bearing

Table 3. Complications during surgery, postoperative, and reasons for revision

Study	Bearing	Patients *n*	THAs *n*	Surgical complications *n (%)*	Post-operative complications *n (%)*	Number of revisions *n (%)*	Reasons for revision *n (%)*	Moment of revision
RANDOMIZED CONTROLLED TRIALS								
Atrey (2018)	CoPE[a]	29	29	NR	Wear: 4 (13.8) Pain: 1 (3.4)	5 (17.2)	Wear: 4 (13.8) Pain: 1 (3.4)	Mean 16 yr
	CoC[h]	28	29	NR	Aseptic loosening cup: 1 (3.4) Head fracture: 1 (3.4) Infection (septic): 1 (3.4) Trunnionosis: 1 (3.4)	4 (13.7)	Aseptic loosening cup: 1 (3.4) Head fracture: 1 (3.4) Infection (septic): 1 (3.4) Trunnionosis: 1 (3.4)	15 yr 14 yr 13 yr 14 yr
Beaupre (2015	CoPE[b]	44	44	NR	Dislocation: 5 (11.4)	3 (6.8)	Recurrent dislocation: 3 (6.8)	<5 yr (2x), 7yr
	CoC[h]	48	48	NR	Dislocation: 2 (4.2) Periprosthetic fracture: 1 (2.1)	0 (0)	-	NR
Kim[#] (2013)	CoPE[c]	100	100	NR	Dislocation: 1 (1.0)	1 (1.0)	Recurrent dislocation: 1 (1.0)	NR
	CoC[f]	100	100	Periprosthetic fracture: 2 (2.0)	Squeaking: 13 (13.0) Dislocation: 1 (1.0)	1 (1.0)	Recurrent dislocation: 1 (1.0)	NR
Cai (2012)	CoPE[d]	50	62	Periprosthetic fracture: 1 (1.6)	Osteolysis stem: 3 (4.8) Dislocation: 2 (3.2) Deep vein thrombosis: 1 (1.6) Leg length discrepancy: 1 (1.6)	3 (4.8)	Aseptic loosening cup: 1 (1.6) Leg length discrepancy: 1 (1.6) Recurrent dislocation: 1 (1.6)	NR
	CoC[g]	43	51	Liner fracture: 1 (2.0)	Squeaking: 2 (3.9) Delayed wound healing: 1 (1.9) Dislocation: 1 (1.9) Infection: 1 (1.9)	2 (3.9)	Infection: 1 (1.9) Recurrent dislocation: 1 (1.9)	NR

Table 3. Continued

Amanatullah (2012)	CoPE[d]	146	161	Periprosthetic fracture: 1 (0.6)	Heterotopic ossification: 41 (25.5) Dislocation: 9 (5.6) Trochanteric bursitis: 5 (3.1) Infection: 5 (3.1) Deep vein thrombosis: 2 (1.2) Migration: 2 (1.2) Pulmonary embolism: 1 (0.6) Leg length discrepancy: 1 (0.6) Wear: 1 (0.6)	3 (1.9)	Recurrent dislocation: 2 (1.2) Infection: 1 (0.6)	Before discharge, 5yr NR
	CoC[h]	166	196	Liner fracture: 2 (1.0) Periprosthetic fracture: 1 (0.5) Sciatic nerve injury: 1 (0.5)	Heterotopic ossification: 59 (30.1) Dislocation: 10 (5.6) Infection: 7 (3.6) Squeaking: 6 (3.1) Migration: 4 (2.0) Deep vein thrombosis: 3 (1.5) Pulmonary embolism: 2 (1.0) Liner fracture: 2 (1.0) Leg length discrepancy: 2 (1.0) Head fracture: 1 (0.5) Wear: 1 (0.5)	11 (5.6)	Recurrent dislocation: 4 (2.0) Aseptic loosening stem: 3 (1.5) Liner fracture: 2 (1.0) Head fracture: 1 (0.5) Infection: 1 (0.5)	3mo, 6mo, 1yr, 4yr NR 3 yr, 5 yr 2 yr 3 mo
Lewis (2010)	CoPE[d]	NR	26	Periprosthetic fracture: 2 (7.7)	NR	1 (3.8)	Pain: 1 (3.8)	6 yr
	CoC[h]	NR	30	Periprosthetic fracture: 1 (3.3)	Dislocation: 1 (3.3)	1 (3.3)	Recurrent dislocation: 1 (3.3)	4 yr
Hamilton (2010)	CoPE[c]	87	87	Periprosthetic fracture: 1 (1.1)	Delayed wound healing: 2 (2.3) Dislocation: 4 (4.6)	2 (2.3)	Recurrent dislocation: 2 (2.3)	NR
	CoC[g]	177	177	Periprosthetic fracture: 5 (2.8) Liner fracture: 1 (0.6) Nerve injury: 1 (0.6)	Delayed wound healing: 9 (7.7) Dislocation: 5 (2.8) Osteolysis stem: 3 (1.7) Infection: 2 (1.1) Liner fracture: 2 (1.1) Periprosthetic fracture: 2 (1.1)	5 (2.8)	Aseptic loosening stem: 2 (1.1) Liner fracture: 1 (0.6) Infection: 2 (1.1)	NR

Table 3. Continued

Pitto (2008)	CoPE[c]	20	20	NR	NR	0 (0)	-	NR
	CoC[f]	20	20	NR	NR	0 (0)	-	NR
Ochs* (2007)	CoPE[a]	31	31	NR	Femoral nerve weakness: 2 (6.5) Deep vein thrombosis: 1 (3.2)	1 (3.2)	Aseptic loosening cup: 1 (3.2)	1 week
	CoC[f]	35	35	NR	Dislocation: 1 (2.9) Infection: 1 (2.9)	1 (2.9)	Infection: 1 (2.9)	NR
Sonny Bal (2005)	CoPE[a]	241	250	NR	Dislocation: 10 (4.0) Deep vein thrombosis: 4 (1.6) Delayed wound healing: 4 (1.6) Leg length discrepancy: 2 (0.8) Periprosthetic fracture: 2 (0.8)	6 (2.4)	Recurrent dislocation: 5 (2.0) Aseptic loosening cup: 1 (0.4)	NR
	CoC[f]	238	250	Liner fracture: 1 (0.4)	Dislocation: 7 (2.8) Periprosthetic fracture: 6 (2.4) Delayed wound healing: 5 (2.0) Deep vein thrombosis: 4 (1.6)	1 (0.4)	Recurrent dislocation: 1 (0.4)	NR
Pitto (2003)	CoPE[d]	27	27	NR	NR	0 (0)	-	NR
	CoC[f]	23	23	NR	NR	0 (0)	-	NR
Pitto (2001)	CoPE[a]	24	25	NR	NR	0 (0)	-	NR
	CoC[f]	25	25	NR	NR	0 (0)	-	NR
NON-RANDOMIZED COMPARATIVE STUDIES								
van Loon[p] (2021)	CoPE[a]	27	27	Periprosthetic fracture: 1 (3.7)	Delayed wound healing: 2 (7.4) Peroneal nerve injury: 2 (7.4)	3 (11.1)	Wear: 2 (7.4) Aseptic loosening stem 1 (3.7)	NR
	CoC[g]	34	34	Periprosthetic fracture: 2 (25.8)	Delayed wound healing: 4 (11.7)	2 (5.9)	Aseptic loosening stem 1 (2.9) Infection (late): 1 (2.9)	NR
Feng[r] (2019)	CoPE[c]	62	77	NR	Dislocation: 3 (3.9) Squeaking: 2 (2.6) Periprosthetic fracture: 1 (1.3) Infection: 1 (1.3)	1 (1.3)	Periprosthetic fracture: 1 (1.3)	NR
	CoC[g]	71	93	NR	Squeaking: 8 (8.6) Dislocation: 6 (6.5)	0 (0)	-	N/A

Table 3. Continued

Schmidt[p] (2003)	CoPE[d]	30	30	NR	0 complications	0 (0)	-	N/A
	CoC[f]	30	30	NR	0 complications	0 (0)	-	N/A
REGISTRY STUDIES								
Epinette (2016)	CoPE[c]	NR	5232	NR	NR	46 (0.9)	Not specified	NR
	CoC[f]	NR	16182	NR	NR	273 (1.7)	Not specified	NR
Jameson (2013)	CoPE[a,c]	NR	4681	NR	NR	82 (1.8)	Not specified	NR
	CoC[g]	NR	10540	NR	NR	216 (2.1)	Not specified	NR

Abbreviations: CoC: Ceramic-on-ceramic CoPE: Ceramic-on-Polyethylene; n = number; NR = not reported; THA = Total Hip Arthroplasty;
** characteristics were reported at final follow-up instead of baseline*
 # Bilateral total hip arthroplasty
a: conventional PE liner, b: cross-linked PE liner, c: highly cross-linked PE liner, d: ultra-high-molecular-weight PE liner, e: sort of PE liner not specified, f: third generation ceramic bearing, g: fourth generation ceramic bearing, h: generation ceramic bearing not specified, p: prospective non-randomized comparative study, r: retrospective non-randomized comparative study
Note: numbers and percentages may not count up to total or 100% due to missing numbers

DISCUSSION

This systematic review and meta-analysis showed a significantly lower risk of cup revision in primary THA with a press-fit modular cup using CoPE bearing compared to CoC in registry studies, based on very low-quality GRADE evidence. The RCTs and non-randomized comparative studies showed no difference, based on low-quality GRADE evidence. Since this outcome is based on only two registry studies and RCTs and non-randomized comparative studies showed no difference, this result should be considered preliminary. In literature, four other systematic reviews comparing both bearings were identified and showed similar results. [18-21] However, these reviews investigated RCTs only, included fewer RCTs, or did not distinguish in fixation method. [18-21] The most recent review investigated only CoHXLPE bearing and included fewer studies but two different from our. [18] One of these studies used a zirconium head and the other a sandwich cup, making both studies not suitable for our inclusion. Registry studies did not split complications and reasons for revision and since this methodological study type was the only one showing a difference in overall revision, this could explain why our study showed no difference on the secondary outcomes: complications and reasons for revision. To our knowledge, this is the first systematic review focused on the revision between CoC and Co(HXL)PE bearing in press-fit cups only in THA.

Focused on loosening as a reason for revision, no significant differences were observed. The aforementioned systematic reviews supported this outcome by showing no difference in loosening as well. [18-21] Recent literature suggests that more early aseptic loosening occurs in CoC, due to the influence of the stiff bearing on osseointegration during the transition from primary to definitive stability. [5] In long-term, the main reason for revision in literature remains aseptic loosening based on wear-induced osteolysis of PE. [2] That no difference was found in this review could be attributed to the difference in follow-up time between studies.

Dislocation showed no significant difference in all study designs. In line with three of the abovementioned reviews that investigated dislocation, we found a trend of a lower risk of dislocation in CoC bearing in RCTs, which was not significant. [19-21] Most included studies reported the use of larger femoral head size in CoC, which is used more often in CoC due to the correlation of bigger head size with higher volumetric wear in CoPE. [50] A bigger head size increases the range of motion as well, which results in a lower chance of impingement and hereby fewer dislocations in CoC. [51] Nevertheless, the included studies showed a surprisingly high incidence of 28mm small heads being used, which might declare the high rates of dislocation in some of the studies. The highest RR of Beaupre et al. showed a lower risk of dislocation in CoC as well. [35] The

long-term follow-up and use of cross-linked PE instead of HXLPE in this study both increase the risk of wear and hereby the long-term risk of dislocation. [52] The difference between studies in follow-up time and types of PE inlay might be the reason why the RR of dislocation differed between studies and no difference was observed after pooling.

The infection showed no significant difference between bearings, which was supported by three of the abovementioned reviews that investigated infection. [19-21] A recent German registry study showed a significantly lower risk of revision for periprosthetic joint infection (PJI) at three years follow-up for CoC compared to CoPE using propensity score matching analysis. [53] Unfortunately, no crude data was available about the overall revision rates to include this study in our analysis. Nevertheless, their outcomes on infection as the reason for revision are important to keep in mind when choosing a bearing. In addition, Pitto et al. showed a lower risk of infection in CoC on long-term. [10] One of the theories to explain this difference is that higher hydrophilicity and wettability in CoC results in a lower bacterial attachment to the bearing. As mentioned in both studies, more long-term follow-up research and microbiologic data are needed to confirm the potential benefits of CoC on PJI in THA.

Postoperative periprosthetic fracture showed no difference between bearings, but a trend of a lower risk of periprosthetic fracture in CoPE. In literature, the higher incidence of wear-induced osteolysis and difference in the mechanical transmission of forces on the stem, are presumed to result in a different biologic response in a more elastic CoPE bearing, which might result in a lower risk of periprosthetic fracture. [54]

Focused on bearing-related complications, squeaking was mostly reported in CoC and widely differed between studies. This was supported by three of the previously mentioned systematic reviews investigating squeaking. [19-21] The difference between studies might be explained by the generation of the ceramic liner, since a third-generation ceramic liner showed an incidence of 13.0%, compared to a fourth-generation liner with an incidence of 3.9% and 2.6% in two studies. [36,38,41] A recent registry study comparing revisions between both generations showed six revisions (6.5%) in a third generation because of squeaking and zero out of 54 (0.0%) in a fourth-generation. [55] Several studies investigated the phenomenon of squeaking, but its etiology is still a point of discussion. One of the main reasons for squeaking to occur might be disruption of fluid lubrication, which can be caused by a lack of fluid or particles between the head and cup. [56] Factors influencing this process are patient factors, for example, BMI, implant characteristics, implant positioning, and biomechanical factors, like wear, extreme loading, or micro-fractures. [57,58] Although wear in CoC is limited, the fourth-generation ceramic bearings were invented to improve wear properties and improve its resistance against (micro-)

fractures, achieved using a slightly different alloy and a different manufacturing process. [57,59] Although squeaking is a multifactorial problem with a wide variation of incidence in literature, the improved features of the fourth-generation ceramics might declare the difference in the incidence of squeaking in our study.

Another bearing-related complication is a ceramic head or liner fracture, which was mostly seen in CoC, but only reported by a few studies. Although ceramic fracture is one of the greatest concerns of the use of this articulation, a recent meta-analysis showed that improvement of the ceramic leads to less ceramic fracture. [4] Compared to the incidence of wear as a complication of Co(HXL)PE, the incidence of both complications was more or less comparable. Although wear is improved by the process of (highly) cross-linking in CoPE bearing, CoC bearings hold a potential to decrease wear up to wear rates below 0.001 mm/year. [3] Wear was unfortunately only reported by two studies, in which the highest incidence was seen in a conventional PE liner with 16.5 years follow-up. [34] To adequately investigate ceramic fracture and PE wear, more long-term research is needed in the same sort of PE liners and same-generation ceramic bearings, since the incidence of both complications will increase over time.

Another important factor to keep in mind when choosing a bearing is the cost of CoC which is three times more expensive than CoPE. [35] In all studies, CoC was placed in younger patients, except for the study of Cai et al. [36] In addition, the prevalence of THA increases with a shift to a younger age, combined with a still increasing life expectancy. [60] Hereby, the performance of the implant needs to prove itself for a longer period and in more active younger people. This is comparable to the in vitro hip simulation study of De Fine et al., in which in the worst-case wear scenario CoC outstands CoHXLPE. [61] The abovementioned revision rates and complications need to be considered when choosing a bearing.

Strengths

This is to our knowledge the first review to report on press-fit cups in THA only. Moreover, it is the first review to report both RCTs and non-randomized comparative and registry studies on this subject. We used the PRISMA statement guidelines, Cochrane risk of bias assessment, MINORS risk of bias assessment, and the GRADE level of evidence tool to assess the quality of evidence, to provide a transparent method of reporting the best available evidence on this subject and provide a more objective interpretation of our results.

Limitations

The statistical heterogeneity of our results was high in registry studies due to big cohorts with small 95%CI and only two studies included. This resulted in an HR with a wide 95%CI which was slightly significant, which is important when interpreting this result. Clinical heterogeneity was seen due to several kinds of bias. An important limitation was the risk of lead time bias, due to differences in follow-up time between the different studies and this bias might be present between subjects in registry studies as well. This can influence the incidence of several complications or reasons for revision and more important, bearing-related complications like wear and ceramic fracture. This increases the risk of outcome bias as well, which is also increased since we combined all sorts of PE bearings, which can have an influence on the incidence of wear-related reasons for the revision. Another limitation was baseline imbalance since we were not able to perform correction for baseline characteristics, which can influence the incidence of complications and reasons for revision. Another potential difference in the baseline is an incidence of screw fixation, since several studies mentioned the option of potential screw fixation, without reporting the number of THAs placed with additional screws. [35,36,39,48] Another clinical limitation is that loosening was not split between the cup and stem in most studies, excluding analysis of potential differences between bearings. Methodological heterogeneity was seen in the included registry studies, since these only report on complications leading to revision, the total number of complications may be underestimated and can differ from other study designs. At last, reasons for revision in registry studies were often not broken down by bearing or fixation, limiting the amount of included registry studies.

The lower risk of overall revision in registry studies of primary THA with a press-fit modular cup using CoPE bearing compared to CoC should be considered preliminary since this outcome was just slightly significant, based on very quality low-quality GRADE evidence and based on only two studies with several limitations. Since no difference was observed in the other methodological designs and the separate reasons for revision showed no significant difference in all designs either, no preference for CoC or CoPE can be expressed, and therefore both seem suitable options based on the available literature.

More comparative long-term studies are needed to confirm the potential advantages of wear-reduction of both bearings since the currently available literature is limited.

Acknowledgments

We would like to thank F.A. van Etten-Jamaludin, clinical librarian, for the help with the literature search.

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APPENDICES

Appendix 1. Search Strategy

PubMed (Medline):

("Arthroplasty, Replacement, Hip"[Mesh] OR "Hip Prosthesis"[Mesh] OR THA[tiab]) OR (("Arthroplasty"[Mesh:NoExp] OR "Arthroplasty, Replacement"[Mesh] OR "Prostheses and Implants"[Mesh:NoExp] OR "Joint Prosthesis"[Mesh:NoExp] OR "Hip Prosthesis"[Mesh] OR arthroplast*[tiab] OR replacement*[tiab] OR prosthes*[tiab]) AND ("Hip Joint"[Mesh] OR "Hip"[Mesh] OR hip[tiab] OR hips[tiab])) AND ("Ceramics"[Mesh] OR ceramic*[tiab] OR alumina[tiab] OR CoC[tiab] OR biolox*[tiab]) AND ("Polyethylenes"[Mesh] OR polyethylene*[tiab] OR poly ethylene*[tiab] OR polytene*[tiab] OR polythene*[tiab] OR CoPE[tiab] OR CoHXLPE[tiab]) AND ("Treatment Outcome"[Mesh] OR "Prognosis"[Mesh:NoExp] OR aseptic[tiab] OR loosening[tiab] OR revision*[tiab] OR reoperat*[tiab] OR survival[tiab] OR failure*[tiab] OR complication*[tiab])

EMBASE (OVID):

#	Searches
1	arthroplasty/ or total arthroplasty/ or exp hip arthroplasty/ or replacement arthroplasty/ or exp hip replacement/ or exp "orthopedic prosthesis and orthosis"/ or joint prosthesis/ or exp hip prosthesis/ or (arthroplast* or replacement* or prosthes*).ti,ab,kw.
2	exp hip/ or (hip or hips).ti,ab,kw.
3	1 and 2
4	exp total hip prosthesis/ or THA.ti,ab,kw.
5	3 or 4
6	ceramics/ or ceramic prosthesis/
7	(ceramic* or alumina or CoC or biolox).ti,ab,kw.
8	6 or 7
9	polyethylene/ or polyethylene derivative/
10	(polyethylene* or poly ethylene* or polytene* or polythene* or CoPE or CoHXLPE).ti,ab,kw.
11	9 or 10
12	treatment outcome/ or exp treatment failure/ or prognosis/ or prosthesis complication/ or exp prosthesis loosening/
13	(aseptic or loosening or revision* or reoperat* or survival or failure* or complication*).ti,ab,kw.
14	12 or 13
15	5 and 8 and 11 and 14

Cochrane Library

ID	Search
#1	((arthroplast* or replacement* or prosthes*) and (hip*)):ti,ab,kw
#2	(THA):ti,ab,kw
#3	#1 or #2
#4	(ceramic* or alumina or CoC or biolox):ti,ab,kw
#5	(polyethylene* or poly ethylene* or polytene* or polythene* or CoPE or CoHXLPE):ti,ab,kw
#6	#3 and #4 and #5

ClinicalTrials.gov

hip arthroplasty | ceramic* or polyethylene*

Appendix 2. Quality assessment of risk of bias, summary of the included randomized controlled trials

Study	**Selection bias** Random sequence generation	**Selection bias** Allocation concealment	**Performance bias** Blinding of participants	**Detection bias** Blinding of primary outcome assessors	**Attrition bias** Incomplete primary outcome data	**Reporting bias** Selective reporting	**Other sources of bias** Funding, baseline characteristics of trial arms	**Key reasons for study considered at high risk of bias**
Atrey et al. (2018)	+	+	+	+	?	+	?	
Beaupre et al. (2016)	+	+	?	?	+	+	+	
Kim et al. (2013)	+	+	?	?	+	?	?	
Cai et al. (2012)	+	+	?	?	+	+	+	
Amanatullah et al. (2011)	+	+	?	+	−	?	?	Randomization using sealed envelopes, resulted in variation in number of cases per group (196 vs. 161), 38.4% loss to follow-up at 5-years
Hamilton et al. (2010)	+	+	?	?	+	?	+	
Lewis et al. (2010)	+	+	+	?	?	+	+	
Pitto et al. (2008)	+	+	?	?	?	?	?	
Ochs et al. (2007)	+	?	?	?	?	?	?	
Sonny Bal et al. (2005)	+	+	?	?	+	+	?	
Pitto et al. (2003)	?	?	?	?	+	+	?	
Pitto et al. (2001)	+	+	?	?	+	+	?	

Appendix 3. Quality assessment of risk of bias, summary of the included cohort and registry studies

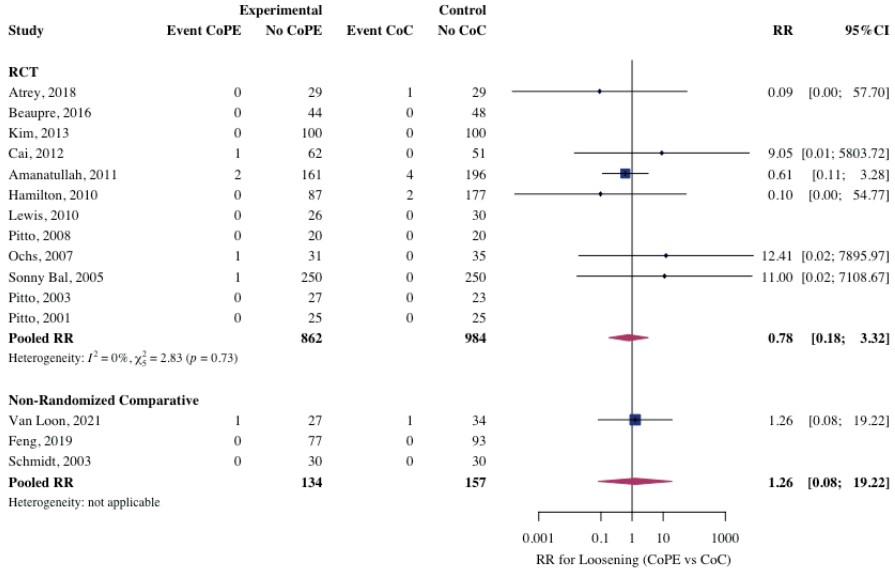
Study	Methodological items for non-randomized studies score (MINORS) *												Total #
	1	2	3	4	5	6	7	8	9	10	11	12	
RCT													
Atrey et al. (2018)	0	2	2	1	0	2	1	2	2	2	1	1	**16**
Beaupre et al. (2016)	2	2	2	2	0	2	1	0	2	2	2	2	**19**
Kim et al. (2013)	2	1	2	2	1	2	2	2	2	2	0	2	**20**
Cai et al. (2012)	2	2	2	2	0	2	0	0	2	2	2	1	**17**
Amanatullah et al. (2011)	2	2	2	1	1	2	1	0	2	2	1	1	**17**
Hamilton et al. (2010)	2	2	2	2	0	2	2	2	2	2	2	1	**21**
Lewis et al. (2010)	2	2	2	2	1	2	2	0	2	2	1	1	**19**
Pitto et al (2008)	2	2	2	1	1	2	1	2	2	2	2	1	**20**
Ochs et al. (2007)	2	2	2	1	1	2	1	0	2	2	1	1	**17**
Sonny Bal et al. (2005)	2	1	2	2	2	2	1	1	2	2	1	1	**19**
Pitto et al (2003)	2	1	2	1	0	2	1	0	2	2	0	1	**14**
Pitto et al (2001)	2	2	2	1	0	2	1	1	2	2	0	1	**16**
Non-randomized comparative studies													
van Loon et al. (2021)	2	2	2	1	0	2	1	0	2	2	1	2	**17**
Feng et al. (2019)	2	1	2	1	0	2	2	0	2	2	1	1	**16**
Schmidt et al. (2003)	1	2	2	2	1	2	2	0	2	2	2	1	**19**
Registry studies													
Epinette et al. (2016)	2	2	2	2	0	2	2	0	2	2	1	2	**19**
Jameson et al. (2013)	2	2	2	2	0	2	2	0	2	2	0	2	**18**

** The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate).*
 # The global ideal score being 16 for non-comparative studies and 24 for comparative studies

Appendix 3. Continued

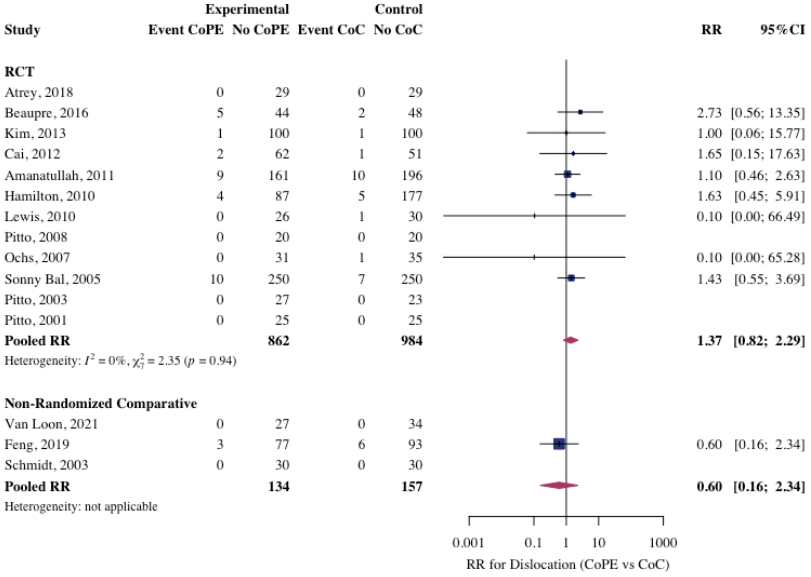
1. A clearly stated aim: the question addressed should be precise and relevant in the light of available literature
2. Inclusion of consecutive patients: all patients potentially fit for inclusion (satisfying the criteria for inclusion) have been included in the study during the study period (no exclusion or details about the reasons for exclusion)
3. Prospective collection of data: data were collected according to a protocol established before the beginning of the study
4. Endpoints appropriate to the aim of the study: unambiguous explanation of the criteria used to evaluate the main outcome which should be in accordance with the question addressed by the study. Also, the endpoints should be assessed on an intention-to-treat basis.
5. Unbiased assessment of the study endpoint: blind evaluation of objective endpoints and double-blind evaluation of subjective endpoints. Otherwise the reasons for not blinding should be stated
6. Follow-up period appropriate to the aim of the study: the follow-up should be sufficiently long to allow the assessment of the main endpoint and possible adverse events
7. Loss to follow up less than 5%: all patients should be included in the follow up. Otherwise, the proportion lost to follow up should not exceed the proportion experiencing the major endpoint
8. Prospective calculation of the study size: information of the size of detectable difference of interest with a calculation of 95% confidence interval, according to the expected incidence of the outcome event, and information about the level for statistical significance and estimates of power when comparing the outcomes
9. An adequate control group: having a gold standard diagnostic test or therapeutic intervention recognized as the optimal intervention according to the available published data
10. Contemporary groups: control and studied group should be managed during the same time period (no historical comparison)
11. Baseline equivalence of groups: the groups should be similar regarding the criteria other than the studied endpoints. Absence of confounding factors that could bias the interpretation of the results
12. Adequate statistical analyses: whether the statistics were in accordance with the type of study with calculation of confidence intervals or relative risk

Appendix 4. Relative risk (RR) for loosening of components during follow-up of CoPE compared to CoC in modular primary total hip arthroplasty with a press-fit cup



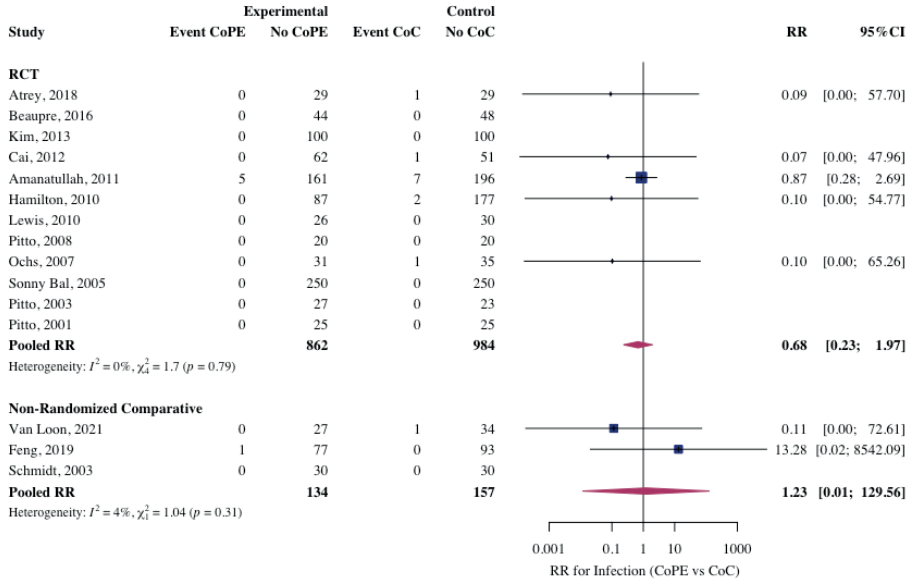
Note: not estimable RR due to no events in both subgroups are left empty

Appendix 5. Relative risk (RR) for dislocation during follow-up of CoPE compared to CoC in modular primary total hip arthroplasty with a press-fit cup



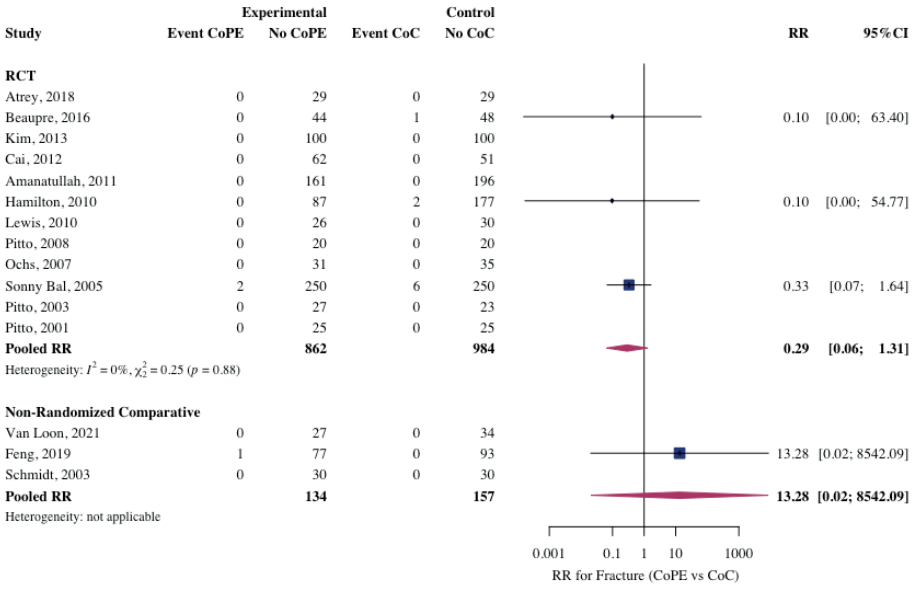
Note: not estimable RR due to no events in both subgroups are left empty

Appendix 6. Relative risk (RR) for infection during follow-up of CoPE compared to CoC in modular primary total hip arthroplasty with a press-fit cup



Note: not estimable RR due to no events in both subgroups are left empty

Appendix 7. Relative risk (RR) for postoperative periprosthetic fractures during follow-up of CoPE compared to CoC in modular primary total hip arthroplasty with a press-fit cup



Note: not estimable RR due to no events in both subgroups are left empty

Part 3

Influence of bearing choice on the primary stability and early revision rate of the press-fit acetabular component

Chapter 7

Ceramic-on-ceramic articulation in press-fit total hip arthroplasty as a potential reason for early failure, what about the survivors: a ten year follow-up

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International Orthopaedics (2021) 45(6):1447-1454

Abstract

Purpose: In press-fit total hip arthroplasty (THA), primary stability is needed to avoid micromotion and hereby aseptic loosening, the main reason for early revision. High aseptic loosening revision rates of the seleXys TH+ cup (Mathys Medical) with Ceramys ceramic-on-ceramic (CoC) bearing are seen in literature. Since CoC is presumed to overcome long-term wear-related revisions, the reason for early failure of this cup is important to clarify. The aim is to investigate its ten-year outcomes and differentiate between potential causes and identify risk factors for aseptic loosening.

Methods: Retrospective screening of a prospectively documented series of 315 THAs was performed. Primary outcome was cumulative incidence of cup revision due to aseptic loosening. Secondary outcomes were component revision and reoperation. Additionally, potential predictive factors for aseptic loosening were evaluated.

Results: At the median follow-up of 9.7 years [IQR 4.4; 10.3], 48 TH+ (15.2%) were revised due to aseptic loosening. Competing risk analysis showed a ten-year cumulative incidence of cup revision due to aseptic loosening of 15.6% (95% CI 12.0–20.2). Stabilization of early revision rates was observed, following a high rate of respectively 81.3% (n = 39) and 95.8% (n = 46) within the first two and three years. No significant predictive factors for aseptic loosening were found.

Conclusion: The ten-year results of seleXys TH+ cup with Ceramys CoC bearing showed an unacceptable high aseptic loosening rate, which stabilized over time after a high early failure incidence. This could be attributed to a problem with osseointegration during the transition of primary to definitive stability.

INTRODUCTION

During press-fit total hip arthroplasty (THA), the initial primary stability of the uncemented acetabular cup during implantation is the most important factor for survival of the implant. [1,2] Sufficient primary stability, avoiding micromotion, is needed to form fibrous or fibrocartilaginous tissue, and subsequently bony tissue, which causes osseointegration. [3] Micromotion jeopardizes osseointegration and therefore definitive secondary stability, which can cause aseptic loosening of the implant, one of the main reasons for early revision in THA. [4,5,6] Focusing on the long term, aseptic loosening caused by wear-induced osteolysis is regarded as the main limitation of prosthesis survival. [7,8] To overcome both of these problems, the search for the perfect implant still continues. Ceramic-on-ceramic (CoC) is one of the options to overcome wear and late revisions. This hard-on-hard bearing shows wear rates of 5 μm/year compared with 50 μm/year in ceramic-on-polyethylene (CoPE) bearing during 20 years. [9]

The press-fit seleXys TH+ cup (Mathys Medical) with a flattened pole and thick wall to prevent deformation was specially designed for both ceramic and polyethylene and metal-on-metal inlays. The titanium alloy cup has a surface of a corundum-blasted microstructure for optimal roughness (Ra 6–12 μm) with an equatorial macrostructure with tetrahedrons (TH+) with a height of 0.65 ± 0.1 mm. The initial fixation results from a 2-mm oversizing of the cup compared with the last used reamer size. Short-term results of this implant were previously published by our research group and showed a total of 17 (6.6%) aseptic revisions, with a 1-year survival of 87.4% (SE 3.8%) using the Kaplan-Meier method. [10] Another study showed a 2-year survival of 92% for the same acetabular cup with another ceramic bearing. [11] Mid-term analysis of the same implant showed an aseptic loosening rate of 10% after 48.6 months. [12] Since CoC seems to be a good option to overcome wear and late revisions, the reason for early failure of this type of implant is important to clarify. Although different theories were discussed in the three aforementioned studies, to our knowledge, no other study published long-term results after the osseointegration phase of three years. [10,11,12]

The aim of this study is to investigate the ten-year outcomes of this acetabular component and to differentiate between potential causes and identify risk factors for aseptic loosening. These outcomes can be helpful to contribute to the search of the perfect implant.

Our hypothesis was that the TH+ acetabular component would stabilize over time after a period of high early failure rate.

MATERIALS AND METHODS

Ethical approval

Ethical approval of this retrospective cohort study was given by the local ethics committee review board. The design and reporting were performed in accordance to the Strengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement. This research was conducted in regard of the Declaration of Helsinki.

Study design and setting

We retrospectively collected the ten-year follow-up outcomes of our prospectively documented series elective total hip arthroplasty procedures with a seleXys TH+ cup performed between January 2009 and October 2010. The short-term outcomes of this study were published earlier by our research group with a smaller cohort since not all patients had reached a meaningful minimal follow-up term. [10] All prospectively documented data were checked for correctness and complemented if necessary. The retrospective screening of patient records after ten years of follow-up was performed by a researcher (J.L.) that was not involved in the surgical process. When no additional information was available, patients were considered to be lost to follow-up. The last date of follow-up at the hospital, date of death or date of cup revision was used to calculate the follow-up time. All outcomes were checked by a second researcher (I.N.S.), also not involved in the surgical process.

Eligibility

All indications for THA included in this study were primary osteoarthritis (OA), secondary OA due to prior osteotomy, prior osteosynthesis or failure of conservative treatment of a hip fracture, rheumatoid arthritis, avascular necrosis or congenital dysplasia of the hip, and femoral fractures close to the joint. Indications were categorized as primary versus secondary OA or primary traumatic treatment. If initial cup stability was not achieved and additional screw fixation was needed, patients were excluded from this study.

Surgical procedure and product information

All procedures were performed at Tergooi using an anterolateral approach under standard antibiotic prophylaxis consisting of 2-grams cefazoline pre-operatively and two doses of 2-grams post-operatively. All THA procedures were performed by three experienced orthopaedic surgeons or under their direct supervision. The preparation of the acetabulum and femur was according to the surgical technique described by the manufacturer of the implants. After implantation of the seleXys TH+ cup (Mathys Medical), a Ceramys (Mathys Medical) ceramic insert of aluminia-thoughened zirconia (ATZ) was used in all cases. We used the Mathys CBH stem or Mathys offset stem, which is a forged rough-blasted surface

stem made of a titanium-aluminum-niobium alloy. If a longer stem was needed, we used a 20% longer Zimmer Alloclasic Zweymuller revision stem (Zimmer GmbH, Winterthur, Switzerland). Neck length was available in four different sizes to gain optimal stability of the whole implant. The aimed femoral offset and leg length were measured accordingly to be identical to the contralateral side. Ceramic heads of 32 mm were used in cups up to 50 mm and 36-mm heads for cups of 52 mm and larger, both with matching inlays. After surgery, standard post-operative rehabilitation under supervision of a physical therapist consisted of immediate full weight bearing with crutches for six weeks. Patients were assessed in a standard care follow-up protocol with X-rays at six, 12, 26, and 52 weeks post-surgery and yearly afterwards.

Outcomes

Patient demographics and implant information were recorded at baseline, including age, gender, indication for THA (primary or secondary OA or primary traumatic treatment), duration of surgery, cup size, head size, stem size, and complications during surgery and during post-operative follow-up.

The primary outcome was cup revision due to aseptic loosening. Progressive radiolucency with pain during weight bearing or clear displacement of more than 3–5 mm and inclination more than 3°–5° was defined as loosening. [13,14,15] If purulent discretion, positive cultures peri-operatively, or high suspicion due to high infection parameters (CRP or leukocytes) were seen, cases were defined as septic loosening.

Secondary outcomes were component revision, stated as a procedure by which the cup, the stem, or both were revised and re-operation for any reason. Additionally, potential predictive factors for revision due to aseptic loosening were evaluated.

Statistical analysis

Statistical analyses were performed with Statistical Package for Social Sciences (SPSS) version 26.0 (SPSS Inc. Chicago, IL). Distribution of continuous variables was assessed using the Shapiro-Wilk tests. Normally distributed variables are stated as medians with interquartile ranges (IQRs). Categorical data are described as numbers with accompanying proportions. Since follow-up was long and the population relatively old, both Kaplan-Meier (KM) and competing risk (CR) analyses (with death as competing risk) were performed to determine the survival of the cup. Survival of the cup was expressed as cumulative revision rates and cumulative revision incidence, respectively. The association between potential predictive factors and cup revision was assessed by use of univariate Cox regression analyses and expressed as hazard ratio (HR) with 95% confidence intervals (CIs). Statistical significance was considered if p-values were less than 0.05.

RESULTS

A total of 315 elective total hip procedures in 307 patients were performed. **Table 1** shows the baseline characteristics of the 307 patients and operative information of the 315 elective total hip procedures performed on these patients. Peri-operative complications occurred in seven cases (2.2%) with five fractures of the greater trochanter (1.6%), one fissure around the stem treated conservatively (0.3%), and one fausse route (0.3%) which was operated again the day after. Complications related to the surgical site were post-operative bleeding (0.3%), haematoma (0.6%), and persistent wound leakage (1.3%). Two patients (0.6%) died respectively 22 and 30 days after surgery after post-operative organ failure, due to deterioration of congestive heart failure in one case and acute kidney failure in the other patient. No ceramic liner fracture was observed in our study. Hip dislocation occurred in three cases (1.0%).

Table 1. Baseline characteristics and operative information of the 315 elective total hip procedures performed on 307 THA patient.

Characteristic	Outcome
Gender, n (%)	
• Female	216 (68.6)
• Male	99 (31.4)
Age at operation in years, median [IQR]	71 [64; 77]
Indication, n (%)	
• Primary OA	274 (86.9)
• Secondary OA	37 (11.7)
• Primary traumatic treatment	4 (1.3)
Operation time in minutes, median [IQR]	55 [43; 69]
Cup size in mm, median [IQR]	52 [52; 54]
Head size in mm, n (%)	
• 32	77 (24.4)
• 36	238 (75.6)
Stem size, median [IQR]	5 [4; 6]
Stem type, n (%)	
• Mathys CBH	297 (94.3)
• Mathys CBH Offset	14 (4.4)
• Alloclassic Zweymuller revision stem	4 (1.3)
Neck length, n (%)	
• Small	129 (41.0)
• Medium	120 (38.1)
• Large	65 (20.6)
• Extra-large	1 (0.3)

Primary outcome

Competing risk analysis demonstrated a 10-year cumulative incidence of cup revision, due to aseptic loosening, of 15.6% (95% CI 12.0–20.2). A total of 12 cases (3.8%) were lost to follow-up, and 57 died during follow-up (18.1%). (**Figure 1**) With a median follow-up of 9.7 years (IQR 4.4; 10.3), a total of 48 TH+ (15.2%) were revised due to aseptic loosening. In five cases (1.6%), the stem was revised due to aseptic loosening as well. Follow-up time ranged from one month up to 11 years. The median time point of cup revision was 15.8 months (IQR 10.3; 22.9). Respectively, 81.3% (n = 39) and 95.8% (n = 46) of all cup revisions for aseptic loosening were performed within the first two and three years. One cup was revised after 50 months following ongoing complaints two years post-surgery. A bone scintigraphy performed just before revision confirmed aseptic loosening. The second late revision was performed 9.0 years post-surgery. This patient presented with complaints three years earlier showing migration of the cup on X-ray. Revision was postponed due to mild complaints in preference of the patient. All retrieved cups showed a lack of bony ingrowth on the implant. **Figure 2** displays an example of aseptic loosening in our study.

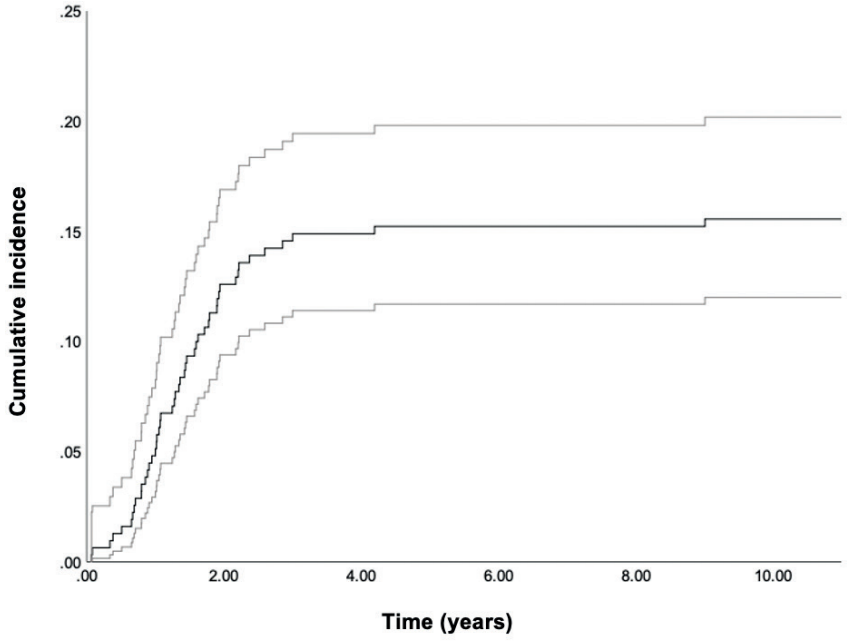

Figure 1. Cumulative incidence of cup revision over time, with upper and lower limits of 95%CI.

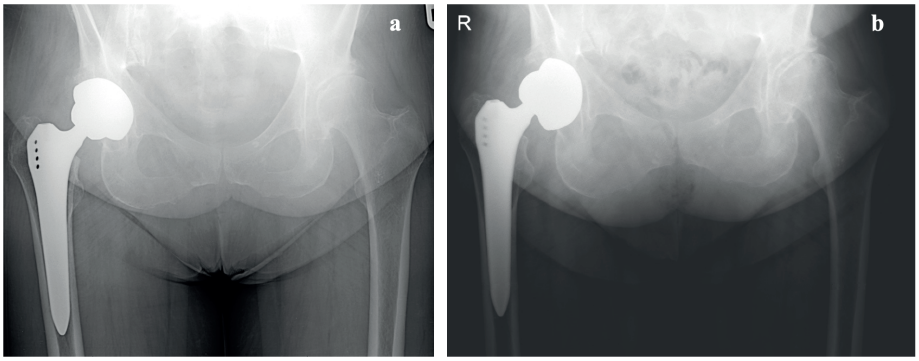

Figure 2. Example of a case with aseptic loosening. **a.** Direct postoperative X-ray **b.** X-ray at 9 months follow-up with clear loosening of the cup.

Secondary outcomes

Cumulative revision rates at ten-year follow-up are shown in **Table 2**. Component revision was performed in 56 (18.8%) patients. A total of 45 (14.2%) cup revisions were performed of which 43 (13.6%) due to aseptic loosening and two cases (0.6%) due to infection. Three stem revisions (1.0%) were performed due to aseptic loosening. Both the stem and cup were revised in eight cases (2.6%) with five cases (1.6%) due to aseptic loosening and three resection arthroplasties according to Girdlestone (1.0%) due to infection.

In 62 cases (20.8%), any re-operation was performed. In addition to the 56 component revisions, five periprosthetic fractures (1.6%) needed re-operation, and one exploration without intervention (0.3%) was performed due to complaints of inexplicable pain.

Univariate Cox regression analyses for determining predictive factors for revision due to aseptic loosening showed no significant outcomes as presented in **Table 3**.

Table 2. Cumulative revision rates in % (95% CI) after ten-years follow-up for all endpoints; using Kaplan-Meier analysis; n = number of events.

Endpoint at ten-years follow-up	n	Cumulative ten-years revision rate in % (with 95%CI)
Cup revision (aseptic loosening)	48	16.1% (12.0-20.2)
Component revision	56	18.8% (14.3-23.3)
Reoperation	62	20.8% (16.1-20.8)

Table 3. Hazard Ratios (HR) for potential predictive factors for cup revision due to aseptic loosening (with 95% CI).

Predictive factor	Hazard ratio (with 95%CI)	p-value
Male gender	0.87 (0.46-1.64)	0.66
Age	1.24 (0.69-2.22)	0.48
Primary vs. secondary OA	2.07 (0.64-6.67)	0.22
Cup size	1.02 (0.92-1.13)	0.71
Stem size	0.88 (0.74-1.05)	0.15
Head size (36 vs. 32)	0.91 (0.48-1.71)	0.76

DISCUSSION

The main finding of this 10-year follow-up retrospective cohort study of 315 THA with the seleXys TH+ acetabular cup (Mathys Medical) with a ceramic-on-ceramic bearing is an unacceptable high cumulative revision incidence (15.2%) due to aseptic loosening, which stabilizes over time after a period of high early failure. Although this cup is withdrawn from the market, the reason for failure still remains unclear. This outcome confirms our hypothesis and is consistent with a same trend in literature, where revision rates of 8% after two-year follow-up and 10% after 48.6 months are shown. [11,12] Revision due to aseptic loosening was seen after a median of 1.32 years (0.86–1.90) with 96% revised within three-year follow-up. Two additional cases showed complaints and signs of aseptic loosening long before revision. Our main outcome is less likely to be due to a problem with the primary stability since the initial reaming and press-fit feeling during surgery were satisfactory and comparable with other designs. This indicates a problem with subsequent transition from primary to definitive stability by osseointegration.

Our theory is that after implantation of the cup, primary stability, mainly obtained by press-fit, decreases over time. Subsequent transition to secondary stability is achieved by an increase in osseointegration, which is influenced by several factors. These processes can initially result in a decrease of the overall stability of the cup, which can bring the implant at risk for loosening if osseointegration is threatened. An increase of overall stability to the definitive stability of the implant is obtained when osseointegration becomes sufficient. This theory was stated before by our research group and is visualized in **Figure 3**. [10]

Several studies in literature could confirm this theory using radiostereometric analysis (RSA) measuring migration by translation and rotation, which is observed mostly in the first six months post-operatively and stabilizes in two to three years post-operatively by osseointegration. [16,17,18,19,20] These results are supported by studies measuring periacetabular bone mineral density (BMD), which changes during osseointegration, showing loss of BMD in the first six months after surgery and restores to baseline in at least two years. [21,22,23] Brodt et al. stated that a limitation of failure of the TH+ to the period of osseointegration could be ruled out. [12] Since the period of RSA migration and change of BMD is covering the majority of aseptic loosening in our study, it refutes the statement of Brodt et al. and funds our theory of a problem with osseointegration. [12]

Osseointegration can be threatened by several factors. For example, implant design, by the biocompatibility, microscopic structure, and macroscopic design of the cup. The seleXys TH+ cup has a titanium alloy, which has good biocompatibility with bone. [24] The microscopic texture is a corundum blasted roughened surface which has a highly osteoconductive nature. [25] Furthermore, the macroscopic cup design has a greater influence on stability than surface modification if a rough surface is chosen. [26] The macroscopic cup design of the TH+ has tetrahedrons with a height of 0.65 ± 0.1 mm on the peripheral ring, as shown in **Figure 4**.

Literature has shown that macroscopic spikes in this area decrease primary stability and since the load on the implant is transferred to this acetabular rim, the TH+ becomes more vulnerable to loosening. [27,28] The Allofit cup (Zimmer) has the same cup design, except for comparable shaped smaller teeth of 0.4–0.6 mm height on the whole surface of the cup, as shown in **Figure 4**. This cup shows an 11-year survival rate of 98% with only one aseptic acetabular loosening. [29]

Another specific feature of the TH+ design is that the rim protrudes 4 mm from the acetabulum. This could lead to impingement between the cup and neck and can provoke loosening during transition from primary to secondary stability. A large cohort study of different retrieved cup designs showed that rim impingement occurs in 56% of the implants with a higher occurrence among components with an elevated rim, making it unlikely that rim impingement would not occur in the TH+. [30] Brodt et al. compared the TH+ with a control group with a Cerafit-R cup (Ceraver, Roissy, France), which had the same lateral overlap of 4 mm without a high rate of aseptic loosening, as visualized in **Figure 4**. [12] Since the impingement force gets transferred to the bone-implant interface through the bearing and only leads to aseptic loosening in the TH+ cup and not in comparable cup designs, it becomes more likely that one of the reasons of failure are the characteristic bigger teeth of tetrahedrons only located at the peripheral rim.

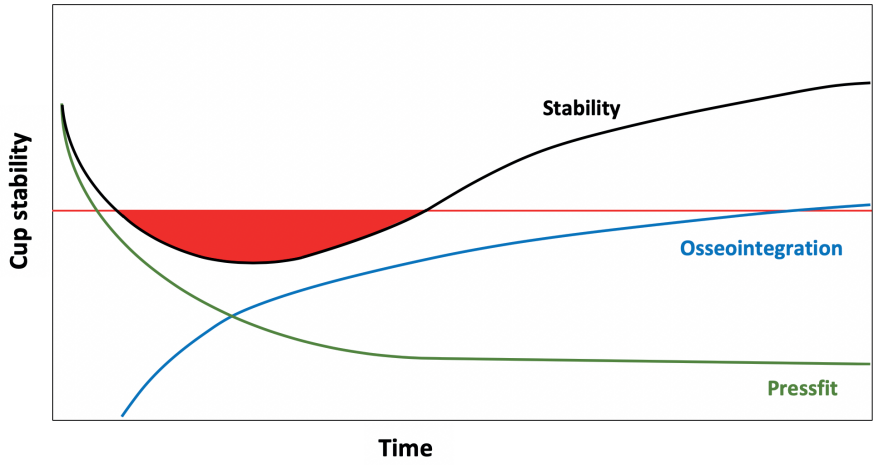

Figure 3. Distribution of primary and secondary stability over time. The minimum stability needed for safe fixation is indicated with the red line. In the red area the cup is at risk for loosening if transition from pressfit to definitive stability by osseointegration is jeopardized.

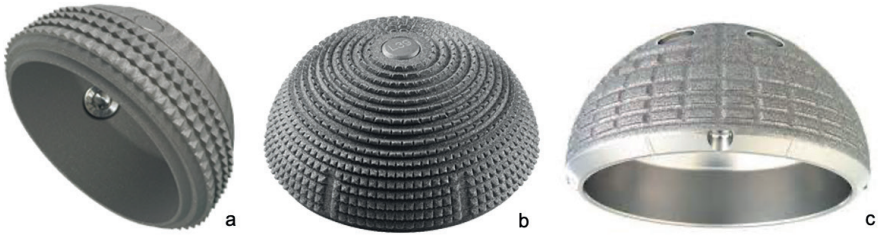

Figure 4. Macroscopic cup design of the **a**. SeleXys TH+ (Mathys Medical) **b**. Allofit (Zimmer) **c**. Cerafit-R (Ceraver).

The bearing can influence transition to definitive stability by its friction and stiffness. CoC bearings have the lowest friction between the head and cup compared with all other articulations in several biomechanical studies, excluding this as a potential reason for bone-implant interface failure. [31, 32] The total stiffness of the implant can be raised by a ceramic bearing. As a result, the forces of normal weightbearing and rim impingement get less absorbed by the coupling and implant than in CoPE and get transferred to the bone-implant interface. This causes shear forces which jeopardize the initial press-fit and hamper osseointegration. Several studies mentioned that hard bearings like CoC might have an influence on the transition to definitive stability by osseointegration, but there is still a lack of evidence. [33,34,35] Biomechanical analysis of several implants showed that the combination of the TH+ with a Ceramys inlay is the

stiffest. [36] Ilchmann et al. showed an 8% revision rate at two years of the TH+ with a much lower stiffness Bionit ceramic inlay, and this inlay had good mid-term results with different cups with a revision rate of 1.4% and 1.0%; thus, the loosening in the study of Ilchmann will probably be due to the cup. [37,38] Our higher two-year revision rate of 12.4% indicates that the stiffness can be a reason to explain the difference in survival. However, the study of Brodt et al. showed that half of their revisions were a TH+ with a polyethylene liner. RSA showed that another CoC bearing compared with MoPE had no difference in migration after two years. [39] Since these results were only seen in the aforementioned two studies with a small number of patients, their outcomes support that the problem of the high aseptic loosening rate of the TH+ is multifactorial and the stiff ceramic bearing is one of the main reasons.

Other factors than the implant or bearing are surgical technique, the status of the implant bed bone quality, undisturbed healing phase, loading conditions, and patient-specific conditions like age, comorbidity, medication, or intoxications. [40] Patient-related factors showed no differences in our short-term follow-up study when compared with an equally matched group with another cup with CoC bearing. In this study, the same patients were included and the same experienced surgeons used the same approach with the same rehabilitation program for all patients. Even though patient-related factors were not the main focus of this study, and more power might be needed to show significant differences, these outcomes indicate that it is more likely that the implant and its bearing are the reason for aseptic loosening.

Focusing on the long-term survival rate of our ten-year study of CoC bearing in THA, a revision rate of 18.8% was observed, resulting in a survival rate of 82.2%. In literature, divergent survival rates of CoC on long-term are observed, with a 15-year follow-up study showing a survival rate of 92%, whereas another 20-year follow-up study showed a survival rate of 99.7%. [41, 42] Our higher survival rates can be explained by the fact that our cohort showed an extremely high early revision rate, since stabilization of revision procedures was observed, with 95.8% (n = 46) of the revisions performed in the first three years.

Based on the outcomes of this study complemented with available literature, we believe that the macroscopic cup design with big tetrahedrons only at the peripheral rim together with stiff Ceramys bearing of the TH+ could be the main reasons for aseptic loosening. These factors can make the implant vulnerable for loosening due to shear forces on the bone-implant interface in combination with loss of stability and may interfere with the process of osseointegration. This can reduce bony ingrowth and thus long-term stability, causing migration and aseptic loosening on both the short and long

term. [43] Larger cohorts or RSA studies are needed to confirm the role of bearings on primary stability, osseointegration, and revision in THA.

CONCLUSIONS

The 10-year results of seleXys TH+ cup with Ceramys CoC bearing showed an unacceptable high aseptic loosening rate, which stabilized over time after a high early failure incidence. This could be attributed to a problem with osseointegration during the transition of primary to definitive stability.

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7

Chapter 8

Higher risk of 2-year cup revision of ceramic-on-ceramic versus ceramic-on-polyethylene bearing: analysis of 33,454 primary press-fit total hip arthroplasties registered in the Dutch Arthroplasty Register (LROI)

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HIP International (2022) 00(0) ; 1-8

Abstract

Background and purpose: The influence of bearing on short-term revision in press-fit total hip arthroplasty (THA) remains under-reported. The aim of this study was to describe 2-year cup revision rates of ceramic-on-ceramic (CoC) and ceramic-on-polyethylene (CoPE).

Patients and methods: Primary press-fit THAs with one of the three most used cups available with both CoC or CoPE bearing recorded in the Dutch Arthroplasty Register (LROI) were included (2007–2019). Primary outcome was 2-year cup revision for all reasons. Secondary outcomes were: reasons for revision, incidence of different revision procedures and use of both bearings over time.

Results: 2-year Kaplan-Meier cup revision rate in 33,454 THAs (12,535 CoC; 20,919 CoPE) showed a higher rate in CoC (0.67% [95% CI, 0.54–0.81]) compared to CoPE (0.44% [95% CI, 0.34–0.54]) (p = 0.004). Correction for confounders (age, gender, cup type, head size) resulted in a hazard ratio (HR) of 0.64 [95%CI, 0.48–0.87] (p = 0.019). Reasons for cup revision differed only by more cup revision due to loosening in CoC (26.2% vs.1 3.2%) (p = 0.030). For aseptic loosening a revision rate of 0.153% [95% CI, 0.075–0.231] was seen in CoC and 0.058% [95%CI 0.019–0.097] in CoPE (p = 0.007). Correction for head size resulted in a HR of 0.475 [95% CI, 0.197–1.141] (p = 0.096). Incidence of different revision procedures did not differ between bearings. Over time the use of CoPE has increased and CoC decreased.

Conclusions: A higher 2-year cup revision rate in press-fit THA was observed in CoC compared to CoPE. Cup loosening was the only significantly different reason for revision and seen more often in CoC and mostly aseptic. Future randomized controlled trials need to confirm causality, since the early cup revision data provided has the potential to be useful when choosing the bearing in press-fit THA, when combined with other factors like bone quality and patient and implant characteristics.

INTRODUCTION

The literature suggests that the main reason for late revisions in press-fit total hip arthroplasty (THA) is aseptic loosening of the cup caused by wear-induced osteolysis of polyethylene (PE) liners. [1-7] Despite the process of crosslinking to improve wear rates, ceramic-on-ceramic (CoC) still remains one of the best options to overcome liner wear. CoC shows wear rates below 0.001 mm/year compared to 0.072 mm/year in conventional ceramic-on-polyethylene (CoPE), 0.042 in metal-on-highly cross-linked PE (MoHXLPE) and 0.030 mm/year in ceramic-on-highly cross-linked PE (CoHXLPE). [8] Despite this, combinations of polyethylene liners with a ceramic head remain the most used bearing in THA in The Netherlands. [9] The influence of bearing on infection, dislocation and aseptic loosening in explanations of early revision of the cup remains underreported. [1,7,10] No differences in periprosthetic joint infection between bearings were observed at 6 months; nevertheless, at 15 years significantly less infections were seen in CoC. [11] Revision because of dislocation was seen less in CoC compared to CoPE at 9 years, due to a bigger head size in CoC. [12] Focusing on aseptic loosening of the cup, higher early revision rates in CoC are seen, which might be caused by the bearing itself. [13] In stiff CoC bearings, a less physiologic load transfer to the bone-implant interface is seen, resulting in increased micromotion. [14,15] This jeopardises osseointegration and following transition to secondary stability due to failure of ingrowth and can cause aseptic loosening of the cup. Evidence of hard-onhard bearings on this process is still limited. [16,17] While life expectancy and prevalence of THA increase, there has been a shift to younger age groups of patient over the last decades. [18] This emphasizes the need for research to find an implant with low wear and complication rates and long survival.

Our primary goal was to describe the 2-year cup revision rates of CoC and CoPE. Following that, the reasons for revision, incidence of different revision procedures and use of both bearings over time will be described.

Our hypothesis was that a higher early revision rate may be observed in CoC compared to CoPE. We expect that reasons for revision will differ between both groups, with more aseptic cup loosening in CoC, and a decrease in use of CoC over time.

MATERIALS AND METHODS

Data sources

The Dutch Arthroplasty Register (LROI) is a nationwide population-based registry that has recorded information on joint arthroplasties in the Netherlands since 2007. It was

initiated by the Netherlands Orthopedic Association (NOV) and had a completeness up to 99% for primary

THAs and 98% for hip revision arthroplasties in 2020. [19] The LROI database provides information on patient characteristics, surgical procedure and prosthesis characteristics, registered by all the hospitals in The Netherlands at the time of the primary operation by barcode scanning. The information about the prosthesis characteristics is supplied by implant manufacturers and distributors in The Netherlands, using a registration form. The vital status of all patients is obtained from Vektis, the national health insurance database in The Netherlands. An opt-out system is used by the LROI to obtain informed consent by patients.

Data collection and patients

Eligible patients were registered in the LROI as having received a primary press-fit THA with either a CoC or CoPE bearing, from 2007 until the end of the follow-up period on 31 December 2019. Only the 3 most frequently implanted cup types available with both CoC and CoPE bearing were selected, since a selection of more cups would have resulted in more heterogeneity in cup type and thereby statistically may have interfered with our goal to analyse the effect of bearing type on outcomes. Moreover, most cup types registered in the LROI are not available with both CoC and CoPE bearing. The indications for THA in this study were primary osteoarthritis (OA), osteonecrosis, acute femoral neck fracture and secondary osteoarthritis due to hip dysplasia. All press-fit THAs included for this study were defined as a procedure in which the cup was a press-fit uncemented implant, with every conventional stem. Since polyethylene liners are mainly differentiated by their wear characteristics, which will not occur within a 2-year follow-up, all kinds of liners, either conventional, (highly) cross-linked or other PE based liners, were amalgamated into 1 group, named as CoPE throughout this paper. The patient demographics recorded were age, gender, American Society of Anesthesiologists (ASA) score, body mass index (BMI), indication for THA (categorized as primary OA or other) and prior operation to the hip. Prosthesis characteristics recorded were cup size, head size, stem size, and surgical approach. Charnley Classification and smoking were also recorded, but only recorded in the LROI since 2014. We chose a minimal observation period of 2 years as the cut off point for revision rate, as previous radiostereometric analysis (RSA) studies suggest that early cup migration, which can result in loosening, is mostly seen in the first 6 months after implantation and stabilises within 2–3 years. [20,21]

Primary outcome

Primary outcome was the early cup revision rate for all reasons within the first 2 years after implantation. This outcome was analyzed when comparing CoC with CoPE in the

3 most used cup types available with both CoC and CoPE bearing in the LROI. When indicated, this outcome was corrected for patient factors (age, ASA score, gender), indication for surgery, surgical approach, cup type, cup size or head size. Since a minimal available follow-up of 2 years was necessary for this outcome, only those THAs implanted from the beginning of the LROI in 2007 until 31 December 2017 were selected for this research question.

Secondary outcomes

Secondary outcomes were reasons for early cup revision, incidence of revision procedures performed and use of both bearings over time from 2007 till 2019. Separately from the reasons for early cup revision, the 2-year revision rate for aseptic loosening of the cup was calculated. Aseptic cup revision was defined as a procedure where at least the cup was exchanged or removed, without signs of infection as stated in the LROI. When a revision of the cup was performed, this procedure was scored in the LROI as either an isolated cup revision, total revision or resection arthroplasty according to Girdlestone. The aforementioned secondary outcomes were compared between CoC and CoPE in the 3 most used cup types available with both CoC and CoPE bearing in the LROI.

Statistical analysis

Revision of the cup for all reasons was the endpoint of the primary analysis. 2-year revision rates were calculated for both CoC and CoPE using Kaplan-Meier analysis, as mortality was not considered a competing risk at this short term. [21] Comparison of the revision rates was performed by use of a Log Rank test. Crude as well as multivariable Cox proportional Hazard models were used to calculate Hazard Ratios (with 95% confidence interval [CI]) for early revision of CoPE compared to CoC. The following confounders were entered into our analysis: age; gender; indication for surgery (OA, osteonecrosis, acute femoral fracture, hip dysplasia); cup size; and head size. For all added covariates, proportional hazards assumption was visually assessed by use of log-minus-log curves. [23] For secondary outcomes the reasons for early cup revision and the type of revision procedures performed if early cup revision was done, were expressed in numbers with accompanying proportions. This was compared between the groups using chi square tests. Separately, aseptic loosening of the cup as reason for early revision was considered endpoint in the secondary analysis. As described for the primary analysis, 2-year revision rates were calculated and compared by use of a Log Rank test and Cox proportional Hazard model. A p-value <0.05 was considered significant. Yearly numbers of the CoC and CoPE bearings were described to assess changes over time. Statistical analyses were performed with Statistical Package for Social Sciences (SPSS) version 26.0 (IBM Corp., Armonk, New York, USA).

Ethical standards

The dataset and analysis were performed in compliance with the standards of the LROI regulation on research and registry data. The design and reporting of this study were done in accordance with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement. This research was in compliance with the Helsinki Declaration.

Methodological safeguards to prevent bias

Only the data of the patients meeting our inclusion criteria were provided to our research team by the LROI. We analyzed the data blinded. Cups were categorized in cup A, B and C, based on the three most used implant types available in the LROI with both CoC and CoPE bearing. Unblinding for manufacturer of the cups was performed after the writing of the results section.

RESULTS

From 2007 to 2019 a total of 326,606 THAs were registered in the LROI. In 97,013 THAs a press-fit cup was implanted with either a CoC (N = 17,197) or CoPE (N = 79,816) bearing and reached a 2-year follow-up (2007–2017). A total of 33,454 of these THAs used one of the three most used cup types available with both CoC and CoPE bearing. This group included 12,535 CoC and 20,919 CoPE THAs. The baseline characteristics of these procedures are shown in **Table 1**.

Focused on 2-year cup revision due to all reasons, the overall 2-year cumulative cup revision rate was 0.53% [95% confidence interval (CI), 0.45–0.60]. Pooled analysis for CoC and CoPE was performed since no significant interaction between bearing and cup type was observed. A total of 84 CoC bearing THAs were revised at 2 years, resulting in a revision rate of 0.67% [95% CI, 0.54–0.81). In CoPE 91 revisions were performed and a revision rate of 0.44% [95% CI, 0.34–0.54) was observed. The results of the Kaplan-Meier analysis are shown in **Figure 1**. This resulted in a significantly lower hazard of early revision in CoPE (hazard ratio [HR] 0.65 [96% CI, 0.48–0.87]) (p = 0.004). After adjustment for confounders (age, gender, cup type, head size) this outcome remained significant (HR 0.64 [95% CI, 0.44–0.93]) (p = 0.019) in favour of CoPE over CoC.

Table 1. Baseline characteristics of patients with press-fit THA performed from 2007 to 2017 in The Netherlands with 1 of the 3 most used cup types available with both CoC and CoPE bearing (n=33,454)

	CoC (n=12,535)	CoPE (n=20,919)
Gender, n (%)		
Male	4914 (39)	7463(36)
Female	7596 (61)	13424 (64)
Age, mean (SD)	65.5(9.9)	67.4 (9.8)
BMI, mean (SD)	27.3 (4.4)	27.3(4.6)
ASA, n (%)		
I	3748 (31.0)	4031 (19.3)
II	7153 (59.2)	14584 (69.9)
III-IV	1183 (9.8)	2252 (10.8)
Prior operation, n (%)	269 (2.3)	448 (2.3)
Charnley, n (%) *		
A	2306 (50.8)	6297 (44.0)
B	2177 (48.0)	7735 (54.0)
C	57 (1.2)	288 (2.0)
Diagnosis, n (%)		
Osteoarthritis	11538 (92.0)	19249 (92.0)
Other	997 (8.0)	1670 (8.0)
Smoker, n (%) *	741 (14.4)	1641 (11.5)
Approach, n (%)		
Anterior	4878 (39.5)	7333 (35.1)
Anterolateral	579 (4.7)	1123 (5.4)
Direct lateral	1694 (13.7)	2890 (13.8)
Posterolateral	5176 (42.0)	9500 (45.5)
Other	11 (0.1)	28 (0.2)
Cup type, n (%)		
Pinnacle, DePuySynthes	8783 (70.1)	10765 (51.5)
Exceed ABT, Zimmer-Biomet	3696 (29.5)	6769 (32.4)
Trident Tritanium, Stryker	56 (0.4)	3385 (16.2)
Cup size mm, mean (SD)	53.9 (3.4)	53.5 (3.3)
Head diameter mm, n (%)		
28	1050 (8.4)	4772 (22.8)
32	2038 (16.3)	12131 (58.0)
36	9447 (75.4)	4016 (19.2)

CoC, ceramic-on-ceramic; CoPE, ceramic-on-polyethylene; BMI, body mass index; SD, standard deviation
* numbers do not add up to total due to missing values
Early cup revision due to all reasons

Overall reasons for early cup revision

The reasons for early cup revision are shown in **Table 2**. Overall, more cup revisions due to loosening were observed in CoC than CoPE (p = 0.03). After adjustment for head size, Log-regression analysis showed an OR 0.398 [95% CI, 0.158–1.00] for revision due to dislocation of CoC compared to CoPE (p = 0.05).

Early cup revision due to aseptic loosening

The Kaplan-Meier analysis showed an overall 2-year cumulative cup revision rate due to aseptic loosening of 0.094% [95% CI, 0.054–0.132]. In CoC a total of 19 cup revisions due to aseptic loosening were observed, with a revision rate of 0.153% [95%CI 0.075–0.231]. CoPE showed a revision rate of 0.058% [95%CI 0.019–0.097] with a total of 12 revisions of the cup due to aseptic loosening. This difference resulted in a HR of 0.378 [95%CI 0.183–0.778] of CoPE compared to CoC (p = 0.007). After adjustment for confounders (head size) an HR of 0.475 [95%CI 0.197–1.141] was observed of CoPE over CoC (p = 0.096). The reason why there is a small difference in the numbers of cup loosening mentioned in **Table 2** and the number of cup revisions due to aseptic loosening is due to the fact that loosening may also occur in cases with other reasons for revision as well, like septic revision cases.

Incidence of revision procedures

The incidence of different cup revision procedures is shown in **Table 3**. Overall, the revision procedures performed did not significantly differ between CoC and CoPE (p = 0.09).

Incidence of CoC and CoPE bearing in THA

In **Figure 2** the absolute incidence of CoC and CoPE bearing in THAs as registered in the LROI are shown over time. From the start of the LROI in 2007 till 2011, an increase in the number of THAs performed with CoC bearing was observed. This incidence has decreased in recent years, whereas the incidence of CoPE is still increasing from the beginning of the LROI until now.

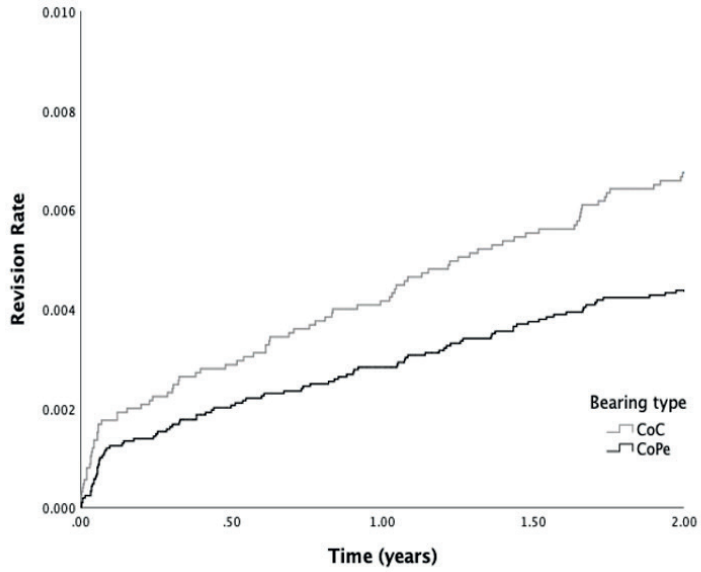

Figure 1. Revision rate of press-fit THA performed from 2007–2017 in The Netherlands with one of the three most used cup types between CoC (N = 12,535) and CoPE (N = 20,919) bearing.

Table 2. Reasons for revision in cup revision of press-fit THAs from 2007 to 2017 in The Netherlands, in numbers with proportions (%).

	CoC	**CoPE**	
	(n=84)	**(n=91)**	**p-value**
Infection	21 (25.0)	30 (33.0)	0.25
Wear of inlay	2 (2.4)	0 (0)	0.23
Periprosthetic fracture	2 (2.4)	6 (6.6)	0.28
Dislocation	22 (26.2)	25 (27.5)	0.85
Cup loosening	22 (26.2)	12 (13.2)	**0.03**
Periarticular ossification	0 (0)	1 (1.1)	1.00
Other	20 (23.8)	21 (23.1)	1.00
Missing	0 (0)	0 (0)	1.00

CoC, ceramic-on-ceramic; CoPE, ceramic-on-polyethylene.
Since a patient may have more than 1 reason for revision of the cup, the total can exceed 100%.

Table 3. Revision procedures performed in case of cup revision in press-fit THAs from 2007 to 2017 in The Netherlands, in numbers with proportions (%).

	CoC	**CoPE**
	(n=84)	**(n=91)**
Girdlestone (infection)	11 (13.1)	21 (23.1)
Cup revision	44 (52.4)	50 (54.9)
Total revision	29 (34.5)	20 (22.0)

CoC, ceramic-on-ceramic; CoPE, ceramic-on-polyethylene.

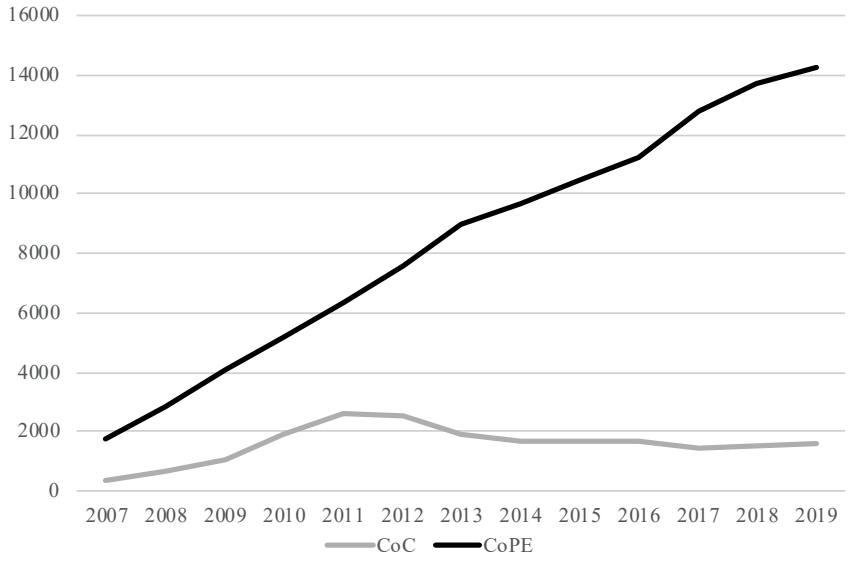

Figure 2. Absolute number of CoC and CoPE bearing in press-fit THA over time from 2007–2019 in The Netherlands (N = 129,358), horizontal axis: years; vertical axis: number of THA procedures.

DISCUSSION

The main finding of this LROI observational study is an approximately 2-fold higher 2-year cup revision rate for all reasons observed in CoC. This was in line with our hypothesis. Nevertheless, early revision risk for both articulations was very low. To our knowledge, this is the first arthroplasty register study showing results focused on the 2-year cup revision risk between CoC and CoPE in THA. Moreover, recent systematic reviews have not shown significant differences in revision rates on short to mid-term

either. [24,25] The fact that both systematic reviews showed no significant difference in revision rate between bearings could be attributed to the lower number of THAs included in all separate studies and the difference in follow-up time between studies in combination with the fact that different reasons for revision occur on different time-points in both bearings.

In line with our hypothesis, the reasons for revision differed significantly between bearings. The first main reason for early revision was loosening. Our outcomes showed significantly more loosening and aseptic loosening in CoC, which was in line with our hypothesis. A recent national registry funded this with an HR of 0.65 [95% CI, 0.58–0.73] for CoC and 0.46 [95% CI, 0.38–0.55] for CoXLPE for revision due to aseptic loosening when compared to metal-on-polyethylene (MoPE) at a mean followup of 4.4 years. [26] Our hypothesis is based on the fact that after uncemented cup implantation, the primary stability obtained by press-fit decreases over time. The transition to secondary stability is obtained when osseointegration becomes sufficient.13 Harder bearing couplings, like CoC, raise the total stiffness of the implant. [27] In this way, the forces on the implant are less absorbed by the bearing and are transferred to the interface between the bone and the cup. We theorise that this jeopardises osseointegration and results in migration of the cup and as a result can cause failure of ingrowth of the cup and thereby aseptic loosening and revision. Focused on migration, Zhou et al. [17] found no increased early migration in CoC compared to metal-on-cross-linked PE bearing. More randomized RSA between CoPE and CoC should be done to confirm whether migration rates are even higher in CoC, without always resulting in aseptic loosening.

The second major reason for early revision was dislocation, which showed no difference between bearings. After correction for head size, the odds for revision due to dislocation were higher in CoC, but not significantly. In CoC larger femoral head sizes are used more often, since in CoPE their use is associated with higher volumetric wear. [28] However, the use of a bigger head size is presumed to increase range of motion, causing less impingement and as a result fewer dislocations. [29] Another registry study observed dislocation as reason for revision at 9 years in 20% in CoC, compared to 33% in CoPE and 30% in CoHXLPE, which was declared by the use of a bigger head size in CoC. [12] This higher risk of dislocation at longterm can be explained by its correlation with wear, which only occurs on long-term in CoPE. [30] These results suggest that our odds of revision after correction for head size were not significant in the short-term but raise the idea that this might become significant in the longer term due to wear in CoPE.

The last main reason for early revision was infection, which did not differ between bearings. A recent systematic review reported no significant difference in rate

of prosthesis infection based on the existing clinical data between bearings. [31] Additionally, Pitto and Sedel showed no difference in revision rate due to infection within six months. [11] Our results support this by showing no potential advantage of bearing on infection in the short term. However, the difference in Girdlestone procedures was higher in CoPE, which might be influenced by the number of cases of infection in this group. Since this procedure has an important impact on patients and the performance of THA after reimplantation, this outcome should be considered in clinical planning.

Since early cup revision is multi-factorial (e.g. patient characteristics, implant design, position, alignment, biocompatibility, microscopic structure, macroscopic design, surgical approach) it is hard to investigate a specific factor. Several confounders were seen in our study, like age, gender and cup type. Many studies have suggested that these factors can have an influence on a higher risk of overall revision, like a specific cup type, a lower age at the moment of surgery and female gender. [32–35] Although the higher incidence of revision in CoC was still significant after correction for these confounders in our study, it shows that the aetiology of early revision is multi-factorial. Focusing on aseptic loosening, in older patients, due to the reduced quality and density of the subchondral trabecular bone, in which the cup is inserted after reaming, there may be an increase in its elasticity. [36,37] Since a lower bone density contributes to cup migration, this can complicate achievement of sufficient primary stability for transition to secondary stability. [38] However, osteoarthritis (OA) might change

this relationship of age and quality of subchondral bone, since in late-stage OA the density, volume and thickness of the subchondral bone increases, which increases the stiffness of the bone bed for implantation. [36,39] Moreover, bone quality is influenced by many factors, like bone mineralization disorders, bone remodelling disorders, collagen disorders, inflammatory conditions like rheumatoid arthritis, physical activity, genetics, smoking, obesity and nutrition deficiencies. [40,41] All the above-mentioned factors could lead to impaired bone quality, which might theoretically increase the risk of aseptic loosening in combination with a stiff CoC bearing resulting in impaired osseointegration. Thus the idea is raised that it might be preferable for CoC to be used only in younger patients and patients with no impaired bone quality. Further research needs to determine if the aforementioned factors like age and OA stadium might relate to increased chance of aseptic loosening. However, most variables usually happen concurrently, which might complicate isolated research on one of these factors.

Our study showed that the incidence of THAs using CoPE is still growing and the usage of CoC is shrinking. An explanation might be that ceramic inserts are up to three times more expensive than PE. [42] Nevertheless, CoC is more often placed in younger

patients and therefore needs longer durability. Long-term cost analysis, which has not been performed between CoC and CoPE to our knowledge, needs to clarify whether differences in outcomes, complications and revision rates are cost-effective to the cost of both bearings.

Limitations

First, since this national registry study is based on observational data, this study cannot conclude causality. Secondly, there is indication bias, which cannot be discounted when comparing different articulation combinations. Thirdly, revision due to aseptic loosening is a rare event, even in our study register; therefore, no survival analysis with correction for confounders was possible in this multi-factorial problem. Fourthly, we combined all different types of PE inserts in one group. This could influence other reasons for revision than aseptic loosening, like wear. Fifthly, wear as reason for revision was observed twice in CoC. Liner fractures are not separately reported in the LROI, which is an important shortcoming of the LROI, since this is one of the main concerns of the use of CoC. However, since wear does not occur in CoC, these two cases are most likely to have been revised due to a ceramic liner fracture. Sixthly, the use of additional screws is not separately reported in the LROI and therefore its potential confounding effect on revision has not been analyzed in our study. However, studies in the literature report that screws have no effect on migration, wear and (early) revision. [43–45] Finally, revision rates may differ from the literature since this research was focused on reasons for cup revision only and a notable group was reported as 'other' mentioning the reason for revision, which was not reported in the LROI.

Implications for further research

Since the aetiology of early revision is multi-factorial, more randomized controlled studies using the same implant need to be performed to eliminate baseline variability. Moreover, more randomized controlled RSA studies need to be performed between CoC and CoPE to identify risk factors for migration and potential resulting aseptic loosening.

CONCLUSION

A higher 2-year cup revision rate in press-fit THA was observed in CoC compared to CoPE. Cup loosening was the only significantly different reason for revision and seen more often in CoC and mostly aseptic. Future randomized controlled trials need to confirm causality, since the early cup revision data provided have the potential to be useful when choosing the bearing in press-fit THA, when combined with other factors like bone quality and patient and implant characteristics.

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8

Chapter 9

Five year cup and stem migration for ceramic-on-ceramic and ceramic-on-polyethylene bearing in press-fit hip arthroplasty. A randomized controlled radiostereometry trial

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Submitted

Abstract

The inelasticity of ceramic bearings might affect primary stability and migration of implants in press-fit total hip arthroplasty (THA). In this randomized controlled trial we compared mid-term migration patterns of the uncemented Delta TT cup and H-MAX S stem between ceramic and polyethylene liners. Patients receiving primary press-fit THA were randomized between a ceramic (n=28) or polyethylene (n=25) liner. To predict the risk of long-term aseptic loosening, migration was measured using model-based radiostereometric analysis (RSA) at baseline, 1.5, 3, 6, 12, 24 and 60 months postoperatively. At five-year follow-up, mean proximal cup translation was 0.56mm (95%CI 0.37–0.74) in ceramic and 0.58mm (95%CI 0.25–0.90) in polyethylene. Mean adduction was 1.05˚ (95%CI 0.27–1.82) in ceramic and 0.78˚ (95%CI -0.16–1.71) in polyethylene. Mixed modeling showed that all between-group effects were ≤0.20mm for translation and ≤0.22˚ for rotation at five years postoperatively (p≥0.23). Most cup migration occurred up to three months, stabilizing within six months. Mean stem subsidence was 2.09mm (95%CI 0.89–3.29) in ceramic and 2.55mm (95%CI 0.97–4.12) in polyethylene. Most stem migration occurred up to 1.5 months, stabilizing afterwards. All between-group effects were ≤0.75mm for translation and ≤1.41˚ for rotation (p≥0.26). Similar five-year migration patterns of the press-fit Delta TT cup and H-MAX S stem were observed between ceramic and polyethylene liners. After initial migration, implants in both groups showed secondary stabilization, which is promising for long-term survival.

INTRODUCTION

One of the main reasons for long-term revision in press-fit total hip arthroplasty (THA) is aseptic loosening caused by wear induced osteolysis of polyethylene (PE) liners. [1,2] Highly cross-linked PE (HXLPE) has been developed to decrease wear rates. However, ceramic-on-ceramic (CoC) is presumed to have even lower wear rates compared to ceramic-on-HXLPE. [3] One of the disadvantages of ceramic (CE) is its higher stiffness compared to PE, while an elasticity modulus similar to bone is known to reduce stress-shielding, promoting osseointegration. [4] Literature shows a higher risk of two-year cup revision in CoC compared to CoPE in press-fit THA. [5] We theorize that CoC could cause a more direct load transfer to the bone-implant interface and increase micromotion of the cup, which could jeopardize osseointegration and transition to long-term stability. [6] To promote osseointegration, implants are continuously developed, which resulted in trabecular titanium implants like the Delta TT cup and the hydroxyapatite coated rough macro-textured H-MAX S stem (LimaCorporate, Villanova San Daniele del Friuli, Italy). [7-10] While these developments may enhance osseointegration, initial stability remains an important factor for osseointegration to occur. Stability of the implant can be accurately assessed by measuring migration patterns using radiostereometric analysis (RSA), predicting the risk for long-term aseptic loosening. [11-13] At two years postoperatively we found no significant differences in migration patterns between Delta TT cups with a PE and CE liner. [14] To our knowledge no RSA studies comparing mid-term migration of a press-fit cup and stem between CoC and CoPE are performed so far. The objective of this randomized controlled trial was to compare five-year migration patterns of both the Delta TT cup and the H-MAX S stem between either a CE or PE liner.

METHODS

Ethical approval

Ethical approval was granted by the local medical ethics committee (registration number NL44230.100.13) and the study was registered at ClinicalTrials.gov (NCT03093038). The design and reporting were performed in accordance with the Consolidated Standards of Reporting Trials (CONSORT) principles and conducted according to the Declaration of Helsinki.

Study design

This single center randomized controlled trial was performed in patients between 18 and 75 years of age undergoing primary unilateral press-fit THA at the OLVG (Amsterdam, The Netherlands) between October 2014 and February 2016 (level of evidence: II).

Randomization was performed using an online randomization program between either a highly cross-linked ultra-high molecular weight polyethylene liner (UHMWPE X-Lima, LimaCorporate, Villanova San Daniele del Friuli, Italy) (PE group) or a BIOLOX® delta ceramic liner (CeramTec GmbH, Plochingen, Germany) (CE group) while receiving the same Delta-TT cup (LimaCorporate) and H-MAX S stem (LimaCorporate) (**Figure 1**). Patient demographics and medical history were recorded at baseline and postoperative complications were registered. Patient-reported outcomes were collected up to five years postoperative, measuring quality of life using the EuroQol five-dimensions (EQ5D-3L) and physical function using the Hip disability and Osteoarthritis Outcome Score Physical Function Short form (HOOS-PS) and Oxford Hip Score (OHS). The focus of this study is on the mid-term results up to five years of the Delta TT cup and the H-MAX S stem. For further details on patient eligibility, informed consent, surgical procedure, implant specification, sample size calculation and RSA set-up, we refer to the previously published two-year results of the Delta-TT cup. [14]

Figure 1. Example of the Delta TT press-fit cup and H-MAX S press-fit stem (LimaCorporate, Villanova San Daniele del Friuli, Italy) with a BIOLOX® Delta ceramic insert and femoral head (CeramTec GmbH, Germany)

Radiostereometric analysis

Primary outcome was migration measured with RSA of the acetabular and femoral component over time. Baseline RSA radiographs were acquired within three days postoperatively before weightbearing and follow-up radiographs at 1.5, 3, 6, 12, 24 and 60 months after implantation. Double examinations of RSA images were performed at one-year follow-up to measure precision of the RSA technique. (**Table 1**) The anonymized RSA radiographs were analyzed using model-based RSA Software, version 4.2 (RSA*core*, Department of Orthopaedics, LUMC, The Netherlands). Cup migration was calculated

Table 1. Precision calculation presented as the upper limit of the 95% confidence interval (mean + (1.96*SD)) of the measurement error of the double RSA examination at 1-year follow-up.

Implant	Translation (mm)			Rotation (degrees)			MTPM (mm)
	Lateral-medial (X)	*Distal-proximal (Y)*	*Posterior-anterior (Z)*	*Anterior tilt (X)*	*Internal rotation (Y)*	*Adduction (Z)*	
Delta TT cup (N=49)	0.441	0.213	0.368	0.734	0.955	0.686	-
	Lateral-medial (X)	*Distal-proximal (Y)*	*Posterior-anterior (Z)*	*Anterior tilt (X)*	*Internal rotation (Y)*	*Adduction (Z)*	
H-MAX S stem (N=46)	0.185	0.463	0.328	0.293	1.034	0.243	1.101

using a 3D Hemispherical Elementary Geometrical Shape (EGS) model (**Figure 2**). [15] Stem migration was calculated using a combined 3D stem and femoral head model, based on computer aided design (CAD) information. [16] Migration was calculated following the recommendations by Valstar et al. [17] The meaning of positive translation (X-axis: medialization, Y-axis: cranialization, Z-axis: anterior migration) and positive rotation (X-axis: anterior tilt, Y-axis: internal rotation or anteversion, Z-axis: adduction/decrease of inclination) are shown in **Figure 2**. For the stem, Maximum Total Point of Motion (MTPM) was calculated, which is the translation of the point on the stem model that moved the most. To prevent loss of data, a marker configuration model (MC-model) was used when necessary. [18] Migration results up to two years postoperatively in this report may differ slightly from results in the two-year report, due to the addition of the five-year RSA acquisition. [14] In several patients less bone markers were available for migration calculations and as a result migration calculation over the entire follow up has been done with the lesser number of available markers.

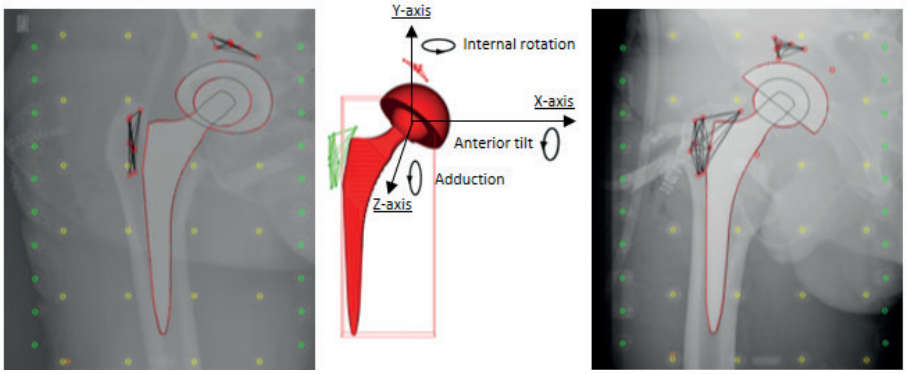

Figure 2. RSA model and coordinate system used to present migration along and rotation around the X-, Y- and Z-axis. Directions as presented in the figure indicate positive migration values

Explorative analysis

As an explorative analysis the relation between migration of the Delta-TT cup and the H-MAX S stem was investigated using Pearsons Correlation coefficient for Y-axis translation and secondly for total translation. The aim was to investigate if increased migration in either the cup or stem, is correlated to increased migration in the other component. We hypothesize that micromotion in the cup and stem could be related, especially with a stiff bearing. Translation on the Y-axis was investigated since this is a predictor of loosening for both components in literature and the total translation was calculated to approximate overall translation of the implant. [11,19,20] For both the cup and the stem, total translation was defined as: $\sqrt{((\text{translation X-axis})^2 + (\text{translation Y-axis})^2 + (\text{translation Z-axis})^2)}$. Both outcomes were presented overall and separately for both bearings in a table for all time points and scatter plots at 1.5, 3 and 6 months, since at these time points most migration is expected due to initial settling of the implants.

Statistics

The initial power analysis was performed for the primary outcome (cup migration at two years). We aimed for a minimum of 16 patients in each group at five-year follow-up, to be able to detect a difference between groups with the magnitude of one standard deviation, with 80% power and alpha=0.05. Statistical analyses were performed with SPSS Statistics version 27.0 (IBM Corp. Armonk, New York, United States). To assess cup and stem migration a mixed model analysis was performed, with bearing (PE vs. CE) as the primary independent value of interest. Primary outcome was the effect of bearing over the five-year follow-up period on implant migration. Group differences were separately analyzed at each time point including time as a categorical factor variable and a time-by-group interaction term. Differences were considered significant for p-values below 0.05.

Table 2. Demographic details, indication for THA and implant information for the 2 study groups. Values are reported as mean (range) or number (%)

Variable	CE GROUP N = 27	PE GROUP N = 25
Age [years]	58.2 (40.0 – 71.0)	59.8 (40.0 – 70.0)
BMI [kg/m²]	25.7 (19.8 – 35.4)	27.4 (20.0 – 35.4)
Gender [male]	14 (52)	14 (56)
Indication for THA		
Osteonecrosis	24 (88.9)	24 (96)
Primary OA	2 (7.4)	1 (4)
OA and DDH	1 (3.7)	-
Cup size		
50	3 (11.1)	5 (20)
52	4 (14.8)	2 (8)
54	4 (14.8)	7 (28)
56	11 (40.7)	3 (12)
58	2 (7.4)	3 (12)
60	3 (11.1)	4 (16)
62	-	1 (4)
Stem size		
8	1 (3.7)	-
9	5 (18.5)	3 (12)
10	6 (22.2)	3 (12)
11	3 (11.1)	6 (24)
12	6 (22.2)	8 (32)
13	3 (11.1)	4 (16)
14	2 (7.4)	-
15	1 (3.7)	-
16	-	1 (4)

BMI = Body Mass Index; OA: osteoarthritis ; DDH: developmental dysplasia of the hip ; PE = polyethylene; CE = ceramic

RESULTS

A total of 28 patients were included in the CE group and 25 patients in the PE group. **Figure 3** presents the flowchart of patient selection and follow-up. Demographic details, patient characteristics and implant information are reported in **Table 2**. As is shown in **Figure 4**, improvement on patient-reported outcomes over time was similar in the two groups and clinically relevant from baseline up to five years. An MC-model was used for two cups (1 CE, 1 PE) and two stems (1 CE, 1 PE) to prevent data loss. At five-year follow-up, 23 Delta TT cups and 22 H-MAX S stems were available in the CE group and 18 Delta-TT cups and 15 H-MAX S stems were available in the PE group for RSA analysis (**Figure 3**).

Radiostereometric analysis of the cup

Mean migration of the Delta TT cup with a CE or PE liner is displayed in **Figure 5** and presented in detail with between group effects up until five-year follow-up in **Table 3**. Between group effects between CE and PE were not different at any time point (all p>0.108). Migration of the cup occurred mostly between baseline and three months postoperatively, after which it stabilized and remained stable from two to five-years follow-up in both the CE and PE group. The Delta TT cup showed a mean proximal translation (Y-axis) of 0.53mm (95%CI 0.36–0.70) and 0.56mm (95%CI 0.37–0.74) in the CE group and 0.51mm (95%CI 0.27–0.74) and 0.58mm (95%CI 0.25–0.90) in the PE group at two and five-year follow-up respectively. For inclination (Z-axis) a mean adduction of 0.75˚ (95%CI 0.01–1.49) and 1.05˚ (95%CI 0.27–1.82) in the CE group and 0.49˚ (95%CI -0.18–1.16) and 0.78˚ (95%CI -0.16–1.71) in the PE group was observed at two and five-year follow-up respectively.

For translation, between group effects over a five year period on the X, Y and Z-axis were 0.25mm (95%CI -0.12–0.62, p = 0.181), 0.03mm (95%CI -0.17–0.24, p = 0.736) and 0.06mm (95%CI -0.18–0.31, p = 0.589). For rotation, between group effects over a five year period on the X, Y and Z-axis were respectively 0.17˚ (95%CI -0.27–0.61, p = 0.452), 0.19˚ (95%CI -0.47–0.85, p = 0.562) and 0.37˚ (95%CI -0.40–1.14, p = 0.337). Individual cup migration patterns are presented in **Appendix 1 & 2**. One cup with a PE insert, showed increased migration on all parameters at two years, with ongoing migration, apart from Y-axis rotation, from two to five years postoperative. However, the increase in cranial migration reduced from two to five years, with 2.0mm at one year, 2.8mm at two years and 3.0mm at five years postoperatively. Separate analysis without this cup showed no significant outcomes. At five years postoperatively there were no clinical signs of aseptic loosening for any of the cups.

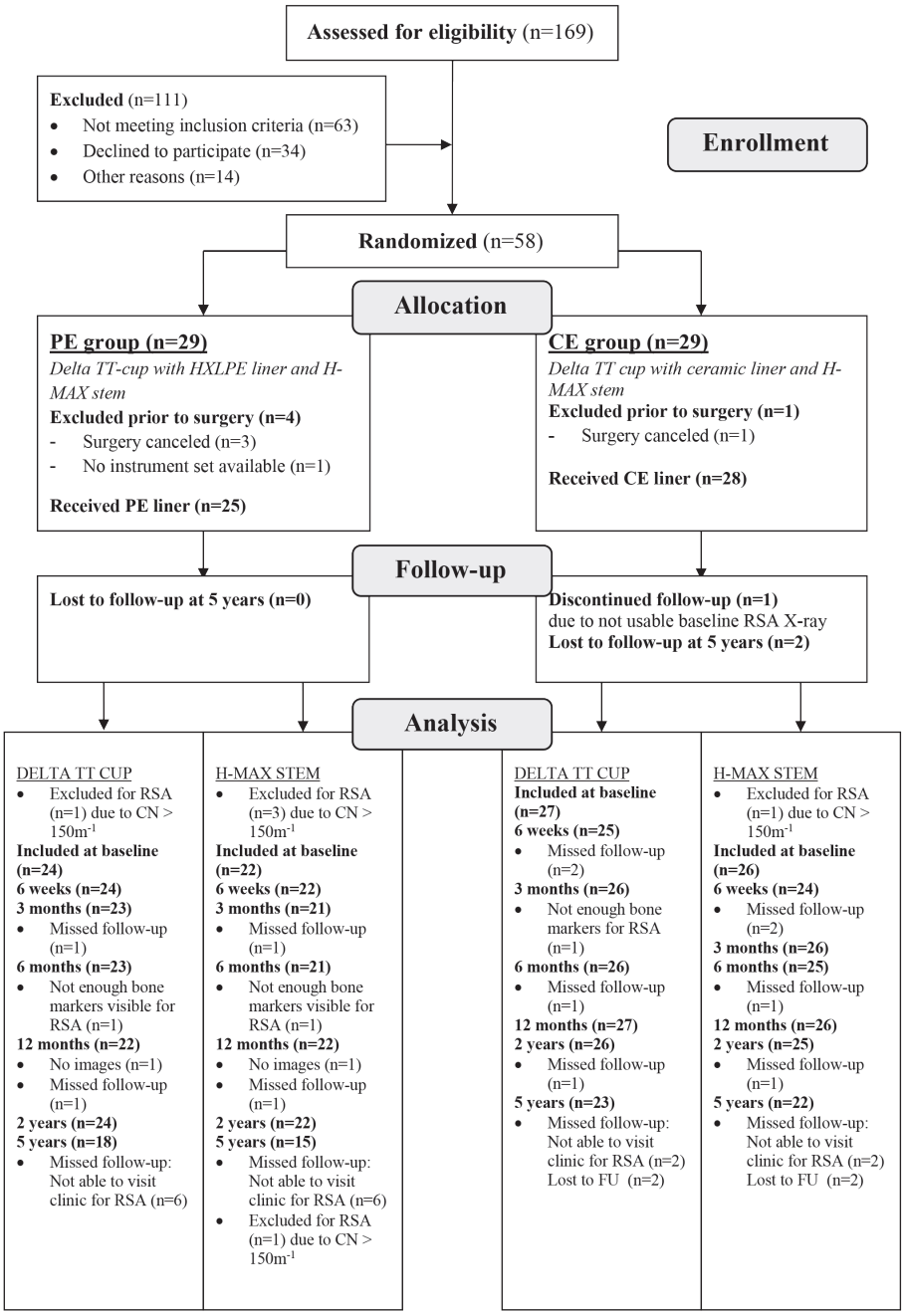

Figure 3. Flow-chart of patient enrollment and follow-up

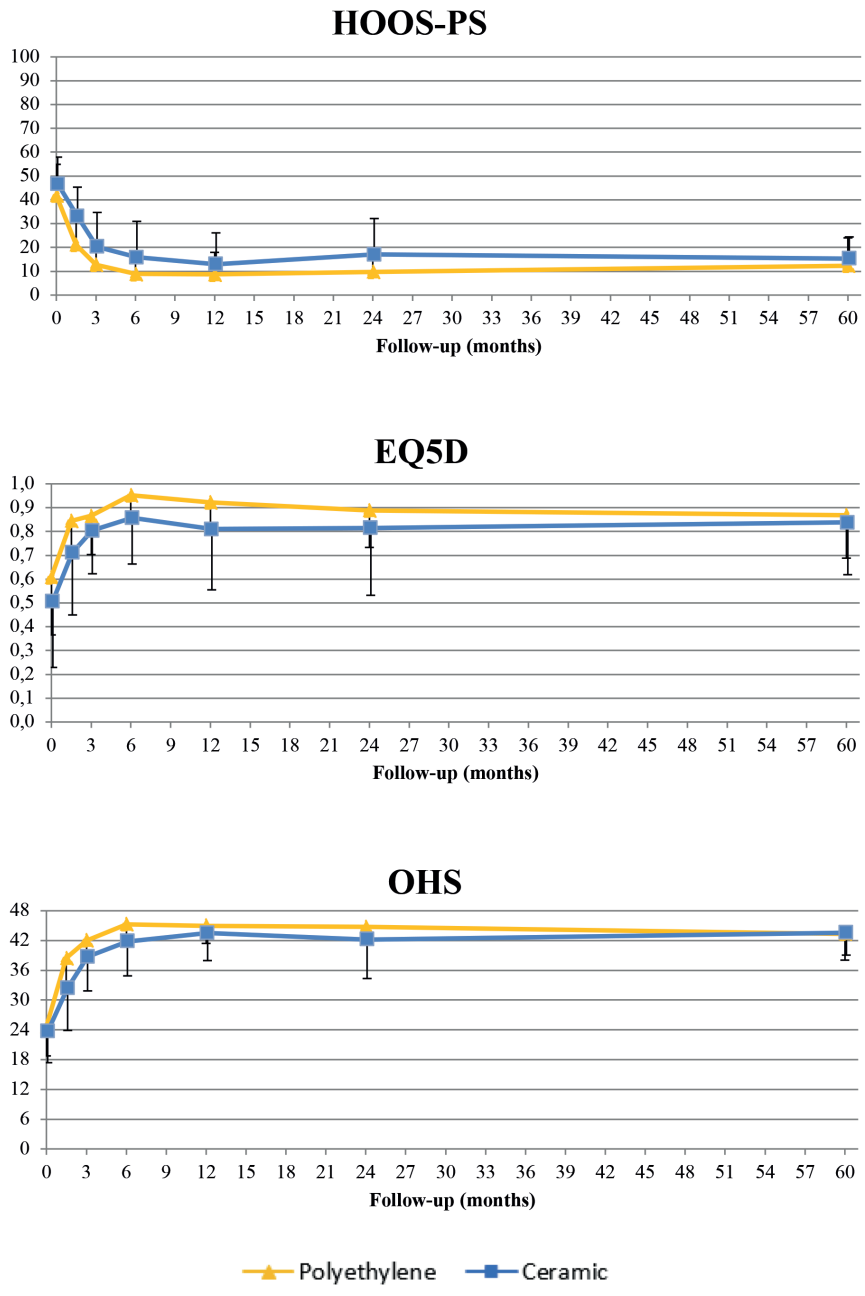

Figure 4. Mean (SD) improvement in patient-reported outcome (PROMs) in the two study groups throughout the five-year follow-up period

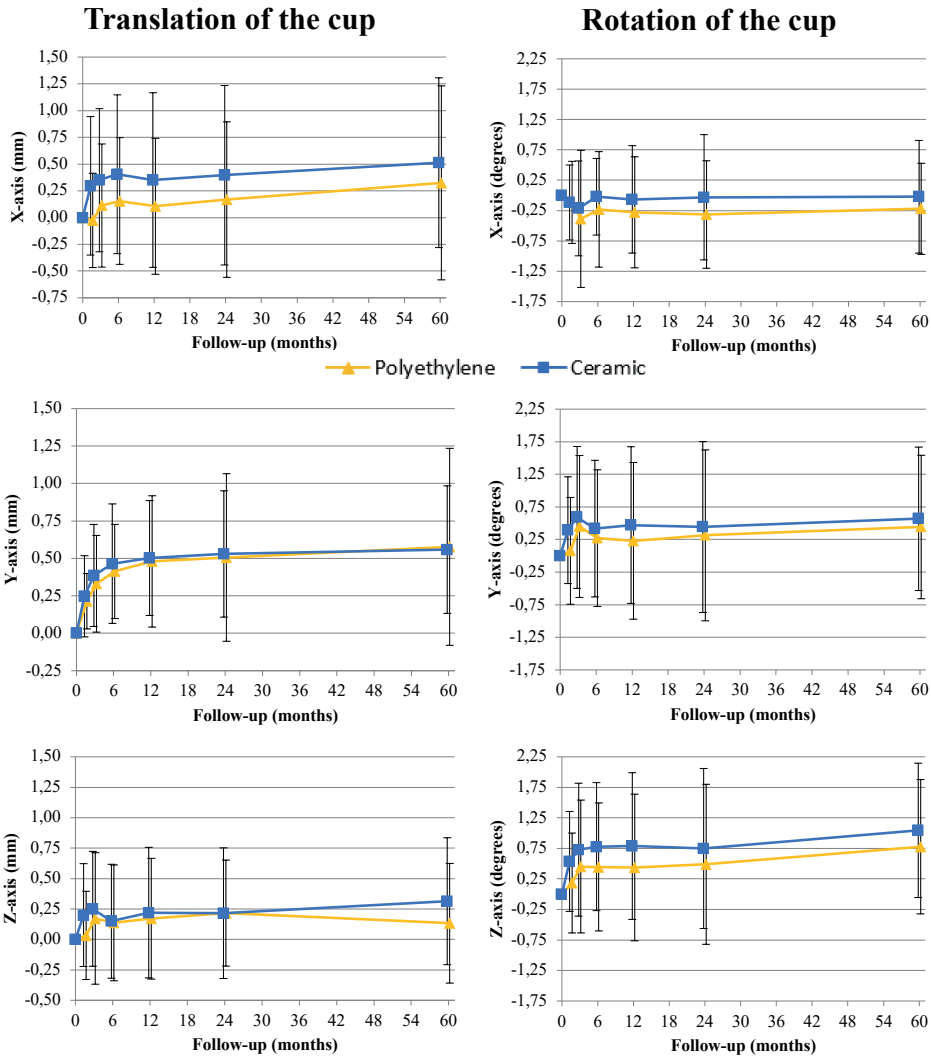

Figure 5. Mean translation and rotation of the Delta TT cup with a polyethylene (PE) or ceramic (CE) liner over time with 95%CI

Table 3. Mean migration of the cup in all directions at all time points during follow-up.

Outcome		CE				PE				CE vs. PE			
				95%CI				95%CI		95%CI			
		N	Mean	Lower bound	Upper bound	N	Mean	Lower bound	Upper bound	Between group diff.	Lower bound	Upper bound	p-value
Tx	1.5mo	25	0.30	0.03	0.56	24	-0.03	-0.21	0.16	0.31	-0.07	0.70	0.108
	3mo	26	0.35	0.08	0.62	23	0.11	-0.14	0.36	0.21	-0.18	0.60	0.279
	6mo	26	0.41	0.11	0.70	23	0.16	-0.10	0.41	0.25	-0.14	0.63	0.204
	1yr	27	0.35	0.03	0.67	22	0.11	-0.18	0.39	0.26	-0.13	0.64	0.188
	2yr	26	0.40	0.06	0.73	24	0.17	-0.14	0.48	0.23	-0.15	0.62	0.231
	5yr	23	0.51	0.17	0.86	18	0.32	-0.13	0.77	0.20	-0.19	0.59	0.315
Ty	1.5mo	25	0.25	0.13	0.36	24	0.21	0.14	0.29	0.03	-0.19	0.25	0.769
	3mo	26	0.39	0.25	0.52	23	0.33	0.19	0.47	0.06	-0.16	0.27	0.613
	6mo	26	0.46	0.30	0.63	23	0.41	0.28	0.55	0.05	-0.16	0.27	0.620
	1yr	27	0.50	0.35	0.65	22	0.48	0.29	0.67	0.03	-0.19	0.25	0.767
	2yr	26	0.53	0.36	0.70	24	0.51	0.27	0.74	0.02	-0.20	0.23	0.889
	5yr	23	0.56	0.37	0.74	18	0.58	0.25	0.90	-0.04	-0.26	0.18	0.729
Tz	1.5mo	25	0.20	0.03	0.37	24	0.03	-0.12	0.19	0.13	-0.13	0.29	0.321
	3mo	26	0.25	0.06	0.44	23	0.17	-0.06	0.41	0.06	-0.20	0.33	0.626
	6mo	26	0.15	-0.04	0.34	23	0.14	-0.07	0.34	0.01	-0.25	0.27	0.948
	1yr	27	0.22	0.01	0.43	22	0.17	-0.05	0.39	0.05	-0.21	0.31	0.697
	2yr	27	0.22	-0.001	0.43	24	0.22	0.03	0.40	-0.02	-0.28	0.24	0.893
	5yr	23	0.31	0.09	0.54	18	0.13	-0.11	0.38	0.16	-0.10	0.43	0.227

Table 3. Continued

Rx	1.5mo	25	-0.12	-0.37	0.14	24	-0.11	-0.40	0.17	0.02	-0.45	0.50	0.917
	3mo	26	-0.21	-0.53	0.10	23	-0.39	-0.88	0.10	0.19	-0.28	0.66	0.426
	6mo	26	-0.02	-0.28	0.23	23	-0.23	-0.64	0.18	0.13	-0.34	0.60	0.578
	1yr	27	-0.06	-0.41	0.28	22	-0.28	-0.68	0.13	0.20	-0.28	0.67	0.409
	2yr	26	-0.03	-0.45	0.39	24	-0.31	-0.69	0.06	0.29	-0.18	0.76	0.219
	5yr	23	-0.02	-0.42	0.38	18	-0.22	-0.59	0.15	0.17	-0.30	0.65	0.471
Ry	1.5mo	25	0.39	-0.07	0.86	24	0.08	-0.27	0.42	0.27	-0.41	0.96	0.430
	3mo	26	0.59	0.02	1.16	23	0.45	-0.02	0.92	0.11	-0.58	0.79	0.753
	6mo	26	0.42	-0.10	0.94	23	0.27	-0.18	0.72	0.25	-0.43	0.94	0.460
	1yr	27	0.47	-0.11	1.05	22	0.23	-0.30	0.76	0.25	-0.44	0.93	0.473
	2yr	26	0.44	-0.16	1.05	24	0.31	-0.24	0.87	0.11	-0.57	0.79	0.750
	5yr	23	0.57	-0.08	1.21	18	0.44	-0.11	0.99	0.11	-0.59	0.80	0.759
Rz	1.5mo	25	0.54	0.04	1.03	24	0.18	-0.19	0.55	0.36	-0.47	1.18	0.389
	3mo	26	0.73	0.14	1.32	23	0.45	-0.08	0.99	0.26	-0.56	1.08	0.525
	6mo	26	0.78	0.12	1.44	23	0.45	-0.13	1.03	0.36	-0.46	1.18	0.389
	1yr	27	0.79	0.11	1.47	22	0.44	-0.18	1.05	0.40	-0.42	1.22	0.337
	2yr	26	0.75	0.01	1.49	24	0.49	-0.18	1.16	0.27	-0.55	1.09	0.516
	5yr	23	1.05	0.27	1.82	18	0.78	-0.16	1.71	0.22	-0.62	1.06	0.607

Radiostereometric analysis of the stem

Migration of the H-MAX S stem with a CE or PE liner is shown in **Figure 6** and presented in detail with between group effects up until five-year follow-up in **Table 4**. Between group effects for mean migration were not different between CE and PE at any time point (p>0.173). Migration of the stem occurred mostly in the first 1.5 months postoperatively and remained stable after this time point. Stem migration was most pronounced for negative translation (= subsidence) on the Y-axis, rotation on the Y-axis and MTPM. H-MAX S stems showed a mean subsidence in the CE group of 2.03mm (95%CI 0.94–3.11) and 2.09mm (95%CI 0.89–3.29) at two- and five-year follow-up respectively and 2.87mm (95%CI 1.58–4.15) and 2.55mm (95%CI 0.97–4.12) in the PE group.

For translation, between group effects over a five year period on the X, Y and Z-axis were 0.01mm (95%CI -0.41–0.43, p = 0.952), 0.68mm (95%CI -0.89–2.26, p = 0.388) and 0.15mm (95%CI -0.29–0.60, p = 0.492). For rotation, between group effects on the X, Y and Z-axis were 0.09˚ (95%CI -0.34–0.52, p = 0.677), -1.54˚ (95%CI -4.00–0.93, p = 0.215) and 0.15˚ (95%CI -0.37–0.68, p = 0.564) respectively. MTPM showed a between group effect of -1.52mm (95%CI -4.14–1.10, p = 0.249).

Individual stem migration patterns are presented in **Appendix 3 & 4**. At five years postoperatively there were no clinical signs of aseptic loosening of any of the stems.

Explorative analysis cup vs. stem migration

The results of the correlation between cup and stem migration are presented in **Table 5** and **Figure 7**. For Y-axis translation, all correlation coefficients were negative indicating that proximal migration of the cup coincided with distal migration of the stem. Pearson correlation coefficients ranged from -0.32 (12 months) to -0.41 (60 months) in the ceramic (CE) group and from -0.21 (12 months) to -0.29 (1.5 months) in the polyethylene (PE) group.

For total translation, all correlation coefficients were positive, indicating more migration of the cup coincided with more migration of the stem. Pearson correlation coefficients ranged from 0.23 (12 months) to 0.41 (1.5 months) in the CE group and from 0.31 (60 months) to 0.78 (1.5 months) in the PE group.

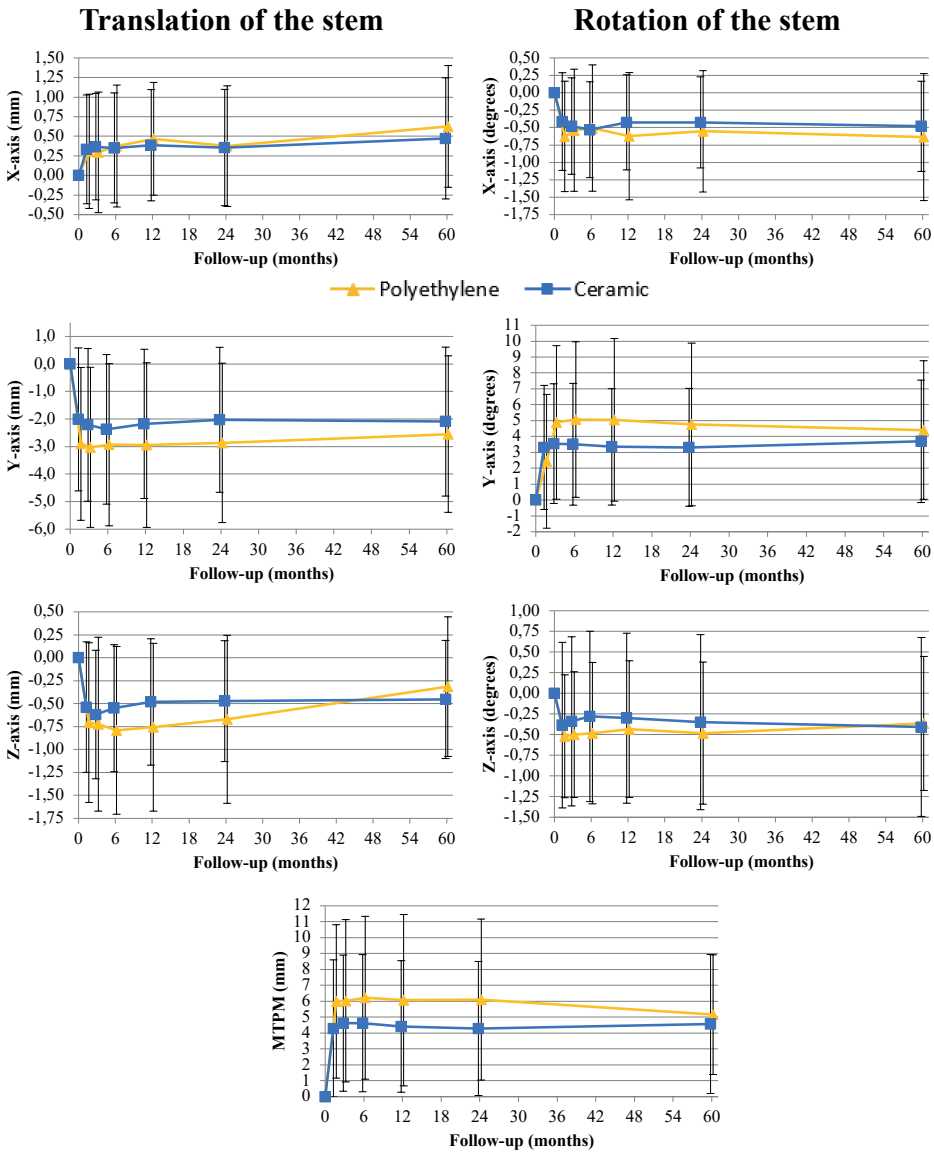

Figure 6. Mean translation and rotation of the H-MAX S stem with a polyethylene (PE) or ceramic (CE) liner over time with 95%CI

Table 4. Migration of the stem in all directions at all time points during follow-up

Outcome		CE				PE				CE vs. PE			
				95%CI				95%CI			95%CI		
		N	Mean	Lower bound	Upper bound	N	Mean	Lower bound	Upper bound	Between group diff.	Lower bound	Upper bound	p-value
Tx	1.5mo	24	0.33	0.04	0.63	22	0.31	-0.01	0.63	0.04	-0.38	0.46	0.86
	3mo	26	0.37	0.09	0.64	21	0.29	-0.06	0.65	0.07	-0.35	0.49	0.75
	6mo	25	0.35	0.06	0.64	21	0.38	0.02	0.73	-0.05	-0.47	0.37	0.82
	1yr	26	0.39	0.10	0.67	20	0.47	0.13	0.80	-0.00	-0.42	0.42	0.99
	2yr	25	0.36	0.05	0.66	22	0.37	0.03	0.72	0.01	-0.41	0.43	0.95
	5yr	22	0.47	0.13	0.82	15	0.63	0.20	1.06	-0.03	-0.48	0.39	0.90
Ty	1.5mo	24	-2.01	-3.11	-0.92	22	-2.90	-4.13	-1.67	0.67	-0.91	2.24	0.40
	3mo	26	-2.21	-3.33	-1.09	21	-3.03	-4.35	1.70	0.72	-0.86	2.30	0.36
	6mo	25	-2.37	-3.49	-1.25	21	-2.93	-4.27	-1.59	0.60	-0.97	2.18	0.45
	1yr	26	-2.17	-3.27	-1.08	20	-2.95	-4.35	-1.55	0.68	-0.90	2.26	0.39
	2yr	25	-2.03	-3.11	-0.94	22	-2.87	-4.15	-1.58	0.68	-0.89	2.26	0.39
	5yr	22	-2.09	-3.29	-0.89	15	-2.55	-4.12	-0.97	0.75	-0.83	2.33	0.35
Tz	1.5mo	24	-0.54	-0.84	-0.24	22	-0.71	-1.09	-0.32	0.13	-0.33	0.59	0.57
	3mo	26	-0.62	-0.90	-0.34	21	-0.72	-1.15	-0.29	0.11	-0.34	0.57	0.62
	6mo	25	-0.55	-0.84	-0.26	21	-0.79	-1.21	-0.38	0.23	-0.23	0.69	0.32
	1yr	26	-0.48	-0.76	-0.20	20	-0.76	-1.18	-0.33	0.26	-0.20	0.71	0.26
	2yr	25	-0.47	-0.74	-0.20	22	-0.67	-1.08	-0.26	0.15	-0.30	0.61	0.51
	5yr	22	-0.45	-0.74	-0.17	15	-0.31	-0.74	0.11	-0.02	-0.48	0.44	0.94

Table 4. Continued

Rx	1.5mo	24	-0.41	-0.71	-0.12	22	-0.63	-0.98	-0.28	0.18	-0.26	0.63	0.41
	3mo	26	-0.48	-0.76	-0.20	21	-0.54	-0.94	-0.14	0.03	-0.41	0.47	0.91
	6mo	25	-0.53	-0.81	-0.25	21	-0.51	-0.92	-0.09	0.02	-0.43	0.46	0.94
	1yr	26	-0.43	-0.70	-0.15	20	-0.62	-1.05	-0.20	0.15	-0.30	0.59	0.51
	2yr	25	-0.43	-0.70	-0.16	22	-0.55	-0.94	-0.17	0.08	-0.36	0.53	0.71
	5yr	22	-0.48	-0.77	-0.19	15	-0.64	-1.14	-0.13	0.08	-0.37	0.53	0.71
Ry	1.5mo	24	3.31	1.66	4.96	22	4.87	2.71	7.04	-1.48	-3.96	1.00	0.24
	3mo	26	3.55	2.03	5.07	21	4.90	2.67	7.12	-1.42	-3.91	1.05	0.25
	6mo	25	3.51	1.93	5.09	21	5.24	2.96	7.52	-1.71	-4.19	0.77	0.17
	1yr	26	3.35	1.87	4.82	20	4.85	2.34	7.35	-1.57	-4.05	0.91	0.21
	2yr	25	3.32	1.78	4.85	22	5.11	2.84	7.37	-1.66	-4.13	0.822	0.19
	5yr	22	3.69	1.98	5.40	15	4.01	2.20	5.81	-1.41	-3.90	1.07	0.26
Rz	1.5mo	24	-0.39	-0.81	0.04	22	-0.52	-0.85	-0.19	0.18	-0.35	0.71	0.51
	3mo	26	-0.34	-0.75	0.07	21	-0.50	-0.85	-0.15	0.19	-0.34	0.72	0.47
	6mo	25	-0.28	-0.70	0.15	21	-0.48	-0.87	-0.09	0.19	-0.34	0.72	0.47
	1yr	26	-0.30	-0.71	-0.12	20	-0.30	-0.72	0.12	0.13	-0.40	0.66	0.62
	2yr	25	-0.35	-0.79	0.09	22	-0.48	-0.86	-0.10	0.14	-0.39	0.67	0.61
	5yr	22	-0.41	-0.89	0.07	15	-0.36	-0.81	0.08	0.07	-0.47	0.60	0.81
MTPM	1.5mo	24	4.29	2.47	6.11	22	5.99	3.85	8.13	-1.52	-4.15	1.10	0.25
	3mo	26	4.63	2.90	6.35	21	6.03	3.71	8.35	-1.39	-4.01	1.24	0.29
	6mo	25	4.62	2.84	6.40	21	6.22	3.89	8.55	-1.58	-4.21	1.04	0.23
	1yr	26	4.42	2.75	6.09	20	6.07	3.55	8.59	-1.55	-4.18	1.08	0.24
	2yr	25	4.29	2.55	6.03	22	6.11	3.87	8.35	-1.63	-4.26	0.99	0.22
	5yr	22	4.57	2.64	6.51	15	5.16	3.08	7.24	-1.48	-4.11	1.15	0.26

Complications

One patient (CE group) needed early revision of the femoral head and antibiotic treatment due to a periprosthetic joint infection. One other patient (PE group) visited the hospital three times because of recurrent dislocation and pain in the groin and a distally migrated stem. This stem showed subsidence of 8mm at 1.5 months postoperatively which stabilized afterwards and rotation about the Y-axis was 7° and 10° at 1.5 and 24 months respectively. Revision surgery of the stem and liner was performed at 3.5 years postoperatively. Two patients reported occasional squeaking in the operated hip with a CoC bearing, however they did not require revision surgery.

Table 5. Pearson correlation coefficients (r) for translation of the cup vs. the stem for translation on the Y-axis and total translation of the implants

		Ceramic				Polyethylene			
	Time (months)	r	95%CI		p-value	r	95%CI		p-value
			Lower Bound	Upper Bound			Lower Bound	Upper Bound	
Y-axis	1.5	-0.39	-0.69	0.01	0.06	-0.29	-0.63	0.16	0.20
	3	-0.39	-0.68	0.01	0.06	-0.27	-0.63	0.18	0.23
	6	-0.38	-0.67	0.02	0.06	-0.27	-0.63	0.18	0.24
	12	-0.32	-0.63	0.08	0.11	-0.21	-0.60	0.26	0.37
	24	-0.37	-0.67	0.03	0.07	-0.26	-0.61	0.18	0.25
	60	-0.41	-0.71	0.01	0.06	-0.27	-0.69	0.28	0.33
Total Translation	1.5	0.41	0.01	0.70	0.05	0.78	0.53	0.90	0.00
	3	0.39	-0.00	0.68	0.05	0.36	-0.09	0.69	0.11
	6	0.34	-0.06	0.65	0.09	0.48	0.06	0.76	0.03
	12	0.23	-0.17	0.57	0.25	0.34	-0.13	0.68	0.15
	24	0.32	-0.09	0.63	0.13	0.36	-0.08	0.68	0.10
	60	0.36	-0.08	0.68	0.10	0.31	-0.24	0.71	0.26

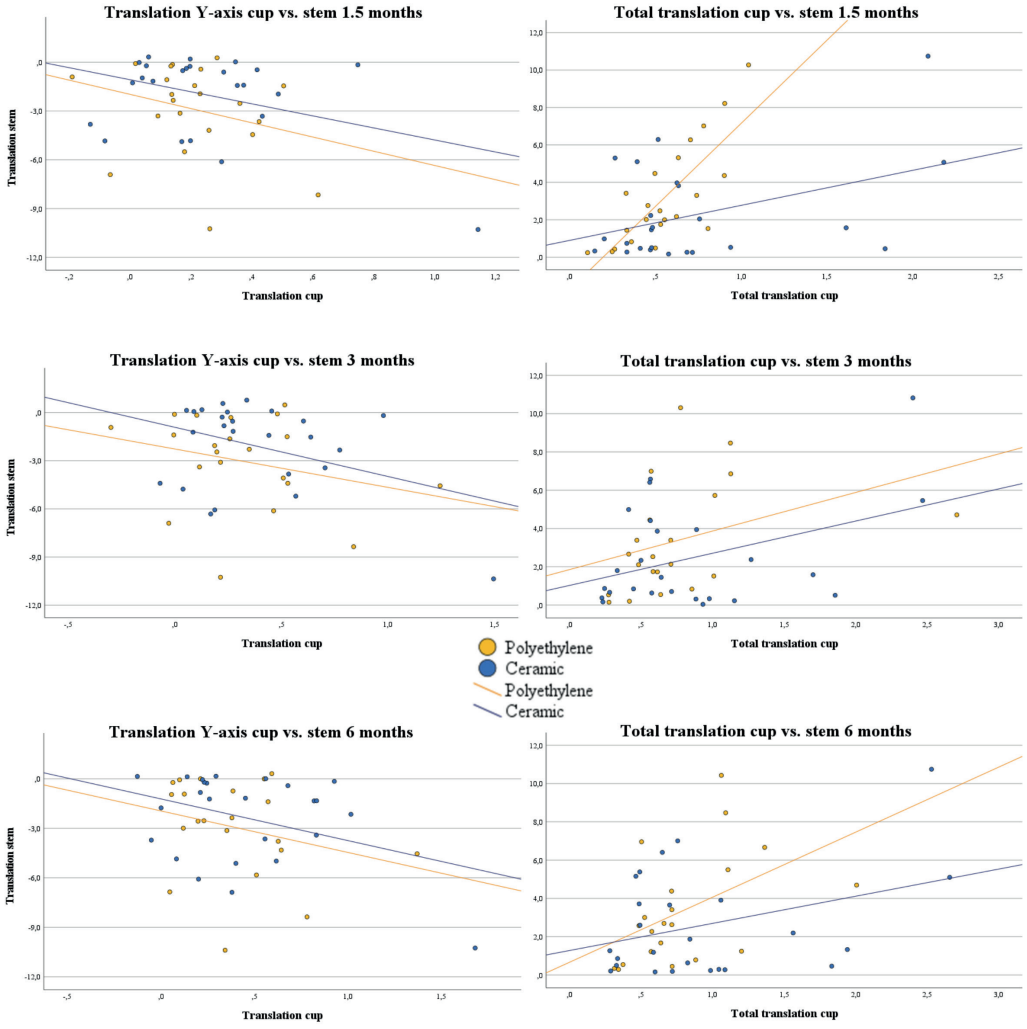

Figure 7. Explorative analysis of translation of the cup vs. the stem on the Y-axis and total translation the calculated center of gravity of both the cup and stem

DISCUSSION

This randomized controlled RSA trial with five-year follow-up found no significant differences in mean migration of the press-fit Delta TT cup and H-MAX S stem between CE and PE liners when using the same ceramic head. While a trend is seen of more migration on some parameters for Delta-TT cups in the CE group and for H-MAX S stems in the PE group, between-group effects are small and none reach statistical significance. To our knowledge only one other RCT RSA study, besides the previously published two-year results of this study, assessed cup migration between CoC and CoPE in press-fit THA, both showing no difference at two-years postoperatively. [14,20] Petricarini et al. also showed safe ingrowth of the Delta TT cup without using RSA at five years. [21]

Important parameters predicting aseptic loosening of the cup are cranial migration and change in inclination. [11,12,22] Pijls et al. proposed a threshold of 0.2mm for mean proximal translation at two years for both cemented and uncemented cups as considered acceptable, above 1.0mm being unacceptable and between both values at risk for having revision rates higher than 5% at ten years. [12] According to these thresholds, the Delta TT cup would be classified 'at risk' with a mean proximal translation of 0.51mm (95%CI 0.27–0.74) and 0.58mm (95%CI 0.25–0.90) in the PE group at two and five-year follow-up respectively and 0.53mm (95%CI 0.36–0.70) and 0.56mm (95%CI 0.37–0.74) in CE. The threshold of Pijls et al. is the best available threshold to predict the risk of cup loosening. However, the majority of cups in Pijls et al. were classified 'at risk' and only a limited number of press-fit RSA studies were included. Press-fit components are expected to show more migration compared to cemented components because of the fixation method and settling phase, therefore more research is needed to develop specific migration thresholds for press-fit cups. Nieuwenhuijse et al. proposed thresholds for individual patient proximal cup translation of 1.76mm and rotation of 2.53˚ about the Z-axis (indicating an increase in inclination) at two years. [11] In our study only one cup in the PE group showed mid-term migration above the threshold for proximal translation, indicating that this cup might be at risk for long-term aseptic loosening.

A recent registry study in the Dutch Arthroplasty Register (LROI) showed a higher two-year cup revision rate in press-fit THA in CoC compared to CoPE, with cup loosening as the only significant different reason for revision. [5] The registry study included a higher number of patients than our study and analyzed the three most frequently used cups available. A higher sample size increases the chance to detect significant differences, however registry studies cannot conclude on causality. In our study patients were randomized, minimizing the risk of bias and all patients received the same cup, stem and ceramic head.

Literature shows that both low bone mineral density (BMD) and impaired bone quality caused by rheumatoid arthritis (compared to osteoarthritis) contribute to increased cup migration. [23,24] More research is needed to investigate whether osseointegration is jeopardized when using a stiff CE liner in these subgroups.

Focused on the stem, most migration was seen in the first 1.5 months after surgery and was mostly subsidence on and rotation about the Y-axis. Slightly higher mean stem migration on all parameters was seen in PE compared to CE, but it did not reach statistical significance. Literature shows that the cup remains the weakest link in THA and is spherical, making it more vulnerable for migration in different directions, whereas the conical stem would be limited in its migration by the surrounding shape of the femur. [25] Streit et al. found an association between early subsidence in press-fit collarless stems with aseptic femoral loosening and set a threshold of 2.7mm subsidence at two-years for individual patients. [19] In our study, 8 out of 25 (32%) H-MAX S stems in the CE group and 9 out of 22 (41%) in PE showed subsidence above this threshold at two-years. Speculating on the cause of high early subsidence incidence, this could be attributed to the fact that the H-MAX S is a collarless press-fit stem, which is mentioned to show more early migration, but should not be interpreted as inferior osseointegration. [26] Streit et al. mentioned that a more implant specific approach might be preferred to predict failure, due to different design features of each stem. [19] Van der Voort et al. suggest that in press-fit stems, stabilization of migration might be more suitable to predict unsafe stems as compared to the absolute value of migration. [26] Therefore, caution is needed when predicting long-term results for stems based on their initial subsidence, especially if this is followed by early stabilization, as seen in our study and in literature, which could be part of the normal settling of a prosthesis. [27]

In our study, one CE patient required revision surgery of the stem, due to recurrent luxation. This stem showed distal migration of 8mm at 1.5 months postoperatively. As mentioned above, more H-MAX S stems showed high early subsidence: two other patients (1 CE, 1 PE) showed distal migration of >10mm at 1.5months postoperatively, rotation about the Y-axis was 4.1 and 4.3 in the first patient and 12.7 and 13.3 in the second patient at 1.5 and 24 months respectively. These subjects were free of complaints during further follow-up and since all stems showed early stabilization, the reason for this revision remains unclear. Considering that this was only one subject, the H-MAX S stem is found to be a safe option to use in THA regardless of bearing type.

Our explorative analysis shows correlation for increase in cup migration with an increase in stem migration in press-fit THA up to five years, both with CE and PE liners. To our knowledge, this is the first study to explore the relation between cup and stem

migration. We theorize that when increased micromotion in the cup and stem are related, osseointegration might be insufficient, potentially by impaired bone quality. Further research in combination with BMD measurements would help to investigate a potential relation between cup- and stem migration and the influence of bearing.

Strengths and limitations

An important strength of this study is the randomized RSA design comparing mid-term migration of a press-fit cup and stem between CoC and CoPE bearing. This study is of high clinical relevance, since RSA is important for the introduction of new implants according to the Dutch Guideline for total hip prosthesis. [28] In our study, a variation in individual migration patterns is observed. Variation in migration is known to be higher in press-fit implants compared to cemented implants and may complicate to detect differences in small groups. A limitation of our study is that at five-year follow-up only 18 cups and 15 stems were available for RSA analysis in the PE group, since some patients were unwilling or not able to visit the clinic due to chronic illness, work or moving away from the hospital. Furthermore we did not perform BMD measurements. To investigate the influence of bearing on migration more comprehensively, we recommend experiments in larger trials with long-term follow-up. Moreover we recommend follow-up on long-term clinical functioning of these implants and the incidence of osteolysis, loosening and wear.

Similar five-year migration patterns of the press-fit Delta TT cup and H-MAX S stem were observed between ceramic and polyethylene liners. Implants in both groups showed secondary stabilization after a phase of initial migration. The results are promising for long-term survival of these implants with both a polyethylene and ceramic liner.

Acknowledgements

LimaCorporate provided financial support to compensate for study-related costs, however was not involved in data collection, analysis and interpretation of results. We would like to thank all patients for their willingness and time to participate in our study, our colleagues from the radiology department and JointResearch and V.A.B. Scholtes for their relevant contribution to the study.

Prof R.W. Poolman has obtained speakers fees and research support from LimaCorporate and Waldemar Link GmbH & Co. KG.

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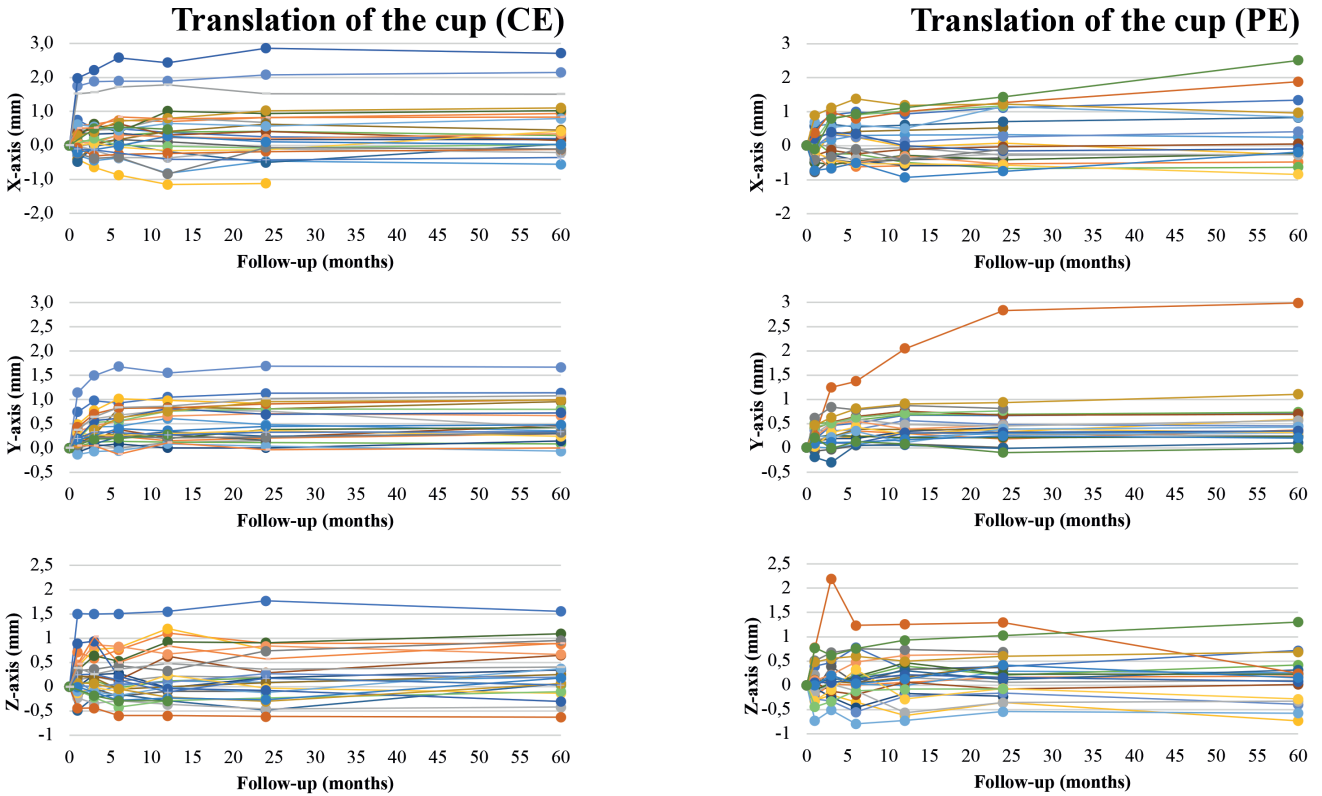
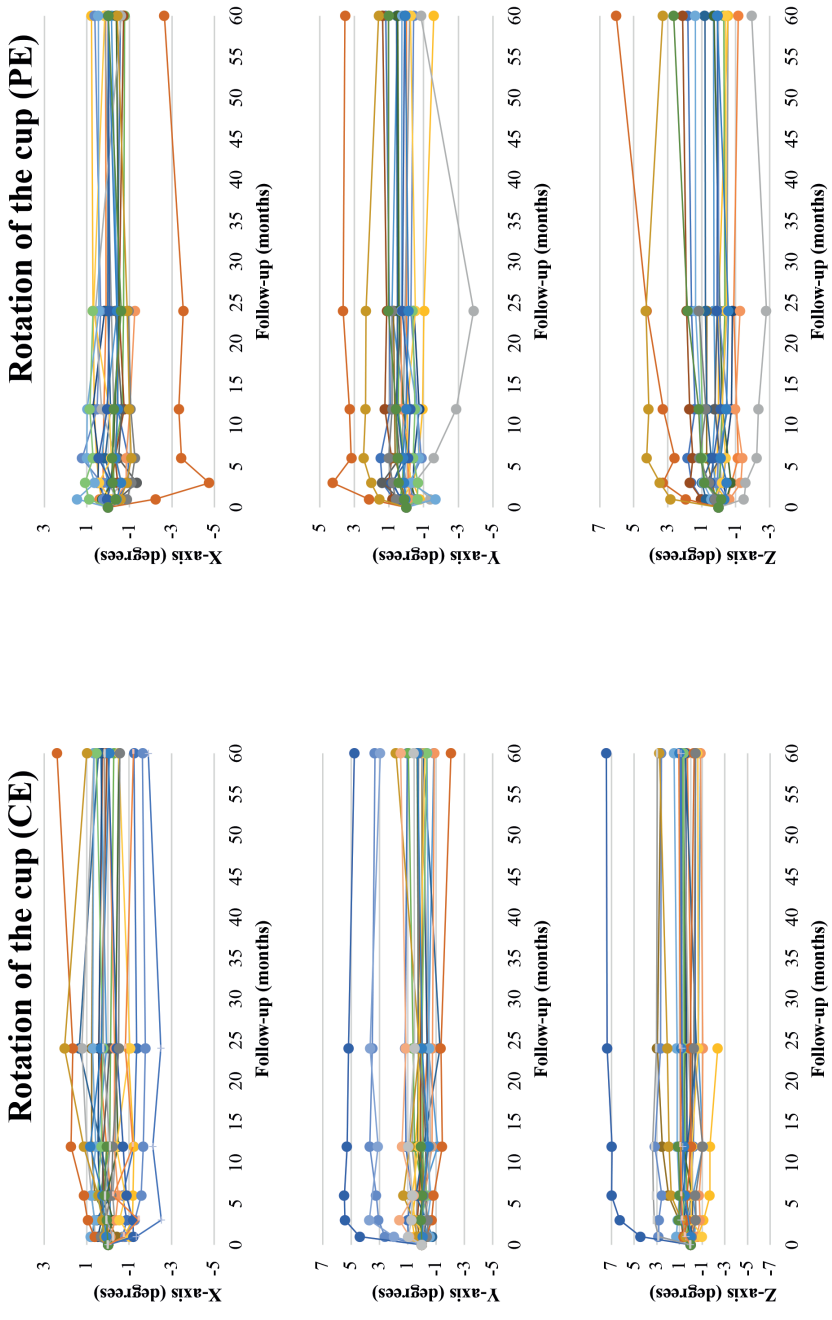
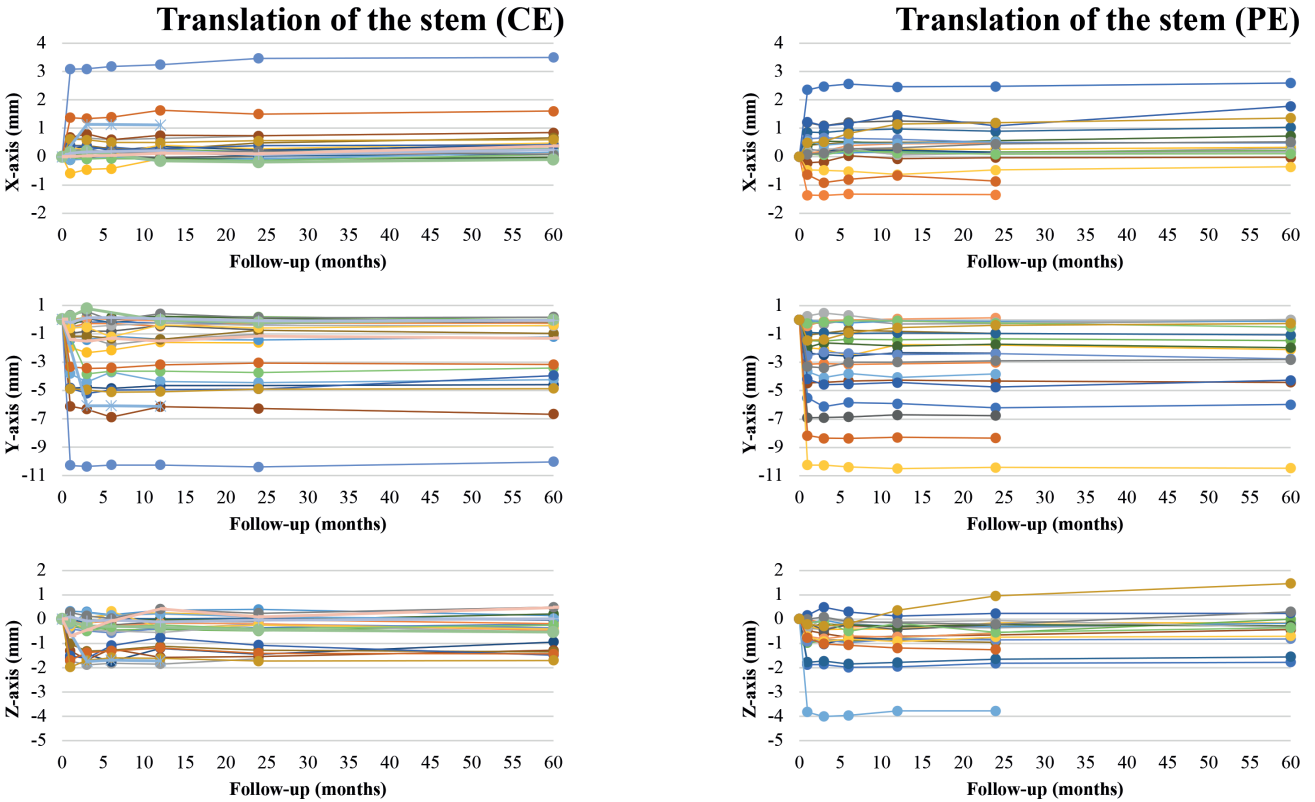


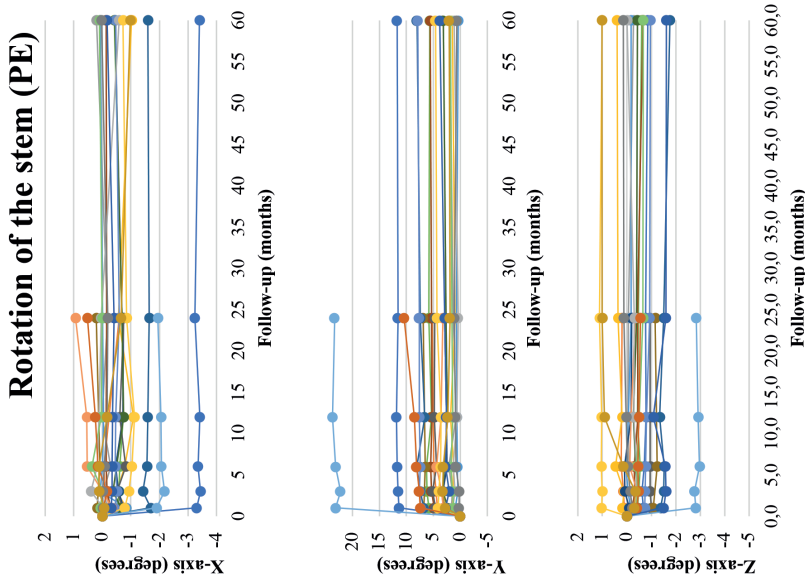
Appendix 1. Individual translation patterns of the cup with a ceramic liner (left) or polyethylene liner (right)



Appendix 2. Individual rotation patterns of the cup with a ceramic liner (left) or polyethylene liner (right)



Appendix 3. Individual translation patterns of the stem with a ceramic liner (left) or polyethylene liner (right)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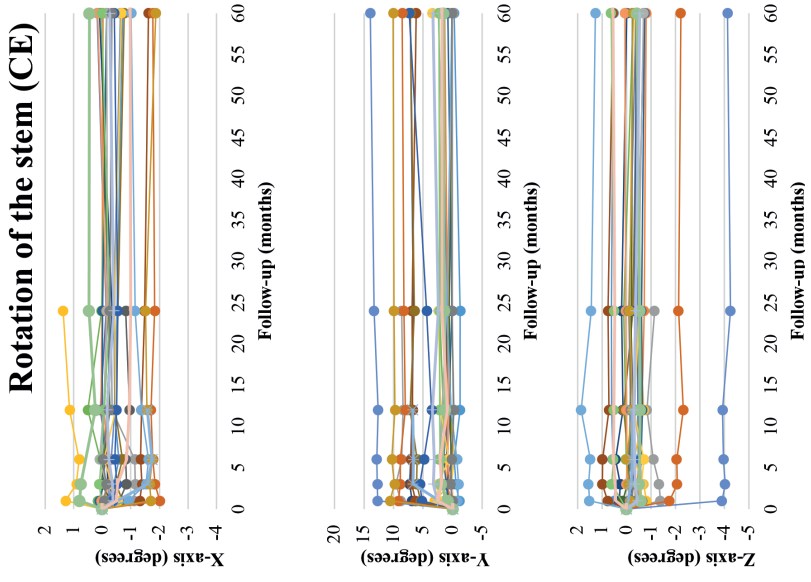
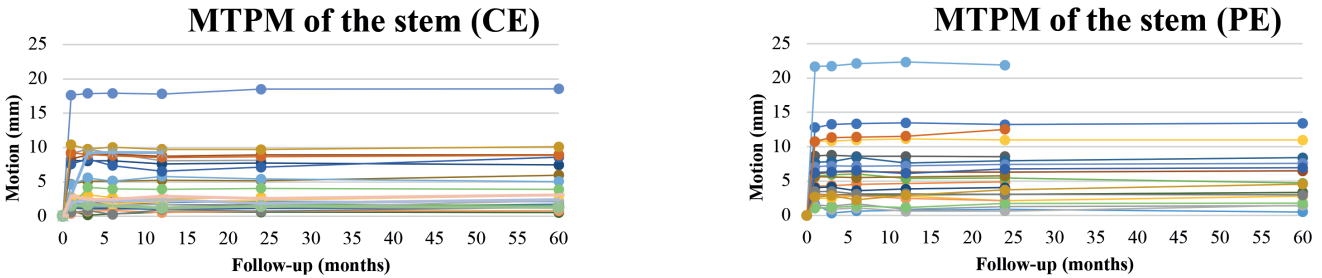
X-axis (degrees)
Y-axis (degrees)
Z-axis (degrees)
Follow-up (months)


Rotation of the stem (CE)
X-axis (degrees)
Y-axis (degrees)
Z-axis (degrees)
Follow-up (months)



Appendix 4. Individual rotation patterns and patterns of Maximum Total Point of Motion (MTPM) of the stem with a ceramic liner (left) or polyethylene liner (right)

Chapter 10

General discussion

GENERAL DISCUSSION

Since the introduction of low-friction total hip arthroplasty (THA), several long-term follow-up studies of this metal-on-polyethylene design have shown survivorship of THA of 85 to 96% at 25 years and 78% up to 35 years. [1-4] Due to improvement of implants and bearings, like for example highly cross-linked PE (HXLPE), revision rates have decreased. The Dutch Arthroplasty Register (LROI) showed a 13-year cumulative revision percentage of 5.2 using competing risk analysis for all THAs registered in the LROI up to 2021. [5] To keep improving the performance and survival of THA, more robust registry data, large cohort studies and more precise measurement research such as radiostereometric analysis (RSA) is needed, since differences in revision rates become smaller due to improvement of THA. RSA has the potential to demonstrate significant but smaller differences in wear and migration, and hereby to better predict survival between implants and bearings compared to other methods. These small differences are highly clinically relevant, since the prevalence of THA and the life expectancy are still increasing. As a result, the longevity of THA needs to increase to provide patients with a lifetime solution. With more than one million THAs placed yearly worldwide, even a small improvement of 0.1% affects more than 1,000 patients. [6, 7] Therefore, the results of this thesis will contribute to the ongoing improvement of THA.

Part 1 - Primary stability of the press-fit acetabular component

The first aim of this thesis was to gain insight in options to ease the estimate of the obtained press-fit by the definitive implant, by use of more precise measurement tools and to investigate their influence on primary stability. Long-term survival of press-fit implants is influenced by many factors. Primary stability, achieved by the initial fixation, is the most important factor to avoid both early and long-term loosening of the acetabular component in THA and determines the survival. Insufficient press-fit can lead to increased early migration, in which fibrous tissue attachment instead of osseointegration occurs, which is also a predictor for long-term aseptic loosening. [8] Henys et al. stated that the orthopaedic surgeon alone must decide about the mechanical state of the implant during surgery. [9] In line with this, Brulc et al. reported that unsuccessful press-fit fixation entirely depends on the surgeon and the surgical approach. [10] Nevertheless, it is a challenge to objectively measure the mechanical state or stability during surgery. In case the surgeon is in doubt of the achieved primary stability, additional reaming, a bigger cup, a cemented cup, or screw fixation can be applied. However, augmentation with screws is not proven to enhance the stability of press-fit cups on long-term and does not improve revision rates. [11, 12] Therefore, sufficient press-fit stability becomes even more important and should be secured intra-operatively. Although instruments like inclinometers or even robot assisted THAs are

invented to help cup positioning, tools available to objectively measure initial stability are lacking. Michel et al. measured the impaction force during implantation and reported that their impact analysis was related to the biomechanical stability of the implant, which however not resulted in a tool to use in clinical setting. [13] Another method to test the expected stability of the definitive implant, is the use of trial cups, of which to our knowledge no studies were published in literature. The size between the last used reamer, the corresponding trial cup and definitive implant differ, and this difference can differ between various manufacturers and implant brands as well, leaving the orthopaedic surgeon with a subjective feeling. Moreover, these trial cups never mimic the size of the definitive implant, because of the fear that the press-fit fixation might get lost, since this principle is based on placement of a cup in a underreamed acetabular cavity. [14, 15] The biomechanical study in **Chapter 2,** proves the concept that primary stability of the implant is not lost when mimicking the definitive press-fit by pre-expansion of the acetabular cavity using a dynamic trial fitting device called the X-pander® in ex vivo setting using bovine calf acetabula. [16] A limitation of **Chapter 2** that should be kept in mind, is that this device was only tested in bovine acetabula and all implantations were performed by one orthopaedic surgeon, while keeping in mind that literature mentioned that the factor for success of press-fit fixation is primarily dependent on the surgeon. [10] This shows the additional strength of **Chapter 3**, in which the advantage of the X-pander® was validated, by 45 experienced international orthopaedic surgeons. [17] This chapter reported that in both primary and revision cases this tool gave more reliable information than traditional trial cups, surgeons felt more confident in achieving press-fit, usage resulted in additional reaming or change of cup size, led to better cup insertion, could lead to the use of less additional screws and they supported the use of this tool instead of traditional trial cups. [17] However, this feasibility study carries the risk of selection bias, since the orthopaedic surgeons participating in this study might be more motivated to volunteer for this study. Since most orthopaedic surgeons are used to the fact that primary stability is a subjective feeling based on experience, they do not always use trial cups either, which might limit the use of the X-pander® in their hands. Nevertheless, the X-pander® could still be beneficial and used especially in difficult cases with troublesome achievement of primary stability during implantation or when this is expected during acetabular preparation. In less experienced hands of for example residents, fellows or less experienced orthopaedic surgeons, the X-pander® teaches them how sufficient primary stability should feel without placement of a wrong sized cup and could reduce the risk of complications, like loosening or acetabular fractures.

Hereby, **Part 1** has proven the concept of dynamic trial fitting and achieved in its aim to gain insight in the options to ease the estimate of the obtained press-fit by the definitive implant by use of a more precise measurement tool and its influence on primary

stability. Dynamic trial fitting can help to achieve sufficient press-fit by accurate sizing and assessment of the reamed acetabulum without affecting primary stability. Since no other studies about dynamic trial fitting were found in literature, **Chapter 2** and **Chapter 3** are the first to report the advantages of this concept and leave room for further improvement of intra-operatively used measurement tools.

Part 2: Bearing surfaces in total hip arthroplasty

Since the introduction of low-friction design THA, the ideal bearing has been a point of discussion. The advice in the guideline 'Total Hip Arthroplasty' of the Dutch Orthopaedic Association (NOV) is to use either a metal or ceramic head and a cross-linked polyethylene insert. CoC is mentioned as an option in certain cases of younger non-obese patients, in which a large head size (≥32mm) can be used, due to the lowest volumetric wear. [18] This guideline also stated that long-term comparative studies between all bearings, especially in press-fit THA, are limited. The incidence of use of metal and ceramic heads widely differs between national arthroplasty registries, with for example more metal heads used in Australia, England, Wales and Sweden, and more ceramics in New Zealand, The United States of America, Germany, Italy, and The Netherlands. [19-26] Since Co(HXL)PE is used more often compared to Mo(HXL)PE in The Netherlands and CoC holds the potential to overcome wear as seen in (HXL)PE, this thesis focused on the comparison of Co(HXL)PE and CoC. [25] In the LROI, all THAs registered up to 2021 implanted with Co(HXL)PE accounted for 60.3% and with CoC for 6.4%. [25] Therefore, the second aim of this thesis was to determine if CoPE, CoHXLPE or CoC shows better outcomes in press-fit THA.

Wear

One of the greatest concerns of PE bearings is wear and the potential of resulting wear-induced osteolysis. [27] Over the last years the use of conventional PE has reduced due to the invention of CoHXLPE, which shows the clinical importance of **Chapter 4**. [28] This study showed a higher statistically significant wear rate of -0.021 mm/year in medial direction in CoPE, whereas CoHXLPE showed no significant wear in this direction. [28] Moreover, in proximal direction, a higher wear rate of 0.033 mm/year was seen in conventional PE compared to a non-significant rate of 0.003 mm/year in CoHXLPE. [28] In **Chapter 5** a wear rate of 0.130 mm/year was observed in CoPE. [29] The wear rates found in both studies were comparable to literature, since Callary et al. found a mean proximal wear rate ranging from 0.00 to 0.06 mm/year in a systematic review including 12 primary THA cohorts with two to ten years of follow-up. [30] Kurtz et al. found a mean two-dimensional femoral head penetration rate after weighted-average analyses of 0.042 mm/year based on 1,503 hips with a HXLPE liner and 0.137 mm/year based on 695 hips with a conventional PE liner in a systematic review with

a minimal 5-year follow-up. [31] The difference in wear rates of CoPE between both **Chapter 4 and 5** and literature can be explained due to the difference in measurement methods, heterogeneity of the implants, bearings, and surgical techniques. [28, 29] Although the method used in **Chapter 5** to measure wear is validated and widely used, the RSA technique used in **Chapter 4** is the golden standard due to a higher precision and could detect wear earlier during follow-up. [28, 29] Another important reason is the difference in the length of the follow-up between **Chapter 4 and 5** and was also a problem in the systematic reviews, since relatively more wear occurs later in the longevity of the implant. [28, 29] Although RSA is superior in accuracy for the measurement of wear, limitations of RSA were also observed in **Chapter 4**. [32, 33] Measurement of negative wear rates in CoHXLPE was seen, which could be attributed to the accuracy range, which is 0.022 to 0.086mm depending on the direction of measurement. [34] Since the total wear in HXLPE in both medial and proximal direction was below this accuracy range, more long-term research is needed to measure more cumulative wear over time and hereby overcome imprecision due to reduced wear rates in HXLPE. The superiority of HXLPE on revision and osteolysis rates has been reported in recent systematic reviews with a minimum of five and ten-years follow-up, without showing a difference in clinical outcome. [35, 36] This trend was also reported in the narrative review of Langlois et al. updating the best available research, which showed the same result seen in registry studies. [37] The fact that these studies report their outcomes regardless of head type and fixation method, shows the clinical relevance of **Chapter 4 and 5,** reporting their outcomes in specific bearings and specifically for press-fit THA. [28, 29]

Focused on bearings that do not show wear-induced osteolysis, CoC is the most used and promising with in biomechanical research the lowest friction factor of all bearings. [38] In **Chapter 5** we showed wear rates of 0.130 mm/year in CoPE and 0.000 mm/year in CoC in cranial direction. [29] In literature wear rates below 0.001 mm/year are described for CoC and 0.030 for CoHXLPE and 0.072 for CoPE. [39] The lower wear rates of CoC are result of the superior lubrication due to the hydrophilic surface of the ceramic, the better biocompatibility of ceramic particles, high chemical stability and the higher resistance to damage compared to other bearings. [40, 41] Controversially, in vitro it was observed that if very high local volumetric concentration on ceramic occurs, wear particles exists and there is a potential for osteolysis due to a local inflammation reaction induced by these particles. [42] In a microscopic retrieval study of revised THAs, ceramic debris was found in surrounding tissues, in which larger size alumina wear particles are presumed to be generated during microseparation of the head and inlay during swing phase and rim impingement. [43-45] This shows that correct placement of the cup is important in CoC to overcome macroscopic wear particles produced by rim impingement. The same finding to prevent wear in PE was observed in **Chapter 5**, showing that inclination

should be below 45 degrees, since in line with literature cup inclination is an important predictive factor for PE wear as well. [29, 46-48] However, the amount of wear particles in CoC in vitro, will presumably not be reached in patients due to a difference in loading concentration and extremely low wear rates in vivo. [42] Affatato et al. supported this, reporting that ceramic produces no wear particles and very low wear. [49] Hereby, the occurrence of significant wear in CoC in vivo still remains a point of discussion. This might be one of the reasons why wear analysis of CoC by RSA to date is not performed in literature to knowledge yet.

Regarding the second aim of this thesis to determine which bearing showed better outcomes in press-fit THA, focused on wear, **Chapter 4 and 5** and literature show that HXLPE is preferred over PE. [35-37, 50-57] Since CoC outperforms CoHXLPE regarding wear rates, this bearing can be a good alternative to overcome PE wear induced osteolysis on long-term, especially in younger patients, which need a longer longevity of the implant. Due to wear reduction by improvement of bearings, it becomes more important to investigate what the effect of wear for especially CoHXLPE will be on longer term, like at least 20 years.

Revision

Since wear is only one important factor influencing revision, choice between both bearings should be made on overall survival and other reasons for revision as well. In **Chapter 6** we reported that CoC has a higher risk of overall revision in modular press-fit THA compared to CoPE. [58] Other systematic reviews with different inclusion criteria or less studies included, found no difference. [50-53, 57, 59] Only one systematic review performed in patients under 60-years showed in sub analysis that CoC has a lower risk for revision at 10-years, compared to PE. [59] However, two of the four studies including this sub analysis were MoPE compared to CoC and were therefore unjustly included and accounted for 89.1% of the weight. Although **Chapter 6** was the first study including registry studies compared to other reviews, the found difference in revision was only seen in two registry studies with several limitations and not in RCTs and non-randomized cohort studies. Also, this was based on a very low-quality GRADE evidence and therefore this result should be considered preliminary. Moreover, in **Chapter 6** important limitations were the risk of lead time bias, the high statistical heterogeneity and baseline imbalance, which should be kept in mind when interpreting the differences in revision. An important baseline imbalance might be introduced by the fact that CoC is placed more often in younger patients. Focused on overall revision in this group, national registry data of the National Joint Registry investigating revision in patients receiving a THA ≤20 years showed a survival of 99% in CoPE at 5-years and 98% in CoC. [60] However, survival at 10 to 12-years shown in survival plots, declined in CoPE to just above 80%, whereas CoC remained stable around the 98%.

[60] A French multicenter trial including 941 THAs in patients younger than 30 years with a mean follow-up of six years showed a higher risk of revision in hard-on-soft bearings, like CoPE when compared to hard-on-hard bearings like CoC with an OR of 3.42 and the main reasons for revision being mentioned aseptic loosening (51%) and wear (24%). [61] In a study investigating revision in the LROI by the five-year survival of primary THA in patients younger than 55 years, cox-regression analysis showed a significant lower risk of revision of CoC compared to CoPE with a HR of 0.77. [62] In a recent meta-analysis in patients aged 30 years old or less, the lowest annual revision rate was observed in uncemented ceramic-on-ceramic bearing of 0.063%/year compared to 0.17%/year in hard-on-soft bearing. [63]

Focused on specific reasons for revision, in **Chapter 5 and 6** we showed no difference in dislocation, infection and periprosthetic fracture. [29, 58] This was in line with the other abovementioned systematic reviews as well. [50-53, 57, 59] According to Migaud et al. the time to first revision differed between CoC and other bearings like Co(HXL)PE. [64] The wide variation in follow-up between studies in **Chapter 6** could influence the incidence of the different reasons for revision and can be the reason that no difference was found in **Chapter 6**. [58] For dislocation, since wear in Co(HXL)PE increases the risk of dislocation; for infection, which was seen less in CoC at both three and nine years follow-up in two different studies; and for periprosthetic fracture, which is linked to wear induced osteolysis and a difference in biologic response in more elastic Co(HXL)PE bearing. [65-70] A reason that **Chapter 5** found no difference in reasons for revision, could be the fact that this study was non-randomized, in which both the indication bias for one of both bearings and the difference in patient characteristics could be confounders influencing the chance of the abovementioned reasons for revision. [29] One of the main concerns against using CoC in literature is the fear of ceramic fracture. Recent research found that fracture of ceramic is rare and occurs in one in 1,000 patients who receive a ceramic coupling. [71] In addition, a recent meta-analysis showed an incidence of 0.9/1,000 patient-year in the third-generation forte CoC group compared to 0.5/1,000 patient-year in the fourth-generation Delta CoC group. [72] Moreover, Toni et al. reported even a lower complication rate of ceramic fracture with an incidence of 0.08% in 2,879 THAs in 10 years and mentioned that this complication is often caused by incorrect surgical technique and should not limit the use of ceramic bearing. [73] When comparing the incidence of ceramic fracture as a bearing related complication of CoC to wear of Co(HXL)PE as its bearing related complication, Epinette et al. found no significant difference in survivorship between CoC and CoHXLPE with a minimum follow-up of 10-years and these bearing related complications as the endpoint. [74] Moreover, the randomized trial of Venditolli et al. found that after 20-years follow-up CoC bearing provided safer revision rates when compared to MoPE when using an uncemented cup, without any ceramic fracture observed. [75]

Another important feature of CoC bearing to keep in mind when counseling patients for THA, is the incidence of squeaking. Although it was not reported in **Chapter 5** and the incidence widely differed between studies in **Chapter 6**, this CoC specific problem can influence patients daily living. [29, 58] Improvement of ceramic has shown that the incidence of squeaking has been reduced, resulting in less revisions because of squeaking. [41] Although ceramic fracture and component related noise like squeaking are still significantly more present in CoC compared to Co(HXL)PE in literature, overall revision rates remain comparable.

The second aim of this thesis was to determine which bearing showed better outcomes in press-fit THA. Focused on revision, in **Chapter 6** we showed higher revision rates in CoC compared to Co(HXL)PE, but this result should be considered preliminary due to limitations of this study. Moreover, a potential superiority of CoC in younger patients regarding revision was seen in literature. Since a decrease of all reasons for revision and component-related complaints is seen due to improvement of both bearing couplings over the last decades and no differences in clinical functioning are found so far, literature remains controversial to prove the preference for one certain universal bearing. Since we analyzed the outcomes in one age group in **Chapter 6**, future research should focus on separate analysis in age groups, since a difference in outcomes is expected. Although reasons for revision might differ between bearings, no overall difference in reasons for revision was found in **Part 2**. Since the improvement of ceramic has led to less ceramic fracture, the fear of ceramic fracture should no longer be a limitation against using this bearing.

Clinical functioning

Focused on clinical functioning, in **Chapter 5** we showed no difference based on the Harris Hip Score. [29] Although this study was not randomized, which might influence this outcome by baseline imbalance and indication bias, literature showed no difference in clinical results between bearings as well. [76-78] In addition, in **Chapter 4** we found no difference either, but this study was not powered on clinical outcomes. Since the focus of both **Chapter 4 and 5** was not on clinical functioning and literature showed no difference either, this thesis cannot conclude any preference regarding the second aim of this thesis to investigate better outcomes on clinical functioning between bearings in patient reported outcome measurements (PROMs).

Part 3 - Influence of bearing choice on the primary stability and early revision rate of the press-fit acetabular component

The main causes for early revision of total hip arthroplasty are infection, dislocation, aseptic loosening and postoperative periprosthetic fracture. [79] However, the influence of bearing on reasons for revision remains underexposed. The third main aim of this

thesis is to investigate the potential influence of CoC and Co(HXL)PE on short-term revision and complication rates, specifically focusing on primary stability of the cup.

Focused on early aseptic loosening, in **Chapter 7** we aimed to identify risk factors for this cause. [80] Several risk factors can influence the process of transition from initial primary stability obtained by press-fit to definitive secondary stability by osseointegration, including macro- and microscopic cup design, implant design, position, alignment, biocompatibility, surgical approach and patient characteristics including bone quality. [81, 82] The last potentially important factor that is often mentioned in literature to bring osseointegration at risk, is bearing choice like a hard-on-hard CoC bearing, but there is still a lack of evidence. [83-87] In **Chapter 7** we presented the theory that a CoC bearing raises the total stiffness of the implant and as a result, the forces of weight bearing and potential rim impingement get less absorbed compared to a hard-on-soft Co(HXL)PE bearing. [80] These forces are transferred to the bone-implant interface and can cause shear forces which can jeopardize the initial press-fit. As a result, too much initial migration can result in failure of ingrowth by osseointegration since fibrous tissue instead of bone is formed and can hereby result in migration and even early aseptic loosening. [8] The review of Sunfeldt et al. supports our abovementioned theory that micromotion affects the implant stability, may have a harmful effect on the bone bed, inhibits bone transformation and thereby subsequent loosening of the implant can occur. [88] This theory is supported in **Chapter 8** by reporting significantly more cup loosening in the first two-years after placement in CoC, which was mostly aseptic and resulted in a higher two-year cup revision rate in CoC compared to CoPE in the LROI. [89] Although we could not conclude causality in **Chapter 8** as this was a registry study with observational data, this study showed no interaction with cup type. As discussed earlier in **Chapter 6,** we showed a higher risk of overall revision in modular press-fit THA in CoC compared to CoPE. However, this result was only seen in two registry studies and not in other study designs and no difference in the reasons for revision was reported. [58] All these chapters together with literature indicate a potential relation between CoC and a higher risk of early revision, due to aseptic loosening. Since initial migration does not always need to lead to aseptic loosening, the goal of the RSA study in **Chapter 9** was to further confirm our theory by comparison of initial migration between CoC and CoPE when using the same press-fit cup. [90] Since an important limitation of both **Chapter 7 and 8** was the risk of indication bias due to a non-randomized cohort setting, which might have influenced the chance of loosening as well, **Chapter 9** was performed in a randomized setting. However, in **Chapter 9** we showed no statistically significant difference in mean migration between CoC and CoHXLPE. [90] A limitation of **Chapter 9** was the variation in individual migration patterns complicating to detect differences in small groups. Nevertheless, only two other studies in literature priorly

reported migration patterns between CoC and Co(HXL)PE, also without showing a significant difference, of which one was the same cohort as **Chapter 9** reporting the short-term results. [90-92] Although it was not significant, in **Chapter 9** we showed more mean cup migration in CoC compared to CoHXLPE for especially rotation on the Z-axis in CoC, which is together with translation on the Y-axis an important predictor for aseptic loosening. [93] This can become highly clinically relevant in specific cases. For example, increased cup migration is seen in uncemented cups in female THA patients with low systemic bone mineral density. [94, 95] This can be related to the patients age as well, since ageing reduces the quality and density of the subchondral trabecular bone, which could influence osseointegration and cup stability as well. [96, 97] In patients with rheumatoid arthritis (RA) increased cup migration is observed compared to patients with osteoarthritis (OA). [98] However, OA itself can impair osseointegration and implant stability as well. [96, 99] Disorders affecting bone mineralization and remodeling, inflammatory conditions, physical activity, genetics, smoking, obesity and nutrition deficiencies have their influence on the bone quality and thereby osseointegration as well. [100, 101] In line with this, Garcia-rey et al. found that survival of THA for patients under 40 years receiving CoC bearing was mainly restricted due to the chance of aseptic loosening and was related to the initial hip disease, which were respectively avascular necrosis, congenital hip dysplasia, post-traumatic arthritis and RA. [56] Another even more important factor is the implant itself, which might declare the difference between the rates of aseptic loosening in **Chapter 7 and 9**. [80, 90] The implant design, position, alignment, biocompatibility and surface preparation resulting in a specific macro- and microscopic design of a cup, are all factors that potentially affect the initial stability and hereby the motion after implantation. [102, 103] In case a potentially less stable cup due to the design is used in combination with CoC this can potentially result in catastrophic revision rates as seen in **Chapter 7,** which is supported with high early failure rates of this cup in literature as well. [86, 104, 105] In case a safe cup is used, it can be theorized that the less physical load transfer in CoC does not always have to result in aseptic loosening, but can still result in more mean initial migration compared to CoHXLPE as reported in **Chapter 9**. [90] Moreover, the migration patterns in **Chapter 9** showed that the difference in mean migration stayed more or less the same over the follow-up period, showing comparable migration curves. [90] This indicates that the difference in migration between both bearings mostly occurs in the first period after implantation, during the phase of initial settling. Especially in patients with the aforementioned disorders or risk factors for impaired bone quality, primary stability can be insufficient. Hereby it can be theorized that cups with a CoC bearing have a wider and larger 'at risk' area which starts earlier during the phase of transition to definitive stability as presented in **Chapter 7** and are therefore more and during a longer period at risk for migration and loosening. [80] Another important thing that should be kept in mind

is that if early migration does not result in early aseptic loosening, it still can hamper long-term outcomes by increasing the long-term revision chance of aseptic loosening as well. [93, 106]

Focusing on the third aim of this thesis to investigate the potential influence of the bearing on revision and complications rates, this thesis succeeded to provide a theory about the influence of hard-on-hard bearings on the primary stability of the cup as presented in **Part 3.** Together the **Chapters 7, 8 and 9** complement each other in the theory that in the multifactorial process of aseptic loosening, which is influenced by many factors, the (hard-on-hard) bearing choice seems an important factor, together with the cup design, bone quality and correct placement of the cup.

FUTURE CONSIDERATIONS

Research

Since primary stability is the most important factor to avoid both early and long-term loosening of the acetabular component in THA, this should be secured intra-operatively. The concept of dynamic trial fitting has been proven helpful. In **Part 1** we achieved to gain insight on how to ease the estimate of the obtained press-fit by the definitive implant by use of more precise measurement tools and their influence on primary stability. Hereby this concept holds the potential to prevent early and long-term revision and could replace traditional trial cups in press-fit THA. Nevertheless, future in vivo studies are necessary to prove their safety and superiority over traditional trial fitting in humans, with for example RSA. A potential research set-up would be randomized controlled trial between primary press-fit THAs implanted with for trial fitting either traditional trial cups being used in one group or a dynamic trial fitting device like the X-pander® in the other group, to predict primary stability of the definitive implant. Additional to this, participants could be double randomized on bearing between CoC and CoHXLPE as well, since as reported in **Part 2** wear in CoC still remains point of discussion and to further fund the theory as presented in **Part 3** about the influence of CoC on the primary stability of the cup. This should be performed in a randomized setting avoiding indication bias and in larger cohorts to ease detecting differences in small groups, especially due to the low wear rates in CoHXLPE, and to avoid underpowering with long-term follow-up and the accompanying potential loss to follow-up. The primary outcome will be migration measured using RSA by blinded researchers to investigate primary stability after implantation, transition to secondary stability and long-term migration or loosening. The secondary outcomes will be wear, also measured using RSA, clinical functioning by long-term follow-up of potential complications, reasons for revision and by follow-up of

patient reported outcome measurements (PROMs). Another secondary outcome will be to explore the hypothesis of the higher risk of aseptic loosening in patients with a lower BMD in combination with CoC, by taking BMD measurements at baseline. For follow-up, ideally 20-years or even lifetime RSA surveillance is needed to observe a potential difference in long-term revision, wear, and loosening.

With this extensive research set-up with double randomization several research questions can be addressed. At first, the potential value of the X-pander® can be proven by measuring its safety based on initial migration and the risk of long-term loosening by RSA. Secondly, this research could investigate if dynamic trial fitting can be more important to use in certain bearings to achieve sufficient primary stability by the double randomization design. Thirdly, the question if wear even occurs in CoC can be finally addressed. In the fourth place, the influence of bearing on migration can be further investigated, especially in larger cohorts focused on long-term revision and the hypothesis of a higher risk of aseptic loosening in patients with a lower BMD in combination with CoC can be examined. At last, by follow-up of clinical functioning by measurement of complication and revision rates and PROMs, this set-up can help to research if either a CoHXLPE or CoC bearing is preferred based on both short and long-term outcomes. Ideally this set-up needs to be tested in subgroups as well, for example in different age and BMD groups to see if different patient groups need different bearings for the best outcomes focused on all aforementioned outcomes. For example, these outcomes need to prove if the improved wear characteristics of HXLPE might be enough wear-resistant in younger patients on long-term compared to the better wear resistance of CoC.

Another important research question in line with this is cost-effectiveness of both bearings. CoC is three times more expensive than Co(HXL)PE bearing. [107] This might be one of the reasons why in **Chapter 8** we showed a decrease in the use of CoC bearing over the last decade in The Netherlands. [89] Fawsitt et al. concluded that the cheapest implant combination is the most-effective in the oldest patient group. [108] However, a more expensive CoC bearing can become cost-effective when it overcomes a(n) (extra) revision especially in young patients, which is supported by the higher survivorship of CoC in younger patients in the aforementioned studies. [60-63] Hart et al. however found that in young patients receiving THA, CoC was the most commonly used bearing, but from 2006 to 2016 Co(HXL)PE became the most used bearing in the United States of America. [109] Therefore, further investigation on the higher costs of CoC in younger patients is needed, since these costs might earn itself back due to a better longevity and might therefore not limit its use in this group. In addition to the proposed research set-up, a cost-utility analysis should be performed in a separate observational setting,

focusing on healthcare costs, complication rates, revision rates and PROMs in large cohorts with ideally lifetime surveillance, especially in younger patients receiving THA.

Another option to overcome the potential increased migration, in case CoC is the preferred bearing of use, could be cemented fixation. Since this is outside the scope of this thesis, further research randomized between both fixation methods focused on migration and loosening with RSA and clinical (PROMs and revision rates) outcomes is needed. Especially in cases with a potentially higher risk of loosening (for example in patients with lower BMD), this research should investigate if cementation could be an alternative to press-fit fixation in case a CoC bearing is preferred to overcome the higher chance of early aseptic loosening. Moreover, cost-effectiveness as mentioned above, needs to determine if one of both fixation methods might be preferred.

Clinical setting

Focused on clinical setting, the advice of the guideline 'Total Hip Arthroplasty' of the Dutch Orthopaedic Association (NOV) is to use either a metal or ceramic head and a cross-linked polyethylene insert and they mention that CoC is an option in certain cases of younger non-obese patients. [18] Although literature and the results of **Part 2 and 3** are not fully conclusive to present a universal preference regarding bearing choice, the results of this thesis can be used to propose a more patient specific approach. With **Part 2** we attribute to the available literature and agree that when a ceramic head with polyethylene inlay is used, HXLPE should be used over conventional PE whenever available. [35-37, 50-57] However, focused on the advice regarding CoC, this could be more precise about a recommendation when CoC can be used. Since CoC can be a good alternative to overcome wear and since younger patients need a longer longevity of the implant and mostly have good bone quality, CoC might be better to be reserved for younger patients, which is advised by several other studies as well, reporting higher survival. [110, 111, 60-63] To keep in mind is the theory presented in **Part 3** that if the bone quality is impaired or gaining primary stability is troublesome, CoC might better not be used to avoid the potential higher risk of aseptic loosening caused by impaired osseointegration as a result of increased initial migration due to micromotion in this stiff bearing, especially in combination with implants with more troublesome achievement of sufficient press-fit fixation.

According to this thesis, a better recommendation could be that in younger patients a CoHXLPE or CoC bearing are both a feasible option and that CoC could be considered more often due to its wear advantages, without the fear for fracture of the ceramic, but implantation of CoC should be restricted to cases in which no impaired bone quality is expected or to cases gaining primary stability intraoperatively is not troublesome. Since

dynamic trial fitting is a potential option to replace traditional trial cups, especially in cases which troublesome achievement of primary stability is expected, its use should be considered more often in press-fit THA when using a CoC bearing. To avoid troublesome fixation or loosening in patients with known low BMD or an older age the advice should be to use a HXLPE insert in this group. In this group the use of dynamic trial fitting to obtain sufficient press-fit intraoperatively can be helpful as well. To specify certain age limits for both younger and older patients more research needs to be performed as mentioned above. However, strict age restricted use of bearings is not preferred either, since other patient characteristics like bone quality, the activity of the patient, medical history and (dis)advantages of both bearings should always be considered when choosing bearing as well.

CONCLUSIONS

1. Dynamic trial fitting can help to achieve sufficient press-fit for the definitive implant, without affecting its primary stability.

2. Dynamic trial fitting holds the potential to replace traditional trial cups due to accurate sizing and eases the estimate of the obtained press-fit of the definitive implant by more precise assessment of the reamed acetabulum and could thereby prevent both early and long-term revision in press-fit THA.

3. CoHXLPE outstands CoPE on the outcomes regarding wear rates and conventional PE should therefore be avoided whenever possible.

4. CoC is a good alternative for Co(HXL)PE focused on better outcomes regarding wear reduction. However, more research is needed to confirm potential (wear) advantages on long-term and cost-effectiveness of both bearings, especially in different age groups.

5. Systematic review of literature showed a lower risk of overall revision in press-fit THA with a modular cup and CoPE bearing compared to CoC in registry studies. This outcome should be considered preliminary since no difference was found in other methodological designs and this outcome was based on only two studies of very low-quality and with several limitations and no difference was observed for all reasons for revision separately.

6. The unacceptable high aseptic loosening rate at ten-years follow-up of the SeleXys TH+ cup in combination with a CoC bearing, which stabilized after a high early failure incidence, could be partially attributed to the influence of CoC on osseointegration during the transition of primary to definitive stability.

7. In the Dutch Arthroplasty Register (LROI) press-fit THAs with CoC bearing showed a higher two-years cup revision rate compared to CoPE, with cup loosening as the only significant different reason for revision and seen more often in CoC and mostly aseptic. Future randomized research is needed to confirm causality.

8. Similar five-years migration patterns of the press-fit Delta TT cup were observed between CoC and CoHXLPE bearing using RSA. The higher mean migration throughout the follow-up period in CoC was not statistically significant and both groups showed secondary stabilization after initial migration.

9. CoC is thought to be a potential key factor for the multifactorial problem of early migration and potential resulting aseptic loosening in press-fit total hip arthroplasty.

10. CoC and CoHXLPE are both a feasible option for younger patients in press-fit THA, but CoC could considered more often due to the wear advantages, without the fear for fracture of the ceramic. However, CoC should be restricted to cases in which no impaired bone quality is expected or to cases in which gaining primary stability intraoperatively is not troublesome, to overcome the potential higher risk of early aseptic loosening. For older patients HXLPE is considered the option of choice.

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Chapter 11

Summary
Dutch summary – Nederlandse samenvatting

SUMMARY

Since the introduction of low-friction total hip arthroplasty (THA), implants and bearings are continuously improved to reduce revision rates and thereby increase the longevity of the implant. In press-fit THA the stability of the implant and wear are the main important factors for survival, in which the bearing is assumed to play an important role. The goals of this thesis were to gain insight in options to ease the estimate of the obtained press-fit by the definitive implant during implantation, by use of more precise measurement tools and to investigate their influence on primary stability; to determine if ceramic-on-polyethylene (CoPE), ceramic-on highly cross-linked polyethylene (CoHXLPE) or ceramic-on-ceramic (CoC) shows better outcomes in press-fit THA and to investigate the potential influence of these bearings on short-term revision and complication rates, specifically focusing on primary stability of the cup.

Part 1: Primary stability of the press-fit acetabular component

After implantation of the cup, the primary stability needs to be sufficient. Thereafter press-fit stability decreases and osseointegration increases, resulting in the definitive stability of the implant. [1] During this transition to secondary stability the cup is vulnerable for increased migration. As a result, fibrous tissue attachment can occur, bringing the cup at risk for both short- and long-term loosening. [2,3] One of the most important factors in achieving sufficient primary press-fit is the intra-operative feeling during implantation. To test the expected stability of the implant, trial cups can be used. However, these never mimic the size of the definitive implant due to the fear of loosening press-fit, by which the choice for the definitive size of the implant remains substantially a subjective feeling of the orthopaedic surgeon. In **Chapter 2** we showed that a dynamic trial fitting device called the X-pander®, which mimics the definitive press-fit by pre-expansion of the acetabulum, can be safely used without jeopardizing primary stability of the cup. [4] Hereby this tool can be used to obtain a more precise measurement during implantation, which can be especially helpful in less experienced hands and in difficult revision cases. The potential of the X-pander® was supported by our findings in **Chapter 3**, since experienced surgeons reported that the X-pander® gave more reliable information on press-fit feeling, they felt more confident in achieving press-fit, usage resulted in additional reaming or change of cup size, led to better cup insertion and could lead to use of less additional screws, when used in both primary and revision cases compared to trial cups. [5] Therefore, they supported the use of this tool instead of traditional trial cups. Although trial fitting may not be used in all cases by experienced orthopaedic surgeons, the X-pander® can be beneficial when achievement of primary stability is troublesome in both primary and revision THA cases and in less experienced hands of residents, fellows or less experienced orthopaedic surgeons

to learn how sufficient primary stability can be obtained and should feel. Regarding the first aim of this thesis, the X-pander® holds the potential to replace trial cups and to prevent placement of wrong sized cups and reduce the accompanying risks and complications, and to prevent early and long-term revision by easing the estimate of the obtained press-fit by the definitive implant during implantation by use of a more precise measurement intraoperatively, without affecting primary stability.

Part 2: Bearing surfaces in total hip arthroplasty

The ideal bearing in press-fit THA remains point of discussion. Ceramic-on (highly cross-linked) polyethylene is one of the most used bearings. A concern against (HXL) PE is the wear and potential resulting wear-induced osteolysis. Although cross-linking reduces this risk, long-term results are still limited. In **Chapter 4** we showed that total 3D wear was less in THAs implanted with HXLPE instead of conventional PE at 5-years follow-up. [6] Ceramic-on-ceramic bearing results in even lower to no wear rate at all. Since comparative research between CoC and Co(HXL)PE is limited, in **Chapter 5** we compared both bearings. After 10-year follow-up this research showed lower wear rates in CoC compared to CoPE, with cup inclination as a predictive factor for wear and no differences in complications, Harris Hip Score and radiological findings. [7] Regarding the second aim of this thesis, focused on which bearing shows better wear outcomes in press-fit THA, HXLPE is preferred over PE and CoC can be a good alternative to overcome PE wear induces osteolysis on long-term, especially in younger patients, which need a longer longevity of the implant. These wear rates become important when a difference in revision rates would be seen. In **Chapter 6** the difference in revision between CoC and CoPE was investigated, which showed a lower risk of overall revision in registry studies of primary THA with a press-fit modular cup using CoPE compared to CoC. [8] Since this outcome was based on only two registry studies with several limitations and very low-quality GRADE evidence and the other methodological designs showed no preference for one of both bearings, this result should be considered preliminary. Moreover, a potential superiority of CoC in younger patients regarding revision was seen in literature. Since a decrease of all reasons for revision and component-related complaints is seen due to improvement of both bearing couplings over the last decades and no differences in clinical functioning are found so far, literature remains controversial to prove the preference for one certain universal bearing. Since the improvement of ceramic has led to less ceramic fracture, the fear of ceramic fracture should no longer be a limitation against using this bearing. Since the outcomes were analyzed in one group in **Chapter 6,** future research should focus on separate analysis in age groups, since a difference in outcomes is expected for both wear and revision.

Part 3: Influence of bearing choice on the primary stability of the press-fit acetabular component

One of the main causes for early revision is aseptic loosening. Therefore, in **Chapter 7** a cohort of prospectively documented press-fit THAs with a high early revision rate was investigated, with the aim to identify risk factors for early revision due to aseptic loosening. The transition from initial primary stability to definitive stability by osseointegration can be influenced by factors such as the macro- and microscopic design of the cup, the implant position, alignment, biocompatibility, surgical approach, and patient characteristics including bone quality. [9,10] As a result the implant can become at risk for loosening. In **Chapter 7** we showed a high aseptic loosening rate, which stabilized after a high early failure incidence. [7] As a reason for this high early failure rate, both the macroscopic cup design and CoC bearing were mentioned. In **Chapter 7** we also presented the theory that the total stiffness of the implant is raised by the hard-on-hard CoC bearing and as a result the forces on the implant are less absorbed by the implant itself compared to Co(HXL)PE and are transferred to the bone-implant interface. At this site the resulting shear forces can jeopardize the initial press-fit, hamper osseointegration and can result in migration of the cup and, if too much migration is observed, aseptic loosening as well. The results of **Chapter 8** supported this theory, by showing a higher two-year cup revision rate in CoC compared to Co(HXL) PE in the Dutch Arthroplasty Register (LROI) with significantly more cup loosening as the reason for revision in CoC, which was mostly aseptic. [11] Since migration does not always have to result in loosening, migration between CoC and CoHXLPE was investigated in press-fit THA in a randomized setting using RSA in **Chapter 9**. [12] This study showed no statistically significant difference in mean migration between CoC and CoHXLPE, although the mean cup migration in CoC was higher during five-years follow-up. [12] Since cup migration and the risk of aseptic loosening are multifactorial, it can be theorized that in cases with more risk factors for loosening, CoC might increase this risk. Altogether, focusing on the third aim of this thesis, CoC is thought to be a potential reason for the multifactorial problem of early migration and potential resulting aseptic loosening in press-fit total hip arthroplasty.

According to this thesis, sufficient primary stability during implantation is a crucial factor for survival of the implant in THA. Therefore, dynamic trial fitting devices could be considered for use in clinical practice to avoid troublesome fixation, since they are safe regarding the primary stability of the implant. More long-term randomized RSA studies, especially in cases with impaired bone quality in combination with BMD measurements, are needed to further confirm superiority of one of both bearings and to investigate cost-effectiveness. Upon that time, this thesis shows that CoC and CoHXLPE are both a feasible option for younger patients in press-fit THA, but CoC could be considered more

often due to the wear advantages, without the fear for fracture of the ceramic. However, CoC should be restricted to cases in which no impaired bone quality is expected or to cases gaining primary stability intraoperatively is not troublesome, to overcome the potential higher risk of early aseptic loosening. For older patients HXLPE is considered the option of choice.

DUTCH SUMMARY – NEDERLANDSE SAMENVATTING

Sinds de introductie van de totale heupprothese (THP), zijn de implantaten en articulaties continu verbeterd om revisie aantallen te verminderen en de levensduur van de implantaten te verbeteren. In press-fit THPs zijn de primaire stabiliteit van het implantaat en de slijtage van de articulatie de belangrijkste factoren die de overleving beïnvloeden, waarbij de materialen van de articulatie een belangrijke rol spelen. De doelen van deze thesis zijn om inzicht te verkrijgen in de opties om een betere intra-operatieve inschatting te maken van de stabiliteit van het definitieve implantaat, door middel van preciezere meetinstrumenten en de rol hiervan op de primaire stabiliteit te bepalen; om te bepalen of keramiek-op-polyethyleen (CoPE), keramiek-op-highly cross-linked polyethyleen (CoHXLPE) of keramiek-op-keramiek betere uitkomsten in press-fit THPs laat zien en om de potentiële invloed van deze articulaties op korte-termijn revisie en complicaties te onderzoeken, in het bijzonder de invloed op de primaire stabiliteit van de cup.

Deel 1: Primaire stabiliteit van de press-fit acetabulum component

Na implantatie van de cup moet de primaire stabiliteit voldoende zijn voor de transitie die daarop volgt waarbij de press-fit afneemt en osseointegratie optreedt, wat resulteert in de definitieve stabiliteit van het implantaat. [1] Gedurende deze overgang naar secundaire stabiliteit is de cup kwetsbaar voor migratie. Hierdoor kan fibreuze hechting optreden, waardoor de cup het risico loopt op korte en lange termijn loslating. [2,3] Een van de meest belangrijke factoren voor het verkrijgen van voldoende primaire stabiliteit is het intra-operatieve gevoel tijdens implantatie, welke afhangt van het subjectieve gevoel van de orthopedisch chirurg. Om de te verwachten stabiliteit van het implantaat te testen kunnen proefcups worden gebruikt. Echter bootsen deze niet de grootte van het definitieve implantaat na, vanwege de vrees voor het verlies van press-fit, waardoor de keuze voor de grootte van het definitieve implantaat vooral een subjectief gevoel blijft. In **Hoofdstuk 2** lieten we zien dat een dynamisch proefpasinstrument genaamd de X-pander®, die de definitieve press-fit nabootst door pre-expansie van het acetabulum, veilig kan worden gebruikt zonder de primaire stabiliteit van de definitieve cup in gevaar te brengen. [4] Hierdoor kan dit instrument worden gebruikt om een preciezere meting te verkrijgen tijdens implantatie, wat vooral in minder ervaren handen en moeilijke revisie casus zinvol kan zijn. De potentie van de X-pander® werd ondersteund door de resultaten in **Hoofdstuk 3**, doordat ervaren orthopedisch chirurgen rapporteerden dat wanneer zij dit instrument gebruikten en vergeleken met proefcups tijdens primaire en revisie casuïstiek, de X-pander® meer betrouwbare informatie gaf over het press-fit gevoel, ze meer zelfverzekerd waren in het verkrijgen van press-fit, het gebruik resulteerde in extra reamen of het aanpassen van de keuze voor de definitieve

cup grootte, het leidde tot betere cup implantatie, het zou kunnen leiden tot minder additionele schroeffixatie en dat ze het gebruik van dit instrument promoten boven het gebruik van proefcups. [5] Hoewel proefcups niet in alle casus door ervaren orthopedisch chirurgen worden gebruikt in de praktijk, kan de X-pander® wel voordelig zijn wanneer primaire stabiliteit lastig verkregen kan worden in zo wel primaire als revisie casuïstiek en in minder ervaren handen van orthopeden in opleiding, fellows of minder ervaren orthopeden om te leren hoe voldoende primaire stabiliteit kan worden verkregen en zou moeten voelen. Aangaande het eerste doel van deze thesis, heeft de X-pander® de potentie om proefcups te vervangen en plaatsing van een verkeerde maat cup te voorkomen; alsmede de bijkomende gevolgen en complicaties en hierdoor korte en lange termijn revisie te voorkomen, door het mogelijk makkelijker verkrijgen van voldoende press-fit door een preciezere meting hiervan tijdens de operatie, zonder de primaire stabiliteit aan te tasten.

Deel 2: articulaties in totale heupprothesen

De meest ideale articulatie voor een press-fit THP blijft een discussiepunt. CoHXLPE is één van de meest gebruikte articulaties. Een reden tegen het gebruik van (HXL) PE is slijtage en het mogelijke gevolg van slijtage-geïnduceerde osteolyse. Hoewel cross-linking dit risico reduceert, zijn lange termijn resultaten nog steeds beperkt. In **Hoofdstuk 4** toonden we aan dat de totale 3D slijtage in THPs met HXLPE minder was vergeleken met conventionele PE na 5-jaars follow-up. [6] Een CoC articulatie laat namelijk nog lagere tot zelfs geen slijtage zien. Gezien vergelijkend onderzoek tussen CoC en Co(HXL)PE beperkt is, hebben we in **Hoofdstuk 5** beide articulaties vergeleken. [7] Dit onderzoek toonde minder slijtage in CoC vergeleken met CoPE na 10-jaar follow-up, waarbij inclinatie van de cup een voorspellende factor voor slijtage van PE was. Daarnaast werden geen verschillen in complicaties, de Harris Hip Score (HHS) en radiologische uitkomsten gezien. Aangaande het tweede doel van deze thesis, gekeken naar welke articulatie minder slijtage laat zien in een press-fit THP, heeft HXLPE de voorkeur boven PE en kan CoC een goed alternatief zijn om PE-slijtage geïnduceerde osteolyse op lange termijn te voorkomen, wat vooral in jonge patiënten de voorkeur heeft, welke een langere levensduur van het implantaat nodig hebben. Het verschil in slijtage wordt belangrijk wanneer een verschil in revisie zou worden gezien. In **Hoofdstuk 6** hebben we het verschil in revisie tussen CoC en CoPE onderzocht, waarbij een lager risico op revisie werd gezien in CoPE in register studies wanneer deze articulatie werd vergeleken met een CoC articulatie in een press-fit primaire THP met een modulaire cup. [8] Gezien deze uitkomst was gebaseerd op twee register studies met verscheidene limitaties welke van zeer lage kwaliteit GRADE bewijslast waren en tevens studies met een ander methodologisch design geen verschil lieten zien, dient dit resultaat als voorbarig te worden beschouwd. Bovendien wordt een potentiële superioriteit gezien

voor CoC in jongere patiënten gekeken naar revisie in de literatuur. Gezien een afname van alle redenen van revisie en articulatie gerelateerde klachten wordt gezien door verbetering van materialen de afgelopen jaren en geen verschillen in klinische functie worden gezien tot dusver, blijft de literatuur controversieel om een voorkeur voor één universele articulatie aan te wijzen. Gezien de verbetering van keramiek heeft geleid tot minder fracturen hiervan, dient de angst voor keramiek fracturen het gebruik niet meer te belemmeren. Gezien in **Hoofdstuk 6** alle uitkomsten in één groep werden bekeken zal verder onderzoek gefocust op losse analyses in leeftijdsgroepen noodzakelijk zijn, gezien een verschil in uitkomsten voor slijtage en revisie wordt verwacht.

Deel 3: Invloed van articulatie keuze op de primaire stabiliteit van de press-fit acetabulum component

Een van de hoofdoorzaken van vroege revisie is aseptische loslating. In **Hoofdstuk 7** hebben we daarom een prospectief cohort van press-fit THPs onderzocht welke een hoog vroeg revisiepercentage lieten zien, met als doel risicofactoren voor vroege revisie door aseptische loslating te identificeren. [7] De overgang van de primaire stabiliteit naar definitieve stabiliteit door osseointegratie kan worden beïnvloed door factoren zoals het macro- en microscopisch ontwerp van de cup, de positie, uitlijning en biocompatibiliteit van het implantaat, de chirurgische benadering en patiëntkarakteristieken, inclusief botkwaliteit. [9,10] Hierdoor kan het implantaat het risico op loslating lopen. In **Hoofdstuk 7** werd een hoog percentage aseptische loslating gezien, welke stabiliseerde na een hoog vroeg falingspercentage. Als redenen voor dit hoge percentage werden het macroscopisch ontwerp van de cup en de CoC articulatie genoemd. [7] In **Hoofdstuk 7** benoemden we ook de theorie dat de totale stijfheid van het implantaat toeneemt door een hard op hard articulatie zoals CoC. [7] Hierdoor worden de krachten op het implantaat minder geabsorbeerd door het implantaat zelf en hierdoor meer overgedragen naar het bot-prothese oppervlak, in vergelijking met CoHXLPE. De resulterende schuifkrachten ter plaatse kunnen de initiële stabiliteit in gevaar brengen, osseointegratie hinderen en hierdoor resulteren in migratie van de cup en wanneer dit te veel wordt zelfs in aseptische loslating. De uitkomsten van **Hoofdstuk 8** ondersteunden deze theorie met een hoger 2-jaars cup revisiepercentage in CoC vergeleken met Co(HXL)PE in de Landelijke Registratie Orthopedische Interventies (LROI) met significant meer loslating van de cup als reden voor revisie in CoC, welke veelal aseptisch was. [11] Gezien migratie niet altijd hoeft te resulteren in loslating onderzochten we in **Hoofdstuk 9** de migratie tussen CoC en CoHXLPE in press-fit THPs in een gerandomiseerde setting door middel van RSA. [12] Deze studie liet geen significant verschil in gemiddelde migratie zien tussen CoC en CoHXLPE, hoewel de gemiddelde migratie wel hoger was in CoC gedurende 5-jaars follow-up. Gezien cupmigratie en het risico op loslating een multifactorieel probleem zijn, is het te veronderstellen dat in patiënten met risicofactoren voor loslating, CoC

deze kans kan vergroten. Alles tezamen, gekeken naar het derde doel van deze thesis, wordt CoC gezien als een potentiële factor in het multifactoriële probleem van vroege migratie en mogelijk daaropvolgende aseptische loslating in press-fit THP.

Volgens dit proefschrift is voldoende primaire stabiliteit tijdens implantatie cruciaal voor overleving van het implantaat gebruikt voor press-fit THPs. Daarom zouden dynamische proefpasinstrumenten moeten worden overwogen om te gebruiken in de klinische praktijk om problemen met moeizame press-fit fixatie te voorkomen, gezien ze de primaire stabiliteit van het definitieve implantaat niet in gevaar brengen. Meer lange termijn gerandomiseerd RSA-onderzoek is noodzakelijk, vooral in groepen met verminderde botkwaliteit, om een voorkeur van één van beide articulaties te bevestigen en kosteneffectiviteit te bevestigen. Tot die tijd, laat dit proefschrift zien dat CoC en CoHXLPE beide een geschikte optie zijn in press-fit THP voor jongere patiënten en dat CoC vaker zou moeten worden overwogen door de voordelen van minder slijtage, zonder de angst voor keramiek fracturen. Echter, CoC gebruik dient te worden beperkt tot gebruik in patiënten waarin geen verminderde botkwaliteit wordt verwacht en in casus waarbij het verkrijgen van primaire stabiliteit tijdens de operatie niet moeizaam gaat, om zo het potentiële verhoogde risico op vroege aseptische loslating te voorkomen. Voor oudere patiënten is HXLPE de optie van voorkeur.

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PHD PORTFOLIO

PhD student:	Justin van Loon
PhD supervisors:	prof. dr. G.M.M.J. Kerkhoffs
PhD co-supervisors:	dr. D. Haverkamp & dr. K.T.M. Opdam
PhD period:	2017-2023

PhD training

Courses	**Year**	**Workload (ECTS)**
Medical Literature: searching for a CAT	2020	0.1
Practical Biostatistics	2020	1.4
e-BROK	2020	1.5
PubMed (e-learning)	2022	0.1
Endnote (e-learning)	2022	0.1
Correct citation (e-learning)	2022	0.1

Oral presentations	**Event**	**Year**	**Workload (ECTS)**
Ceramic-On-Ceramic Versus Ceramic-On-Polyethylene, A Comparative Study With 10-Years Follow-Up.	EHS Congress	2021	0.5
Two-year Cup Revision in Ceramic-On-Ceramic and Ceramic-On-Polyethylene B earing. Analysis of 33,454 Primary Press-fit Total Hip Arthroplasties Registered in the Dutch Arthroplasty Register (LROI).	EHS Congress	2021	0.5
Comparison of 5-year cup and stem migration between a ceramic and polyethylene liner in press-fit total hip arthroplasty. A randomized controlled trial using radiostereometric analysis **Shared first authorship, presentation made by J. van Loon, presented by A.D. Klaassen*	NOV-jaarcongres	2022	0.5

Poster presentations	Event	Year	Workload (ECTS)
Ceramic-On-Ceramic Versus Ceramic-On-Polyethylene, A Comparative Study With 10-Years Follow-Up.	EFORT Congress	2021	0.5
Ceramic-On-Ceramic Articulation In Press-Fit Total Hip Arthroplasty As A Potential Reason For Early Failure, What About The Survivors: A Ten-Years Follow-Up.	EFORT Congress	2021	0.5
Ceramic-On-Ceramic Versus Ceramic-On-Polyethylene, A Comparative Study With 10-Years Follow-Up.' EHS Congress	EHS Congress	2021	0.5

(Inter)national conferences	Year	Workload (ECTS)
World Arthroplasty Congress 2021	2021	1.0
EFORT Congress	2021	1.0
European Hip Society – 14th International Congress	2021	0.5
Nederlands Orthopaedische Vereniging Congres	2021-present	1.0

Other scientific activities	Year	Workload (ECTS)
Editor 4Arthroscopy/4Bone	2018	2.0
Editor-in-Chief 4Arthroscopy	2018-2019	2.0
Editor-in-Chief 4Bone	2019-2021	5.0
Invited peer-reviewed for: Gait & Posture	2021-present	0.2
Invited peer-reviewed for: International Orthopaedics	2021-present	0.4

Teaching

Lecturing	Year	Workload (ECTS)
Anatomy and embryology teacher - University of Amsterdam (including several musculoskeletal system lectures and dissection practicals)	2017-2019	>30.0
Anatomical Lecture 'Lower Extremity' - Master Academy VCMS	2019	0.3

Other	Year	Workload (ECTS)
Guest lecture: 'Posterior Ankle Impingement Syndrome (PAIS) in ballet dancers.' - Keuzeonderwijs 'Arts en Topsport'	2019	0.5
Guest lecture: 'Posterior Ankle Impingement Syndrome (PAIS) in ballet dancers.' - Keuzeonderwijs 'Arts en Topsport'	2021	0.5

LIST OF PUBLICATIONS

Publications in this thesis

Hoornenborg D, **van Loon J**, de Waard S, Sierevelt IN, Opdam KTM, Kerkhoffs GMMJ, Haverkamp D. Dynamic trial fitting by an expanding trial cup does not jeopardize primary acetabular component stability.
Clinical Biomechanics 2020; 78:105077

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Submitted
**co-first authors*

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Journal of Dance Medicine and Science. 2021; 15;25(1):24-29
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ACKNOWLEDGEMENTS – DANKWOORD

Een proefschrift schrijven in je vrije tijd, het is een mooie uitdaging en nog gelukt ook. Iets waar een hoop tijd, doorzettingsvermogen, motivatie, (on)geduld, creativiteit, inspiratie, aanmoediging en de nodige afleiding voor noodzakelijk was om dit doel te bereiken. Hier hebben dan ook vele personen direct en indirect een belangrijke bijdrage aan geleverd, waarvoor ongelofelijk veel dank.

De belangrijksten wil ik daarom graag in het bijzonder bedanken:

Promotor, **prof. dr. G.M.M.J. Kerkhoffs.**
Beste Gino, toen het plan kwam om van mijn onderzoek een promotietraject te maken, was jij gelijk overtuigd om mij te begeleiden. Jouw rol in de besluiten om mij kansen te bieden als promovendus en AIOS, is voor mij van grote betekenis. Hiervoor wil ik je dan ook hartelijk bedanken. Ik kijk uit naar onze samenwerking tijdens mijn opleiding tot orthopedisch chirurg, waarbij ik hoop nog meer inspiratie, vaardigheden en kennis van je op te mogen doen.

Co-promotor, **dr. D. Haverkamp**.
Beste Daniël, als enthousiaste student klopte ik bij je aan in het Slotervaart, omdat ik meer onderzoek wilde doen binnen de orthopedie. Na een mooi project volgden er meer en hebben we er samen een proefschrift van gemaakt. Jouw wetenschappelijke enthousiasme en kennis zijn aanstekelijk en een groot voorbeeld voor mij als promovendus. Daarnaast was je altijd bereikbaar voor overleg en advies. Jij hebt mij gaandeweg geleerd een zelfstandig onderzoeker te zijn. Ontzettend veel dank voor al je feedback, aanmoediging, inspiratie en de prettige samenwerking. Opdat er in de toekomst nog vele mooie projecten samen mogen volgen.

Co-promotor, **dr. K.T.M. Opdam.**
Beste Kim, toen je zelf nog midden in je promotie zat, nam je mij als student onder je hoede. Het beruchte 'PAIS injectie stuk' wat ons vele uren en frustratie heeft gekost was hierin het begin. Jij introduceerde mij bij Daniël en hebt vervolgens bijgedragen aan het ontwikkelen van mijn proefschrift. Jouw hulp hierbij was onmisbaar, waarvoor veel dank. Vol geduld hielp jij mij met goed advies en stond jij klaar voor al mijn vragen. Hierbij was je altijd even vrolijk, relaxed en 'to-the-point', wat ik enorm waardeer. Ik hoop in de toekomst nog vaak met je te mogen samenwerken.

Leden van de promotiecommissie, **prof. dr. Maas, prof. dr. Oostra, dr. Schafroth, dr. ten Broeke, prof. dr. Schreurs en prof. dr. ir. Tuijthof,** hartelijk dank dat u zitting wilden nemen in mijn promotiecommissie en voor de beoordeling van mijn proefschrift. Ik kijk uit naar de openbare discussie.

Daarnaast wil ik mijn dank uitspreken naar alle patiënten die in de onderzoeken hebben meegedaan.

Beste **Inger Sierevelt**, jouw bijdrage aan dit proefschrift is van grote waarde geweest voor mij. Als groentje binnen de wereld van de methodologie en statistiek heb jij mij ondersteund en begeleid. Wanneer een analyse opnieuw gedaan moest worden of ik iets niet begreep schoot jij te hulp en was geen vraag te veel. Ik herinner mij nog goed dat je richting het einde van mijn proefschrift zei dat ik bovengemiddelde statistische kennis had voor iemand binnen de orthopedie. Dit grootse compliment zal ik nooit vergeten, maar had ik nooit kunnen waarmaken zonder jou. Ik kan je niet genoeg bedanken voor de samenwerking en de gezelligheid tijdens onze overleggen.

Dan mijn paranimfen, **Jan Jaap de Graeff en Koos de Wit.**
Jan Jaap, na onze kennismaking in de Epsteinbar was er al snel een klik, met een waardevolle vriendschap tot gevolg. Ik geniet van je humor, goede adviezen, eerlijkheid en directheid. De manier waarop wij vaak hetzelfde denken en op één lijn zitten zegt genoeg. Daarnaast is nu ook onze wetenschappelijke samenwerking een feit en zijn we beiden in opleiding tot orthopedisch chirurg. Nadat jij tijdens een van de vele mooie feestjes mijn knieschijf had gereponeerd was er weinig twijfel meer mogelijk dat jij een succesvol orthopeed zou worden. Ik hoop dan ook dat we in de toekomst nog eens samen in de kliniek mogen staan.

Koos, hoe we elkaar nou eigenlijk hebben gevonden is volgens mij nog steeds een raadsel. Iets via de studie, racefietsen of via via op het AMC. Echter is één ding zeker, de waardevolle match is er. Ik geniet van je vrolijkheid, enthousiasme en oprechte interesse. Daarnaast kan ik ook altijd op je rekenen voor een avontuur op de racefiets, wat een heerlijke uitlaatklep is en de ideale afleiding. Ik hoop dat we nog vele jaren op avontuur mogen op onze racemonsters en de aansluitende borrels.

Mannen, jullie zijn prachtgozers. Ik ben trots dat jullie tijdens mijn verdediging naast mij staan. Jullie weten hoe zeer ik jullie en onze vriendschap waardeer. Op nog vele mooie momenten en avonturen samen.

Hierbij kunnen de mooie weekenden met **Michel Klaver** natuurlijk niet onbesproken blijven. Mies, je bent een topgozer en ik kan erg genieten van je gezelligheid, humor, zelfs je huilkaters en natuurlijk niet te vergeten de whisky proeverijen samen.

Prof. dr. R.W. Poolman.
Beste Rudolf, voor het missende stukje van de puzzel in mijn proefschrift, kwam jij te hulp geschoten. Jouw verfrissende ideeën en kritische blik zijn van grote waarde geweest om de laatste onderzoeken af te ronden die nodig waren om dit proefschrift tot een geheel te vormen. Hiervoor wil ik je hartelijk bedanken. Gezien jouw grote wetenschappelijke interesse hoop ik dat we nog mooie projecten mogen vervullen in de toekomst.

Dr. A.M.J.S. Vervest.
Beste Ton, al snel nadat ik was begonnen als semi-arts in Tergooi begon onze wetenschappelijke samenwerking voor de TH+ studie. Daarnaast ben ik je zeer dankbaar voor de kansen die jij mij hebt geboden in Tergooi, jouw steun (en die van **dr. M.J. de Vos**, waarvoor tevens grote dank) om te solliciteren voor de opleiding tot orthopedisch chirurg en de mogelijkheid die jij mij hebt geboden om mijn contract te verlengen in Tergooi waardoor ik dit proefschrift verder kon afronden. Daarnaast dank voor hoe jij mijn ongeremde enthousiasme voor de orthopedie in banen hebt weten te leiden tijdens mijn periode als ANIOS.

Co-auteurs, allen veel dank voor jullie hulp en begeleiding. Zonder jullie was het niet mogelijk geweest de artikelen af te ronden en was dit proefschrift niet tot stand gekomen.

Beste **stafleden en collega A(N)IOS van de orthopedie in Tergooi**. Na bijna 2 jaar met jullie te hebben mogen samenwerken, wil ik jullie hartelijk bedanken voor alle kansen en leerzame momenten. Na een leerzame periode als semi-arts heb ik bij jullie mijn eerste stappen als arts gezet binnen de orthopedie en ben ik mede door mijn opgedane ervaring bij jullie in opleiding gekomen. Tevens veel dank voor alle gezelligheid en ik hopelijk tot in de toekomst.

Many thanks, to the **Orthopaedic Surgery at the Victoria Hospital**, Cape Town, South-Africa, for giving me the opportunity to gain my first orthopaedic surgical experience. In special I want to thank **Abbas Omar** and **Hammaad Gamieldien** for everything you taught me in theatre, your hospitality, the laughs we had and the nice chips we ate at Vic. I hope to see you again in the future and to collaborate in the theatre again.

Daarnaast wil ik iedereen van de **Anatomilie** bedanken: Roelof-Jan, Roeland, Lida, Petra, Mara, Inge, Carl en alle geweldige (oud) collega studentassistenten anatomie. Dit warme nest van slimme koppen heeft mij een hoop geleerd over de anatomie van onder andere het bewegingsapparaat. Daarnaast weet ik zeker dat ik hierdoor altijd betrokken zal willen blijven bij onderwijs. Tenslotte waren de uitjes, borrels en de niet te vergeten anatomieweekenden ronduit fantastisch. Bedankt voor de mooie tijd en ik kijk vol trots terug naar deze periode.

Mort, jij mag hier uiteraard niet ontbreken. Als jouw papa in de introductieweek leerde ik je kennen, waarna we al snel huisgenoten werden en de rest is geschiedenis. Ik geniet van je enthousiasme, humor, onze goede gespreken, gezellige avonden, mooie vakanties en de inspiratie en frisse blik die jij brengt met je soms licht verhoogd associatief denken. Dank voor je steun, inspiratie, wijze woorden en vooral een hoop gezelligheid. Je bent een topgozer.

Maten uit Zeeland, Nathan, Bram, Michel, Leroy, Arend, Thomas, Rens, Sake en Boris. Onze vriendschappen lopen ver terug naar de middelbare en zelfs de basisschool. Ondanks dat niet iedereen altijd bij kon houden waar ik mee bezig was, stonden jullie altijd voor me klaar. Ook al zijn we allemaal totaal andere richtingen opgegaan, hebben we veel moois met elkaar beleefd. Ik ben trots dat we dat nog steeds mooie momenten met elkaar blijven meemaken. Op nog vele mooie herinneringen.

Ook **al mijn andere vrienden vanuit Amsterdam en omgeving**, die ik gaandeweg tijdens mijn studie heb leren kennen in introductieweken, als huisgenoten, door de Epsteinbar, als Epcie, als BuReCo, door VCMS, door de MFAS, als collega's tijdens mijn vooropleiding in het OLVG of op welke manier dan ook, ik ben jullie allen ontzettend dankbaar voor jullie steun en afleiding op welke manier dan ook. Ik zal hier geen rij met namen gaan opsommen, maar ik weet zeker dat de juiste personen zich aangesproken voelen.

Mijn **bestuur van VCMS** wil ik bedanken voor hun steun, gezelligheid, motivatie en chirurgische inspiratie. Irina, Roger, Bas, Manou, Amaran en Loes, jullie ongekende ambities en grootse ideeën hebben mij gestimuleerd om mijn onderzoek verder vorm te geven naast mijn bestuursfunctie bij VCMS. Ik kijk vol trots terug op wat wij neer hebben gezet als team en uiteraard naar de gesneuvelde wasbak tijdens onze orthopedische praktijkmodule.

Lieve **familie de Koning**, jullie hebben mij met open armen ontvangen en ik prijs mij gelukkig dat Marlou zo'n ontzettend gezellige, lieve en leuke familie heeft. Ik kan onwijs genieten van de momenten samen. Dank voor jullie liefde en steun.

Lieve **Ramon en Vincent**, ondanks dat ik fysiek inmiddels het kleinste broertje ben, kan ik mij geen betere oudere en jongere broer wensen. **Ramon,** als oudere broer heb ik veel van je mogen leren. Op veel punten zitten wij op één lijn en denken wij hetzelfde, wat ik als zeer waardevol ervaar in onze momenten samen. **Vincent,** als jonger broertje hebben wij elkaar positief beïnvloed, al kostte het wellicht wat tijd dat in te zien. De afgelopen jaren zijn wij verder naar elkaar toegegroeid, waar ik zeer dankbaar voor ben.
Ik weet dat ik altijd bij jullie terecht kan en waardeer onze momenten samen enorm. We zijn onmiskenbaar broers, al zijn onze eigenschappen en kwaliteiten soms nogal uiteenlopend. Echter is 1 ding zeker, jullie volgen jullie eigen pad vol ambitie en ik ben onwijs trots op wat jullie bereikt hebben. Ik waardeer enorm hoe jullie mij altijd hebben gesteund.

Lieve **pap en mam**, zonder jullie was ik hier niet gekomen. Jullie hebben mij altijd onvoorwaardelijk gesteund en het volledige vertrouwen gegeven. Mijn dankbaarheid voor jullie support, op welke manier dan ook, is niet uit te drukken in woorden. Geen wild idee of vraag om hulp was voor jullie te gek. Jullie altijd oprechte interesse in mij als persoon, mijn studie, onderzoek en andere bezigheden heb ik als enorm waardevol en stimulerend ervaren. Ik ben jullie eeuwig dankbaar voor de kansen die jullie mij hebben geboden. Ik ben ongelofelijk trots op jullie en hoe jullie altijd voor mij klaar staan. Als eerste in de familie ben ik arts geworden, in opleiding gekomen en nu ook gepromoveerd, mede dankzij jullie steun. Dit proefschrift is voor jullie.

Lieve **Marlou**, de laatste woorden van dit boekje wil ik afsluiten met mijn woorden en grote dank voor jou. Ik was net aan dit onderzoek begonnen toen ik jou leerde kennen. Jouw geduld, positiviteit, energie, steun en onbevangen enthousiasme hebben mij verder geholpen wanneer dat nodig was. De tijd en ruimte die je mij altijd hebt geboden om dit proefschrift te schrijven of door andere taken van mijn bordje te nemen, ben ik je enorm dankbaar voor. Jij staat altijd voor mij klaar en mede hierdoor heb ik mijn promotie kunnen afronden. Ik ben ongelofelijk trots op ons en kijk uit naar alle mooie avonturen die ons nog te wachten staan.
Ik ben gek op je.

CURRICULUM VITAE

Justin van Loon was born on the 12th of March 1995 in Vlissingen, the Netherlands as the second of three brothers. In 2013 he graduated from the Gymnasium at the Christelijke Scholengemeenschap Walcheren (CSW) in Middelburg. Later that year he started medical school at the University of Amsterdam.

After obtaining his Bachelor of Science degree in July 2016, Justin started working as a teaching-assistant anatomy at the Academic Medical Center (AMC) after a few months of travelling. Teaching students of several studies anatomy and the principles of the complete dissection of the cadaver, boosted his enthusiasm for anatomy of the musculoskeletal system. In combination with his interests for biomechanics, sports, surgery and technology, his passion for orthopaedic surgery was born. During this period, he commenced his orthopaedic research activities with a project focused on Posterior Ankle Impingement Syndrome in Ballet Dancers under supervision of dr. K.T.M. Opdam at the AMC. The next research project he started was focused on primary stability of the acetabular component in press-fit total hip arthroplasty under supervision of dr. D. Haverkamp at the Slotervaart Medical Center in Amsterdam. By extending this project, supported by prof. dr. G.M.M.J. Kerkhoffs, this ultimately resulted in this thesis. Next to his teaching and research activities, Justin was a member of the Dutch Surgical Society for Medical Students (VCMS) board for two years. In this function, he was involved in the organization of extra-curricular activities focused on surgical education, including orthopaedics, for interested medical students throughout the Netherlands. Justin combined these activities with its medical internships. He gained his first practical experience in the operation room, during an elective in orthopaedic surgery in Victoria Hospital, Cape Town, South-Africa. This was followed by a senior internship orthopaedic surgery at Tergooi hospital, Hilversum, under supervision of dr. A.M.J.S. Vervest. After obtaining his medical degree (cum laude) he started working as a resident not-in-training (ANIOS) in the orthopaedic surgery department of the Tergooi hospital. From October 2021 until March 2023 Justin started his orthopaedic training as a resident (AIOS) in general surgery at the OLVG, Amsterdam. From April 2023 he continued his training as a resident (AIOS) in orthopaedic surgery at the Spaarne Gasthuis.

Justin lives in Amsterdam with his girlfriend Marlou de Koning. Besides his passion for orthopaedics, he likes race cycling, cooking, other sport activities and enjoying social life with friends and family.