Turun yliopisto
University of Turku

PRIMARY AND REVISION HIP REPLACEMENT: A UNIVERSITY HOSPITAL DATABASE AND REGISTRY STUDY

Inari Kostensalo

TURUN YLIOPISTON JULKAISUJA – ANNALES UNIVERSITATIS TURKUENSIS
Sarja - ser. D osa - tom. 1125 | Medica - Odontologica | Turku 2014

University of Turku

Faculty of Medicine
Department of Orthopedics and Traumatology
Institute of Clinical Medicine
Doctoral Program of Clinical Investigation

Supervised by

Adjunct professor Keijo Mäkelä, MD, PhD
Department of Orthopedics and Traumatology
Turku University Hospital and University of Turku
Turku, Finland

Adjunct professor Petri Virolainen, MD, PhD
Department of Orthopedics and Traumatology
Turku University Hospital and University of Turku
Turku, Finland

Reviewed by

Adjunct professor Jukka Kettunen, MD, PhD
Department of Orthopedics and Traumatology
Kuopio University Hospital and
the University of Eastern Finland
Kuopio, Finland

Professor Juhana Leppilahti MD, PhD
Department of Orthopedics and Traumatology
Oulu University Hospital and University of Oulu
Oulu, Finland

Opponent

Adjunct professor Teemu Moilanen, MD, PhD
School of Medicine, University of Tampere
Coxa Hospital for Joint Replacement
Tampere, Finland

The originality of this thesis has been checked in accordance with the University of Turku quality assurance system using the Turnitin OriginalityCheck service.

ISBN 978-951-29-5810-8 (PRINT)
ISBN 978-951-29-5811-5 (PDF)
ISSN 0355-9483
Painosalama Oy - Turku, Finland 2014

With love
to Mikael

ABSTRACT

Inari Kostensalo – Primary and Revision Hip Replacement: a University Hospital Database and Registry Study

From the Department of Orthopedics and Traumatology, Institute of Clinical Medicine, Faculty of Medicine, Doctoral Program of Clinical Investigation, University of Turku, and Turku University Hospital, Turku, Finland

Annales Universitatis Turkuensis
Painosalama Oy, Turku, Finland 2014

Large-headed total hip arthroplasty (THA) and hip resurfacing arthroplasty (HRA) with metal-on-metal (MoM) bearings became popular during the last decade. Recently, it has become evident that the large-head MoM hip implants are associated with increased revision rates despite their theoretical advantages. The purpose of this study was to evaluate the early results of primary MoM hip replacements and of acetabular revisions.

I analyzed retrospectively the results of four MoM implant designs and the survival rate of acetabular revisions with impaction bone grafting, as documented in the Turku University Hospital database. Further, I evaluated the correlation between femoral head size and dislocation rate, and used the Finnish Arthroplasty Register data to compare the survival of three large-head MoM THAs to analogous HRAs.

The early results for the Magnum M2A–ReCap THA were good. A larger head size decreased the risk of dislocation. Articular surface replacement (ASR) THA yielded inferior results compared to analogous HRA. For two other designs the results were similar. The R3–Synergy THA yielded inferior results compared to the reference implants. The survival of acetabular reconstructions with impaction bone grafting was inferior compared to previous reports.

In conclusion, the early results of the Biomet ReCap–Magnum design were promising, and large head sizes decreased the dislocation rate. The survival of different MoM hip implant designs varied. The survival of new designs and techniques may be inferior to those reported by the clinics where implants are developed. An important caveat is that early promising results of new devices may rapidly worsen. New implants need to be introduced in a controlled fashion to the market; here, arthroplasty registers are a valuable tool that needs to be used.

Keywords: Hip, osteoarthritis, total hip arthroplasty, hip resurfacing arthroplasty, dislocation rate, metal-on-metal bearing, adverse reaction to metal debris, revision total hip arthroplasty, impaction bone grafting

TIIVISTELMÄ

Inari Kostensalo – Ensivaiheen ja uusintaleikattujen lonkan tekonivelten tulokset: yliopistosairaalan ja proteesirekisterin aineistoon perustuva tutkimus.

Ortopedian ja traumatologian klinikka, Kliinisen lääketieteen laitos, Lääketieteellinen tiedekunta, Turun yliopiston kliinisen lääketieteen tohtoriohjelma, Turun yliopisto ja Turun yliopistollinen keskussairaala, Turku, Suomi

Annales universitatis Turkuensis
Painosalama Oy, Turku, Finland 2014

Isonuppiset, metalli-metalli-liukupintaiset lonkan tekonivelet sekä pinnoitetekonivelet yleistyivät viime vuosikymmenen aikana. Isonuppisia, metalli-metalli-liukupintaisia lonkan tekoniveliä käytettäessä on kuitenkin ilmennyt uusintaleikkaustarpeen kasvaminen niiden teoreettisista eduista huolimatta. Tämän tutkimuksen tarkoituksena oli arvioida metalli-metalli-liukupintaisten lonkan tekonivelleikkausten sekä luunpakkausmenetelmällä tehtyjen lonkkamaljakon uusintaleikkausten tuloksia.

Tutkimuksessa analysoin takautuvasti neljän metalli-metalli-liukupintaisen tekonivelmallin pysyvyystuloksia, sekä luunpakkaus-menetelmällä tehtyjen lonkkamaljakon uusintaleikkausten tuloksia Turun Yliopistollisen Keskussairaalan aineiston perusteella. Lisäksi tutkin lonkan tekonivelen nuppikoon ja sijoiltaanmenoriskin välistä yhteyttä Suomen Endoproteesirekisterin aineistoon perustuen. Teimme myös rekisteripohjaisen tutkimuksen kolmen eri metalli-metalli liukupintaisen totaalilonkkaproteesin uusintaleikkausriskistä ja vertasimme niitä vastaavien pinnoiteproteesien uusintaleikkausriskiin.

Lyhyen aikavälin tulokset Magnum M2A – ReCap totaalilonkkaproteesille olivat hyviä. Suurempi nuppikoko oli selvästi yhdistettävissä pienempään sijoiltaanmenoriskiin. Lyhyen aikavälin seurannassa ASR pinnoiteproteesin pysyvyys oli vastaavaa totaalilonkkaproteesia parempaa, mutta kahden muun verratun parin välillä ei ollut eroa uusintaleikkausriskissä. R3 – Synergy totaalilonkkaproteesin tulokset olivat huonommat kuin vertailumalleilla. Birmingham pinnoiteproteesin pysyvyystulokset ja lonkkamaljakon luunpakkausmenetelmällä tehtyjen uusintaleikkausten pysyvyystulokset olivat huonommat kuin kehittäjäklinikoiden tulokset.

Johtopäätöksenä totesimme että alkuvaiheen tulokset ReCap-Magnum-implanttia käytettäessä olivat hyvät. Isojen nuppikokojen käyttö vähensi tekonivelen sijoiltaanmenon riskiä. Metalli-metalli-liukupintaisten lonkkaimplanttien alkuvaiheen pysyvyystulokset vaihtelivat. Lonkan tekonivelleikkausten tulokset saattavat olla huonompia kuin mitä implantin tai tekniikan kehittäneen klinikan julkaisemat tulokset ovat olleet. Metalli-metalli-liukupintaisten lonkkaproteesien ongelmat ovat sittemmin osoittautuneet yleisiksi. Uudet tekonivelmallit tulee ottaa käyttöön hallitusti jatkuvassa proteesirekisteriseurannassa.

Avainsanat: Lonkkanivel, nivelrikko, lonkan tekonivelleikkaus, lonkan pinnoitetekonivel, sijoiltaanmenoriski, metalliliukupintainen tekonivel, metallihierre-haittavaikutus, lonkan tekonivelen uusintaleikkaus, luunpakkaus

TABLE OF CONTENTS

ABBREVIATIONS

AAOS	American Academy of Orthopedic Surgeons
ALVAL	aseptic lymphocyte-dominated vasculitis-associated lesion
ARMD	adverse reaction to metal debris
ASR	articular surface replacement
BHR	Birmingham hip resurfacing
CI	confidence interval
CoC	ceramic-on-ceramic
HHS	Harris Hip Score
HR	hazard ratio
HRA	hip resurfacing arthroplasty
HXLPE	highly cross-linked polyethylene
ICD	International Classification of Diseases
LDH MoM THA	large-diameter head metal-on-metal total hip arthroplasty
MARS MRI	metal artefact reduction sequence magnetic resonance imaging
MoM	metal-on-metal
MoP	metal on polyethylene
MRI	magnetic resonance imaging
OA	osteoarthritis
RA	rheumatoid arthritis
RR	risk ratio
THA	total hip arthroplasty
THR	total hip replacement

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original papers, which will be referred to in the text by their Roman numerals.

I Kostensalo I, Seppänen M, Mäkelä K, Mokka J, Virolainen P, Hirviniemi J. Early results of large head metal-on-metal hip arthroplasties. Scand J Surg 2012;101(1):62-5.

II Kostensalo I, Junnila M, Virolainen P, Remes V, Matilainen M, Vahlberg T, Pulkkinen P, Eskelinen A, Mäkelä KT. Effect of the femoral head size on revision risk for dislocation after total hip arthroplasty. A population-based analysis of 42,379 primary procedures from the Finnish Arthroplasty Register. Acta Orthop 2013 Aug;84(4):342-7.

III M Junnila, I Kostensalo, P Virolainen, V Remes, M Matilainen, T Vahlberg, P Pulkkinen, A Eskelinen, A Itälä, K Mäkelä. Hip resurfacing arthroplasty versus large head metal on metal total hip arthroplasty – comparison of three designs from the Finnish Arthroplasty Register. Scand J Surg 2014 103(1):54-9.

IV Kostensalo I, Junnila M, Mokka J, Virolainen P, Vahlberg T, Mäkelä KT. Three metal-on-metal implants from the same manufacturer – A midterm survival analysis of BHR, BHR–Synergy and R3–Synergy implants. Acta Orthop Belgica 2014 80(2):222-7.

V Kostensalo I, Seppänen M, Virolainen P, Mokka J, Koivisto M, Mäkelä K. Acetabular reconstruction with impaction bone grafting in total hip revision arthroplasty. Submitted.

The original communications have been reproduced with the permission of the copyright holders.

1. INTRODUCTION

Total hip arthroplasty (THA) is the treatment of choice of severe osteoarthritis of the hip joint and is one of the most cost-effective surgical treatments (Lavernia and Alcerro 2011; Pivec et al. 2012). The golden standard material for THA bearings has been polyethylene-on-metal for several decades, but hard-on-hard bearing surfaces are also available: ceramic-on-ceramic (CoC), metal-on-metal (MoM), and metal-on-ceramic. Hip implants may be fastened to bone with bone cement or without bone cement through bony ingrowth. Currently, most cemented prostheses are used with metal-on-polyethylene or ceramic-on-polyethylene bearing surfaces and the polyethylene cup is cemented directly on to the pelvic bone. Hard-on-hard options may be used with uncemented acetabular fixation. Theoretically, polyethylene has higher wear rates than hard-on-hard bearings (Silva et al. 2005; Lusty et al. 2007). Large femoral heads lead to more volumetric wear than smaller heads in metal-on-polyethylene implants, which may increase the risk of osteolysis (Clarke and Manley 2008).

The most common surgical complications after THA and hip resurfacing arthroplasty (HRA) are osteolysis and aseptic loosening, infection, periprosthetic fracture, dislocation and, lately, soft tissue problems associated with MoM bearings. Revision surgery may be demanding because of soft tissue destruction due to adverse reactions to metal debris (ARMD). Bone loss is often associated with revision surgery and can be managed with different types of revision prostheses, metal augments and bone autografts and allografts. Impaction bone grafting is a technique to treat bone loss in revision THA.

During the last decade, MoM hip implants became popular due to the theoretical advantages of decreased wear, a large femoral head size and a low dislocation rate. MoM bearing surfaces may be used in association with both traditional THA and HRA. In THA, the femoral head is cut and the stem is implanted into femoral cavity. In HRA, the femoral head is resurfaced with a cemented metal cap and the femoral neck is preserved. HRA was developed as a more natural and less invasive procedure (Amstutz and Le Duff 2012). The acetabular component in HRA might be used with a modular head for THA.

The short-term to midterm results of many MoM devices were promising (Steffen et al. 2008; Ollivere et al. 2009; Zhang et al. 2010; McMinn et al. 2011). Gradually, however, results were published on complications related to the metal bearings, such as ALVAL-reactions (aseptic lymphocyte-dominated vasculitis-associated lesion) and pseudotumors (Campbell et al. 2010; Delaunay et al. 2010; Natu et al. 2012). Currently, these reactions are also called ARMD-reactions. As the severity and frequency of these complications emerged as substantial clinical issues, national authorities released recommendations to abandon the use of MoM bearings in THA (NJR 2007). In Finland, the Finnish Arthroplasty Association has recommended that surgeons are not to use any

MoM devices until more data from their safety would be available (Suomen Artroplastia yhdistys 2012).

It is not all that easy to tracing and identify problems related to metal bearings. Patients may have a wide range of symptoms or no symptoms. Clinical symptoms predicting ARMD are pain, swelling, prosthetic squeaking and subluxation sensations. High chromium and cobalt levels in the blood may predict ARMD, but with poor sensitivity and specificity (MacNair et al. 2013; Sidaginamale et al. 2013). Metal artefact reduction sequence magnetic resonance imaging (MARS MRI) is a reliable screening tool, but its availability for diagnosis and follow-up is limited (Nawabi et al. 2014).

The purpose of this thesis was to study early survival results of large-headed MoM THA and HRA. In addition, our aim was to evaluate the survival of acetabular revisions performed with the impaction bone grafting technique.

2. REVIEW OF THE LITERATURE

2.1 PRIMARY HIP REPLACEMENT

Modern THA was introduced in the 1960's when Charnley's cemented low-friction implants came on the market. Prior to that, common belief was that it was the synovial fluid which was responsible for flow joint friction. Sir John Charnley realized, however, that friction depended on the constitution of the joint surfaces rather than on the synovial fluid. His first attempt to develop low-friction THA contained teflon bearings (Charnley 1966, Waugh 1990), but it turned out that these implants developed quite soon soft tissue masses due to wear, and revision rates were high. His second bearing option was a metal-on-polyethylene implant, which appeared to be safe (Waugh 1990).

Currently, the fixation options used in THA are cementation and cementless fixation through bony ingrowth of porous surfaces (Pivec et al. 2012). The first implants developed by Charnley were used cemented fixation (Waugh 1990), but since aseptic loosening was a relatively common complication of these implants, porous coated cementless fixation was developed, since the risk of aseptic loosening of cementless stems compared to cemented stems is reduced (Wechter et al. 2013). Aseptic loosening of a cementless stem after bony ingrowth is rare, although cementless polyethylene cups do become aseptic loosened through wear and osteolysis.

The benefit of cement fixation is that the early periprosthetic fracture rate is lower than of uncemented implants (Berry 1999). Cement may strengthen the bone cavity from the inside which reduces the risk of fracture. Cemented hips are more suitable for elderly patients with lower activity requirements (Bagarić et al. 2014; Mäkelä et al. 2014).

The most common approaches for THA are the posterior approach and anterolateral approach of Hardinge. HRAs were usually performed through the posterior approach. A minimally invasive technique has theoretical advantages, e.g., less soft tissue trauma, rapid recovery and reduced post-operative pain due to a small incision (Smith, Blake, and Hing 2011). However, there is a risk for component malpositioning and an increased risk of transient lateral femoral cutaneous nerve palsy. Several studies have shown no significant functional or clinical difference between standard and minimally invasive approaches (Wall and Mears 2008; Mazoochian et al. 2009; Smith et al. 2011).

2.1.1 Bearing surface options

Conventional metal-on-polyethylene bearing surfaces of uncemented THA are associated with a high rate of wear particle induced osteolysis and aseptic loosenings. In the late 1990's highly cross-linked and thermally treated polyethylenes came available (Jameson et al. 2011). These materials are claimed to decrease osteolysis by a reduced wear rate

(Kurtz et al. 2011). One factor which, nevertheless, causes higher wear rates is oxidation in polyethylene bearings (Costa et al. 1998), since oxidation decreases the homogeneity of these bearings. Third generation polyethylenes are infused with antioxidants to minimize this effect (Gómez-Barrena et al. 2009). Laboratory tests and midterm clinical results with these new polyethylenes have been promising (Callary et al. 2013; Snir et al. 2014).

CoC bearings have optimal tribologic properties, biologically inert wear and, at least theoretically, high durability due to extreme hardness. The most catastrophic complications follow implant breakage. The first generation CoC bearings in the 1970's were made of aluminium oxide. These bearings had a relatively high breakage rate (Sedel 2000). The materials currently used are third-generation aluminium oxide or zirconium oxide and breakage rates have reportedly been no more than 0.004% to 0.7% (Willmann 2000; Choy et al. 2013). CoC bearings have also a tendency to squeak audibly (Yang et al. 2007; Restrepo et al. 2008; Jarrett et al. 2009). Squeaking is associated with implant positioning and with young, heavier and taller patients. Squeaking may not affect patient satisfaction (Sexton et al. 2011).

MoM bearings in THA were introduced in the 1960's (Dandy and Theodorou 1975). The results were inferior compared to traditional polyethylene-on-metal bearings and MoM bearings were almost forgotten for over three decades. In the early years of the 21st century, second generation metal bearings came on the market. Now the bearings were made on chromium-cobalt and were claimed to cause less wear metal on polyethylene bearings (Clarke and Manley 2008; Lombardi et al. 2011).

2.1.2 Hip resurfacing arthroplasty

In HRA, the femoral head is covered with a metal cap and not, as in THA, replaced with a total stem. Acetabular component is similar in THA and HRA. Due to a preserved femoral neck, the anatomical result after HRA may be more natural.

HRA was thought to have advantages over THA, e.g., improved range of motion and hip function, bone preservation, lower dislocation rates and easier and safer revision operation in case of failure (Johansson et al. 2000; Burroughs et al. 2005; Shimmin et al. 2008). Originally, HRA was designed mainly for young patients with osteoarthritis, whose likelihood to have a revision procedure later in life is higher than for elderly patients. Promising early results extended the indications to other diagnoses, e.g., femoral head necrosis. Patients with HRA are thought to remain more active and to have better functions of daily living than patients with THA. Some evidence supporting this assumption has been published (Baker et al. 2011). Patients treated with HRA are often younger and more physically active, which may bias patient selection. HRA requires a larger opening than THA, and soft tissue trauma is larger despite the bone preserving features.

In the 1980's hip resurfacing prostheses with polyethylene-on-metal bearings were introduced (Tan et al. 2013). Results were inferior than with standard THA and these prostheses were abandoned (Amstutz and Le Duff 2012).

HRA was regularly used instead of THA for treatment of young and active patients in the early 21st century. The Birmingham hip resurfacing arthroplasty (BHR (Smith & Nephew, Memphis, USA)) was one of the most common HRA models. Other common HRA designs were the Articular Surface Replacement (ASR) (DePuy, Warsaw, USA), the ReCap HRA (Biomet, Warsaw, USA), the Converse Plus (Wright Medical Technology, Arlington, USA) and the Durom (Zimmer, Warsaw, USA) models. The BHR may have a lower risk for early revision compared to other HRAs (Johanson et al. 2010). Some studies show better functional results for HRA in ten year follow-up studies compared to THA (Baker et al. 2011). Other studies have not found statistically significant functional differences in 4 - 5 year follow-up studies where THA and HRA have been compared (Parsons and Edlin 2012; Larkin et al. 2013; Whitehouse et al. 2013).

Midterm results have shown high survival rates for HRA (Steffen et al. 2008; Ollivere et al. 2009). Survivorship as high as 99% and 98% at 10 and 13 years have been reported among patients under 55 years treated with HRA (McMinn et al. 2011). Ten-year survivorships as high as 94% and six-year survivorship 97% has been published for BHR HRA (Treacy et al. 2011; Reito et al. 2011). The reported results of HRA compared to THA have been inferior, and an almost 3-fold revision rate of HRA has been reported compared to THA (Johanson et al. 2010), while the ASR revision rate has been 4-fold compared to the BHR revision rate (Underwood et al. 2011). The 7-year survival rate of ASR HRA has been as low as 51% (Reito et al. 2013). The Durom HRA survival rate has been 95.2% at 3 years (Leclercq et al. 2013) and 88.2% at 5 years of follow-up (Naal et al. 2011).

Refinement of surgical techniques and experience seem to improve survival rates (Witjes et al. 2009; Treacy et al. 2011). Hospitals that operated less than 70 HRA annually had an almost 4-fold risk for early revision compared to hospitals that performed a larger amount of operations (Johanson et al. 2010). Female patients seem to be at a double risk for early HRA revisions compared to males ("Medical Device Alert"; Johanson et al. 2010; Naal et al. 2011).

2.1.3 Large-diameter head metal-on-metal total hip arthroplasty

The MoM articulation was considered to allow larger femoral head sizes without increasing wear (Dowson et al. 2004; Silva et al. 2005). A MoM prosthesis is considered to have a large diameter when the femoral head is 36 mm in diameter or more (G Singh et al. 2013). A large femoral head size increases the range of motion, improves stability and reduces impingement (Burroughs et al. 2005) and it decreases the risk for dislocation as the jump distance increases (Byström et al. 2003). The jump distance is the distance

that femoral head must travel before dislocating from the hip socket. These advantages led to an increased use of large-diameter femoral head MoM THAs (LDH MoM THA). LDH MoM THA was considered to allow correction of anatomical abnormalities in the femoral neck, which would reduce the risk of impingement compared to HRA.

Recently, there has been an increasing concern related to the wear debris generated from the taper junction (also known as the trunnion) of LDH MoM THAs (Pastides et al. 2013). A larger femoral head allows more offset, which increases the micromotion between the head center and the trunnion (Elkins et al. 2013). This wear process is called "trunnionosis" (Pastides et al. 2013). Contributing factors that have led to an increase in the incidence of trunnionosis might be short trunnion length, ridged surface and the use of larger femoral head sizes (Langton et al. 2012). Trunnionosis is associated with the development of adverse reaction to metal debris (ARMD) (Vundelinckx et al. 2013).

The effect of trunnion wear has been also documented in non-MoM THAs (Mao et al. 2012; Walsh et al. 2012), although, trunnionosis is obviously more common in large-headed MoM implants (Fricka et al. 2012).

2.2 COMPLICATIONS AFTER TOTAL HIP ARTHROPLASTY AND HIP RESURFACING ARTHROPLASTY

The most common surgical complications associated with MoM THA and HRA are aseptic loosening and periprosthetic osteolysis, dislocation, infection, periprosthetic fracture and ARMD.

2.2.1 Aseptic loosening

Aseptic loosening of the cup due to wear debris-induced osteolysis is a common late term complication (Iannotti et al. 1986). It can lead to component migration, instability or fracture. The amount of wear debris depends on positioning of the components and implant materials (Callanan et al. 2011). Aseptic loosening of a truly osteointegrated uncemented stem is rare, but the uncemented stem may not always osteointegrate early after surgery due to poor bone quality or an undersized component. The stem may subside and cause a periprosthetic fracture, which is called early loosening of the stem.

2.2.2 Dislocation

Until 2003, prosthetic component dislocation was one of the most common indications for reoperation, second only to component loosening (Vaughn 1993; Byström et al. 2003). Since then, the dislocation rate has decreased significantly (Krenzel et al. 2010; Jameson et al. 2011), which is thought to be associated with the increased use of larger head sizes.

The last decade has shown that a larger femoral head size decreases indeed the occurrence of dislocations (Byström et al. 2003; Krenzel et al. 2010; Dudda et al. 2010; Jameson et al. 2011). Dislocation rates as low as 0.05% have been reported when femoral components over 36 mm in diameter have been used (Lombardi et al. 2011). There is a significantly increased risk of revision due to dislocation as the femoral head size decreases; the risk is especially high when a small diameter femoral component is used with an uncemented acetabular component (Conroy et al. 2008). A large British study has documented a significant decrease in dislocation rates between 2006 and 2009, but with no change in the overall revision rates (Jameson et al. 2011). Two significant changes in hip surgery were introduced during that time: femoral heads with a larger diameter and the posterior approach became more popular (Jameson et al. 2011).

The clearest change in dislocation rate occurs when the head size increases from 28 mm to 32 mm (Wang et al. 2012), and the dislocation rate with 28 mm diameter femoral heads is fourfold compared to 32 mm diameter femoral heads (Byström et al. 2003).

The posterior approach is more prone to cause revision for dislocation than the straight lateral or anterolateral approach (Byström et al. 2003; Enocson et al. 2009; Krenzel et al. 2010). An improved repair technique can be used to reconstruct the posterior soft-tissue sleeve during the posterior surgical approach to prevent dislocation (Mahoney and Pellicci 2003). Patients who underwent THA because of a femoral fracture had dislocation rate on 2% when the anterolateral approach was used. The risk for dislocation was 14% when the operation was performed through posterolateral approach. The risk for dislocation was 12% with the posterolateral approach and posterior repair (Enocson et al. 2009). The difference between the posterolateral approach with posterior repair and without posterior repair was not significant in one study (Enocson et al. 2009), while in another study posterior repair significantly decreased the dislocation rate when the posterior approach was used from 4% to 0% (Mahoney and Pellicci 2003).

The primary indication for THR is associated with the dislocation rate. THRs indicated by dislocated hip fractures are known for instability (Johansson et al. 2000; Furnes et al. 2001), and a dislocation rate of 6% has been reported (Enocson et al. 2009). When THA was indicated by developmental hip dysplasia, 3% of patients had dislocation (Wang et al. 2012).

After revision arthroplasty, the dislocation rate is three times higher than the dislocation rate after primary hip arthroplasty (Khatod et al. 2006). It has been reported that after conversion from hip hemiarthroplasty to THA, the dislocation rate is higher compared to first-time revision from THA to THA (Sah and Estok 2008). The indication for revision affects the dislocation rate also after revision surgery. In one study, 14.7% of the patients who underwent revision for the treatment of a deep prosthesis infection had dislocation after the revision, while only 1.7% of patients whose revision was due to aseptic loosening had dislocation after the revision (Hartman and Garvin 2006).

The effect of the duration of the primary operation on the dislocation rate has been examined in many studies, and no significant correlation has been reported (Byström et al. 2003; Khatod et al. 2006). A high preoperative range of motion is a risk for dislocation, and the risk is even greater if the high range of motion is combined with surgery via the posterior approach and the use of a femoral head with a diameter under 32 mm (Krenzel et al. 2010).

The risk for redislocation is significantly higher than the risk for first-time dislocation (Mahoney and Pellicci 2003), and thus prevention of the first dislocation is critical. The femoral head size is the most important predictor of dislocation. The posterior approach is also a significant risk factor for dislocation and this risk cannot necessarily be reduced with posterior repair. Component malpositioning, posterior approach and a small femoral component size are also the most important risk factors for early dislocation (Nishii et al. 2004; Patel et al. 2007; Dudda et al. 2010).

2.2.3 Prosthetic infections

Prosthetic infection may be a septic, life-threatening complication. In the acute phase, a prosthetic infection may be cured with surgical lavation and debridement with in combination with prolonged antimicrobial medication. A chronic infection requires usually an amotion of the implant and a two-stage revision. Prosthetic infections are associated with high morbidity and mortality (Pivec et al. 2012). Prosthetic infection need to be considered in the differential diagnosis in revisions due to aseptic loosening. The prevalence of prosthetic infections varies from 1% to 3% after primary THA (Fitzgerald 1995; Dale et al. 2011), but rises significantly after revisions (James et al. 1982; Blom et al. 2003).

2.2.4 Periprosthetic fractures

A periprosthetic fracture is a serious complication after THA and HRA and the treatment depends on the fracture type and stability of the implant. Femoral periprosthetic fractures are more common than acetabular fractures (Masri et al. 2004). The overall postoperative periprosthetic femoral fracture rate after primary THA varies from 1% to 3% (Berry 1999; Park et al. 2003; Cook et al. 2008). Periprosthetic femoral fractures in the short-term are often associated with an improper choice of implant or technical problems. The risk for late periprosthetic fractures increases after 10 years due to osteolysis, especially among elderly patients (Cook et al. 2008).

Periprosthetic femoral fractures may be treated conservatively, by surgical osteosynthesis (wiring, plates, and/or cortical strut bone grafts) or by revision arthroplasty (Park et al. 2011). Periprosthetic femoral fractures associated with THA are usually classified by the Vancouver classification system (Masri et al. 2004). The classification records the location of the fracture, the stability of the prosthesis and the surrounding

bone stock. Thus, type A fractures include trochanteric fractures, in type B the fracture is in the stem area and in type C the fracture is located below the stem.

An important risk factor for periprosthetic fractures is osteolysis and aseptic loosening of the implant (Sarvilinna et al. 2004). Other predictors of periprosthetic fractures are female gender, high age and the indication for surgery (J Singh et al. 2013). In the same study, cemented implants had 30% lower risk for early periprosthetic fracture compared to uncemented implants. Cement is thought to strengthen bone cavity from inside and, therefore, to decrease the periprosthetic fracture risk (Thomsen et al. 2008). Cook et al. reported a 0.8% fracture rate at 5 years and 3.5% at 10 years after primary implant in cemented THA (Cook et al. 2008), while Berry (Berry 1999) reported from the Mayo clinic a fracture incidence of 5.4% for uncemented THAs, 0.3% for cemented THAs and 1.1% overall. The study consisted more than 23, 000 hips operated between 1969 and 1999. The fracture incidence after revision surgery was much higher, 4.0% (Berry 1999).

Femoral neck fractures after HRAs occur predominantly early after the operation (Shimmin and Back 2005; Zustin et al. 2010; Matharu et al. 2013) with a subsequent incidence peak 10 years after surgery (Carrothers et al. 2010; Zustin et al. 2010). The second peak may be associated with neck thinning over time. The overall prevalence of femoral neck fractures in HRA is reportedly 1.1% at a mean follow-up time of 5.5 years (Matharu et al. 2013). This figure comes close to the periprosthetic fracture rates of THA (Cook et al. 2008; J Singh et al. 2013).

2.2.5 Complications related to metal-on-metal articulations

Metal debris may enter the hip joint when large-head MoM articulations are used for THA, where there is a risk of trunnion wear and corrosion. After LDH MoM THA and HRA, the chromium and cobalt ion concentrations may be elevated not only in hip joint, but also in the serum, plasma and urine of the patient (Hartmann et al. 2013). High metal ion levels in the blood are associated with complications related to MoM bearing surfaces (MacNair et al. 2013; Mokka et al. 2013).

MoM bearing surface related complications are becoming common. When these problems first appeared, they were considered to be reactions related to aseptic lymphocytic vasculitis (aseptic lymphocyte-dominated vasculitis-associated lesion or ALVAL-reactions), but later research has shown that ALVAL-reactions are only a part of this problem. Rather, direct toxicity of cobalt and chromium is currently thought to be involved in the development of MoM reactions of the hip joint. At the moment metal bearing and trunnionosis related complications are commonly called adverse reactions to metal debris or ARMD. ARMD is a spectrum of changes involving pure metallosis, ALVAL and granulomatous inflammation (Natu et al. 2012). ARMD may include soft tissue necrosis, pseudotumors and hip joint effusion. Clinically, patients

may be symptomless or experience groin pain, clicking, a sensation of subluxation and palpable masses in the groin area (Mokka et al. 2013). In MRI ARMD may be seen as a fluid collection or a solid mass (Toms et al. 2008). ARMD is more common among female patients, and the risk increases when components of small size are used and the inclination angle is high (de Haan et al. 2008; Glyn-Jones et al. 2009).

ARMD may appear as pseudotumors. Pseudotumors are fluid collections and/or soft tissue masses associated with MoM bearings. These sterile, inflammatory tumors are neither malignant nor infectious, but they might indicate revision due to groin pain, a palpable mass or paresthesia (Pandit et al. 2008; Bisschop et al. 2013). The prevalence varies between studies from 0.1% (Beaule et al. 2011) to no less than 69% (Chang et al. 2012; Matthies et al. 2012). In a study of Bisschop et al. (2013), 28% of the patients had pseudotumor five years after surgery, but only 28% of these pseudotumors were symptomatic. In a recent meta-analysis, the prevalence varied from 0% to 6.9% (Wiley et al. 2013). A blood cobalt level >85 nmol/L predicts pseudotumor formation (Wiley et al. 2013). In one study the prevalence of pseudotumors was significantly higher among female patients: it was 13.1% at six years for women under 40 years and 6.1% at eight years for women over 40 years vs. 0.5% for men (Glyn-Jones et al. 2009). Pseudotumors have been associated with high metal ion levels in many (Pandit et al. 2008; Hart et al. 2009; Langton et al. 2010), but not all studies. Thus, Matthies et al. (2012) found no correlation between serum metal ion levels nor cup position and pseudotumor prevalence (2012).

Symptomless pseudotumors may be found by metal artefact reduction sequence magnetic resonance imaging (MARS MRI). Sonography may also be used to identify solid or cystic masses (Fang et al. 2008). MRI findings can be compared to each other and grading systems have been designed for this (van der Weegen et al. 2014). Of these systems the one published by Anderson (normal, infection or varying severity of MoM disease) is the most appropriate one for pseudotumor severity grading (van der Weegen et al. 2014).

2.2.5.1 Metal ion release

Persons no harboring metal devices or otherwise lacking metal exposure have immeasurably low levels of chromium and cobalt in their serum. In a study of Sidaginamale et al. (Sidaginamale et al. 2013) 3.22% of 3042 persons without a MoM implant had a blood chromium level >2µg/L and 0.033% had a blood cobalt level >2µg/L. The highest blood chromium level was 8.6µg/L and the highest blood cobalt value was 6.7µg/L. In patients with a MoM hip device, these concentrations are often at least somewhat elevated. The typical detection limit of cobalt in human serum is 0.3µg/L. Concentrations >50µg/L are considered very high (Hartmann et al. 2013). There is no unequivocal limit above which revision due to a soft tissue reaction or cobalt poisoning needs consideration. The decision to revise is made by a combination

of the individual patient's symptoms, laboratory results and MRI findings. It has been stated that 5µg/L could be used as a limit to detect ARMD (Hart et al. 2011; Mokka et al. 2013). The UK Medicines and Healthcare products Regulatory Agency instructs that patients with serum chromium or cobalt levels >7µg/l should be investigated further for any soft tissue reactions (NJR 2007) Patients with >5µg/L cobalt in their serum have a 4-fold risk for ARMD compared to lower cobalt levels (Bosker et al. 2012). Sidaginamale et al. (Sidaginamale et al. 2013) reported a 94% sensitivity and 95% specificity for serum cobalt levels over 4.5µg/l to detect abnormal metal wear. However, low metal ion levels do not exclude ARMD (MacNair et al. 2013). In some studies, serum chromium and cobalt levels have correlated highly with the cup inclination angle. An inclination angle >50º was associated with increased serum metal-ion levels (de Haan et al. 2008; Hart et al. 2011; MacNair et al. 2013). An acetabular component inclination angle > 60º has been reported to increase the risk for ARMD (Langton et al. 2009; Reito et al. 2011; MacNair et al. 2013), but other large studies have not observed any no correlation between the inclination angle and serum metal-ion levels (Emmanuel et al. 2013; Mokka et al. 2013).

Female gender is a significant risk factor for high serum chromium levels (MacNair et al. 2013). Bilateral prostheses are associated with significantly higher serum metal ion levels than to unilateral prosthesis (MacNair et al. 2013). A further risk factor for elevated serum ion levels is a small femoral head size (≤ 51 mm vs. ≥ 53 mm) (Langton et al. 2008).

The metal ion levels in patients treated with hip resurfacing prosthesis may be similar to those of patients with MoM THAs (Moroni et al. 2011). In studies comparing the metal ion levels in the blood of patients with types of HRA, patients with BHR had higher blood ion concentrations than patients who had ASR or Metasul MTHR (Langton et al. 2009). Male patients with BHR HRA stand out as having higher blood metal ion levels compared to other HRA designs (Witzleb et al. 2006; Langton et al. 2009).

Metal ions released into the blood are largely cleared by the kidneys and excreted into the urine. Nephrotoxicity studies do not indicate that there are any renal effects in the midterm or short term (Corradi et al. 2011; J. Yang et al. 2011).

Several case reports on systemic cobalt toxicity have been published. Gilbert et al. reported a patient with hypothyroidism, dilated cardiomyopathy, pericardial effusion, liver failure and polycythemia after bilateral MoM THA (Gilbert et al. 2013). These are the classical signs of cobalt poisoning. The diagnosis was confirmed by biopsies and analysis of hip aspiration fluid. Cardiomyopathy due to cobaltism has been reported in at least seven other patients (Machado et al. 2012; Zywiel et al. 2013), although causality has not always been unequivocal (Machado et al. 2012). Interestingly, however, one patient had a symptomatic improvement after removal of the MoM hip replacement (Machado et al. 2012). A patient has reportedly died because of cobalt-induced cardiomyopathy. This patient had undergone revision surgery to after fracture of a CoC component and

was fitted with a MoP device. He developed classical cobalt toxicity, the hip device was removed and he underwent cobalt chelation therapy, but died in spite of these efforts (Zywiel et al. 2013).

The neurological manifestations of cobalt toxicity may include optic atrophy, deafness and limb paresthesia (Royal and Hospitals 2000). In one case report, the patient developed blindness, deafness and lower limb paresthesia and removal of the implant provided some improvement (Rizzetti et al. 2009).

Permanent metal ion exposure may be a cancer risk due to chromosomal damage (Daley et al. 2004). The overall short-term cancer risk of modern MoM hip arthroplasties is not increased (Mäkelä et al. 2012; Brewster et al. 2013), but the incidence of basalioma and soft-tissue sarcomas was significantly higher in a MoM cohort than in non-MoM cohort (Mäkelä et al. 2014). Since soft tissue sarcomas are extremely rare, this may still be a chance finding.

2.3 REVISION SURGERY

The demand for primary THA is increasing, and this will raise the demand for revision surgery. However, the revision rate has remained relatively constant over time (Kurtz et al. 2005; Kurtz et al. 2007). Aseptic loosening is one of the most common reasons for revision hip arthroplasty (Hailer et al. 2010; Karam et al. 2012). Aseptic loosening is usually associated with loss of bone stock from both the acetabular and the femoral side. Repair of this bone stock is a major problem in revision surgery (van Haaren et al. 2007).

Acetabular bone deficiency may be classified according Paproskys acetabular defect classification. Class I means minimal bone loss with no component migration and intact acetabular walls; class II moderate bone loss and destruction of medial and/or superior walls; and class III acetabular bone defects, severe bone loss and destruction of the acetabular rim (Paprosky et al. 1994; Yu et al. 2013). Another classification of acetabular defects has been presented by the AAOS. In this classification type I means segmental deficiency with significant rim defect; type II cavitary defects medially or posteriorly; type III combined cavitary and segmental deficiency; type IV pelvic discontinuity; and type V arthrodesis.

On the femoral side the Endo-Klinik classification from I to IV is generally used. Grade I is minimal bone stock loss and IV the most severe. Femoral bone deficiency can be treated with impaction bone grafting, megaprosthesis or structural allografts (Ornstein et al. 2009; Buttaro et al. 2012). The results with regard to an acceptably low frequency of aseptic loosening and minor bone loss have been satisfactory (Ornstein et al. 2009). The most common complication after these revisions is periprosthetic fracture; the incidence varies from 4% to 32% (Pekkarinen et al. 2000; Halliday et al. 2003).

2.3.1 Impaction bone grafting in acetabular bone deficiency

Impaction bone grafting with a cemented polyethylene cup has been widely used for over 30 years to reconstruct major acetabular defects in primary and revision hip replacement surgery. Procedures are managed according to principles established by Slooff et al. and Schreurs et al. (Slooff et al. 1993; Slooff et al. 1996; Schreurs et al. 2001; Schreurs et al. 2004).

The original impaction bone grafting technique, also known as Slooff's procedure, was described in 1993 (Slooff et al. 1993). In this technique, acetabular cavities are tightly impacted with morselized femoral head or with a cancellous graft alone. The graft may be impacted against a wire mesh and the acetabular component is cemented on top of the graft. Long-term and midterm results have been favorable, and with aseptic loosening as the endpoint, survival rates have been over 90% in many studies (Slooff et al. 1996; Welten et al. 2000; Schreurs et al. 2001; de Kam et al. 2010; van Egmond et al. 2011). Short-term studies show high, over 95% survival rates (Comba et al. 2006). The surgical technique is demanding and some studies have reported less satisfactory outcomes in non-tertiary referral centers (Azuma et al. 1994; van Haaren et al. 2007). The etiology of graft reabsorption are unknown and results may be unpredictable (Azuma et al. 1994; van Haaren et al. 2007).

In one recent study results of impaction bone grafting in AAOS type III and IV acetabular bone deficiencies were not as good as presented above (van Haaren et al. 2007). However, the grafts in this inferior study were not washed before impaction (van Haaren et al. 2007), and authors suggested that it may have worsened the mechanical stability and affected to results (Arts et al. 2006). Bone graft washing is thought to increase friction and to allow tighter impaction by removing fat and bone marrow from the graft. In addition, bone graft washing reduces the risk of bacterial infection (Hirn et al. 2001).

Bone graft size affects graft survival. Large and washed bone grafts tend to have the least cup migration and cement penetration seems to be better when larger grafts are used (Ullmark and Nilsson 1999). Washing itself does not influence cement penetration but bone graft incorporation is affected (Arts et al. 2006).

Bone grafts are of human origin and must be sterilized before recipient contact to prevent transmission of bacteria and viruses. Traditionally, freezing has been the golden standard sterilization procedure. Fresh frozen bone is stored in -80ºC in accordance with bone bank protocols (AATB 2014). Since freezing leaves some concern of residual viral or prion contamination, some centers prefer irradiated bone grafts (Tomford 1995).

2.3.2 Revision after metal-on-metal hip replacement

The indications for a revision operation due to ARMD after MoM hip replacement are not unambiguous. If the patient has severe symptoms like hip pain, clicking, sensation

of subluxation or swelling, the decision to revise is easier. Radiographic and laboratory findings provide information about the possibility of metal induced soft tissue reactions. However, there is no definite indication for revision and the decision is often difficult. If a revision is indicated by an ARMD-reaction, the procedure tends to be challenging because of concomitant soft-tissue destruction. All pseudotumor formation needs to be completely resected to avoid recurrence and infection (Liddle et al. 2013).

The outcome of revision surgery indicated by a pseudotumor or gluteus muscle necrosis may be poor. Almost half of the revised hips may encounter a major complication and a third require re-revision during 3 years of follow-up (Grammatopolous et al. 2009). In a study of Liddle et al., the survival rates for revisions due to pseudotumor were comparable with the survival rates for revision performed for any other reason during 30 months of follow-up (Liddle et al. 2013). Of note, however, is that this study included HRA revisions for any reason and did not concentrate on the MoM problem.

Ball et al. reported on the change in metal ion concentrations following revision surgery. Patients with very high (> 20 μg/L) metal ion concentrations had a reduction in the concentration after one year of follow-up, but some patients still had levels > 5 μg/L at that time (Ball et al. 2013).

3. AIMS OF THE PRESENT STUDY

The main purpose of this study was to evaluate the survival rates and complication frequencies of MoM hip implants on the basis of data entered into the Turku University Hospital database and the Finnish Arthroplasty Register. Additional aims were to assess the association between femoral head size and dislocation revision rates and to evaluate the long-term results of acetabular revision operations where impaction bone grafting has been used.

The specific aims of the studies were:

1. To evaluate the short-term clinical results of Biomet Magnum M2A – ReCap total hip replacement. (I)

2. To study the association between femoral head size and dislocation revision rate in primary THA and HRA based on data from the Finnish Arthroplasty Register. (II)

3. To analyze the early outcome of three HRA designs and to compare the outcome with analogous LDH MoM THAs from the data of the Finnish Arthroplasty Register. (III)

4. To assess the short-term to midterm survival results of the metal-on-metal hip devices Birmingham hip resurfacing arthroplasty, Synergy – Birmingham modular hip arthroplasty, and Synergy – R3 total hip arthroplasty in Turku University Hospital. (IV)

5. To evaluate the long-term results of acetabular revisions, based on the Turku University Hospital's data, where a technique of acetabular reconstruction with impaction bone grafting was used for total hip revision arthroplasty. (V)

4. PATIENTS AND METHODS

4.1 PATIENTS

4.1.1 Studies I, IV and V

Studies I, IV and V are retrospective studies based on data collected from the Turku University Hospital's medical records and from the Implant DB database (BCB Medical).

In study I, during the study period between September 2005 and June 2009, a total of 691 cementless MoM THA operations were performed on 635 patients using the Biomet Bimetric stem, the ReCap cup and the M2a-Magnum femoral head. The M2a-Magnum modular head and the ReCap cup are high-carbon, as-cast single-heated components. The system is modular, with different head sizes and the option to adapt the neck length with different length tapers. The main components of the head and acetabular component are produced from a cobalt-chromium alloy that contains a small proportion of molybdenum and carbon. The stem, taper and taper adapters are made of a titanium, aluminium and vanadium alloy (Bosker et al. 2012). All Magnum M2A – ReCap implants were included in the study. Demographic data are presented in Table 1.

Table 1. Patients in study I.

			Harris Hip Score (HHS)		
	Number	**Mean age**	**Preoperative**	**3 months after the surgery**	**1 year after the surgery**
Women	369	65 (25-88)			
Men	266	65 (28-88)			
Total	635	63 (25-88)	59.8	86.4	94.0

In study IV, all BHR HRAs, Synergy – BHR modular hip arthroplasties and Synergy – R3 THAs performed between February 2004 and September 2010 in the Turku University Hospital were included. There were a total of 329 operations on 313 patients during the study time. The BHR cup is a chromium-cobalt monoblock component with a metallic inner surface. R3 is a modular titanium cup with three liner options: plastic, ceramic and metal. Both the BHR cup and the R3 cup with a metal liner can be used with the Synergy stem, except that the head size in the Synergy – BHR modular hip arthroplasty device is, on average, much larger than in Synergy – R3 THA. Demographic data are presented in Table 2.

Table 2. Patients in study IV.

	Number n (%)	Male n (%)	Female n (%)	Age Mean	Harris Hip Score Mean		
					Preoperatively	3 months postoperatively	1 year postoperatively
BHR HRA	249 (75.7%)	175 (81.4%)	74 (64.9%)	52.0	65.8	93.6	97.8
BHR – Syn modular hip replacement	39 (11.9%)	21 (9.8%)	18 (15.8%)	57.8	61.9	86.8	92.3
R3 – Syn THA	41 (12.5%)	19 (8.8%)	22 (19.3%)	62.5	61.8	89.4	97.0
Total	329	215	114	54.0	64.9	92.3	97.2

Study V covered the time period between the years 1999 – 2004 and involved the patients treated at the Turku University Hospital. During this time, a total of 63 acetabular revisions were performed, where impaction bone grafting and a cemented cup were used. There were 62 patients. Demographic data are presented in Table 3.

Table 3. Patients in study V.

	Number	Mean age
Women	42	
Men	21	
Total	63	68 (35-77)

4.1.2 Studies II and III

Studies II and III are based on the data entered into the Finnish Arthroplasty Register.

In study II, all primary THAs and HRAs performed in Finland between 1996 and 2010 were included. If both hips of the same patients had been operated, only the first one was included, making a total of 79,382 hips. Only patients aged 18-100 years at the time of operation were included. Patients without information of femoral head size were excluded. Only the most common implant designs (more than 100 implantations during the study period) were included. Head sizes 28 mm, 32 mm, 36 mm, and 37+ mm of these implants were included, leaving altogether 42,379 hips for final analysis. Data on the implants are presented in Table 4.

Table 4. Implants in study II.

Implant	Implant type	Number of hips	Mean follow-up (years)	Number of hips revised due to dislocation
Elite Plus	Cemented THA	1,291	8.4	10
Lubinus IP & Lubinus SP I & Lubinus SP II/Lubinus IP	Cemented THA	2,666	7.9	78
Exeter Universal/Ex All-poly & Ex Contemporary	Cemented THA	12,119	6.2	159
Spectron/Reflection	Cemented THA	4,192	4.3	27
ML-Taper/MMC & Durom-resurfacing cup	Cementless THA	362	1.5	0
cementless Spotorno/Morscher & Durom- resurfacing cup	Cementless THA	132	4.5	0
Synergy/R3 & BHR- resurfacing cup	Cementless THA	1,225	1.8	0
Biomet Bimetric/Biomet cups	Cementless THA	10,029	5.1	140
ABG I/ABG I & ABG II	Cementless THA	2,075	10.0	25
ABG II/ABG II	Cementless THA	1,897	6.5	16
Accolade & Omnifit & Symax/ Trident	Cementless THA	160	4.4	0
Summit/Pinnacle & ASR-resurfacing cup	Cementless THA	2,045	3.2	11
Corail/ Pinnacle & ASR-resurfacing cup	Cementless THA	411	2.7	2
BHR-resurfacing prosthesis	HRA	1,635	5.3	2
ASR- resurfacing prosthesis	HRA	836	4.2	1
ReCap- resurfacing prosthesis	HRA	587	3.3	1
Durom- resurfacing prosthesis	HRA	287	4.1	0
Conserve Plus- resurfacing prosthesis	HRA	430	2.9	0
Total		42,379	5,6	472

In study III, all Bimetric – Recap THAs (Biomet, Warsaw, USA), ReCap HRAs (Biomet), Synergy – BHR THA (Smith & Nephew, Memphis, USA), BHR HRAs (Smith & Nephew), Corail & Summit ASR THAs (DePuy, Warsaw, USA) and ASR HRAs (DePuy) devices used for hip surgery in Finland during the study period 2001 – 2011 were included. To reduce skewness between HRA and THA, patients older than 85 years were excluded. Also patients with a diagnosis of other reason or rheumatoid arthritis were excluded. All the other diagnoses were included. This yielded a total of 5,464 Bimetric/ReCap THAs, 698 ReCap HRAs, 475 Synergy/BHR THAs, 1,902 BHR HRAs, 632 Corail & Summit/ASR THAs and 979 ASR HRAs and a grand total of 10,150 hips. Demographic data are presented in Table 5.

Table 5. Implants in study III.

Hip Device	n	Mean follow-up (years, range)	Mean age (years, range)	Males %	Implanting period	Operated side, % right	Diagnosis, % primary osteoarthritis
Bimetric/ ReCap THA	5,464	3,1 (0-7,0)	63 (21-85)	54	2005-2011	56	93
ReCap resurfacing	698	4,1 (0-7,7)	56 (25-77)	65	2004-2011	52	96
Synergy/ BHR THA	475	4,0 (0-7,6)	58 (18-82)	55	2004-2011	54	92
BHR resurfacing	1,902	6,0 (0-10,7)	54 (18-83)	69	2001-2011	53	91
Corail & Summit/ ASR THA	632	3,9 (0-7,7)	60 (21-78)	58	2004-2010	54	91
ASR resurfacing	979	5,0 (0-7,8)	56 (25-79)	64	2004-2010	56	96
Total	10,150	4,0 (0-10,7)	60 (18-85)	59	2001-2011	55	93

4.2 METHODS

All data was collected retrospectively from the medical records of the Turku University Hospital, from the Implant DB database (studies I, IV and V) and from the Finnish Arthroplasty Register (studies II and III).

Data on hip and knee total arthroplasties has been collected by the Finnish Arthroplasty Register since the 1980's (Paavolainen et al. 1991). Health care authorities, institutions and orthopedic units are obligated to provide all essential information to the National Institute for Health and Welfare for maintenance of this register, and currently 98% of all implantations are entered. Revisions can be linked to the primary operation by using a personal identification number.

In study I, we evaluated the postoperative complications, indications for reoperation and changes in HHS retrospectively from electronic databases. All patients had two scheduled outpatient visits, the first at two to three months after surgery and the second one year after surgery.

In study II, revision for dislocation was defined as the endpoint. Of all included THAs, 15.0% were LDH MoM THAs. The survival rate for dislocation was evaluated in head size groups 28 mm, 32 mm, 36 mm and 37+ mm, and these groups were compared to one another. The patient's age at day of surgery (18-49 years, 50-59 years, 60-69 years, 70-79 years and 80+ years), gender and time period of operation (1996-2000, 2001-2005, and 2006-2010) were examined as potential confounding factors. Patients who had died or left Finland during the follow-up time were censored at that point.

In study III, the revision risk between three HRA and their analogous THA models were compared. This made a total of three HRA – THA pairs (ReCap HRA vs. Bimetric/ReCap THA, BHR HRA vs. Synergy/BHR THA, and ASR HRA vs. Corail&Summit/ASR THA). The patient's age at the day of surgery, gender, operated side, head size < 50 mm or ≥ 50 mm, primary diagnosis and implant design were examined as potential confounding factors. The effect of age was also analyzed by dividing the patients to those under 55 years and 55 years or older. Revision for any reason served as the endpoint. Revision for aseptic loosening, revision for dislocation, revision for infection and revision for periprosthetic fracture were also studied as separate end-points. Patients who had died or left Finland during the follow-up time were censored at that point.

In study IV, revision operation served as the end-point. All patients had a scheduled follow-up visit at two months and at one year after surgery. Acetabular anteversion and abduction angles, complications and the HHS were evaluated and recorded. Radiolucency around the components was evaluated as a sign of loosening. Blood chromium and cobalt levels were measured in samples obtained from a total of 100 patients. These variables were studied as potential risk factors for revision.

In study V, re-revision for any reason served as the end-point. Acetabular defects were classified according to Paprosky's acetabular defect classification from pre-revision radiographs. The patient's age at the day of index operation, operated side, bilateral operation, indication for primary arthroplasty, primary implant type, reason for index revision, acetabular cup type used in revision, possible simultaneous stem revision, amount of femoral heads used to graft, amount of screws used for impaction bone grafting, mesh usage, rheumatoid arthritis diagnosis and Paprosky's bone defect classification were evaluated as potential risk factors for re-revision.

4.2.1 Statistical methods

All statistical analyses were carried out using the SAS System for Windows, versions 9.2 and 9.3 (SAS Institute Inc, Cary, NC, USA). Implant survival probabilities were assessed using the Kaplan-Meier survival and log-rank test. In study II, a Kolmogorov-type of supremum test was performed to check the proportional hazard assumption. Potential confounding factors were studied by Cox's multiple regression model. Results were expressed by HR and 95% CI. P-values from data obtained from the Cox multiple regression analysis were applied to the Wald test. P-values less than 0.05 were considered statistically significant.

5. RESULTS

5.1 Study I

HHS increased from a preoperative value of 59.8 to 86.4 at three months of follow-up and to 94.0 at one year of follow-up. The most common reason for re-operation was a periprosthetic calcar fracture in the femur. A total of 23 patients required a re-operation. At one year of follow-up, there were no complications associated with the metal bearings.

5.2 Study II

A larger femoral head size was statistically significantly associated with a decreased risk for revision for dislocation. The adjusted risk ratio in the Cox model was 0.40 (95% CI 0.26-0.62, p<0.001) for the 32 mm head size, 0.41 (CI 0.24-0.70, p=0.001) for the 36 mm head size and 0.09 for the 37+ mm (CI 0.05-0.17, p<0.001). Survival charts for the different age groups are presented in Figures 1a-c.

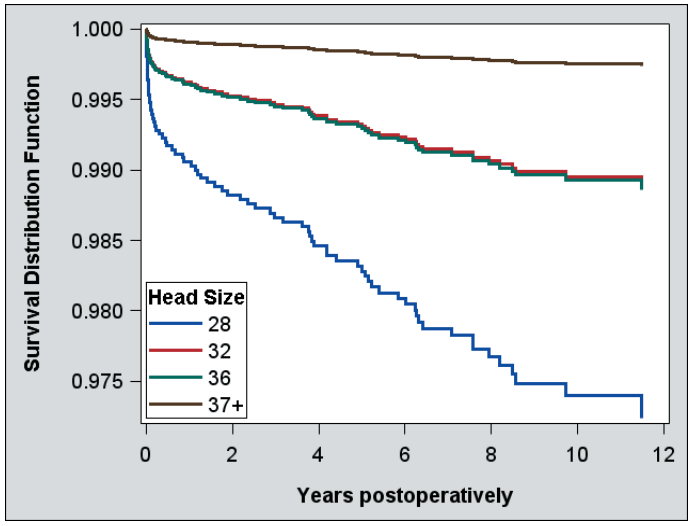

Figure 1a. Survival data of the implants by head size in the age group 50-59 year. Adjustments have been performed for sex and time period. Study II.

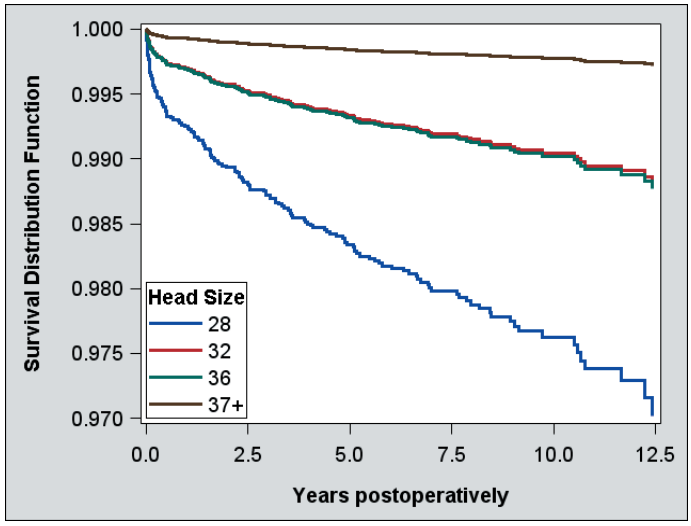

Figure 1b. Survival data of the implants by head size in the age group 60-69 year. Adjustments have been performed for sex and time period. Study II.

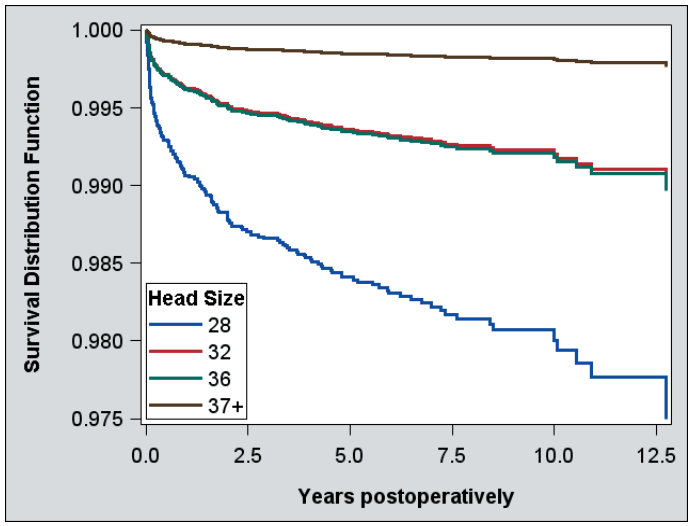

Figure 1c. Survival data of the implants by head size in the age group 70-79 year. Adjustments have been performed for sex and time period. Study II.

The reference group (head size 28 mm) contained 56% of all hips and had the longest follow-up time. Figures 2 a-d show the unadjusted dislocation revision rate divided by the head size groups 28 mm, 32 mm, 36 mm and 37+ mm during the first 30 days, during 1 to 12 months postoperatively and during 2 to 5 years postoperatively.

The revision risk for dislocation did not differ between HRAs and LDH MoM THAs (RR 0.82, CI 0.22- 3.07, p=0.8). Male gender was significantly associated with an increased dislocation revision rate in the Cox model (RR 1.23, CI 1.03 – 1.48, p=0.02). The dislocation

risk was increased during the time period 2006 – 2010 compared to 1996 – 2000 after adjustments for femoral head size in the Cox model (RR 1.41, CI 1.01 – 1.97, p=0.05).

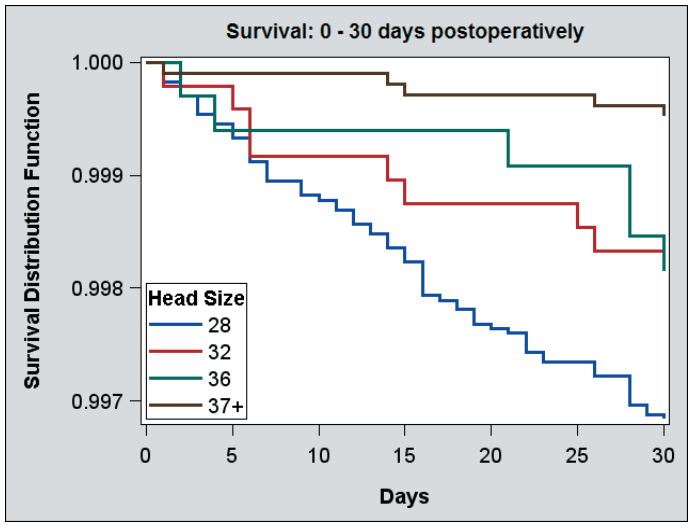

Figure 2a. Unadjusted dislocation revision rate during the first 30 postoperative days by head size. Study II.

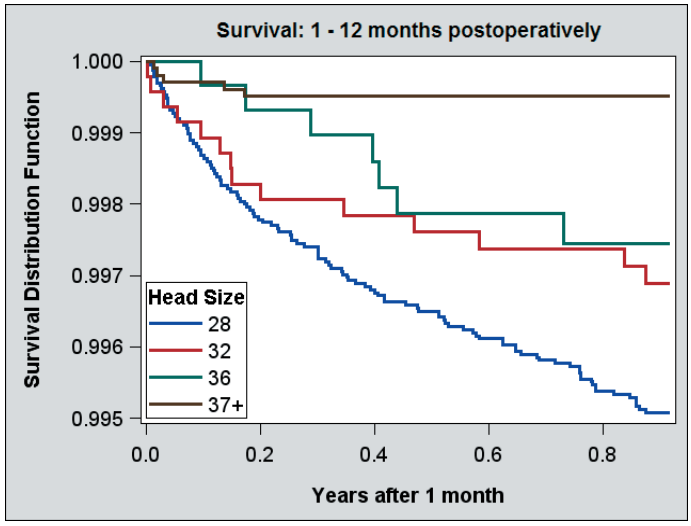

Figure 2b. Unadjusted dislocation revision rate during 1 to 12 months postoperatively by head size. Study II.

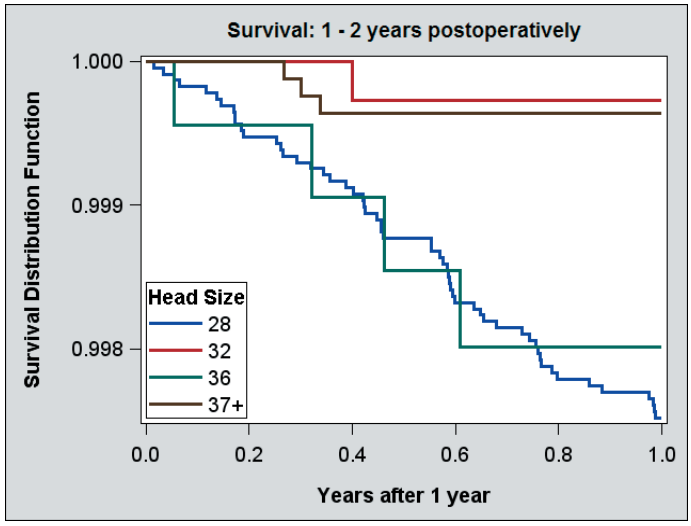

Figure 2c. Unadjusted dislocation revision rate during 1 to 2 years postoperatively by head size. Study II.

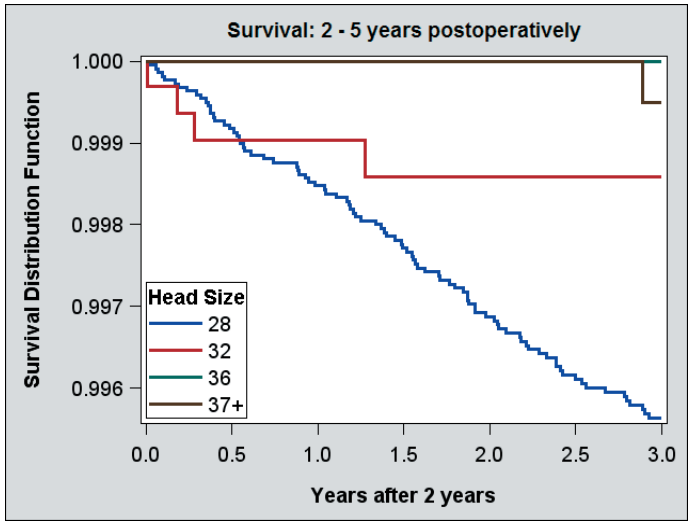

Figure 2d. Unadjusted dislocation revision rate during 2 to 5 years postoperatively by head size. Study II.

5.3 Study III

The revision risk for ASR THA was significantly higher compared to ASR HRA by Cox regression analysis (RR 0.73, CI 0.54 – 0.98; p=0.04). There was no statistically significant difference in revision risk between ReCap HRA and Bimetric – ReCap THA (RR 1.43, CI 0.95-2.14; p=0.09) or BHR HRA and Synergy – BHR THA (RR 1.35, CI

0.75-2.43; p=0.31). Figures 3 a-c show the overall survivals, where revision for any reason was the end-point. Adjustments were made for age at surgery, gender, head size and diagnosis.

There was no difference in the risk of revision due to dislocations, fractures or infections. The risk for revision for aseptic loosening in ASR HRA was statistically significantly lower than of ASR THA. P-values are presented in Table 6.

Table 6. P-values for revision risks for different indications between implant pairs.

Indication	ASR HRA vs. ASR THA	BHR HRA vs. BHR modular hip replacement	ReCap HRA vs. ReCap THA
Dislocation	0.4	0.5	0.7
Fracture	0.2	0.5	0.2
Infection	0.2	0.95	0.1
Aseptic loosening	< 0.001	0.2	0.8

Subgroup analysis showed that elderly women with ReCap HRA had a higher revision risk compared to Bimetric – ReCap THA. Elderly men with ASR THA had a similar revision risk as with ASR HRA. Subgroup analyses are presented in detail in Table 7.

Table 7. Subgroup analysis: age and gender stratification.

	Adjusted RR for revision ReCap HRA/ Bimetric-ReCap (95% CI)	p-value	Adjusted RR for revision BHR HRA/ Synergy-BHR (95% CI)	p-value	Adjusted RR for revision ASR HRA/Corail & Summit-ASR (95% CI)	p-value
Age ≤ 54 years						
Males	0.79 (0.28-2.28)	0.67	2.43 (0.32-18.60)	0.39	0.73 (0.24-2.28)	0.59
Females	1.01 (0.35-2.89)	0.99	1.01 (0.35-2.95)	0.99	1.70 (0.72-4.04)	0.23
Age ≥ 55 years						
Males	0.93 (0.44-1.99)	0.86	1.08 (0.36-3.25)	0.89	0.48 (0.28-0.84)	0.01
Females	3.52 (1.87-6.60)	< 0.001	1.48 (0.52-4.22)	0.46	0.65 (0.41-1.03)	0.07

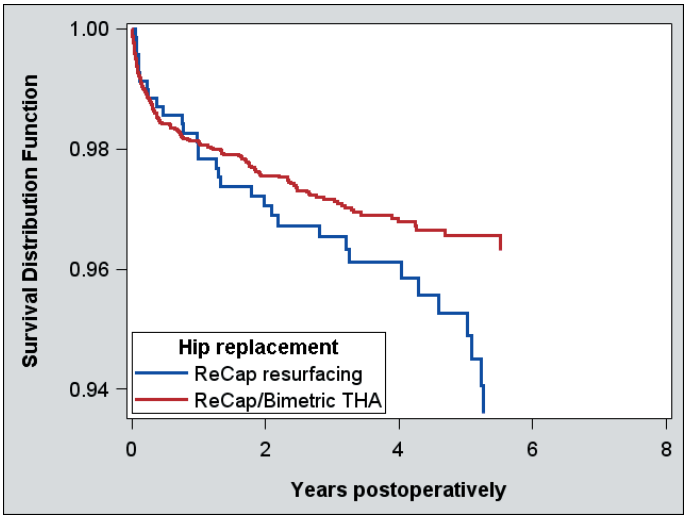

Figure 3a. Cox-adjusted survival curves of ReCap resurfacings and Bimetric – ReCap THAs. Study III.

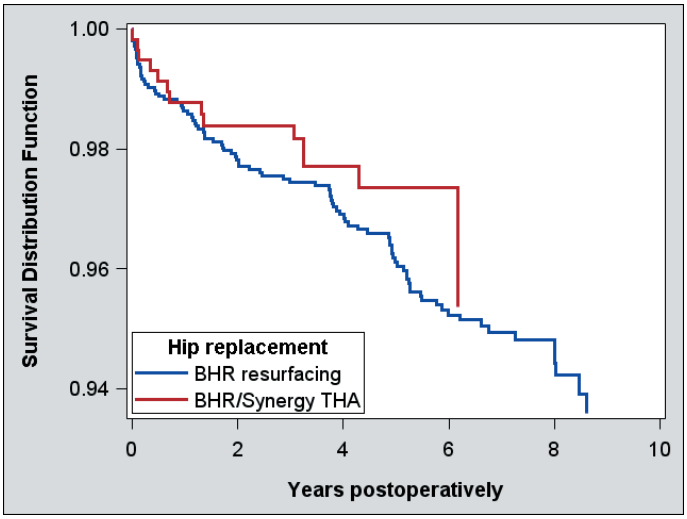

Figure 3b. Cox-adjusted survival curves of BHR resurfacings and Synergy – BHR THAs. Study III.

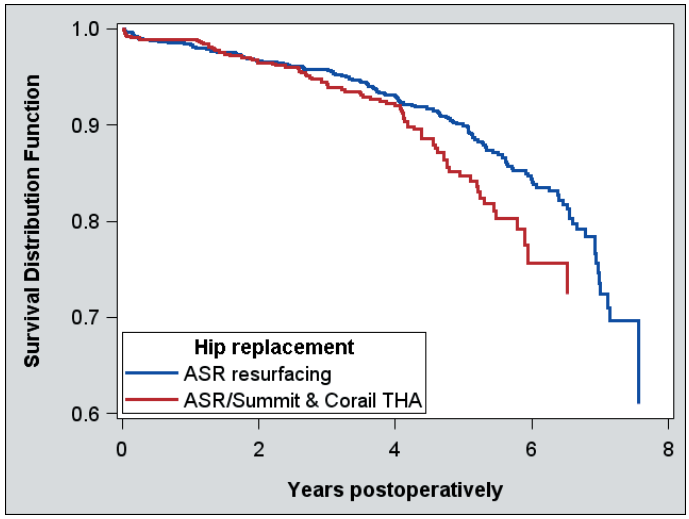

Figure 3c. Cox-adjusted survival curves of ASR resurfacings and ASR THAs. Study III.

5.4 Study IV

At the end of follow-up, the overall survival rate was 87.6% for BHR – BHR HRA, 94.9% for Synergy – BHR modular hip replacement and 80.5% for Synergy – R3 THA. At three years the overall survival rate was 90.5% for BHR – BHR HRA, 94.9% for Synergy – BHR modular hip replacement and 80.5% for Synergy – R3 THA. Survival charts are presented in Figures 4 a-b. In Cox's regression model, a larger femoral head size was associated with lower revision risk rate (p=0.009). The patient's age, gender, cup anteversion or abduction angle were not associated with revision risk. The adjusted risk ratios for revision for any reason according to Cox's model are presented in Table 8.

The concentrations of cobalt and chromium were assessed of 100 patients. Of these patients 77 had undergone hip arthroplasty with BHR HRAs 8 with the Synergy – BHR modular hip replacement and 15 with Synergy – R3 THA. The average overall chromium level was 4.0 µg/l and the average cobalt level was 6.7 µg/l. Forty-six hips were revised during the follow-up time. Five of these revisions were performed for ARMD.

Table 8. Revision risks in study IV. N = number of patients

	3 years follow-up time				Total follow-up time			
	N	**HR**	**CI**	**p-value**	**N**	**HR**	**CI**	**p-value**
Synergy – BHR modular hip replacement	39	1.00			39	1.00		
BHR HRA	249	2.46	0.57 – 10.52	0.2	249	2.64	0.62 – 11.21	0.2
Synergy – R3 THA	41	4.02	0.85 – 19.03	0.08	41	4.46	0.94 – 21.18	0.06

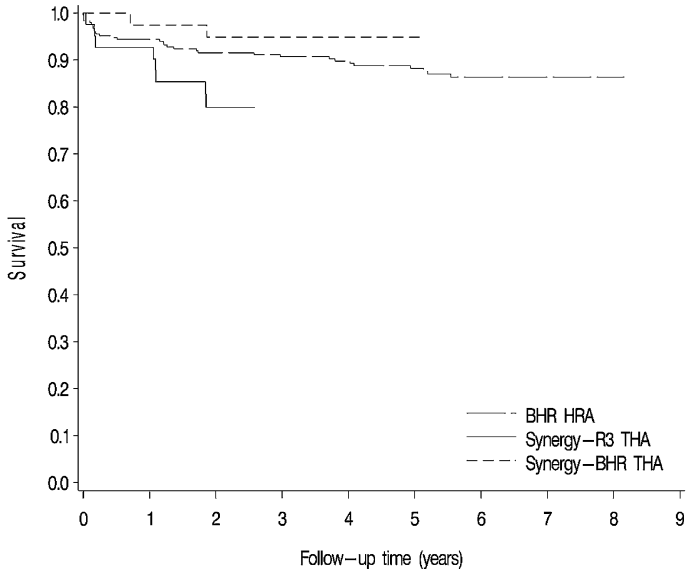

Figure 4a. Kaplan-Meier survival curves for revision risk covering the entire follow-up time (log-rank test, p=0.036). Study IV.

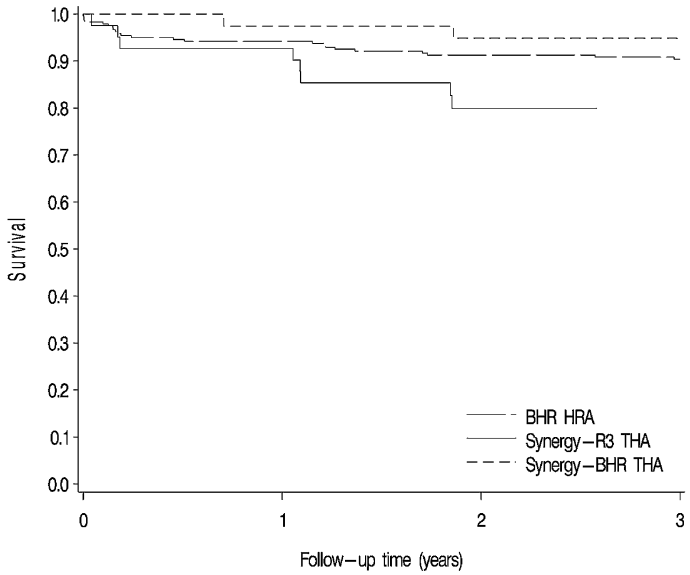

Figure 4b. Kaplan-Meier survival curves for revision risk at three years of follow-up (log-rank test, p=0.048). Study IV.

5.5 Study V

Eighteen of 63 study-hips underwent acetabular re-revision after acetabular impaction bone grafting. The overall survival rate was 71% during the mean follow-up time of 7.4 years (Figure 5). The mean time to re-revision was 4.3 years after the index operation. The

most common reason for re-revision was aseptic loosening of the acetabular component (83% of all re-revisions). Cox's regression model did not reveal any risk factors for re-revision. The results of the logistic regression analysis are presented in Table 9.

Table 9. Logistic regression analysis of the influence of certain variables on re-revision rate.

Variable	RR	CI	p-value
Age	1.02	0.96 - 1.07	0.6
Laterality	1.6	0.52 – 4.89	0.4
Bilateral	1.26	0.11 – 14.88	0.9
Cement fixation in primary arthroplasty	1.72	0.52 – 5.67	0.4
Stem revision	0.32	0.06 – 1.63	0.2
First-time revision versus several revisions	1.45	0.47 – 4.41	0.5
Femoral heads used	0.56	0.06 – 5.44	0.6
Mesh	3.88	0.45 – 33.6	0.2
Gender	0.71	0.23 – 2.21	0.6
Cup	0.60	0.16 – 2.20	0.4
Rheumatoid arthritis	0.20	0.024 – 1.69	0.1
Paprosky classification 1,2 vs. 3	1.58	0.50 – 5.00	0.4

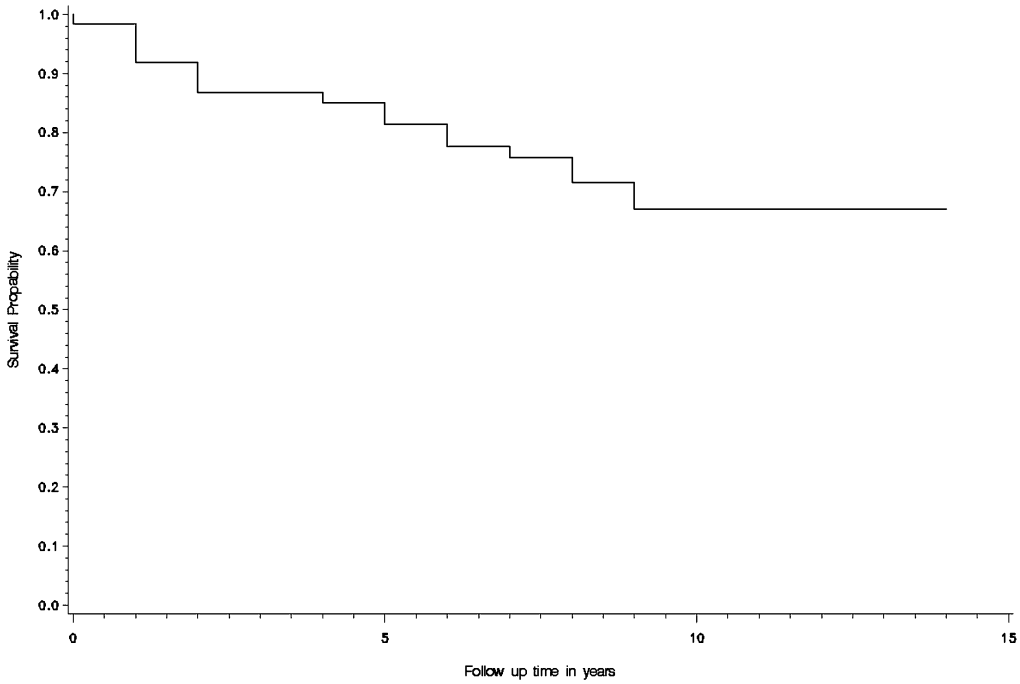

Figure 5. Kaplan-Meier survival chart for acetabular revision with impaction bone grafting. Study V.

6. DISCUSSION

Problems with wear debris, periprosthetic osteolysis and aseptic loosening in traditional MoP THAs created a need for new, more durable bearing materials. The survival of hip implants is limited, and especially young patients require durable implants with a long lifespan and easier revision procedures. MoM bearings allow a larger femoral head size compared to the traditional MoP bearings (Silva et al. 2005). A larger femoral head size allows better functional results and reduces the dislocation rate (Burroughs et al. 2005). Early results of the ReCap-Magnum MoM device were promising in our study, while the early results of the other MoM devices varied. However, the knowledge and experience of using MoM bearings has increased exponentially during studies IV and V. The high frequency of ARMD associated with the ReCap-Magnum (and other MoM study devices) has become common knowledge (Hart et al. 2011; Melvin et al. 2013), and the ReCap-Magnum device was recalled by the Biomet company in 2014.

Dislocation is a serious complication after THA and HRA. A larger femoral head size decreases the dislocation risk (Bartz et al. 2000; Byström et al. 2003). Earlier studies on the dislocation risk in THA have included only a limited number of LDH MoM THAs or HRAs. In study II, a head size 28 mm was associated with a 10-fold risk for revision due to dislocation compared a head size ≥ 37 mm. The 28 mm head size group had significantly longer follow-up time compared the larger head size groups, but this needs to be balanced against the fact that most of the dislocations occurred during the first post-operative year, which accords with earlier studies (Jameson et al. 2011). To ensure freedom from any bias related to different follow-up durations, we performed survival analyses differently for early and late revisions, and the results were similar. After adjusting for head size and other confounding factors in the Cox model, the dislocation revision rate was higher in 2006 – 2010 compared to 1996 – 2000. This might be related to patient selection favoring more sick patients. New implants allow reoperations for dislocation inoperable previously and use of approximately larger head sizes might result in less accurate component positioning. Recurrent dislocations are no longer tolerated, and these hips might be revised more often than earlier. There were practically no dislocations in the head size group ≥ 37mm. Head sizes 32 mm and 36 mm are large enough to decrease the dislocation rate compared to the 28 mm group, but might not cause trunnionosis to as high an extent as larger head sizes. In new, highly crosslinked polyethylenes, the wear rate seems to be similar for sizes 28 mm and 36 mm (Bragdon et al. 2007). Wear rates tend to increase when the head size exceeds 36 mm (Lachiewicz et al. 2009; Bragdon et al. 2012). The posterior approach predisposes to dislocation (Krenzel et al. 2010). Unfortunately, data concerning surgical approach is not available in Finnish Arthroplasty Register. In addition, the register data endpoint is always revision, and data on the patient's quality of life is not available.

Follow-ups to trace MoM hip replacement related complications have been arranged in all units that have implanted MoM prostheses. These systematic follow-ups usually consist of symptom questionnaires, metal ion measurements and MARS MRI for selected patients. There is a wide range of symptoms, laboratory results and radiographic findings associated with metal bearing related complications (Bisschop et al. 2013). Patients may experience pain, swelling, clicking, sensation of subluxation and other symptoms, or have a silent, symptomless ARMD (Mokka et al. 2013). High blood chromium and cobalt levels may predict ARMD. Sidaginamale et al. reported that when serum cobalt levels are >4.5µg/L, this is associated with a sensitivity of 94% and a specificity of 95% with abnormal metal wear rates (Sidaginamale et al. 2013). However, no direct correlation between wear rates and ARMD has been reported (Langton et al. 2011). This poses challenges to follow-up. In our study there was no correlation between blood metal ion levels and ARMD prevalence. The amount of patients was relatively small and ARMD may not yet have emerged during the follow-up time. The overall metal ion level was above the reference values, but the patients whose hips were revised for ARMD had similar metal ion levels as the other patients in the study. The metal ion concentrations of only 100 patients were determined and this may have reduced the possibilities to achieve a statistically and clinically meaningful correlation between metal ion levels and metal bearing related complications.

MARS MRI can be used to detect silent ARMD and to determine the severity of the reaction. It has high sensitivity and specificity in predicting ALVAL (Nawabi et al. 2014). Thomas et al. reported of no correlation between ARMD MRI findings and clinical symptom scores (Thomas et al. 2013).

We were not able to perform MRI in studies I and IV, and there are probably silent MoM hip replacement related complications that went undetected. A later study including partly the same patients as in study I showed a significant amount of silent ARMD (Mokka et al. 2013).

A larger femoral head size seems to be associated with an increased revision risk as a consequence of increased taper corrosion (Dyrkacz et al. 2013). According to this assumption, LDH MoM may produce more metal wear than HRA due to trunnionosis, i.e., corrosion in the junction between the femoral head and the adapter sleeve (Lavigne et al. 2011). In study III, of the three HRA–THA pairs compared, only ASR THA yielded increased revision rates compared to ASR HRA. It has recently become evident that the revision risk of ASR THA is increased compared to that of ASR HRA (Reito et al. 2013). In study IV three different MoM implants from the same manufacturer were compared, and the Synergy – BHR modular hip replacement device was associated with a better outcome than BHR HRA. In the same study, BHR HRA had significantly higher survival rate compared to Synergy – R3 THA. These findings imply that implant survival of HRA is not better than of THA.

Birmingham HRA has had very good midterm survival results (Reito et al. 2011; Treacy et al. 2011; Pailhe et al. 2013). In studies III and IV, BHR HRA had a fair survival rate, but our BHR HRA survival was inferior to the results of studies from development centers and other specialized clinics (Reito et al. 2013; Treacy et al. 2011). The Synergy – R3 implant with MoM bearing surfaces had a very poor outcome already short-term (study IV). A metal liner for R3 acetabular components is no longer in use.

The effect of acetabular inclination and abduction angles on MoM bearing related complications has been discussed (de Haan et al. 2008; Glyn-Jones et al. 2009; Reito et al. 2011; MacNair et al. 2013; Mokka et al. 2013). The optimal abduction angle is between 31° and 50°, and an abduction angle of more than 60° predisposes to ARMD (Langton et al. 2009; Reito et al. 2011). In study IV, five patients underwent revision due to ARMD and all of them had an optimal abduction angle. In the same study, seven patients had an abduction angle of over 60°, but none developed ARMD or had exceptionally high metal ion levels.

The periprosthetic fracture rate has been reported to be similar in THA and HRA (Cook et al. 2008; Steffen et al. 2009; Matharu et al. 2013). Matharu et al. (2013) reported a femoral neck fracture rate after HRA of 1.1% and Steffen et al. (2009) of 1.8%, which are comparable figures to the ones in studies I and IV. Cementing seems to protect from periprosthetic fractures in THA (J Singh et al. 2013). It strengthens the femoral bone cavity from the inside and reduces the risk for periprosthetic fracture. In study III, elderly women with ReCap HRA had a higher revision rate for periprosthetic fracture than ReCap THA. This is probably explained by the high femoral neck fracture rate in this patient group.

The results of revisions conducted for metal bearing related complications (at least regarding pseudotumors) may be worse than after revisions for other reasons (Grammatopolous et al. 2009). There is still a very limited amount of studies on the results of revisions indicated by ARMD, and future research is needed.

Revisions involving large acetabular bone defects are a challenging problem. In study V, we evaluated the Turku University Hospital's results of acetabular revisions with impaction bone grafting and a cemented cup. The overall survival rate was 71% after a mean follow-up time of 7.4 years, which is lower than in earlier studies from development centers (Schreurs et al. 2001; Schreurs et al. 2004). Van Haaren et al. published results that are similar to ours (2007), but in their study the bone chips were not washed, which might have resulted in inferior mechanical stability (Arts et al. 2006). In our study, the grafts were washed three times, twice with water and once with an antimicrobial wash to prevent infection. Our inferior results could be explained by more severe acetabular bone defects, as indicated by the Paprosky classification. In addition, our bone chip diameter was 0.3 – 1.0 cm, which may be slightly too small for optimal bone incorporation (Tägil 2000). Although our results were inferior to most of the earlier studies and although acetabular impaction bone grafting may not always provide

a reliable bone stock, bone grafting has played an important role in acetabular revision surgery before the introduction of trabecular metal cups and other new revision systems.

Our study has some limitations. Studies II and III were register studies using the data of the Finnish Arthroplasty Register. This method does not allow comparisons of the functional results between different study groups. Tracing MoM hip replacement related complications from register data is unreliable. Since MoM complications are a relatively new clinical entity, there is no specific question in the Finnish Arthroplasty Register data collection form concerning revision due to ARMD. Revisions for metal bearing related complication are recorded for example as revisions due to other reasons. The register does not contain information concerning metal ion levels, the surgical approach or radiological examinations to detect silent osteolysis or acetabular abduction and inclination angles. At the moment the ability of the Finnish Arthroplasty Register to detect poor performing implants quickly is poor. Dates of death should be updated to the Finnish Register sooner, to allow a rapid yearly analysis of implant survival of arthroplasty devices. Yearly register reports should be produced and published actively by orthopedic clinicians – preferably on the internet. The Finnish data should be promptly combined with international databases to detect inferior implants as early as possible.

In studies I, IV and V, data was collected retrospectively. In both register and retrospective studies the reliability of the results depends on the accuracy of the input data. We were not able to measure metal ion levels nor to evaluate radiographs of all patients in study IV. In study V, we were not able to measure graft incorporation from post-operative radiographs. In both studies IV and V, revision only served as an end-point. Some of the patients might have aseptic loosening, but due to patient related circumstances revision may not have been performed. In studies I and IV the follow-up time was too short to detect later onset ARMD.

Complications after THA are relatively common in Finland. New implants need to be carefully tested before they are released to the market at large. Although early implant survival of a new device may be good, this will not overrule the possibility of rapidly accumulating complications later on. A revision of the activity of the Finnish Arthroplasty Register is required aimed at detecting inferior implants as early as possible.

7. CONCLUSIONS

Our study leads to the following conclusions:

I. Early short-term results of the Magnum – M2A metal-on-metal THA were good. We did not encounter any metal bearing related complications or dislocations. The functional results improved according to pre- and postoperative Harris Hip Score.

II. A larger femoral head size reduces the need for revisions due to dislocations in THAs and HRAs and, vice versa, a decreased use of larger femoral head sizes for wear issues may increase the amount dislocation revisions in the future. Although attractive from a mechanical point of view, recent unfavorable clinical outcome data of these large headed metal-on-metal prosthesis, generates caution in using these implants.

III. There was no difference in the need for revision between BHR HRAs and THAs or between ReCap HRAs and THAs in the short-term or midterm at a nationwide level. The ReCap LDH MoM adapter sleeve is made of titanium, not of chromium cobalt like in two other models, and this may affect the development of ARMD. The revision risk of the ASR THAs was significantly higher than of the ASR HRAs. The true prevalence of ARMD among patients with metal-on-metal hip implants is not known, and these results need to be updated annually to elucidate if there will be differences between the HRAs and THAs, and between the designs from different manufacturers.

IV. The Synergy – R3 had a poor survival already at short-term. The BHR HRA survival rate was inferior when compared to previous midterm studies. Metal bearing related complications are a serious concern. Our findings support the decision to abandon metal-on-metal devices.

V. Overall implant survival was inferior compared to earlier studies from the development centers. There were no statistically significant risk factors for re-revision of impaction bone grafting with a cemented cup. Impaction bone grafting of acetabular defects in revision total hip arthroplasty may not always provide a reliable bone stock.

8. ACKNOWLEDGEMENTS

This study was carried out in Department of Orthopedics and Traumatology of Turku University Hospital during years 2010 – 2014. This study was financially supported by Research grant of Turku University Hospital (EVO-project), Orion Farmos Research foundation, and Turku University Foundation.

I owe my deepest gratitude to my supervisor Adjuct Professor Keijo Mäkelä. He has been supportive and always found the time to guide me despite of his own busy schedule. He has been the best mentor a beginning orthopedic researcher could imagine. He has created an optimal atmosphere to conduct research and he has been a great role model with a fantastic scientific vision. It has been a privilege to work with him.

I would also like to express my deepest gratitude to my other supervisor Adjunct Professor Petri Virolainen, chief of the Department of Orthopaedics and Traumatology of Turku University Hospital. This thesis would not been possible without his great leadership and scientific wisdom. His attitude during this project has been optimistic and encouraging during all the phases of this thesis.

I am greatly thankful to the reviewers of this thesis, Adjunct Professor Jukka Kettunen and Adjunct Professor Juhana Leppilahti. Their criticism has been constructive and precise. I feel privileged for been able to get feedback from these experienced and open-minded surgeons.

The co-authors of original studies, Matti Seppänen, Mika Junnila, Jari Mokka, Ville Remes, Antti Eskelinen and Ari Itälä, are acknowledged for their contribution to studies and for their encouraging attitude towards this whole project. Especially, Mika Junnila and Matti Seppänen have been supportive and have generously shared their wisdom in science and in general. Joni Hirviniemi and BCB-Medical team have played an important role in gathering the data and I want to thank all of them for their contribution.

My gratitude also goes to Tero Vahlberg, Mari Koivisto, Markus Matilainen and Pekka Pulkkinen for statistical analysis in this thesis. Adjunct Professor Robert Paul is greeted for his linguistic advice.

I want to express my gratitude to all my colleagues in Kainuu Central Hospital for making such a good work atmosphere. My warmest gratitude goes to head of Surgery Kalle Rissanen, who has enabled me to take time off from work to research when needed.

My most sincere gratitude goes to friends and family. You have shown sincere interest to my project, but also reminded me there is more in life than work and research. I want to thank my parents, Sari and Pekka, for your love and support through my life. My siblings, Milla and Joel, thank you for keeping my feet on ground and for your

friendship. I also want to thank my parents-in-law Eila and Tom, for making me feel like part of the family and always providing a place to stay when needed.

My most sincere gratitude goes to my fiancée, Mikael Laaksonen, who has encouraged me with his never ending optimism during all these years. Thank you for being there for me, without you this thesis would never been possible.

Kajaani, August 2014

Inari Kostensalo

9. REFERENCES

AATB Standards for Tissue Banking. 2014. Accessed March 5. http://www.aatb.org/AATB-Standards-for-Tissue-Banking.

Amstutz HC, Harlan C, and Le Duff M. 2012. Hip Resurfacing: A 40-Year Perspective. HSS J. Oct;8(3):275–82.

Arts JJ, Verdonschot N, Buma P, and Schreurs BW. Larger Bone Graft Size and Washing of Bone Grafts prior to Impaction Enhances the Initial Stability of Cemented Cups: Experiments Using a Synthetic Acetabular Model. Acta Orthop. 2006 Apr;77(2):227-33.

Azuma T, Yasuda H, Okagaki K, and Sakai K. 1994. Compressed Allograft Chips for Acetabular Reconstruction in Revision Hip Arthroplasty. J Bone Joint Surg Br. 1994 Sep;76(5):740-4.

Bagarić I, Sarac H, Borovac JA, Vlak T, Bekavac J, and Hebrang A. Primary Total Hip Arthroplasty: Health Related Quality of Life Outcomes. Int Orthop. 2014 Mar;38(3):495-501.

Baker RP, Pollard TC, Eastaugh-Waring SJ, and Bannister GC. A Medium-Term Comparison of Hybrid Hip Replacement and Birmingham Hip Resurfacing in Active Young Patients. J Bone Joint Surg Br. 2011 Feb;93(2):158-63

Ball ST, Severns D, Linn M, Meyer RS, and Swenson FC. What Happens to Serum Metal Ion Levels after a Metal-on-Metal Bearing Is Removed? J Arthroplasty. 2013 Sep;28(8 Suppl):53-5.

Bartz RL, Nobel PC, Kadakia NR, and Tullos HS. The Effect of Femoral Component Head Size on Posterior Dislocation of the Artificial Hip Joint. J Bone Joint Surg Am. 2000 Sep;82(9):1300-7.

Beaulé PE, Kim PR, Powell J, Mackenzie J, Werle J, Antoniou J, Huk O, Vendittoli PA, Lavigne M, Smith F, Naudie D, McCalden R, Bourne R, Schemitsch E, Garbuz D, Greidanus N, Duncan C, Belzile E. A Survey on the Prevalence of Pseudotumours with Metal on Metal Hip Resurfacings in Canadian Academic Centers. J Bone Joint Surg Am. 2011 May;93 Suppl 2:118-21.

Berry DJ. 1999. Epidemiology: Hip and Knee. Orthop Clin North Am. 1999 Apr;30(2):183-90.

Bisschop R, Boomsma MF, Van Raay JJ, Tiebosch AT, Maas M, Gerritsma CL. High Prevalence of Pseudotumors in Patients with a Birmingham Hip Resurfacing Prosthesis. J Bone Joint Surg Am. 2013 Sep 4;95(17):1554-60.

Blom AW, Taylor AH, Pattison G, Whitehouse S, Bannister GC. Infection after Total Hip Arthroplasty. The Avon Experience. J Bone Joint Surg Br. 2003 Sep;85(7):956-9.

Bosker BH, Ettema HB, Boomsma MF, Kollen BJ, Maas M, Verheyen CC High Incidence of Pseudotumour Formation after Large-Diameter Metal-on-Metal Total Hip Replacement: A Prospective Cohort Study. J Bone Joint Surg Br. 2012 Jun;94(6):755-61.

Bragdon CR, Doerner M, Martell J, Jarrett B, Palm H; Multicenter Study Group, Malchau H. The 2012 John Charnley Award: Clinical Multicenter Studies of the Wear Performance of Highly Crosslinked Remelted Polyethylene in THA. Clin Orthop Relat Res. 2013 Feb;471(2):393-402.

Bragdon CR, Greene ME, Freiberg AA, Harris WH, Malchau H. Radiostereometric Analysis Comparison of Wear of Highly Cross-Linked Polyethylene Against 36- vs 28-Mm Femoral Heads. J Arthroplasty. 2007 Sep;22(6 Suppl 2):125-9.

Brewster DH, Stockton DL, Reekie A, Ashcroft GP, Howie CR, Porter DE, Black RJ. Risk of Cancer Following Primary Total Hip Replacement or Primary Resurfacing Arthroplasty of the Hip: A Retrospective Cohort Study in Scotland. Br J Cancer. 2013 May 14;108(9):1883-90.

Burroughs BR, Hallstrom B, Golladay GJ, Hoeffel D, Harris WH. Range of Motion and Stability in Total Hip Arthroplasty with 28-, 32-, 38-, and 44-Mm Femoral Head Sizes: An in Vitro Study. J Arthroplasty. 2005 Jan;20(1):11-9.

Buttaro MA, Costantini J, Comba F, Piccaluga F. The Use of Femoral Struts and Impacted Cancellous Bone Allograft in Patients with Severe Femoral Bone Loss Who Undergo Revision Total Hip Replacement: A Three- to Nine-Year Follow-Up. J Bone Joint Surg Br. 2012 Feb;94(2):167-72.

Byström S, Espehaug B, Furnes O, Havelin LI; Norwegian Arthroplasty Register. Femoral Head Size Is a Risk Factor for Total Hip Luxation: A Study of 42,987 Primary Hip Arthroplasties from the Norwegian Arthroplasty Register. Acta Orthop Scand. 2003 Oct;74(5):514-24.

Callanan MC, Jarrett B, Bragdon CR, Zurakowski D, Rubash HE, Freiberg AA, Malchau H. The John Charnley Award: Risk Factors for Cup Malpositioning: Quality Improvement through a Joint Registry at a Tertiary Hospital. Clin Orthop Relat Res. 2011 Feb;469(2):319-29.

Callary SA, Field JR, Campbell DG. Low Wear of a Second-Generation Highly Crosslinked Polyethylene Liner: A 5-Year Radiostereometric Analysis Study. Clin Orthop Relat Res. 2013 Nov;471(11):3596-600.

Campbell P, Ebramzadeh E, Nelson S, Takamura K, De Smet K, Amstutz HC. Histological Features of Pseudotumor-like Tissues from Metal-on-Metal Hips. Clin Orthop Relat Res. 2010 Sep;468(9):2321-7.

Carrothers AD, Gilbert RE, Jaiswal A, Richardson JB. Birmingham Hip Resurfacing: The Prevalence of Failure. J Bone Joint Surg Br. 2010 Oct;92(10):1344-50.

Chang EY, McAnally JL, Van Horne JR, Statum S, Wolfson T, Gamst A, Chung CB. Metal-on-Metal Total Hip Arthroplasty: Do Symptoms Correlate with MR Imaging Findings? Radiology. 2012 Dec;265(3):848-57.

Choy WS, Kim KJ, Lee SK, Bae KW, Hwang YS, Park CK. Ceramic-on-Ceramic Total Hip Arthroplasty: Minimum of Six-Year Follow-up Study. Clin Orthop Surg. 2013 Sep;5(3):174-9.

Clarke IC, Manley MT; Implant Wear Symposium 2007 Engineering Work Group. How Do Alternative Bearing Surfaces Influence Wear Behavior? J Am Acad Orthop Surg. 2008;16 Suppl 1:S86-93.

Comba F, Buttaro M, Pusso R, Piccaluga F. Acetabular Reconstruction with Impacted Bone Allografts and Cemented Acetabular Components: A 2- to 13-Year Follow-up Study of 142 Aseptic Revisions. J Bone Joint Surg Br. 2006 Jul;88(7):865-9.

Conroy JL, Whitehouse SL, Graves SE, Pratt NL, Ryan P, Crawford RW. Risk Factors for Revision for Early Dislocation in Total Hip Arthroplasty. J Arthroplasty. 2008 Sep;23(6):867-72.

Cook RE, Jenkins PJ, Walmsley PJ, Patton JT, Robinson CM. Risk Factors for Periprosthetic Fractures of the Hip: A Survivorship Analysis. Clin Orthop Relat Res. 2008 Jul;466(7):1652-6.

Corradi M, Daniel J, Ziaee H, Alinovi R, Mutti A, McMinn DJ. Early Markers of Nephrotoxicity in Patients with Metal-on-Metal Hip Arthroplasty. Clin Orthop Relat Res. 2011 Jun;469(6):1651-9.

Costa L, Luda MP, Trossarelli L, Brach del Prever EM, Crova M, Gallinaro P. Oxidation in Orthopaedic UHMWPE Sterilized by Gamma-Radiation and Ethylene Oxide. Biomaterials. 1998 Apr-May;19(7-9):659-68.

Dale H, Skråmm I, Løwer HL, Eriksen HM, Espehaug B, Furnes O, Skjeldestad FE, Havelin LI, Engesaeter LB. Infection after Primary Hip Arthroplasty: A Comparison of 3 Norwegian Health Registers. Acta Orthop. 2011 Dec;82(6):646-54.

Daley B, Doherty AT, Fairman B, Case CP. Wear Debris from Hip or Knee Replacements Causes Chromosomal Damage in Human Cells in Tissue Culture. J Bone Joint Surg Br. 2004 May;86(4):598-606.

Dandy DJ, Theodorou BC. The Management of Local Complications of Total Hip Replacement by the McKee-Farrar Technique. J Bone Joint Surg Br. 1975 Feb;57(1):30-5.

de Haan R, Pattyn C, Gill HS, Murray DW, Campbell PA, De Smet K. Correlation between Inclination of the Acetabular Component and Metal Ion Levels in Metal-on-Metal Hip Resurfacing Replacement. J Bone Joint Surg Br. 2008 Oct;90(10):1291-7.

de Kam DC, Gardeniers JW, Veth RP, Schreurs BW. Total Hip Arthroplasty in Patients under 40 Years of Age And, If Indicated, Reconstruction of Acetabular Defects with Bone Impaction Grafting. Ned Tijdschr Geneeskd. 2010;154:A811.

Delaunay C, Petit I, Learmonth ID, Oger P, Vendittoli PA. Metal-on-Metal Bearings Total Hip Arthroplasty: The Cobalt and Chromium Ions Release Concern. Orthop Traumatol Surg Res. 2010 Dec;96(8):894-904.

Dowson D, Hardaker C, Flett M, Isaac GH. A Hip Joint Simulator Study of the Performance of Metal-on-Metal joints*1Part II: Design. J Arthroplasty. 2004 Dec;19(8 Suppl 3):124-30.

Dudda M, Gueleryuez A, Gautier E, Busato A, Roeder C. Risk Factors for Early Dislocation after Total Hip Arthroplasty: A Matched Case-Control Study. J Orthop Surg (Hong Kong). 2010 Aug;18(2):179-83.

Dyrkacz RM, Brandt JM, Ojo OA, Turgeon TR, Wyss UP. The Influence of Head Size on Corrosion and Fretting Behaviour at the Head-Neck Interface of Artificial Hip Joints. J Arthroplasty. 2013 Jun;28(6):1036-40.

Elkins JM, Callaghan JJ, Brown TD. Stability and Trunnion Wear Potential in Large-Diameter Metal-on-Metal Total Hips: A Finite Element Analysis. Clin Orthop Relat Res. 2014 Feb;472(2):529-42.

Emmanuel AR, Bergin KM, Kelly GE, McCoy GF, Wozniak AP, Quinlan JF. The Effect of Acetabular Inclination on Metal Ion Levels Following Metal-on-Metal Hip Arthroplasty. J Arthroplasty. 2014 Jan;29(1):186-91.

Enocson A, Hedbeck CJ, Tidermark J, Pettersson H, Ponzer S, Lapidus LJ. Dislocation of Total Hip Replacement in Patients with Fractures of the Femoral Neck. Acta Orthop. 2009 Apr;80(2):184-9.

Fang CS, Harvie P, Gibbons CL, Whitwell D, Athanasou NA, Ostlere S. The Imaging Spectrum of Peri-Articular Inflammatory Masses Following Metal-on-Metal Hip Resurfacing. Skeletal Radiol. 2008 Aug;37(8):715-22.

Fitzgerald RH Jr. Infected Total Hip Arthroplasty: Diagnosis and Treatment. J Am Acad Orthop Surg. 1995 Oct;3(5):249-262.

Fricka KB, Ho H, Peace WJ, Engh CA Jr. Metal-on-Metal Local Tissue Reaction Is Associated with Corrosion of the Head Taper Junction. J Arthroplasty. 2012 Sep;27(8 Suppl):26-31.

Furnes O, Lie SA, Espehaug B, Vollset SE, Engesaeter LB, Havelin LI. Hip Disease and the Prognosis of Total Hip Replacements. A Review of 53,698 Primary Total Hip Replacements Reported to the Norwegian Arthroplasty Register 1987-99. J Bone Joint Surg Br. 2001 May;83(4):579-86.

Gilbert CJ, Cheung A, Butany J, Zywiel MG, Syed K, McDonald M, Wong F, Overgaard C. Hip Pain and Heart Failure: The Missing Link. Can J Cardiol. 2013 May;29(5):639.

Glyn-Jones S, Pandit H, Kwon YM, Doll H, Gill HS, Murray DW. Risk Factors for Inflammatory Pseudotumour Formation Following Hip Resurfacing. J Bone Joint Surg Br. 2009 Dec;91(12):1566-74.

Gómez-Barrena E, Medel F, Puértolas JA. Polyethylene Oxidation in Total Hip Arthroplasty: Evolution and New Advances. Open Orthop J. 2009 Dec 24;3:115-20.

Grammatopolous G, Pandit H, Kwon YM, Gundle R, McLardy-Smith P, Beard DJ, Murray DW, Gill HS. Hip Resurfacings Revised for Inflammatory Pseudotumour Have a Poor Outcome. J Bone Joint Surg Br. 2009 Aug;91(8):1019-24.

Hailer NP, Garellick G, Kärrholm J. Uncemented and Cemented Primary Total Hip Arthroplasty in the Swedish Hip Arthroplasty Register. Acta Orthop. 2010 Feb;81(1):34-41.

Halliday BR, English HW, Timperley AJ, Gie GA, Ling RS. Femoral Impaction Grafting with Cement in Revision Total Hip Replacement. Evolution of the Technique and Results. J Bone Joint Surg Br. 2003 Aug;85(6):809-17.

Hart AJ, Ilo K, Underwood R, Cann P, Henckel J, Lewis A, Cobb J, Skinner J. The Relationship between the Angle of Version and Rate of Wear of Retrieved Metal-on-Metal Resurfacings: A Prospective, CT-Based Study. J Bone Joint Surg Br. 2011 Mar;93(3):315-20.

Hart AJ, Sabah SA, Bandi AS, Maggiore P, Tarassoli P, Sampson B, A Skinner J. Sensitivity and Specificity of Blood Cobalt and Chromium Metal Ions for Predicting Failure of Metal-on-Metal Hip Replacement. J Bone Joint Surg Br. 2011 Oct;93(10):1308-13.

Hart AJ, Sabah S, Henckel J, Lewis A, Cobb J, Sampson B, Mitchell A, Skinner JA. The Painful Metal-on-Metal Hip Resurfacing. J Bone Joint Surg Br. 2009 Jun;91(6):738-44.

Hartman CW, Garvin KL. Dislocation of the Hip after Reimplantation for Infection: An Analysis of Risk Factors. Clin Orthop Relat Res. 2006 Jun;447:24-7.

Hartmann A, Hannemann F, Lützner J, Seidler A, Drexler H, Günther KP, Schmitt J. Metal Ion Concentrations in Body Fluids after Implantation of Hip Replacements with Metal-on-Metal Bearing--Systematic Review of Clinical and Epidemiological Studies. PLoS One. 2013 Aug 7;8(8):e70359.

Hirn MY, Salmela PM, Vuento RE. High-Pressure Saline Washing of Allografts Reduces Bacterial Contamination. Acta Orthop Scand. 2001 Feb;72(1):83-5.

Iannotti JP, Balderston RA, Booth RE, Rothman RH, Cohn JC, Pickens G. Aseptic Loosening after Total Hip Arthroplasty. Incidence, Clinical Significance, and Etiology. J Arthroplasty. 1986;1(2):99-107.

James ET, Hunter GA, Cameron HU. Total Hip Revision Arthroplasty: Does Sepsis Influence the Results? Clin Orthop Relat Res. 1982 Oct;(170):88-94.

Jameson SS, Lees D, James P, Serrano-Pedraza I, Partington PF, Muller SD, Meek RM, Reed MR. Lower Rates of Dislocation with Increased Femoral Head Size after Primary Total Hip Replacement: A Five-Year Analysis of NHS Patients in England. J Bone Joint Surg Br. 2011 Jul;93(7):876-80.

Jarrett CA, Ranawat AS, Bruzzone M, Blum YC, Rodriguez JA, Ranawat CS. The Squeaking Hip: A Phenomenon of Ceramic-on-Ceramic Total Hip Arthroplasty. J Bone Joint Surg Am. 2009 Jun;91(6):1344-9.

Johanson PE, Fenstad AM, Furnes O, Garellick G, Havelin LI, Overgaard S, Pedersen AB, Kärrholm J. Inferior Outcome after Hip Resurfacing Arthroplasty than after Conventional Arthroplasty. Evidence from the Nordic Arthroplasty Register Association (NARA) Database, 1995 to 2007. Acta Orthop. 2010 Oct;81(5):535-41.

Johansson T, Jacobsson SA, Ivarsson I, Knutsson A, Wahlström O. Internal Fixation versus Total Hip Arthroplasty in the Treatment of Displaced Femoral Neck Fractures: A Prospective Randomized Study of 100 Hips. Acta Orthop Scand. 2000 Dec;71(6):597-602.

Karam JA, Tokarski AT, Ciccotti M, Austin MS, Deirmengian GK. Revision Total Hip Arthroplasty in Younger Patients: Indications, Reasons for Failure, and Survivorship. Phys Sportsmed. 2012 Nov;40(4):96-101.

Khatod M, Barber T, Paxton E, Namba R, Fithian D. An Analysis of the Risk of Hip Dislocation with a Contemporary Total Joint Registry. Clin Orthop Relat Res. 2006 Jun;447:19-23.

Krenzel BA, Berend ME, Malinzak RA, Faris PM, Keating EM, Meding JB, Ritter MA. High Preoperative Range of Motion Is a Significant Risk Factor for Dislocation in Primary Total Hip Arthroplasty. J Arthroplasty. 2010 Sep;25(6 Suppl):31-5.

Kurtz SM, Gawel HA, Patel JD. History and Systematic Review of Wear and Osteolysis Outcomes for First-Generation Highly Crosslinked Polyethylene. Clin Orthop Relat Res. 2011 Aug;469(8):2262-77.

Kurtz S, Mowat F, Ong K, Chan N, Lau E, Halpern M. Prevalence of Primary and Revision Total Hip and Knee Arthroplasty in the United States from 1990 through 2002. J Bone Joint Surg Am. 2005 Jul;87(7):1487-97.

Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of Primary and Revision Hip and Knee Arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am. 2007 Apr;89(4):780-5.

Lachiewicz PF, Heckman DS, Soileau ES, Mangla J, Martell JM. Femoral Head Size and Wear of Highly Cross-Linked Polyethylene at 5 to 8 Years. Clin Orthop Relat Res. 2009 Dec;467(12):3290-6.

Langton, D J, S S Jameson, T J Joyce, N J Hallab, S Natu, and A V F Nargol. 2010. Early Failure of Metal-on-Metal Bearings in Hip Resurfacing and Large-Diameter Total Hip Replacement: A Consequence of Excess Wear. The Journal of Bone and Joint Surgery. British Volume 92: 38–46.

Langton DJ, Jameson SS, Joyce TJ, Webb JJ, Nargol AV. The Effect of Component Size and Orientation on the Concentrations of Metal Ions after Resurfacing Arthroplasty of the Hip. J Bone Joint Surg Br. 2008 Sep;90(9):1143-51.

Langton DJ, Joyce TJ, Jameson SS, Lord J, Van Orsouw M, Holland JP, Nargol AV, De Smet KA. Adverse Reaction to Metal Debris Following Hip Resurfacing: The Influence of Component Type, Orientation and Volumetric Wear. J Bone Joint Surg Br. 2011 Feb;93(2):164-71.

Langton DJ, Sidaginamale R, Lord JK, Nargol AV, Joyce TJ. Taper Junction Failure in Large-Diameter Metal-on-Metal Bearings. Bone Joint Res. 2012 Apr 1;1(4):56-63.

Langton DJ, Sprowson AP, Joyce TJ, Reed M, Carluke I, Partington P, Nargol AV. Blood Metal Ion Concentrations after Hip Resurfacing Arthroplasty: A Comparative Study of Articular Surface Replacement and Birmingham Hip Resurfacing Arthroplasties. J Bone Joint Surg Br. 2009 Oct;91(10):1287-95.

Larkin B, Nyazee H, Motley J, Nunley RM, Clohisy JC, Barrack RL. Hip Resurfacing Does Not Improve Proprioception Compared With THA. Clin Orthop Relat Res. 2014 Feb;472(2):555-61.

Lavernia CJ, Alcerro JC. Quality of Life and Cost-Effectiveness 1 Year after Total Hip Arthroplasty. J Arthroplasty. 2011 Aug;26(5):705-9.

Lavigne M, Belzile EL, Roy A, Morin F, Amzica T, Vendittoli PA. Comparison of Whole-Blood Metal Ion Levels in Four Types of Metal-on-Metal Large-Diameter Femoral Head Total Hip Arthroplasty: The Potential Influence of the Adapter Sleeve. J Bone Joint Surg Am. 2011 May;93 Suppl 2:128-36.

Leclercq S, Lavigne M, Girard J, Chiron P, Vendittoli PA. Durom Hip Resurfacing System: Retrospective Study of 644 Cases with an Average Follow-up of 34 Months. Orthop Traumatol Surg Res. 2013 May;99(3):273-9.

Liddle AD, Satchithananda K, Henckel J, Sabah SA, Vipulendran KV, Lewis A, Skinner JA, Mitchell AW, Hart AJ. Revision of Metal-on-Metal Hip Arthroplasty in a Tertiary Center: A Prospective Study of 39 Hips with between 1 and 4 Years of Follow-Up. Acta Orthop. 2013 Jun;84(3):237-45.

Lombardi AV Jr, Skeels MD, Berend KR, Adams JB, Franchi OJ. Do Large Heads Enhance Stability and Restore Native Anatomy in Primary Total Hip Arthroplasty? Clin Orthop Relat Res. 2011 Jun;469(6):1547-53.

Lusty PJ, Tai CC, Sew-Hoy RP, Walter WL, Walter WK, Zicat BA. Third-Generation Alumina-on-Alumina Ceramic Bearings in Cementless Total Hip Arthroplasty. J Bone Joint Surg Am. 2007 Dec;89(12):2676-83.

Machado C, Appelbe A, Wood R. Arthroprosthetic Cobaltism and Cardiomyopathy. Heart Lung Circ. 2012 Nov;21(11):759-60.

Macnair RD, Wynn-Jones H, Wimhurst JA, Toms A, Cahir J. Metal Ion Levels Not Sufficient as a Screening Measure for Adverse Reactions in Metal-on-Metal Hip Arthroplasties. J Arthroplasty. 2013 Jan;28(1):78-83.

Mahoney CR, Pellicci PM. Complications in Primary Total Hip Arthroplasty: Avoidance and Management of Dislocations. Instr Course Lect. 2003;52:247-55.

Mao X, Tay GH, Godbolt DB, Crawford RW. Pseudotumor in a Well-Fixed Metal-on-Polyethylene Uncemented Hip Arthroplasty. J Arthroplasty. 2012 Mar;27(3):493.e13-7.

Masri BA, Meek RM, Duncan CP. Periprosthetic Fractures Evaluation and Treatment. Clin Orthop Relat Res. 2004 Mar;(420):80-95.

Matharu GS, McBryde CW, Revell MP, Pynsent PB. Femoral Neck Fracture After Birmingham Hip Resurfacing Arthroplasty: Prevalence, Time to Fracture, and Outcome After Revision. J Arthroplasty. 2013 Jan;28(1):147-53.

Matthies AK, Skinner JA, Osmani H, Henckel J, Hart AJ. Pseudotumors Are Common in Well-Positioned Low-Wearing Metal-on-Metal Hips. Clin Orthop Relat Res. 2012 Jul;470(7):1895-906.

Mazoochian F, Weber P, Schramm S, Utzschneider S, Fottner A, Jansson V. Minimally Invasive Total Hip Arthroplasty: A Randomized Controlled Prospective Trial. Arch Orthop Trauma Surg. 2009 Dec;129(12):1633-9.

McMinn DJ, Daniel J, Ziaee H, Pradhan C. Indications and Results of Hip Resurfacing. Int Orthop. 2011 Feb;35(2):231-7.

Medical Device Alert (Draft) - con155767.pdf. 2014. Accessed March 6. http://www.mhra.gov.uk/home/groups/dts-bs/documents/medicaldevicealert/con155767.pdf.

Melvin JS, Karthikeyan T, Cope R, Fehring TK. Early Failures in Total Hip Arthroplasty – A Changing Paradigm. J Arthroplasty. 2013 Dec 21. [Epub ahead of print]

Mokka J, Junnila M, Seppänen M, Virolainen P, Pölönen T, Vahlberg T, Mattila K, Tuominen EK, Rantakokko J, Aärimaa V, Kukkonen J, Mäkelä KT. Adverse Reaction to Metal Debris after ReCap-M2A-Magnum Large-Diameter-Head Metal-on-Metal Total Hip Arthroplasty. Acta Orthop. 2013 Dec;84(6):549-54.

Moroni A, Savarino L, Hoque M, Cadossi M, Baldini N. Do Ion Levels in Hip Resurfacing Differ from Metal-on-Metal THA at Midterm? Clin Orthop Relat Res. 2011 Jan;469(1):180-7.

Mäkelä KT, Matilainen M, Pulkkinen P, Fenstad AM, Havelin L, Engesaeter L, Furnes O, Pedersen AB, Overgaard S, Kärrholm J, Malchau H, Garellick G, Ranstam J, Eskelinen A. Failure Rate of Cemented and Uncemented Total Hip Replacements: Register Study of Combined Nordic Database of Four Nations. BMJ. 2014 Jan 13;348:f7592.

Mäkelä KT, Visuri T, Pulkkinen P, Eskelinen A, Remes V, Virolainen P, Junnila M, Pukkala E. Risk of Cancer with Metal-on-Metal Hip Replacements: Population Based Study. BMJ. 2012 Jul 25;345:e4646.

Mäkelä KT, Visuri T, Pulkkinen P, Eskelinen A, Remes V, Virolainen P, Junnila M, Pukkala E. Cancer Incidence and Cause-Specific Mortality in Patients with Metal-on-Metal Hip Replacements in Finland. Acta Orthop. 2014 Feb;85(1):32-8.

Naal FD, Pilz R, Munzinger U, Hersche O, Leunig M. High Revision Rate at 5 Years after Hip Resurfacing with the Durom Implant. Clin Orthop Relat Res. 2011 Sep;469(9):2598-604.

Natu S, Sidaginamale RP, Gandhi J, Langton DJ, Nargol AV. Adverse Reactions to Metal Debris: Histopathological Features of Periprosthetic Soft Tissue Reactions Seen in Association with Failed Metal on Metal Hip Arthroplasties. J Clin Pathol. 2012 May;65(5):409-18.

Nawabi DH, Gold S, Lyman S, Fields K, Padgett DE, Potter HG. MRI Predicts ALVAL and Tissue Damage in Metal-on-Metal Hip Arthroplasty. Clin Orthop Relat Res. 2014 Feb;472(2):471-81.

Nishii T, Sugano N, Miki H, Koyama T, Takao M, Yoshikawa H. Influence of Component Positions on Dislocation: Computed Tomographic Evaluations in a Consecutive Series of Total Hip Arthroplasty. J Arthroplasty. 2004 Feb;19(2):162-6

NJR 7th Annual Report 2010.pdf. 2014. Accessed March 2. http://www.njrcentre.org.uk/NjrCentre/Portals/0/NJR 7th Annual Report 2010.pdf.

Ollivere B, Darrah C, Barker T, Nolan J, Porteous MJ. Early Clinical Failure of the Birmingham Metal-on-Metal Hip Resurfacing Is Associated with Metallosis and Soft-Tissue Necrosis. J Bone Joint Surg Br. 2009 Aug;91(8):1025-30.

Ornstein E, Linder L, Ranstam J, Lewold S, Eisler T, Torper M. Femoral Impaction Bone Grafting with the Exeter Stem - the Swedish Experience: Survivorship Analysis of 1305 Revisions Performed between 1989 and 2002. J Bone Joint Surg Br. 2009 Apr;91(4):441-6.

Paavolainen P, Hämäläinen M, Mustonen H, Slätis P. Registration of Arthroplasties in Finland. A Nationwide Prospective Project. Acta Orthop Scand Suppl. 1991;241:27-30.

Pailhe R, Matharu GS, Sharma A, Pynsent PB, Treacy RB. Survival and Functional Outcome of the Birmingham Hip Resurfacing System in Patients Aged 65 and Older at up to Ten Years of Follow-Up. Int Orthop. 2013 Dec 28. [Epub ahead of print]

Pandit H, Glyn-Jones S, McLardy-Smith P, Gundle R, Whitwell D, Gibbons CL, Ostlere S, Athanasou N, Gill HS, Murray DW. Pseudotumours Associated

with Metal-on-Metal Hip Resurfacings. J Bone Joint Surg Br. 2008 Jul;90(7):847-5.

Paprosky WG, Perona PG, Lawrence JM. Acetabular Defect Classification and Surgical Reconstruction in Revision Arthroplasty: A 6-Year Follow-up Evaluation. J Arthroplasty. 1994 Feb;9(1):33-44.

Park MS, Lee YK, Yang KH, Shin SJ. Management of Periprosthetic Femoral Fractures. J Arthroplasty. 2003 Oct;18(7):903-6.

Park SK, Kim YG, Kim SY. Treatment of Periprosthetic Femoral Fractures in Hip Arthroplasty. Clin Orthop Surg. 2011 Jun;3(2):101-6.

Parsons NL, Costa ML, Achten J, Edlin RP, Foguet P, Prakash U, Griffin DR; Young Adult Hip Arthroplasty Team. Total Hip Arthroplasty versus Resurfacing Arthroplasty in the Treatment of Patients with Arthritis of the Hip Joint : Single Centre , Parallel Group , Assessor Blinded , Randomised Controlled Trial. BMJ. 2012 Apr 19;344:e2147.

Pastides PS, Dodd M, Sarraf KM, Willis-Owen CA. Trunnionosis: A Pain in the Neck." World J Orthop. 2013 Oct 18;4(4):161-6.

Patel PD, Potts A, Froimson MI. The Dislocating Hip Arthroplasty. Prevention and Treatment. J Arthroplasty. 2007 Jun;22(4 Suppl 1):86-90.

Pekkarinen J, Alho A, Lepistö J, Ylikoski M, Ylinen P, Paavilainen T. Impaction Bone Grafting in Revision Hip Surgery. A High Incidence of Complications. J Bone Joint Surg Br. 2000 Jan;82(1):103-7.

Pivec R, Johnson AJ, Mears SC, Mont MA. Hip Arthroplasty. Lancet. 2012 Nov 17;380(9855):1768-77.

Reito A, Puolakka T, Elo P, Pajamäki J, Eskelinen A. High Prevalence of Adverse Reactions to Metal Debris in Small-Headed ASR™ Hips. Clin Orthop Relat Res. 2013 Sep;471(9):2954-61.

Reito A, Puolakka T, Pajamäki J. Birmingham Hip Resurfacing: Five to Eight Year Results. Int Orthop. 2011 Aug;35(8):1119-24.

Restrepo C, Parvizi J, Kurtz SM, Sharkey PF, Hozack WJ, Rothman RH. The Noisy Ceramic Hip: Is Component Malpositioning the Cause? J Arthroplasty. 2008 Aug;23(5):643-9.

Rizzetti MC, Liberini P, Zarattini G, Catalani S, Pazzaglia U, Apostoli P, Padovani A. Loss of Sight and Sound. Could It Be the Hip? Lancet. 2009 Mar 21;373(9668):1052.

Royal, Bethlem, and Maudsley Hospitals. 2000. King's College: 374–375.

Sah AP, Estok DM 2nd. Dislocation Rate after Conversion from Hip Hemiarthroplasty to Total Hip Arthroplasty. J Bone Joint Surg Am. 2008 Mar;90(3):506-16.

Sarvilinna R, Huhtala HS, Sovelius RT, Halonen PJ, Nevalainen JK, Pajamäki KJ. Factors Predisposing to Periprosthetic Fracture after Hip Arthroplasty: A Case (n = 31)-Control Study. Acta Orthop Scand. 2004 Feb;75(1):16-20.

Schreurs BW, Bolder SB, Gardeniers JW, Verdonschot N, Slooff TJ, Veth RP. Acetabular Revision with Impacted Morsellised Cancellous Bone Grafting and a Cemented Cup. A 15- to 20-Year Follow-Up. J Bone Joint Surg Br. 2004 May;86(4):492-7.

Schreurs BW, Slooff TJ, Gardeniers JW, Buma P. Acetabular Reconstruction with Bone Impaction Grafting and a Cemented Cup: 20 Years' Experience. Clin Orthop Relat Res. 2001 Dec;(393):202-15.

Sedel, L. Evolution of Alumina-on-Alumina Implants: A Review. Clin Orthop Relat Res. 2000 Oct;(379):48-54.

Sexton SA, Yeung E, Jackson MP, Rajaratnam S, Martell JM, Walter WL, Zicat BA, Walter WK. The Role of Patient Factors and Implant Position in Squeaking of Ceramic-on-Ceramic Total Hip Replacements. J Bone Joint Surg Br. 2011 Apr;93(4):439-42.

Shimmin AJ, Back D. Femoral Neck Fractures Following Birmingham Hip Resurfacing: A National Review of 50 Cases. J Bone Joint Surg Br. 2005 Apr;87(4):463-4.

Shimmin A, Beaulé PE, Campbell P. Metal-on-Metal Hip Resurfacing Arthroplasty. J Bone Joint Surg Am. 2008 Mar;90(3):637-54.

Sidaginamale RP, Joyce TJ, Lord JK, Jefferson R, Blain PG, Nargol AV, Langton DJ. Blood Metal Ion Testing Is an Effective Screening Tool to Identify Poorly Performing Metal-on-Metal Bearing Surfaces. Bone Joint Res. 2013 May 16;2(5):84-95.

Silva M, Heisel C, Schmalzried TP. Metal-on-Metal Total Hip Replacement. Clin Orthop Relat Res. 2005 Jan;(430):53-61.

Singh G, Meyer H, Ruetschi M, Chamaon K, Feuerstein B, Lohmann CH. Large-Diameter Metal-on-Metal Total Hip Arthroplasties: A Page in Orthopedic History? J Biomed Mater Res A. 2013 Nov;101(11):3320-6.

Singh JA, Jensen MR, Harmsen SW, Lewallen DG. Are Gender, Comorbidity, and Obesity Risk Factors for Postoperative Periprosthetic Fractures after Primary Total Hip Arthroplasty? J Arthroplasty. 2013 Jan;28(1):126-31.e1-2.

Slooff TJ, Buma P, Schreurs BW, Schimmel JW, Huiskes R, Gardeniers J. Acetabular and Femoral Reconstruction with Impacted Graft and Cement. Clin Orthop Relat Res. 1996 Mar;(324):108-15.

Slooff TJ, Schimmel JW, Buma P. Cemented Fixation with Bone Grafts. Orthop Clin North Am. 1993 Oct;24(4):667-77.

Smith TO, Blake V, Hing CB. Minimally Invasive versus Conventional Exposure for Total Hip Arthroplasty: A Systematic Review and Meta-Analysis of Clinical and Radiological Outcomes. Int Orthop. 2011 Feb;35(2):173-84.

Snir N, Kaye ID, Klifto CS, Hamula MJ, Wolfson TS, Schwarzkopf R, Jaffe FF. 10-Year Follow-Up Wear Analysis of First-Generation Highly Crosslinked Polyethylene in Primary Total Hip Arthroplasty. J Arthroplasty. 2014 Mar;29(3):630-3.

Steffen RT, Pandit HP, Palan J, Beard DJ, Gundle R, McLardy-Smith P, Murray DW, Gill HS. The Five-Year Results of the Birmingham Hip Resurfacing Arthroplasty: An Independent Series. J Bone Joint Surg Br. 2008 Apr;90(4):436-41.

Steffen RT, Foguet PR, Krikler SJ, Gundle R, Beard DJ, Murray DW. Femoral Neck Fractures after Hip Resurfacing. J Arthroplasty. 2009 Jun;24(4):614-9.

Suomen Artroplastiayhdistys - Extranet. 2014. Accessed March 2. http://www.suomenartroplastiayhdistys.fi/index.php?page=1074&lang=1.

Tan TL, Ebramzadeh E, Campbell PA, Al-Hamad M, Amstutz HC. Long-Term Outcome of a Metal-on-Polyethylene Cementless Hip Resurfacing. J Arthroplasty. 2014 Apr;29(4):802-7.

Thomas MS, Wimhurst JA, Nolan JF, Toms AP. Imaging Metal-on-Metal Hip Replacements: The Norwich Experience. HSS J. 2013 Oct;9(3):247-256.

Thomsen MN, Jakubowitz E, Seeger JB, Lee C, Kretzer JP, Clarius M. Fracture Load for Periprosthetic Femoral Fractures in Cemented versus Uncemented Hip Stems: An Experimental in Vitro Study. Orthopedics. 2008 Jul;31(7):653.

Tomford WW."Transmission of Disease through Transplantation of Musculoskeletal Allografts. J Bone Joint Surg Am. 1995 Nov;77(11):1742-54.

Toms AP, Marshall TJ, Cahir J, Darrah C, Nolan J, Donell ST, Barker T, Tucker JK. MRI of Early Symptomatic Metal-on-Metal Total Hip Arthroplasty: A Retrospective Review of Radiological Findings in 20 Hips. Clin Radiol. 2008 Jan;63(1):49-58.

Treacy RB, McBryde CW, Shears E, Pynsent PB. Birmingham Hip Resurfacing: A Minimum Follow-up of Ten Years. J Bone Joint Surg Br. 2011 Jan;93(1):27-33.

Tägil M. The Morselized and Impacted Bone Graft. Animal Experiments on Proteins, Impaction and Load. Acta Orthop Scand Suppl. 2000 Feb;290:1-40.

Ullmark G, Nilsson O. Impacted Corticocancellous Allografts: Recoil and Strength. J Arthroplasty. 1999 Dec;14(8):1019-23.

Underwood R, Matthies A, Cann P, Skinner JA, Hart AJ. A Comparison of Explanted Articular Surface Replacement and Birmingham Hip Resurfacing Components. J Bone Joint Surg Br. 2011 Sep;93(9):1169-77.

Wall SJ, Mears SC. Analysis of Published Evidence on Minimally Invasive Total Hip Arthroplasty. J Arthroplasty. 2008 Oct;23(7 Suppl):55-8.

Walsh AJ, Nikolaou VS, Antoniou J. Inflammatory Pseudotumor Complicating Metal-on-Highly Cross-Linked Polyethylene Total Hip Arthroplasty. J Arthroplasty. 2012 Feb;27(2):324.e5-8.

van der Weegen W, Brakel K, Horn RJ, Wullems JA, Das HP, Pilot P, Nelissen RG. Comparison of Different Pseudotumor Grading Systems in a Single Cohort of Metal-on-Metal Hip Arthroplasty Patients. Skeletal Radiol. 2014 Feb;43(2):149-55.

van Egmond N, De Kam DC, Gardeniers JW, Schreurs BW. Revisions of Extensive Acetabular Defects with Impaction Grafting and a Cement Cup. Clin Orthop Relat Res. 2011 Feb;469(2):562-73.

van Haaren EH, Heyligers IC, Alexander FG, Wuisman PI. High Rate of Failure of Impaction Grafting in Large Acetabular Defects. J Bone Joint Surg Br. 2007 Mar;89(3):296-300.

Wang L, Trousdale RT, Ai S, An KN, Dai K, Morrey BF. Dislocation After Total Hip Arthroplasty Among Patients With Developmental Dysplasia of the Hip. J Arthroplasty. 2012 May;27(5):764-9.

Waugh, William. 1990. John Charnley: The Man and the Hip. Springer-Verlag London Limited.

Vaughn BK. Managing Chronic Dislocated Total Hip Arthroplasty. Semin Arthroplasty. 1993 Jan;4(1):16-24.

Wechter J, Comfort TK, Tatman P, Mehle S, Gioe TJ. Improved Survival of Uncemented versus Cemented Femoral Stems in Patients Aged < 70 Years in a Community Total Joint Registry. Clin Orthop Relat Res. 2013 Nov;471(11):3588-95.

Welten ML, Schreurs BW, Buma P, Verdonschot N, Slooff TJ. Acetabular Reconstruction with Impacted Morcellized Cancellous Bone Autograft and Cemented Primary Total Hip Arthroplasty: A 10- to 17-Year Follow-up Study. J Arthroplasty. 2000 Oct;15(7):819-24.

Whitehouse MR, Aquilina AL, Patel S, Eastaugh-Waring SJ, Blom AW. Survivorship, Patient Reported Outcome and Satisfaction Following Resurfacing and Total Hip Arthroplasty. J Arthroplasty. 2013 May;28(5):842-8.

Wiley KF, Ding K, Stoner JA, Teague DC, Yousuf KM. Incidence of Pseudotumor and Acute Lymphocytic Vasculitis Associated Lesion (ALVAL) Reactions in Metal-on-Metal Hip Articulations: A Meta-Analysis. J Arthroplasty. 2013 Aug;28(7):1238-45.

Willmann G. Ceramic Femoral Head Retrieval Data. Clin Orthop Relat Res. 2000 Oct;(379):22-8.

Witjes S, Smolders JM, Beaulé PE, Pasker P, Van Susante JL. Learning from the Learning Curve in Total Hip Resurfacing: A Radiographic Analysis. Arch Orthop Trauma Surg. 2009 Oct;129(10):1293-9.

Witzleb WC, Ziegler J, Krummenauer F, Neumeister V, Guenther KP. Exposure to Chromium, Cobalt and Molybdenum from Metal-on-Metal Total Hip Replacement and Hip Resurfacing Arthroplasty. Acta Orthop. 2006 Oct;77(5):697-705.

Vundelinckx BJ, Verhelst LA, De Schepper J. Taper Corrosion in Modular Hip Prostheses: Analysis of Serum Metal Ions in 19 Patients. J Arthroplasty. 2013 Aug;28(7):1218-23.

Yang CC, Kim RH, Dennis DA. The Squeaking Hip: A Cause for Concern-Disagrees. Orthopedics. 2007 Sep;30(9):739-42.

Yang J, Shen B, Zhou Z, Pei F, Kang P. Changes in Cobalt and Chromium Levels After Metal-on-Metal Hip Resurfacing in Young, Active Chinese Patients. J Arthroplasty. 2011 Jan;26(1):65-70.

Yu R, Hofstaetter JG, Sullivan T, Costi K, Howie DW, Solomon LB. Validity and Reliability of the Paprosky Acetabular Defect Classification. Clin Orthop Relat Res. 2013 Jul;471(7):2259-65.

Zhang X, Xu W, Li J, Fang Z, Chen K. Large-Diameter Metal-on-Metal Cementless Total Hip Arthroplasty in the Elderly. Orthopedics. 2010 Dec 1;33(12):872.

Zustin J, Krause M, Breer S, Hahn M, von Domarus C, Rüther W, Sauter G, Morlock MM, Amling M. Morphologic Analysis of Periprosthetic Fractures after Hip Resurfacing Arthroplasty. J Bone Joint Surg Am. 2010 Feb;92(2):404-10.

Zywiel MG, Brandt JM, Overgaard CB, Cheung AC, Turgeon TR, Syed KA. Fatal Cardiomyopathy after Revision Total Hip Replacement for Fracture of a Ceramic Liner. Bone Joint J. 2013 Jan;95-B(1):31-7.