Turun yliopisto
University of Turku

BEARING-SPECIFIC COMPLICATIONS OF TOTAL HIP ARTHROPLASTY: CHARACTERIZATION AND TREATMENT

Jari Mokka

TURUN YLIOPISTON JULKAISUJA – ANNALES UNIVERSITATIS TURKUENSIS
Sarja - ser. D osa - tom. 1213 | Medica - Odontologica | Turku 2015

University of Turku

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

Supervised by

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

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

Reviewed by

Adjunct professor Jorma Pajamäki, MD, PhD
Coxa Hospital for Joint Replacement and
University of Tampere
Tampere, Finland

Adjunct professor Hannu Miettinen, MD, PhD
Department of Orthopedics and traumatology
Kuopio University Hospital and
the University of Eastern Finland
Kuopio, Finland

Opponent

Adjunct professor Minna Laitinen, MD, PhD
Department of Orthopaedics and Traumatology
Tampere University Hospital and
University of Tampere
Tampere, Finland

Cover photo: Jari Mokka

ISBN 978-951-29-6347-8 (PRINT)
ISBN 978-951-29-6348-5 (PDF)
ISSN 0355-9483
Painosalama Oy - Turku, Finland 2015

To Miia, Miisa, Mimi and Miska

ABSTRACT

Jari Mokka: Bearing-specific complications of total hip arthroplasty: characterization and treatment

From the University of Turku, Faculty of Medicine, Department of Orthopaedics and Traumatology, Doctoral program of clinical investigation

Annales Universitatis Turkuensis
Painosalama Oy – Turku, Finland 2015

Hip resurfacing arthroplasty (HRA) and large head metal-on-metal total arthroplasty (LDH MoM THA) gained popularity during the last decade. Adverse reaction to metal debris (ARMD) is a unique complication of metal bearings. ARMD is a complex reaction caused by metal debris from metal-on- metal bearing surfaces and from trunnion corrosion of modular junctions.

We analyzed survivorship of 8059 LDH MoM THAs based on data of the Finnish Arthroplasty Register. We found relatively high short-term survivorship for some LDH MoM THAs, but there were remarkable differences between the devices studied.

After some alarming reports of failing MoM THAs, we studied the first 80 patients who had received a ReCap-M2a-Magnum implant at our institution and evaluated the prevalence of ARMD. We found a high prevalence of pseudotumors, and, because of this, we discontinued the use of MoM bearings and followed up all patients with a MoM THA.

Bone loss due infection, osteolysis or fracture poses a great challenge for reconstructive and fracture surgery. Onlay allografting for both revision and fracture surgery provides mechanical stability and increases bone stock. Bone loss and implant stability must be assessed preoperatively and adequately classified; this provides guidelines for the operative treatment of periprosthetic fractures and revision THA. In our studies on structural allografts union rates were high, although the rates of infections and dislocations were marked.

In summary, early results of the use of LDH MoM devices were encouraging. However, the survival of the LDH MoMs varied. The prevalence of adverse reaction to metal debris was high after application of the ReCap-Magnum THA. New implants should be introduced carefully and under close surveillance by University clinics and arthroplasty registers.

Keywords: Hip, arthroplasty, revision, metal-on-metal, large-diameter-head, resurfacing, ARMD, ALVAL, bone deficiency, classification, salvage arthroplasty, bone grafting, onlay allograft, structural graft, periprosthetic fracture.

TIIVISTELMÄ

Jari Mokka – Lonkan tekonivelen liukupinnalle tyypilliset komplikaatiot ja niiden hoito.

Turun yliopisto, lääketieteellinen tiedekunta, ortopedian ja traumatologian klinikka, Turun yliopiston kliinisen lääketieteen tohtoriohjelma

Annales universitatis Turkuensis
Painosalama Oy – Turku 2015

Lonkan pinnoitetekonivelen (HRA) ja isonuppisen metalli-metalli liukupintaisen tekonivelen (LDH MoM THA) käyttö yleistyi nopeasti viime vuosikymmenen aikana. Metalli-metalli liukupintoihin ja kartioliitoksiin liittyvä metallihierrekomplikaatio (adverse reaction to metal debris, ARMD) liityy lähes yksinomaan metalli-metalli liukupintoihin. Lisääntynyt tekonivelien modulaarisuus lisää metallihierrekomplikaatioiden riskiä.

Tutkimuksessani analysoin 8059 LDH MoM -tekonivelen pysyvyyttä lyhyellä ja keskipitkällä aikavälillä Implanttirekisterin tietoihin perustuen. Pysyvyystulokset olivat hyviä, mutta ne vaihtelivat merkittävästi eri mallien välillä jo lyhyelläkin aikavälillä. Metalli-metalli liukupintaan liittyvien ongelmien raportoinnin yleistyessä teimme retrospektiivisen, 80 ensimmäistä implantoitua ReCap- M2a-Magnum–tekoniveltä koskevan tutkimuksen. Metallihierrekomplikaatio oli yleinen löydös, jonka seurauksena metalli-metalli liukupintaisten tekonivelten käyttö lopetettiin klinikassamme.

Luukato tekonivelen ympärillä johtuu useimmiten infektiosta, osteolyysistä tai murtumasta. Periproteettisten murtumien hoito on vaativaa. Myös luunpuutos lonkan tekonivelen uusintaleikkauksissa aiheuttaa hoidollisia haasteita. Rakenteellisten luunsiirteiden paranemista koskevat tutkimustuloksemme olivat hyvät, mutta myös infektioiden ja sijoiltaanmenojen määrä oli varsin suuri.

Kaiken kaikkiaan varhaiset LDH MoM tekonivelten käyttökokemukset olivat olleet rohkaisevia, mutta kaikki mallit eivät olleet pysyvyydeltään yhdenveroisia. Metalli-metalli liukupintaan ja kartioliitokseen liittyvä metallihierrekomplikaatio (ARMD) oli yleinen ReCap-Magnum-implanttia käytettäessä. Uudet implantit tulee maassamme ottaa käyttöön yliopistosairaaloiden tekonivelyksiköiden valvonnan alla. Tekonivelrekisteri on avainasemassa uusien tuotteiden arvioinnissa jo ennen kuin uusi tekonivelmalli vapautetaan laajaan käyttöön.

Avainsanat: lonkka, tekonivelleikkaus, metalli-metalli liukupinta, isonuppinen tekonivel, pinnoita, ARMD, ALVAL, luun puutos, luokittelu, luusiirre, allografti, rakenteellinen siirre, murtuma.

TABLE OF CONTENTS

ABSTRACT **4**

TIIVISTELMÄ **5**

TABLE OF CONTENTS **6**

ABBREVIATIONS **8**

LIST OF ORIGINAL PUBLICATIONS **10**

1. INTRODUCTION **11**

2. REVIEW OF THE LITERATURE **14**

2.1. Metal-on-metal hip arthroplasty 14

2.1.1. History of metal-on-metal total hip replacement and hip resurfacing arthroplasty 14

2.2. Results of modern metal-on-metal hip replacement arthroplasty and total hip arthroplasty 18

2.2.1. Metal-on-metal related complications 19

2.3. Revision operations and periprosthetic fractures 23

2.3.1. Epidemiology 23

2.3.1.1. Revision operations 23

2.3.1.2. Periprosthetic fractures 24

2.3.2. Classification 25

2.3.2.1. Periprosthetic femoral and acetabular bone loss 25

2.3.2.2. Periprosthetic femoral and acetabular fractures 27

2.3.2.2.1. Vancouver classification of intraoperative periprosthetic fractures. 28

2.3.2.2.2. Vancouver classification of postoperative periprosthetic fractures 28

2.3.2.2.3. Unified Classification System 28

2.3.3. Treatment options 29

2.3.3.1. Treatment of bone deficiency in revision total hip arthroplasty 29

2.3.3.2. Treatment of periprosthetic fractures 31

3. AIMS OF THE PRESENT STUDY **35**

4. PATIENTS AND METHODS....36
4.1. Patients....36
4.1.1. Studies I, III and IV....36
4.1.2. Study II....37
4.2. Methods....38
4.2.1. Study I....38
4.2.2. Study II....39
4.2.3. Study III....39
4.2.4. Study IV....40
4.3. Statistical methods....40

5. RESULTS....42
5.1. Studies based on the Turku University Hospital medical records (I, III and IV)....42
5.1.1. Structural onlay allografts in periprosthetic fractures....42
5.1.2. Structural onlay allografts in revision surgery....43
5.1.3. Adverse reaction to metal debris after LDM MoM....45
5.2. Studies based on the Finnish arthroplasty register....47
5.2.1. Short time survivorship of large diameter MoM head THA's from Finnish arthroplasty register....47
5.2.2. Designs....48

6. DISCUSSION....51

7. CONCLUSIONS....61

8. ACKNOWLEDGEMENTS....62

9. REFERENCES....64

10. ORIGINAL PUBLICATIONS....75

ABBREVIATIONS

AAOS	American Academy of Orthopaedic Surgeons
ALVAL	Aseptic lymphocyte-dominant vasculitis-associated lesion
AOANJRR	Australian Orthopaedic Association National Joint Replacement Registry
ARMD	Adverse reaction to metal debris
ASR	Articular Surface Replacement
ASA	American Society of Anesthesiologists
BCIS	Bone cement implantation syndrome
BHR	Birmingham Hip Resurfacing
BHS	British Hip Society
BOA	British Orthopaedic Association
CI	Confidence interval
CoC	Ceramic-on-ceramic
HHS	Harris hip score
HR	Hazard ratio
HRA	Hip resurfacing arthroplasty
HMWP	High molecular weight polyethylene
HXLPE	Highly cross-linked polyethylene
ICD	International Classification of Diseases
ImplantDB	Implant Data Base
LDH MoM THA	Large-diameter metal-on-metal total hip arthroplasty
MARS MRI	Metal artefact reduction sequence magnetic resonance imaging
MHRA	Medicines and Healthcare Products Regulatory Agency (UK)
MoM	Metal-on-metal
MoP	Metal-on-polyethylene
NARA	Nordic Arthroplasty Register Association
NZ Joint Registry	New Zealand Joint Registry
OA	Osteoarthritis

PTFE	Polytetrafluoroethylene, teflon
PMMA	Polymethylmetacrylate
PFF	Proximal femoral fracture
PPF	Periprosthetic fracture
PVR	Pulmonary vascular resistance
RR	Risk ratio
SAY	Suomen artroplastiayhdistys (Finnish arthroplasty association)
SHAR	Swedish Hip Arthroplasty Register
SOY/FAS	Suomen ortopediyhdistys (Finnish orthopedic association)
SVR	Systemic vascular resistance
THA	Total hip arthroplasty
TissueDB	Tissue Data Base
TKA	Total knee arthroplasty

LIST OF ORIGINAL PUBLICATIONS

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

I Virolainen, P, Mokka, J, Seppänen, M, Mäkelä, KT. Up to 10 years follow up of the use of 71 cortical allografts (strut-grafts) for the treatment of periprosthetic fractures. Scandinavian Journal of Surgery 2010;99(4):240-243.

II Mokka J, Mäkelä KT, Virolainen P, Remes V, Pulkkinen P, Eskelinen A. Cementless total hip arthroplasty with large diameter metal-on-metal heads: short-term survivorship of 8059 hips from the Finnish Arthroplasty Register. Scandinavian Journal of Surgery 2013;102(2):117-123

III Mokka J, Keemu H, Koivisto M, Stormi T, Vahlberg T, Virolainen P, Junnila M, Seppänen M, Mäkelä KT. Experience of structural onlay allografts for the treatment of bony deficiency in revision total hip arthroplasty. Scandinavian Journal of Surgery 2013;102(4);265-270.

IV Mokka J, Junnila M, Seppänen M, Virolainen P, Pölönen T, Vahlberg T, Mattila K, Tuominen EJK, Rantakokko J, Äärimaa V, Kukkonen J, Mäkelä KT. Adverse reaction to metal debris after ReCap- M2A-Magnum large-diameter-head metal-on-metal total hip arthroplasty. Acta Orthopaedica 2013;84(6):549-554

1. INTRODUCTION

Total hip arthoplasty (THA) has revolutionized the treatment of severe hip osteoarthritis (OA). THA is one of the most predictable procedures in orthopedic surgery. Sir John Charnley introduced polymethylmethacrylate (PMMA) cement for fixation of prosthetic components (Charnley 1960), originally discovered by the chemist Otto Röhm (Breusch and Malchau 2005). Charnley also invented the concept of low-friction arthroplasty, a bearing which combined a high-molecular weight polyethylene cup and a metal head of a cemented stem (Charnley 1961). Sir Charnley's inventions evolved into the cemented THA with a metal-on-polyethylene bearing which became the golden standard for prosthetic treatment of the osteoarthritic hip. The treatment was originally reserved for patients with end-stage OA and aged more than 65 years. Sir Charnley was concerned about the long- term survivorship of the prosthesis of young patients. Later on, results based on national arthroplasty registries have proved that cemented total hip arthroplasty (THA) is indeed the method of choice for treating the osteoarthritic hip (Havelin 2000, Puolakka et al. 2001, Malchau 2002, SHAR, NARA). THA has also been labeled as the operation of the century (Learmonth 2007).

Recent studies have shown that the survivorship of conventional THA is inferior among young and active patient compared to elderly, less mobile patients (Daras 2009, Eskelinen et al. 2011). The most common reason for THA failure is aseptic loosening of the components, regardless of the fixation method. Aseptic loosening of the acetabular component is more evident than of the femoral component (Garcia-Cimberlo et al. 2000). Aseptic loosening is often caused by osteolysis generated by biologically active polyethylene wear particles. Alternative bearing couples have been developed to minimize wear and osteolysis. The optimal features of a perfect bearing would include low friction, low volumetric wear, biological inertness, high resistance to wear and fluid film lubrication through the whole gait cycle (Kumar 2014).

Bearings can be divided into hard-on-soft and hard-on-hard bearings. Hard bearings include metal and ceramic surfaces, whereas polyethylene is considered a soft material. First-generation metal-on-metal bearings had a lower wear rate than metal-on-polyethylene bearings (Willert et al. 1996). Loosening was the main reason for failure of the first-generation MoM bearings (August et al. 1986). The ceramic bearing was introduced in France 1970 (Boutin 2000). Ceramic material has several advantages over metal. Scratch resistance, better wettability and biological inertness make it a more favorable bearing for the young and active patient (Sedel 1990). However, ceramic is a brittle material and there is concern about breakage

of the material and noise. Metal-on-metal (MoM) bearings were reinvented by McMinn and colleagues (McMinn et al. 1996) in the 1990's, when the Birmingham Hip Resurfacing (BHR) device was introduced. LDH MoM THAs evolved from resurfacings during the first decade of this millennium, mainly to overcome the risk of HRA neck fracture and to facilitate revision (Lavigne et al. 2011, Gross and Liu 2012). Metal bearings self-polish, which means that small scratches are smoothed in time. Metal as a material is more durable and allows thus larger heads and thinner acetabulum components. Large heads reduce the dislocation rate. These advantages led to widespread use of MoM alloprostheses around the world. The short-term results of large-diameter head metal-on- metal hips were encouraging (Kostensalo et al. 2012). From 2005 to 2012 the ReCap-Magnum (Biomet Warsaw, Ind, USA) was the most commonly used THA in our unit with over 1000 implantations. However, early on there were concerns about the consequences of long-term metal ion release from MoM bearings. The potential mutagenicity and carcinogenicity of long-term exposure to cobalt and chromium ions were a concern, as well (Dumbleton and Manley 2005, Mäkelä et al. 2012, Mäkelä et al. 2014). Recently, it has become obvious that adverse reaction to metal debris (ARMD) are a common metal-on-metal bearing-specific complication (Shimmin et al. 2005, Davies et al. 2005, Pandit et al. 2008 et al, Ollivere et al. 2009, Ebramzadeh et al. 2011). Consequently, the use of metal-on-metal bearing has been largely abandoned due to early and mid-term failures (MRHA 2010, SAY 2012).

Periprosthetic fracture (PPF) is a devastating complication of THA. PPF is the third most common reason for failure of a THA (SHAR 2013). The actual prevalence of PPFs is difficult to establish from literature data alone (Berry 1999). The Mayo Clinic reported a PPF rate of 1% after primary THA and 4% after revision THA (Berry 1999). A Swedish Hip Registry study from 1979 through 2000 reported corresponding figures of 0,4% and 2.1%, respectively (Lindahl et al. 2006). Similar incidences (0,9% and 4.2%) were reported in a study of 52,136 primary and 8,726 revision arthroplasties (Meek et al. 2011). Women over 70 years of age have a twofold risk for early PPF (Meck et al. 2011). The incidence of PPF is likely to rise, as primary operations accumulate as the patients undergoing THA become younger, and the future revision pool is certainly growing (Bozic et al. 2009). Osteolysis due to polyethylene particles is the most important contributor to late PPFs (Harris 2004).

PPFs may be intraoperative or postoperative. Intraoperative fractures are often due to a suboptimal operative technique, poor bone quality of the patient or wrong implant selection (Berry 1999). The PPF fracture rate is clearly higher when cementless primary implants are used and after revision surgery (Masri et al. 2004, Holley et al. 2007). The complexity of the fracture treatment is often dictated by whether the stem is fixed or loose. A loose stem usually means more complicated surgery. The

Vancouver classification of periprosthetic femoral fractures was developed to help treating these complicated cases (Duncan and Masri 1995). Classification takes into account the bone quality of the patient and the stability of the prosthetic stem. The goal of the treatment is to restore the bone stock and the joint function to the level before the fracture.

In revision THA and PPF surgery bone stock may be restored either by autogenous or allologous bone grafting. Structural onlay allografts are used in elective revision surgery as well as fracture surgery. Autogenous bone graft is biologically more active, but it can be used only in morcellized form and its source is limited. Also, donor morbidity has to be taken into consideration. A viable alternative is to take allograft bone from donors either in structural or morcellized form. Bone banking started in Turku in 1968 with an experimental canine bone bank (Aho. 1973). Human bone was deposited for the first time in a bone bank in 1972 and the first batch of bone tissue from living donors was deposited in 1976 (Virolainen et al. 2003). Since then, tissue from this bone bank has been used for clinical purposes.

The purpose of this thesis was to study early survival rates of large diameter MoM THAs; the data originated from the Finnish Arthroplasty Register data. Another purpose was to evaluate the performance of the Biomet ReCap-Magnum device; here, the data originated from the Turku University Hospital patient data base. Special attention was paid on adverse reactions to metal debris. Also, the aim was to evaluate the use of structural bone grafts for revision operations and PPF surgery in the Turku University Hospital.

2. REVIEW OF THE LITERATURE

2.1. Metal-on-metal hip arthroplasty

2.1.1. History of metal-on-metal total hip replacement and hip resurfacing arthroplasty

The first operations to treat symptomatic ostoarthrosis of the hip were interposition arthroplasties, in which a scaffold was placed between the arthritic joint surfaces. The scaffold was made from different materials – including skin, fascia lata and even sterilized pig urinary bladder (Baer 1926). The first implant with some predictability was developed by Smith-Petersen, who developed a mould arthroplasty in which the femoral head was covered with an artificial surfacing made from Vitallium metal, an alloy of 65% cobalt, 30% chromium and 5% molybdenum (Smith-Petersen 1948). The Judet brothers invented an acrylic resurfacing material for the femoral head. The prosthesis was very prone to wear after initial good results (Judet 1950). The hip prosthesis of the Judet brothers was further refined by Thompson and Austin-Moore, who launched metal prosthesis models (Thompson 1952, Moore and Bohlman 1943). Wiles presented the first THA composed of stainless steel components with screw fixation (Wiles 1957). After the introduction of bone cement, McKee and Watson-Farrar developed a technique of cemented metal-on-metal bearing hip replacement, which was in use until the 1970's (McKee and Watson-Farrar 1966). At the same time, Ring developed a cementless metal-on-metal prosthesis (Ring 1968). Other models, e.g., the Russian Sivash (Sivash 1969) and the German Müller (Müller 1970), emerged, as well. These prostheses had a high incidence of failure and thus the MoM models were abandoned, much augmented by the introduction of Charnley's low-friction arthroplasty concept.

Osteolysis and loosening were the main problems of low-friction arthroplasty with metal-on- polyethylene bearings. By the late 1970's it was unequivocally shown that osteolysis was due to a biological reaction between the tissue and polyethylene debris, rather than to cement particles, as originally thought. It has been shown that joint fluid penetrates into the interface of bone and the prosthesis (Schmalzried et al. 1992). The concept of an effective joint space was introduced. Schmalzried and colleagues also discovered that small polyethylene debris activates macrophage phagocytosis and direct resorption of the bone surrounding the prosthetic material. The amount of resorption is proportional to the extent of the inflammatory reaction.

The first signs of periprosthetic osteolysis occur approximately 5 years after primary surgery. Osteolysis and loosening are the major factors that ultimately affect the durability of low-friction THA (Harris 2004). The acetabulum component is more prone

to loosening because the femoral component has a more extended contact area to intact bone (Schmalzried 1992). With this in mind, alternative bearings were further developed, which included re-introduction of meta-on-metal (MoM), and ceramic-on-ceramic (CoC) bearing surfaces. In theory, hard-on-hard bearings undergo much less volumetric wear and the wear particles are more than tenfold smaller compared to hard-on-soft bearings. The particle size influences macrophage activity; particles sized 0.5µm - 10µm are capable of activating macrophages (Sieber et al. 1998).

Although most of the early MoM bearings failed during long-term follow-up, some of the bearings did last for decades (Schmalzried 1996). A deeper understanding of the failure mechanism and improvements in manufacturing processes led to the development of a second-generation of MoM bearings. The first-generation MoM bearings failed mainly because of aseptic loosening, although also local soft tissue reactions were detected (Greenwald et al. 2001). Aseptic loosening was mainly caused by poor manufacturing processes, which caused inadequate clearance between the components. In MoM couples, a polar bearing is desirable and this is achieved by adequate clearance between the cup and the metal head. A fluid film will separate the surfaces. If the clearance is too thin or absent, there is no fluid film lubrication which means excessive wear of the equatorial bearing and component loosening (Learmonth 2007).

Second-generation MoM bearings consisted of devices like the Metasul (Zimmer, Warsaw, IN, USA) modular articulation, which had a 28mm CoCr head and a cup with a sandwich design. The metal bearing surface was molded into a polyethylene modular liner (Rieker et al. 2004). These second generation bearings had improved component sphericity and clearance, and the surface finish had improved. Most of the published second generation MoM research reports deal with the Metasul device (Dumbleton and Manley 2005). Second-generation MoM devices varied by their metallurgical properties, e.g., cast versus wrought steel or high versus low carbon content. Otherwise models like the Biomet M2a 28mm were rather similar in design (Lombardi et al. 2001). It was hoped that improvements in metallurgy would reduce volumetric wear and osteolysis compared to conventional low-friction MoP devices. However, long-term studies showed that, at best, survivorship was equal (Dumbleton and Manley 2005, Neuerburg et al. 2012). The main failure mechanisms were still aseptic loosening and dislocation. In theory, smaller heads (28mm) produce full-film lubrication less likely compared to large heads. Numerous studies have shown that MoM THA produce higher metal ion levels compared to MoP bearings (Jacobs et al. 1998, Sieber and Köttig 1999, Dorr et al. 2000, Grübl et al. 2006). It seems that the biological risks of MoM bearings are greater than of CoC, CoP or MoP bearings, and that the risk will increase over time. In a series of 19 consecutive revisions of second- generation MoM THAs tissue samples were collected for further analysis,

and histologically failed MoM prostheses had triggered a predominantly lymphocytic reaction (aseptic lymphocyte-dominant vasculitis-associated lesion, ALVAL), rather than a granulocytic reaction, which is the case for MoP bearings (Willert et al. 2005).

The developers of third-generation MoM bearing (fig. 1) aimed at producing bone-preserving hip implants. Metallurgical progress allowed manufacturing of larger heads and thinner acetabular components. In contrast to low-friction arthroplasty, large MoM bearings have better frictional characteristics compared with smaller heads (Cuckler 2005). Fluid-film lubrication is complete with larger heads. Another problem – besides wear – that needed to be solved with larger metal heads were dislocations. Dislocation is the third most common complication of arthroplasty, according to joint registries (SHAR, NAR). The incidence is higher in revision arthroplasty than in primary arthroplasty. (Alberton, et al. 2002). The jump distance defines the distance of vertical displacement of the femoral head center required before hip joint dislocation occurs (Sariali et al. 2009). Large femoral heads are associated with a lower dislocation rate than small heads (Kostensalo et al. 2013). Lewinneck described the safe window for acetabular component positioning, where the dislocation risk is at minimum. They found that outside the "safe" range of 15°±10° anteversion and 40°±10° inclination, the dislocation risk increased significantly (Lewinneck et al.1978). The triad of good short-term and mid-term results from the use of second-generation MoM devices, retrieval studies from first-generation MoM devices and poor results of conventional THA in patients under 55 years of age introduced the rebirth of the idea of hip resurfacing. Earlier attempts at resurfacing failed due to material faults and osteolysis. The acetabulum components of the early Charnley surface replacements were made of teflon (PTFE) and the femoral components of metal. Teflon has a friction coefficient close to that of cartilage (Charnley 1960). However, PTFE devices failed early due acetabular component deterioration. Charnley had even placed small particles of PTFE and HMWP under his own skin to assess tissue compatibility, and documented a marked inflammatory reaction to PTFE (Ward 2009). Later on, metallurgical advances allowed larger metal heads and shallower acetabular components – now the development of BHR became possible (McMinn et al. 1996).

Hip resurfacing arthroplasty (HRA) is a bone-conserving alternative to THA. Hip resurfacing may restore joint biomechanics better than conventional THA (Amstutz et al. 1998). Young and active patients will probably outlive any type of conventional low-friction polyethylene bearing. Bone quality and polyethylene wear are the two major factors limiting the survivorship of polyethylene cups (Garcia-Cimberlo et al. 2000, Harris 2004). MoM resurfacing gained popularity in the treatment of young and active patients who needed to avoid polyethylene wear. Models like Converse Plus (Wright Medical Technology, Arlington, Tennessee, USA), McMinn and Corin (Corin

Medical, Cirencester, UK) and BHR (Midlans Medical Technologies, Birmingham, UK) had >97% survivorships in short-term follow-up studies (McMinn et al. 1996, Amstutz et al. 2004). These devices gained rapid popularity among orthopedic surgeons. Theoretically, the ideal patient for HRA was a young (<60 years) active male with healthy proximal bone morphology and a large frame – this is the case when normal anatomy is difficult to restore. As the number of procedures rose rapidly, complication rates increased concomitantly (Shimmin et al. 2005).

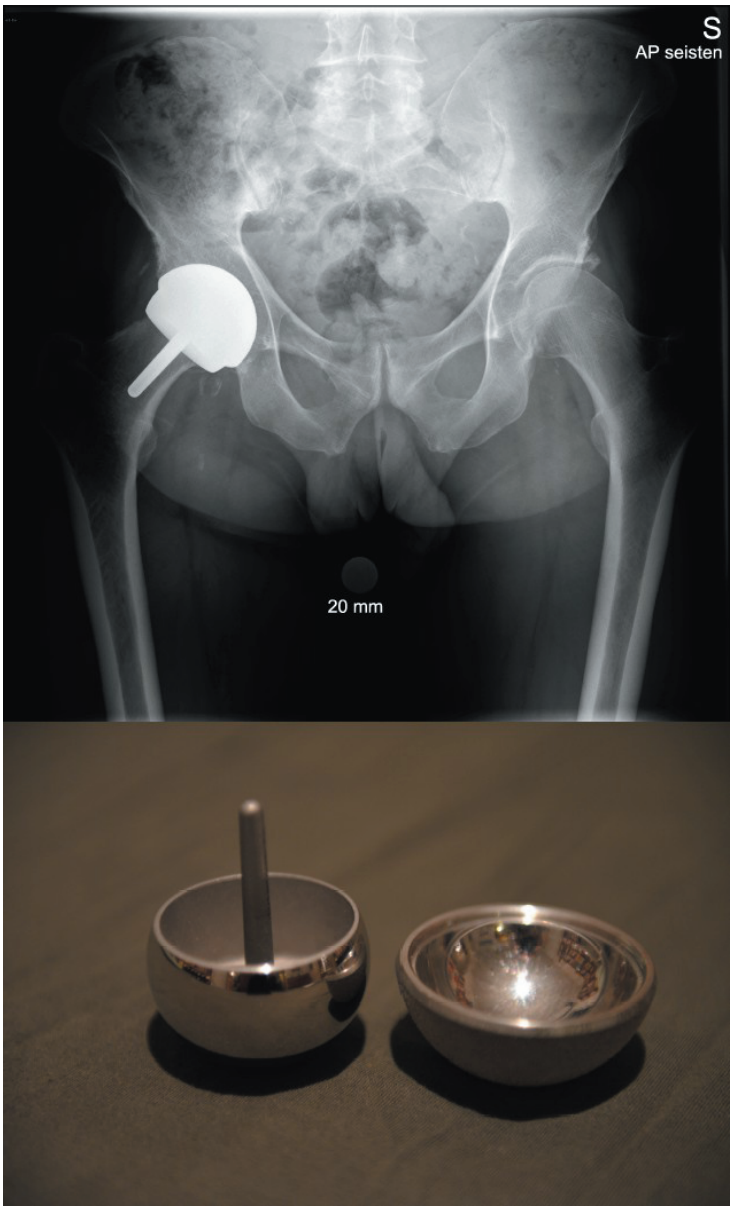

Figure 1. Typical MoM HRA device.

2.2. Results of modern metal-on-metal hip replacement arthroplasty and total hip arthroplasty

Short-term and mid-term studies based on data from single units have shown relatively high survivorships of some HRA devices (Steffen et al. 2008, Ollivere et al. 2009, Baker et al. 2011, Reito et al. 2011 and Treacy et al. 2011, Seppänen et al. 2012). Survivorships in single studies have been around 95% at 5 years (2 – 7 years, CI 83.5 – 99.2%), 95.8% at a minimum of 5 years (CI 94.1 – 96.8%), 93,5% at a minimum of 10 years (CI 89.2 – 95.6%) and 96.7% at 6 years (4.7 – 7.8 years, CI 98.4 – 95%) for BHR. All studies show that survivorship is inferior among females compared to males (Reito et al. 2013). However, a NARA register collaboration paper reported an inferior outcome after HRA compared to conventional THA (Johansson et al. 2010): HRA had a nearly 3-fold risk for revision. According to the NJR 2013 report, all resurfacing arthroplasties, including BHR, were associated with a considerably poorer implant survivorship among women than men. The AOANJRR 2013 report showed that women have a threefold risk for revision after one year compared to males. Survivorship seemed to vary by device. ASR and Durom resurfacings had inferior results compared to BHR. A survival rate of only 51% in 7 years has been reported for the ASR HRA (Reito et al. 2013). Also the Durom HRA is associated with a high revision rate: survivorship is only 88.2% at 5 years (Naal et al. 2011). According to the National Joint Replacement Registry of Australia, ReCap resurfacing has a cumulative 10.8% revision rate at ten years, compared to the Cormet HRA 20.7% at ten years, the ASR HRA 15.4% at five years and the Durom HRA 7.6% at five years (AOANJRR 2013). Malposition of components during the HRA-procedure results in increased wear and soft tissue damage, the main reasons for failing HRA (De Smet et al. 2011). Due to the relatively small head-neck ratio of HRA, the window of correct positioning of the implant is very limited (Schmalzried 2011). If the registers show that short-term results are inferior, the problem is paramount. Langton identified three risk factors associated with high concentrations of Co and Cr ions: the size of the femoral component (<51mm), the inclination and the anteversion of the acetabular component outside of the safe zone, as defined by Lewinneck (Langton et al. 2008). Several other studies have also shown that placing the acetabulum components outside of the optimal orientation increases the risk of pseudotumors (Grammatopoulos et al. 2010, Bosker et al. 2012).

LDH MoM THA devices have similar bearing-related complications as do resurfacings. However, as the modularity of the prostheses grew, a new source of metal-ion release was discovered. Garbuz and colleagues compared identical HRA and LDH MoM THA devices and found that patients with the latter device had elevated blood Co- and Cr-ion levels compared to patients with a HRAs. The only logical explanation seemed

to be wear of the modular junction of the stem and head (Garbuz et al. 2010). In a study comparing Conserve plus HRA and analogous LDH MoM THA, markedly higher Co levels were recorded in the latter group (Beaulé et al. 2011). In a study comparing three HRA and LDH MoM devices, a significantly increased risk for revision was found in ASR XL THA devices compared to ASR HRA (Junnila et al. 2014). Australian data on conventional THA clearly showed that there is an elevated risk of revision of the MoM devices with heads larger than 32mm compared to MoM devices with smaller heads (AOANJRR 2013). The cumulative risk at ten years is 15.5%. Metal-related pathology is the main reason for revision. A MoM head larger than 40mm doubles the risk, as do female gender. Bosker and colleagues reported a high incidence of pseudotumors (39%) in their series of 120 Magnum M2a (Biomet) LDH THAs (Bosker et al. 2012). Several studies have reported alarmingly high failure rates among patients fitted with an ASR XL LDH THAs (Langton et al. 2009, Reito et al. 2013). The Durom LDH MoM THA device has turned out to yield equally poor results; here, the ten year revision rate is 14.5% (Long et al. 2010, Althuizen et al. 2012). Bolland and colleagues reported a 19% revision rate for Synergy/BHR LDH MoM THAs (Bolland et al. 2013). Increased levels of metal ions were measured among patients whose components were planted in an optimal orientation. (Bosker et al. 2012)

Due to the surge of reports on revisions due to ARMD lesions, the Medicines and Healthcare Products Regulatory Agency (MHRA) of the UK launched a Medical Device Alert in 2010 on MoM bearings (MHRA 2010). Also the Finnish Arthroplasty Society did not recommend the use HRAs or LDH MoM THAs due to the increased risk of revisions of these devices (SAY 2012).

2.2.1. Metal-on-metal related complications

HRA MoM complications can be divided into two groups: firstly, problems associated with any hip arthroplasty, e.g., infection, deep venous thrombosis, nerve and vessel damages and heterotrophic ossification, and, secondly, a set of problems which are unique to resurfacings. These include femoral neck fractures, avascular necrosis due to vessel damage and cement, increased metal ion levels and, ultimately, ARMD reactions like pseudotumors (Shimmin et al. 2005, Davies et al. 2005, Pandit et al. 2008 et al, Ebramzadeh et al. 2011). ARMD reactions of HRA are common also to LDH MoM THAs. Ion-levels are increased not only inside the joint capsule but also in serum, blood, urine and the internal organs (Hartmann et al. 2013). High blood metal ion levels are associated with complications related to the bearing surfaces of MoMs (MacNair et al. 2013).

Adverse reactions to metal debris was introduced as an "umbrella" term to describe MoM joint failures associated with pain, aseptic swelling of the joint, soft tissue necrosis and metallosis of the joint (Langton et al. 2009). To combat resurfacing-related neck fractures and femoral neck anomalies where surfacing was impossible, a modular large diameter MoM (LDH MoM) THA was developed. The LDH MoM device consists of a resurfacing-like acetabular component, a conventional femoral stem and a matching large diameter MoM head connected to a stem with an adaptor system developed by the producer (Garbuz et al. 2010, Merti et al. 2010). LDH MoM devices provided good short-time results compared to both conventional THA (Lombardi et al. 2004) and resurfacings (Garbuz et al. 2010). The levels of cobalt and chromium ions after LDH MoM THA were elevated in matching groups of patients with identical HRA bearing surfaces. The only difference with respect to device design was the head- stem morse taper in LDH MoM THAs (Garbuz et al. 2010), which introduced potential extra wear from modularity, a phenomenon called trunnionosis (Pastides et al. 2013). Crevice corrosion initiated by fretting in THA tapers is a complex and multifactorial problem. Taper tribocorrosion from head-neck and other modular junctions, and the toxic and inflammatory responses of soft tissue to this tribocorrosion are still poorly understood. The optimum taper size, for example, is still unknown (Berry et al. 2014). THA in younger active patients will lead to increased stress on the taper and, as a result, there may be a significant taper corrosion and fretting burden over time (Wassef and Schmalzried 2013).

Widespread use of LDH MoM and HRA devices has increased the occurrence of MoM bearing-related complications. Volumetric wear of MoM bearings is 60 – 100 -fold less than of conventional MoP bearings (Cuckler 2005, Grübl et al. 2006), although the particle number is 100-fold (Davies et al. 2005). The first reports from second-generation MoM device bearing complications led to the discovery of ALVAL reactions by histology (Willert et al. 2005). Later it has become obvious that the histological ALVAL reaction is only a small part of a larger problem. Direct cell toxicity of Co- and Cr- ions and allergic reactions to these ions are part of the combined pathology around the hip joint. Local clinical findings of MoM hips are called ARMD (Pandit et al. 2008).

Pseudotumors are a part of the ARMD complex and constitute inflammatory fluid collections with a mixed amount of solitary component. The prevalence of pseudotumors varies from as low as 0.1% (Canadian Hip Resurfacing Study Group 2012) to the highest prevalence of 69% for symptomatic or symptomless ASR hips reported in the literature (Chang et al. 2012). Large pseudotumors have been associated with local destructiveness and require revision surgery (Pandit et al. 2008). However, MRI scans of symptomatic patients have revealed pseudotumors on the asymptomatic side, too (Hart et al. 2009). Asymptomatic pseudotumors occur

often in mildly symptomatic hips with inferior functional outcome scores (Kwon et al. 2011).

Accurate measurements of trace elements are difficult. The physiological Co- and Cr-ion levels in the blood are 0.05 – 0.35 µg/L and 0.1 – 0.4 µg/L, respectively (CRC 2014). Although metal ions released into the blood circulation are largely cleared by the kidneys and excreted with the urine, there has been no evidence of nephrotoxicity in mid- or short-term studies (Corradi et al. 2011, Yang et al. 2011). It would be tempting to use ion levels only to screen for the wear of MoM components. However, currently there is no widely accepted cut-off level for the concentrations of Co- and Cr-ions in the blood. Increased ion levels (over 17 µg/L for Cr and over19 µg/L for Co) have been associated with metallosis in revision surgery (De Smet et al. 2008). Thus, the MHRA and the Finnish Arthroplasty Association have recommended that all patients with MoM hips undergo measurements of Co- and Cr-ions in the blood, and if ion levels exceed 5 µg/L, cross-sectional imaging is advised (MHRA 2010, SAY 2012).

According to study on ReCap-Magnum LDH MoM THA's, patients with Co-ion levels over 5µg/L have a 4-fold risk for ARMD compared to those with lower Co-levels. The Cr-ion level or positioning of the acetabulum component did not correlate with ARMD (Bosker et al. 2012). It has been suggested that evidence of ARMD should be sought/suspected when the Co-and/or Cr-level exceeds 5µg/L (Hart et al. 2011). MoM devices are at risk of failure when the Co- and Cr-ion levels in the blood increase. However, metal-ion analysis alone may not be sufficient to detect ARMD. Rather, soft tissue imaging – ideally MARS MRI – should be used in conjunction with ion concentration assessments (MacNair et al. 2013). The decision to proceed to revision of the prosthesis must be made on the basis of the combination of patient symptoms, ion levels and soft tissue imaging results. The most important symptoms include pain, unexplained discomfort in the groin, clicking and a feeling of subluxation. Pseudotumors may be visible on MARS MRIs in patients with MoM bearings, regardless whether the hip is symptomatic or not (Hart et al. 2012, Hauptfleisch et al. 2012, Thomas et al. 2013), but large pseudotumors may be visible in the groin or trochanteric area without any imaging. Pseudotumors are usually graded by MRI according to the Hart. The Hart Grade I pseudotumor is thin-walled and flat. The Grade IIa pseudotumor is thick-walled or irregular and not flat. In these instances, more than 50% of the walls are not in apposition. The Hart Grade IIb pseudotumor is thick-walled or irregular, and of any shape. The Grade III pseudotumor is solid, and also of any shape (Hart et al. 2012). Pseudotumor revision surgery tends to be complex and the outcome may be poor due soft tissue damage, especially to the abductor mechanism, caused by the pseudotumor (Grammatopoulos et al. 2009).

Cr-ion exposure from MoM bearings has been associated with an increased incidence of genotoxic biomarkers. Furthermore, the Cr-ion has been associated with reproductive dysfunction, e.g., abnormal semen and spontaneous abortions (Keegan et al. 2008). Increased Co-ion levels have been associated with cardiac dysfunction, hypothyroidism, neurological symptoms (loss of vision and deafness) (Steens et al. 2006, Rizetti et al. 2009, Tower et al. 2010) and carcinogenesis (Mäkelä et al. 2012). Even fatal cardiomyopathy as a result of cobalt poisoning has been described after revision hip replacement for a fractured ceramic acetabular component (Zyviel et al. 2013). Pre-existing Co-ion exposure may augment the adverse reaction to metal debris (Posada et al. 2014), which may explain why a level as low as 20μg/L has caused neurological symptoms (Tower et al. 2010). Cobaltism is rare and not unique to MoM bearings, since also excessive corrosion from metal interfaces of other implanted devices may cause cobaltism (Jacobs 2010). The chelating agent ethylenediaminetetra-acetic acid (EDTA) has been successfully used to treat patients with Co-poisoning, together with instant revision surgery of the MoM device.

The effects of permanent long-term Co- and Cr-ion exposure are unknown. The overall short-term cancer risk for contemporary MoM bearings is not increased (Mäkelä et al. 2012, Mäkelä et al. 2014). The incidence of basalioma and soft tissue sarcoma is reportedly increased, but this may still be an incidental finding at this stage (Mäkelä et al. 2014).

The window of safe orientation of the acetabulum components of MoM HRA is even narrower than for conventional MoP THA (Langton et al. 2009). Even optimally oriented LDH MoM components are associated with metal ion release and pseudotumor formation (Bosker et al. 2012). Increased modularity of LDH MoM devices has added a new source of metal ions: a sleeve or adapter between the large diameter head and stem. Trunnionosis is a significant contributor of metal ions (Pandit et al. 2013)

Large-diameter metal on metal total hip arthroplasties should be abandoned, is the advice of the British Orthopaedic Association, the British Hip Society and the Finnish Arthroplasty Society. The same is inferred by the results of the Astralian Orthopaedic Association National Joint Replacement Registry , the Nordic Arthroplasty Register Association, the National Joint Registry and the New Zealand joint registry. Of the HRA only the BHR HRA may have an acceptable track record and it may still have a strictly targeted indication in the patient population of large and active males under 55 years of age. However, the prevalence of pseudotumors among patients fitted with a BHR HRA is high, even higher than previously thought (Skinner and Kay 2011, Bisschop et al. 2013, Reito et al. 2014, Junnila et al. 2015). Systematic and continuous follow-up of the whole MoM HRA and LDH MoM THA population is mandatory.

2.3. Revision operations and periprosthetic fractures

2.3.1. Epidemiology

2.3.1.1. Revision operations

THA is one of the most successful and cost-effective procedures in reducing pain and improving mobility and the quality of life of patients (Berry 1999, Söderman et al. 2000, Learmonth et al. 2007). Throughout the world, life expectancy increases and patients are younger and more active throughout their lives. Thus, patient expectations do not often meet the durability of the implant (Daras 2009). The prevalence of primary and revision operations of the hip and knee is rapidly increasing in the USA (Kurtz et al. 2007). The prevalence of TKA tripled from 1990 to 2002 (Kurtz et al. 2005). The absolute number of revision THA increased with 200%, while the revision burden remained constant. Revision burden is defined as the number of revisions divided by the sum of revisions and primary operations. Data obtained from national joint registries confirms their finding. The revision burden during 1990 – 2002 for hips in the USA was 17.5%, in Norway 15%, in Finland 15.7%, in Australia 18.2% and in Sweden 11.0%. The figure for Sweden is lower and this is partly explained by the implant selection for elderly people. The revision rate in Finland is higher than in the other Nordic countries (Mäkelä et al. 2014).

New technologies and implants are constantly introduced to the market. The history of THA is a sequence of trials and errors. Despite thorough laboratory testing, a certain portion of new inventions will inevitably fail (AOA 2004). Clearly, new devices should be introduced in a more controlled manner in the future than has been the case thus far. Advances made in cementing and operative techniques have improved long-term survivorship, but in younger patients the results of low-friction arthroplasty are still not excellent (Garcia-Cimberlo et al. 2000, Naudie et al. 2004, Pedersen et al. 2014).

The goal of joint registers is to decrease revision surgery and to reveal inferior implants and techniques. Improved quality of treatment also reduces costs. According to joint registries the four most common indications for reoperation are aseptic loosening (incidence decreasing), infection (incidence increasing), dislocation (incidence decreasing) and periprosthetic fractures (incidence increasing), followed by reasons related to MoM bearings (AOA 2014, NJR 2014, SHAR 2014 and THL 2011). USA and Germany are examples of developed countries, which lack a nationwide joint registry (Hayashi 2008). The American Joint Registry started a pilot project in 2011 and currently there are 361 hospitals reporting to it (AJRR 2014).

In the early history of hip prostheses, the generic endpoint was loosening, which was due to implant design and improper implantation technique. The factors

related to long-term success or failure were largely unknown (Schmalzried 1996). The understanding of the failure mechanisms of total joint prostheses is the key to the long-term success. Harris and colleagues reported on the emergence of aggressively growing granulomatous lesions around a cemented stem in 1976. There was no evidence of infection or malignancy (Harris 1976). Initially, the phenomenon was called "cement disease", because osteolysis was believed to be caused mainly by PMMA particles (Jones et al. 1987). Later it was proved that aggressive osteolysis was related to polyethylene bearing wear and that it occurred both in cementless and cemented THAs (Santavirta et al. 1990, Maloney et al. 1990).

Periprosthetic osteolysis is a substantial problem that still jeopardizes the durability of contemporary hip replacement (Harris 1995). It is now known that periprostetic wear debris originates from different sources by different mechanisms. Wear has been described as a process where material is detached from the endoprothesis in the form of debris. According to Archibeck and colleagues (2000), there are different modes of wear. Mode 1 wear originates from the bearing surfaces. Mode 2 wear originates from a modular bearing surface which contacts against a secondary surface like the shell. Mode 3 wear consists of third particle wear. Mode 4 is described as backside wear of the acetabulum component or as fretting of a taper or stem (Archibeck et al. 2000).

An additional form of wear is corrosion. Corrosion occurs when metals are introduced into an environment where they are chemically unstable or the environment is reactive (Ahmad 2006). Corrosion products are generated by metal-on-metal bearing surfaces, but also by modular metal interfaces. MoM wear produces small particles, which induce a lymphocyte-dominant histological reaction (Barry et al. 2014). Taper tribocorrosion liberates Cr-orthophosphates, and the clinical presentation resembles those seen associated with MoM bearing surfaces (Berry et al. 2014). Tribocorrosion may even lead to fracture of the implant.

Particle-induced osteolysis, regardless of the mechanism, will ultimately lead to implant loosening, bone loss and PPFs. Hard-on-hard bearings were developed to minimize PE induced osteolysis. However, fretting, corrosion and wear are still a problem with these new bearings.

2.3.1.2. Periprosthetic fractures

Peripriosthetic fracture is a rare and devastating complication of THA. Periprostetic fractures may be classified as intraoperative, early postoperative and late postoperative fractures. They may also be classified by site as periprosthetic femoral or acetabular fractures. According to various sources, the incidence of femoral PPFs varies from 0.1% to 2.3% for primaries and 2.8% to 7.8% for revisions (Berry 1999, Lindahl 2007, Cook 2008). The risk is highest during the first year after implantation and rises again after 10

years (Lindahl 2007). The incidence of intraoperative fractures is highest for cementless revisions, 20.9% (Berry 1999). Advanced age, female gender and the use of cementless implants are the major factors contributing to periprosthetic fractures (Thien et al. 2014). The risk for PPF is highest for females over 70 years of age and for patients who have undergone revision surgery (Meek et al. 2010). In a Mayo Clinic series, an intraoperative femoral fracture was associated with cementless fixation and revision surgery. After the postoperative period, there was no difference in fracture prevalence by fixation method (Berry 1999). A loose implant, whether cemented or cementless, is at immediate risk for PPF (Lindahl et al. 2006).

Periprosthetic acetabular fractures occur intraoperatively or as a late complication to trauma or a pathological process that reduces the integrity of bone, e.g., osteolysis or malignancy (Chitre et al. 2013). Intraoperative acetabular fracture is a rare but serious complication of cementless primary THA. In a Mayo Clinic series, the incidence of intraoperative acetabular fractures when cementless cups were used was 0.4%. PPFs associated with cemented cups are rare (Haidukewych et al. 2006). The greatest risk for fracture was for revision surgery, elliptical cups and under-reaming of 2mm. When cementless cups are implanted, periprosthetic acetabular fractures may be associated with pelvic discontinuity, especially in elderly patients with poor bone quality. Although fortunately rare, these fractures are difficult to treat, and treatment outcomes may be poor. The prevalence of postoperative fractures is increasing due to an increasing number of primary prostheses. The number of octogenarians who carry a constant risk of falling and who have poor bone quality is also increasing. Young THA patients are at risk of PPFs due to high-energy trauma. Finally, revision surgery itself raises the risk of PPFs. (Berry 1999).

2.3.2. Classification

2.3.2.1. Periprosthetic femoral and acetabular bone loss

Periprosthetic bone loss caused by osteolysis can occur around well-fixed cemented as well as cementless components (Jasty et al. 1991). Because osteolysis may occur in asymptomatic hips, routine follow-up is needed, particularly if designs known to be risky are used and the patients are young and active patients (Berry 2003).

An appropriate classification system helps the clinician to evaluate osteolysis and other bone deficiencies and to evaluate the optimum reconstruction method in each clinical case. A good classification system is reliable and repeatable. Intra-observer reliability means that the same surgeon chooses the same classification repeatedly, while inter-observer reliability means that different surgeons choose the same classification repeatedly (Brown et al. 2014). Bone loss is classified on the basis of

plain radiographs, and the classification can be validated intraoperatively (Yu et al. 2013).

There are several classifications to evaluate femoral or acetabular periprosthetic bone deficiencies. The most often used femoral deficiency classifications are the Endo-Klinik (Engelbrecht and Heinert 1987), Paprosky (Paprosky and Aribindi 2000, Della-Valle et al. 2003) and AAOS classifications (D'Antonio et al. 1993).

The Endo-Klinik femoral bone deficiency classification is relatively simple but may provide less information for a clinician than other classification systems. The hallmark of Endo-Klinik grade I bone deficiency are radiolucent lines confined to the upper half of the femoral bone as signs of loosening of the prosthesis. In Grade II, there are generalized radiolucent zones and endosteal erosion of the upper femur leading to widening of medullary canal. Grade III consists of widening of the medullary cavity by expansion of the upper femur, and Grade IV exhibits gross destruction of the upper third of the femur with involvement of the middle third.

In the Paprosky femoral bone loss classification, type 1 is defined as minimal metaphyseal and diaphyseal bone loss. In Paprosky type 2A, the calcar area is absent and extends just below the intertrochanteric level. Paprosky type 2B includes anterolateral bone loss, and in Paprosky 2C the calcar area is absent and there is posteromedial bone loss. Paprosky types from 3A to 3C go as in type 2, but are combined with diaphyseal bone loss.

In the AAOS femoral bone loss classification, type I is characterized by segmental defects above the lesser trochanter (level 1), within 10cm of the lower edge of the lesser trochanter (level 2) and distal to 10cm below the lesser trochanter (level 3). In AAOS femoral bone loss type II, there are cavitary defects and loss of cancellous or endosteal cortical bone without disruption of the outer cortical shell. In type III, there are combined cavitary and segmental defects, and in type IV there is either rotational or angular malalignment. In AAOS type V, the femoral canal is partially or completely occluded, and in type VI there is discontinuity with a loss of femoral bony integrity. It has been claimed that the AAOS femoral bone loss classification is complicated and that it has poor intra-observer reliability (Gozzard et al. 2003), while the Paprosky classification has good intra-observer and inter-observer reliability (Brown el al. 2014). Still, there is no comprehensive and universal femoral bone loss classification system that is applicable for all types of reconstructions (Haddad et al. 1999).

The most widely used acetabular bone deficiency classifications are the Paprosky (Paprosky et al. 1990, Paprosky et al. 1994) and AAOS classifications (D'Antonio et al. 1989).

Paprosky acetabular deficiency type 1 consists of minimal deformity, an intact rim and intact domes. In type 2A there is enlargement of the acetabulum and only minimal osteolysis. In type 2B, the acetabular dome and superior rim are distorted and in type 2C the medial wall of the acetabulum is distorted. In type 3A there is loss of the superior rim and, often, of the medial wall, the rim is non- supportive and there is superolateral migration. In type 3B there is more than a 50% loss of the superior rim, and both the medial and posterior walls are distorted. The rim is non-supportive, and there is superomedial migration.

In AAOS acetabular deficiency type I, there are segmental deficiencies in peripheral areas either superiorly, anteriorly or posteriorly. In type I, a segmental defect may also occur in the central area. In these cases the medial acetabular wall is absent. Similarly, in AAOS type II there are cavitary deficiencies in the peripheral area either superiorly, anteriorly or posteriorly. In type II, a cavitary defect may also occur centrally while the medial wall is intact. AAOS type III consists of combined deficiencies, type IV of pelvic discontinuity and type V of arthrodesis.

2.3.2.2. Periprosthetic femoral and acetabular fractures

The Paprosky classification is a universal classification of PPFs of the acetabulum (Della Valle et al. 2003). Paprosky type 1 fractures are intraoperative and occur during insertion. They may be either recognized or not recognized during operation, the fracture may be displaced or undisplaced and the component may be either stable or unstable. Paprosky type 2 fractures are intraoperative, and occur during removal of an implant. These fractures are subdivided according to bone loss into fractures involving less than 50% or more than 50% bone stock loss. Paprosky type 3 fractures are defined as traumatic fractures with either a stable or an unstable component. Type 4 fractures are spontaneous fractures involving either less than 50% or more than 50% bone stock loss. Type 5 fractures include pelvic discontinuity and are also subdivided according to bone stock loss into less than 50% or more than 50% bone stock loss. Type 5 includes also fractures associated with pelvic radiation.

The Vancouver classification of periprosthetic acetabular fractures is a simplified version of Paprosky's classification, and takes into account only the stability of the component (Masri et al. 2004, Davidson et al. 2008). It applies only to intraoperative fractures. Type I consists of undisplaced fractures, where the stability of component is not compromised. Type II consists of undisplaced fractures, where the stability of the component may be compromised. Type III fractures are displaced and are associated with compromised stability of the component and no stabilization of the fracture (Davidson et al. 2008).

Also periprosthetic femoral fractures may occur intra-operatively. These include cortical perforations, longitudinal cracks and displaced fractures. The fracture may be comminuted or not (Masri et al. 2004). Intraoperative fractures diagnosed postoperatively are called late intraoperative fractures.

By classifying PPFs the clinician should get an estimate of the bone stock and treatment options. A good classification should include fracture location, stability of the implant and the fracture and quality of the remaining bone stock.

2.3.2.2.1. Vancouver classification of intraoperative periprosthetic fractures.

A group of experts in Vancouver, Canada published a classification for periprosthetic fractures. This classification was the Vancouver classification (Masri et al. 2004). Vancouver type A intraoperative PPFs are proximal metaphyseal fractures. Type A1 fractures are cortical perforations unlikely to compromise implant fixation or to increase the risk for fracture. Type A2 fractures are undisplaced linear cracks, whereas type A3 fractures are displaced or unstable proximal femoral or greater trochanter fractures. Vancouver type B includes proximal diaphyseal fractures. Type B1 fractures are diaphyseal perforations, type B2 fractures are undisplaced diaphyseal cracks, and type B3 fractures are dispalced midfemur fractures. Vancouver type C includes the distal diaphyseal fractures. Type C1 fractures are distal cortical fractures, type C2 fractures are undisplaced distal linear cracks and type C3 fractures are distal and displaced fractures.

2.3.2.2.2. Vancouver classification of postoperative periprosthetic fractures

The most common validated classification of postoperative periprosthetic femoral fractures is the Vancouver classification (Duncan and Masri 1995, Brady et al. 2000, Rayan et al. 2008). Type A fractures occur in the trochanteric region. Type A_g fractures include greater trochanter fractures, whereas type A_L fractures include lesser trochanter fractures. Type B fractures occur around or just distal to the femoral stem. In type B1 fractures the stem is well fixed, while in type B2 fractures the stem is loose, but the bone stock is good. In type B3 fractures the stem is loose and there is severe bone stock loss. Type C fractures occur far from tip of the stem.

2.3.2.2.3. Unified Classification System

Various systems have been adopted to describe various fractures, sometime multiple systems relating to only one bone. Some fractures, e.g., interprosthetic fractures, do not fit into any of the classifications. A new Unified Classification System has been developed to address all PPFs (Duncan and Haddad 2014).

2.3.3. Treatment options

2.3.3.1. Treatment of bone deficiency in revision total hip arthroplasty

Bone deficiency is a multifactorial process caused by stress-shielding, particle-induced osteolysis, implant failure and instability, and infection. Deficient bone stock is a common problem in revision hip arthroplasty.

There are several methods for addressing acetabular and femoral bone deficiency in revision THA. Impaction bone grafting for acetabulum reconstruction (Sloof et al. 1984) and for reconstruction of the proximal femur (Nelissen et al. 1995) are both well described and documented techniques. In the original Slooff techniques, cavities in the acetabulum are tightly impacted with a morsellized femoral head or cancellous graft. A void may be constructed into a contained defect with the use of a wire mesh. The acetabular component is cemented on top of the reconstruction. This technique is demanding, and studies from less developed clinics have less satisfactory outcomes (Kostensalo et al 2015). The reasons for graft reabsorption are unknown and results may be unpredictable (Azuma et al. 1994, van Haaren et al. 2007).

In contemporary acetabular revision surgery, more favorable results have been achieved with the use of porous-coated cementless cups (Della Valle et al. 2004). Porous-coated cups may be the method of choice for acetabular reconstruction (Palm et al. 2007). Acetabular cancellous bone grafting may be used in association with cementless revision cups to fill cavitary and combined defects. Grafts also help to restore the center of rotation and restore the pelvic bone stock for future revisions (Haddad and Rayan 2009).

Structural acetabular allografts can be used in Paprosky type 2A, 2B, 3A and 3D defects (Paprosky et al. 1994), but if less than 50% of host bone contact is achieved, results are poor: the incidence of failure is 26% and of radiological loosening 41% (Chandler et al. 1995). During a follow-up of structural bone grafts covering an average of 16 years, 60% of the reconstructions were either loose or required revision (Shinar and Harris 1997). Porous tantalum metal acetabulum cups and augments were developed to allow reconstruction of more complicated acetabular defects (Sporer and Paprosky 2006). The risk of re-revision due to aseptic loosening is highest with beaded designs and titanium wire mesh designs compared with highly porous trabecular metal designs (Kremers et al. 2012). Acetabular revisions when there is severe bone loss may be addressed with the use of trabecular metal components with which it is possible to achieve adequate fixation close to the anatomical position without the aid of cages (Fletcher et al. 2008). Porous metal is the workhorse of contemporary acetabular reconstruction (Sporer and Paprosky 2006, Pulido et al. 2011).

Failure of the femoral component associated with loss of femoral bone stock is a severe complication of THA. Bone stock deficiency may be due to stress-shielding, osteolysis, fracture or infection. The main objective of a femoral revision is to restore hip biomechanics, to restore the bone stock and to secure implant fixation. Restoring bone stock is particularly important for young patients (Fitzek et al. 2006). There are two techniques that enable restoration of bone stock: impaction bone grafting and cortical onlay allografts. For severe proximal bone loss, a proximal replacing tumor prosthesis is a viable option for elderly patients (Korim et al. 2014). For younger patients, proximal femoral allograft composite plays a role in more severe deficiencies that are not repairable by bone grafting (Rogers et al. 2012).

The Exeter group published original, 18 – 49 month follow-up data on the use of impaction bone grafting to treat 56 hips. Only seven complications were associated with the technique from out of 68 consecutive operations and no hips were reoperated due aseptic loosening (Gie et al. 1993). Twelve hips were not reviewed: nine patients died, one failed to attend, one had an early failure and one had an early PPF. However, a series of 26 impacted hips showed a substantial amount of PPFs (12%) and dislocations (12%) after impaction grafting (Fetzer et al. 2001). The Sloof group presented good results of 33 consecutive femoral impaction bone grafting procedures: a 100% survival rate for loosening or reconstruction failure as an endpoint. Fracture was the major complication and occurred in 12% of the hips (Schreurs et al. 2005). The same group published data of a mean follow-up time of 15 years, and reported a 100% survival rate for the femoral component (Heyligers et al. 2014).

A Swedish registry-based study of 1188 patients from 30 different hospitals also documented excellent long-time survivorship of 94% (70 further revisions in 1188 patients). The main causes for failure were infection and fracture of the femur (33 cases or 47%). Of the 70 revisions, only 57 could be identified by information in the joint register (SHAR) (Ornstein et al. 2009). However, some studies have reported early massive subsidence in 11% of the stems (Eldridge et al. 1997). High complication rates (33%) following femoral impaction bone grafting have also been reported from Finland (Pekkarinen et al. 2000). A specific concern has been the cement mantle which is often incomplete when allografts are used (Masterson et al. 1997). Impaction bone grafting is technically demanding and the learning curve is steep. The operation time is long compared to revisions involving cementless revision. A bone bank is also needed. In spite of some weaknesses, impaction bone grafting may still be a viable option for reconstructing severe (Endo-Klinik IV) deficiencies of the femur.

Cortical structural allografts are a feasible option for restoration of the integrity of the proximal femur with cementless revision hip arthroplasty. Structural onlay

allografts unite with host bone, especially when a morsellized allo- and autogenous graft is used between the structural graft and the vascularized host bone (Gross et al. 2003). Long cementless revision stems combined with structural onlay allografts provide good results in Paprosky type I-IIIA defects with a reported success rate of 96% (Della Valle and Paprosky 2003). An effective inlay technique has also been presented to downsize the femoral canal to accommodate the thickness of the revision component (Fitzek et al. 2006).

An allograft composite or tumor prosthesis is the method of choice for revision of more severe circumferential Type IV femoral defects with a grossly unsupportive isthmus and widening of the femoral canal (Gross and Hutchison 1998, Rogers et al. 2012, Korim et al. 2014).

Cortical onlay and inlay grafts are a safe and efficient method of restoring bones stock in non- circumferentially deficient femurs. However, concern has been expressed about graft-induced viral or bacterial contamination. The clinical infection risk is negligible for morsellized and structural allografts, but is more of a concern when massive allografts are used (Tomford et al. 1990).

In summary, the current method of choice for reconstructing contained acetabular defects is cancellous bone grafting in combination with the use of porous metal augments and porous cementless acetabular components. Structural onlay and inlay allografts in conjunction with long cementless revision stems are the current method of treating segmental and non-circumferential femoral defects. Severe circumferential proximal femoral defects are difficult to treat otherwise than with allograft composites or proximal femoral replacement arthroplasty.

2.3.3.2. Treatment of periprosthetic fractures

The stability of the prosthetic component dictates the choice of the method of fracture repair. The goal of treatment is to maximize hip function by fracture stabilization, prevention of fracture propagation, maintenance of component alignment and stability. The ultimate goal is fracture union (Davidson et al. 2008).

For the treatment of an intraoperative Vancouver type 1 acetabular fracture, a stable component may be left in situ. In intraoperative Vancouver type 2 acetabular fracture with an undisplaced fracture and an unstable component it is important to evaluate the posterior and anterior columns. Usually, additional screw- fixation is adequate. In intraoperative Vancouver type 3 fractures, the acetabular fracture is displaced. Columns have to be reconstructed by internal fixation. If there is pelvic dissociation, reconstruction cages, bone grafting or other revision techniques must be applied to stabilize the fracture and the acetabular component (Chitre et al. 2013).

If an acetabular fracture is not recognized intra-operatively, the stability of the component dictates if treatment is conservative or operative. Close observation is mandatory to detect fixation failures as early as possible, if conservative treatment is chosen (Chitre et al. 2013).

Treatment of the Paprosky type 1 intraoperative fracture depends on the stability of the component. A stable component does not need additional treatment, but additional screw fixation augments the fixation.

Paprosky type 2 acetabular fractures occur intra-operatively during removal of an implant. The pelvis is stabilized with single or double plating. If the bone stock is inadequate, bone grafting or porous metal augments are used. Even a two-stage operation may be considered: first, the pelvis is stabilized and bone stock is reconstructed and then an acetabular component is added in a later stage (Chitre et al 2013).

Treatment of Paprosky type 3 traumatic fractures of the acetabulum depends on pelvic and component stability. Plating of an unstable pelvis is advisable. If unstable, the acetabulum component is revised.

Paprosky type 4 includes spontaneous acetabular fractures. Spontaneous fractures are mainly caused by osteolysis related to plastic wear debris. Spontaneous pelvic discontinuity is one of the most challenging situations for the surgeon doing revision arthroplasty. It is a distinct condition, in which bone loss separates the superior from the inferior aspect of the pelvis (Berry et al. 1999). Clinical series of revisions with ingrowth porous materials and distraction are promising, but long-term data is lacking (Sporer and Paprosky 2006, Roshan et al. 2014). In theory, the best fixation should result by use of both columns, the posterior column by plating and the anterior column by screw fixation, combined with a porous metal cup. This method should be better than cup-cage or fixation of the posterior column alone. There was no significant difference in stability between the posterior plate construct and the cup-cage construct (Gililland et al. 2013). Pelvic discontinuity due to radiation is the result of ischemic necrosis of the bone and impaired osteoblast function (Chung et al. 2010).

The best treatment of intraoperative femoral fractures is prevention by adequate fixation methods. For elderly patients (65 years and over) cemented stems are preferable if fractures are to be avoided (Mäkelä et al. 2014). The learning curve of the residents applying surgery with cementless stems is steep and increases rapidly with the number of periprosthetic fractures. When implant choices are made, it is important to involve residents in training in the process. If consultant orthopedic

surgeons use cementless stems in all patients regardless of bone quality and patient age, so do the residents.

Vancouver type A1 femoral cortical perforations may be ignored or filled with autogenous bone-graft. Vancouver type A2 undisplaced linear cracks are treated with cables, if the femoral component is stable. Prevention of distal propagation of the fracture is mandatory. If the crack of the calcar extends to the metaphyseal region of the femur in Vancouver type A3 fractures, a diaphyseal fixation stem must be used. A displaced greater trochanter fracture must be fixed with a plate, cables or wires. Vancouver B1 diaphyseal cortical perforations should be fixed by bypassing with a revision stem two cortical diameters long or approximately 5cm. Additional structural bone-grafting is needed if the perforation is at the tip of stem. Vancouver B2 displaced diaphyseal fractures should be exposed and fixed with cables, structural grafts and, possibly, plating. Vancouver C1 distal cortical perforations should be bypassed with structural grafts. Vancouver C2 undisplaced linear cracks may be fixed by cables with or without additional structural grafts. Long stable spiral fracture may be even ignored, according to some authorities (Masri et al. 2004).

Vancouver C3 displaced distal femoral fractures are fixed by plating with or without additional structural grafts.

Vancouver A_G fractures of the greater trochanter are usually caused by osteolysis. Operative treatment may be the best treatment option, if dislocation is greater than 2cm, or if the abductor mechanism has been violated. These fractures may also be treated conservatively, because true osseous union of greater trochanteric fractures due to osteolysis is rare.

Avulsions of the lesser trochanter are called Vancouver A_L fractures. These rare fractures are treated conservatively.

Vancouver type B1 fractures occur around a stable stem. They are treated by internal fixation with plates, cables and structural bone grafting, but the outcome may be poor. According to SHAR the reoperation risk is high: 26 additional operations in 88 cases (SHAR). B2 fractures with a loose stem may be misinterpredicted as B1 fractures during the operation (Lindahl et al. 2006). Plate fixation with a structural onlay allograft seems to give a better outcome than plating alone (Gililland et al 2013).

In Vancouver type B2 fractures the stem is always loose. Revision surgery or the stem is performed with a cementless revision femoral component. Additional internal fixation and bone grafting may be required. A cemented femoral revision stem may be used to treat highly selected fractures (Richards et al. 2011). The

Exeter (Stryker, Warsaw, IND, USA) type of polished stem is usually chosen when the cement mantle is repairable (Richards et al. 2011).

In Vancouver type B3 fractures restoring of the bone stock is key. The femoral isthmus is usually not supportive. Proximal allografts should be considered for young patients, when restoration of the bone- stock for future revisions is important (Parvizi et al. 2011, Rogers et al. 2012). Proximal femoral replacement arthroplasty is a viable option for elderly patients (Sewell et al. 2010, Korim et al. 2014). Long, distally fixating stems or fully porous coated stems combined with a modified extended trochanteric osteotomy yield satisfactory results (Fink et al. 2012, Drexler et al. 2014). Vancouver type C fractures can be treated regardless of the fracture by different internal fixation methods.

PPFs are costly for society, and they are associated with high patient morbidity. Lindahl and colleagues studied PPFs based on SHAR in 1979 – 2000. They recorded 1049 fractures, of which 688 were associated with primary surgery and 361 with revision surgery. They reported that the majority of the fractures occurred after the patient had fallen at the same level (75%). "Spontaneous" fractures (37%) occurred in revised hips, but most fractures occurred when the stem was loose. Other, implant-related factors affected the fracture prevalence (Lindal 2005). PPF treatment in Sweden was criticized for the limited use of structural allografts in the treatment of BI and B2 fractures (Lindahl et al. 2006).

In a single-institution series of 99 periprosthetic femoral fractures and a minimum follow-up time of 12 months, the surgical complication rate was no less than 29%, although 86% of the patients did have fracture union (Holley et al. 2007). An observational study of 71 periprosthetic femoral fractures based on data of two hospitals yielded a complication rate of no less than 48%. The re-operation rate in this study was 33%; reoperations were indicated by either implant failure or re-fracture. It was concluded that treatment of PPFs is associated with a high rate of complications and reoperations. The clinical outcome depended on whether complications occurred or not (Zuurmod et al. 2010).

Mortality after surgical treatment of PPFs is significantly higher than after primary THA. In an age and sex-matched cohort study, 106 PPFs, 311 primary total joints and 309 proximal femoral fractures were compared. PPF's and PFF's were associated with higher mortality rates after one year, 32% and 43%, respectively, than primary joint replacements (9%) (Bhattaharrya et al. 2007).

Treatment of PPFs is associated with a high complication rate and increased mortality. PPFs should be treated in specialized units with knowledge and experience of both trauma surgery and revision arthroplasty surgery.

3. AIMS OF THE PRESENT STUDY

The main purpose of this study was to evaluate the short-term survivorship of large-diameter head metal-on-metal total hip arthroplasty based on the Finnish Arthroplasty Register. I also aimed at assessing the prevalence of metal-induced adverse reactions in association with the ReCap-Magnum device in our unit. Other aims were to evaluate the results of structural onlay allografts in the treatment of periprosthetic fractures and in revision arthroplasty surgery.

The specific aims of were:

1) to evaluate the use of cortical onlay allografts in the treatment of periprosthetic femoral fractures (I),

2) to evaluate the results of cortical onlay allografts in reconstructing bone deficiencies in revision total hip arthroplasty (III),

3) to evaluate short-term survivalship of large-head metal-on-metal total arthroplasty based on the Finnish Arthroplasty Register data (II) and

4) to evaluate the prevalence of adverse reactions to metal debris (ARMD) after ReCap- M2a-Magnum metal-on-metal total arthroplasty in our unit (IV).

4. PATIENTS AND METHODS

4.1. Patients

4.1.1. Studies I, III and IV

Studies I, III and IV are retrospective studies based on data collected from the medical records, electronic medical records and the Implant DB and Tissue DB databases (BCB Medical) of patients treated at the Turku University Hospital .

In study I, structural onlay allografts were used in total of 71 patients due to a periprosthetic fracture after THA (52) or TKA (18) during the period of January 1999 and December 2008. One patient had an interprosthetic fracture. Internal fixation with structural onlay allograft augmentation was used in all patients (fig. 2).

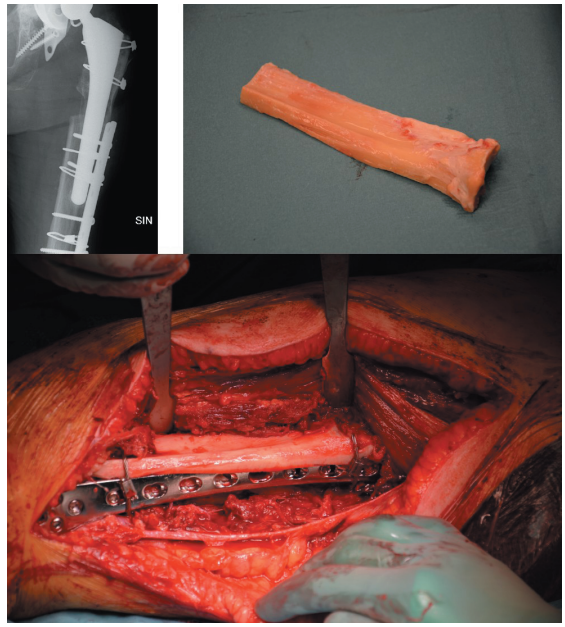

Figure 2. Structural onlay allograft in a periprosthetic fracture.

In study III, register data were compared to patient records. At least one cortical onlay allograft was used in 40 elective THA revisions (40 patients) between January 1999 and August 2010 to reconstruct femoral bone defects at our institution. The initial diagnosis (cause for the primary THA) was recorded. The exact date of the primary THA was not always known. The mean follow-up time after the revision operation was 52 months (range: 12–125 months). If the revised hip was reoperated, the status of the stem and the strut graft were recorded.

In study IV, a ReCap-M2a-Magnum LDH MoM THA was implanted on 80 hips on 74 patients during the period from August 2005 to December 2006. Magnum-ReCap-M2a was introduced at our clinic in August 2005 (fig. 3). The components are made from as-cast single-heated high-carbon cobalt chromium alloy. The system is modular and has a titanium alloy neck adaptor. The stem, taper and taper adapters are made of titanium, aluminium and vanadium alloy. The radial clearance level of the M2a-Magnum articulation is maintained at 75–150 µm. The acetabular component is 6 mm thick at the dome and (on average) 3 mm thick at the rim (Biomet design rationale). Patients were examined between February 2012 and September 2012 with MRI, assessment of serum chromium and cobalt ion levels, the Oxford hip score questionnaire and by clinical examination. The mean follow-up time was 6.0 (5.5–6.7) years. 10 patients could not participate in the follow-up due to medical conditions or death. 5 patients had undergone THA of both hips in one session and 1 patient had had both hips operated but in separate sessions. 27 patients had a MoM hip device in the contralateral hip joint and 40 patients had any hip device.

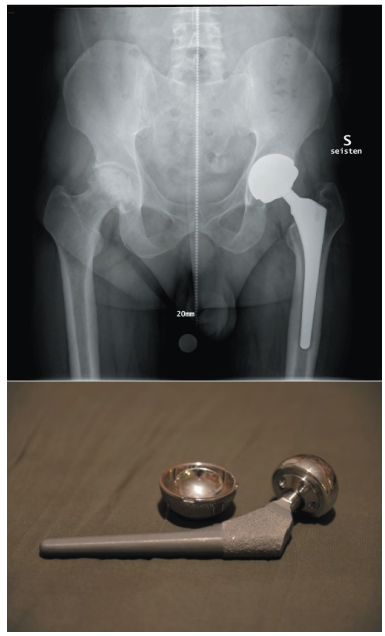

Figure 3. Biomet M2a Magnum – Bi-Metric LDH MoM THA.

4.1.2. Study II

Study II is based on data of the Finnish Arthroplasty Register. The Finnish Arthroplasty Register has been collecting data on total hip replacements since 1980, and it is the second oldest register in the world after the Swedish Hip Arthroplasty

Register. 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 the joint register. Currently, 98% of the implantations are registered. Reoperations can be linked to the primary operation by a personal identification code (Paavolainen et al. 1991, Puolakka et al. 2001).

During the period covering January 2002 through December 2009, the register contains information on 16,978 patients who had undergone conventional MoP THA and on 8,059 patients who had a LDH MoM THA performed for primary or secondary arthrosis. Patients diagnosed with rheumatoid arthritis or for other reasons than primary and secondary arthrosis were excluded. Head size equal or more than 38mm was considered as LDH. Only LDH MoM THA designs more than 100 implantations during the study period were included. Seven different LDH MoM implants were used and included in the registry study: 4,202 ReCap-BiMetric (Biomet) 52%, 2,459 M2a38-BiMetric (Biomet) 31%, 495 ASR-Summit (Depuy) 6%, 432 BHR-Synergy (Smith&Nephwe) 5%, 197 Durom-ML/Taper (Zimmer) 2%, 154 Durom-CLS (Zimmer) 2% and 120 ASR-Corail (Depuy) 1%. Patient data is presented in table 1.

Table 1. Patient demographics in study II (Original publication II).

	LDH MoM THA	Cemented THA
Mean follow-up time, years (range in parenthesis)	2.4 (0.0–7.8)	4.1 (0.0–8.0)
Mean age, years (range in parenthesis)	62 (14–85)	73 (24–85)
Proportion of male patients (%)	54	40
Proportion of primary OA as diagnosis (%)	92	95

LDH MoM THA: large diameter head metal-on-metal total hip arthroplasty; OA: osteoarthritis.

4.2. Methods

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

4.2.1. Study I

In study I, we evaluated the use of structural onlay allografts to treat PPFs. Tissue transplant information was gathered from Tissue DB database, which was developed for the management of bone banks. It provides statistical tools to generate reports on the information stored in database. The tissue DB register data was compared to patient notes. The tibial or femoral allografts were freshly freeze-dried and prepared by the University of Turku Tissue Bank. Before use, all grafts were excised and

prepared under strict aseptic conditions. No alcohol or other chemical agents were applied on the grafts nor were they irradiated.

We evaluated the union rate by examination of plain radiographs and patient notes. We evaluated the rates of the following complications: reoperations, infections, nonunions and malunions.

4.2.2. Study II

In study II, we compared the short-term results of LDH MoM THAs to conventional THAs. The survival rate of LDH MoM THA was compared to that of conventional MoP THA during the same time period. Stratified analysis was performed for males and females aged <55 or ≥55 years. Sub-analyses were made by age and gender with regard to the revision risk of LDH MoM THA compared to the revision risk of conventional MoP THA. The LDH MoM THA group was further analyzed with regard to the impact of the MoM THA device by gender, diagnosis, implant design, hospital production volume and femoral head diameter (≤44 mm, 45-49 mm, 50-55 mm and ≥55mm). The age of the patients was recorded as the age at the time of surgery.

4.2.3. Study III

In study III, we evaluated the use of structural onlay allografts for reconstruction of femoral bone deficiencies. Tissue transplant information was gathered from the Tissue DB register and was compared to patient records. At least one cortical onlay allograft was used in 40 elective THA revisions (40 patients) between January 1999 and August 2010 to reconstruct femoral bone defects at our institution. The initial diagnosis (cause for the primary THA) was recorded. The exact date of the primary THA was not always known. If the revised hip was reoperated, the status of the stem and the strut graft were recorded. The follow-up time of the strut graft was considered to have ended when, in a reoperation, the graft was loose. The follow-up time of the stem was considered to have ended if, in a reoperation, the stem was removed or replaced. Otherwise, the follow-up of a patient was considered to have ended at the time of the last orthopedic note in the medical records. None of the patients died during follow-up. We evaluated the rate of surgical complications, infections, fractures, dislocations and non-unions of the graft and/or the stem. Bone loss was evaluated from radiographs and classified according to Paprosky (Paprosky and Aribidi 2000). Long cementless revision stems were used in all revision surgeries. There were 31 (77,5%) monoblock extensively porous coated stems; 14 Integral (Biomet), 14 Reach (Biomet), 1 Biomet 300, 1 Mallory-Haed (Biomet) and 9 (22,5%) modular distally fixed stems; 8 Link MP (Waldemar Link) and 1 ZMR (Zimmer).

4.2.4. Study IV

In study IV, we evaluated the prevalence of ARMD after ReCap-M2a-Magnum THA and the risk factors associated with ARMD. MRI was used to identify collections of fluid and soft tissue masses (Toms et al 2008, Hart et al. 2012). MRI was performed on 77 hips regardless of patient symptoms. For MRI, 1.5T images were used, carefully optimized to reduce metal-induced artifacts (Hargreaves et al. 2011).

MARS (metal artifact reduction sequence) MRI is a technique that has recently been developed that provides good metal-artifact suppression while minimizing image blurring and scanning time (Eustace et al. 1997, Hart et al 2012). 1 patient with a study implant in both hips underwent computed tomography (CT) because of a pacemaker. 1 patient was identified radiographically as having a loose stem; the device was revised before MRI. An estimate of the volume of periarticular fluid collections and soft tissue masses was made. For this, MRI images were examined in 3 planes for measurement of the maximal anterior-posterior, superior-inferior and medial-lateral diameters. All patients underwent pelvic and hip radiography; the radiographs were used to measure the inclination angle of the cup. Serum levels of cobalt and chromium ions were measured at follow-up. A total score of 42–48 points was considered excellent, 34–41 good, 27–33 fair and 0–26 poor. Separate questions about clicking, a sensation of subluxation and swelling of the hip were asked. The OHS questionnaire was not filled out preoperatively or at routine outpatient visits. All patients were clinically evaluated by 1 of the 5 orthopedic surgeons performing revision surgery at the Turku University Hospital. The prevalence of ARMD after ReCap-M2a-Magnum THA as assessed and the risk factors for ARMD were evaluated. ARMD was considered definite if the patient was revised for ARMD and if the operative finding was compatible with ARMD. ARMD was also considered definite in those cases where a revision operation had not been performed but the serum chromium or cobalt level was ≥ 10 µg/L and/or there was a solid mass or a fluid collection of ≥ 50 mm on MRI (in any plane). In patients who had not undergone surgery, ARMD was considered to be probable or possible either if the serum chromium or cobalt concentration was ≥ 5µg/L and/or if there was a collection of fluid of any size by MRI. We assessed the following risk factors for ARMD: age, gender, side, inclination of the cup, bilaterality, clicking, subluxation sensation, swelling, OHS total score, OHS group 1 (excellent) and OHS group.

4.3. Statistical methods

Any p-values < 0.05 were considered as statistically significant. Confidence Intervals (CI) of 95% was used.

In study II, Kaplan-Meyer analysis was used to calculate the survival probabilities. Survival data was compared with the log-rank test. Adjusted revision rates were calculated using Cox's multiple regression analysis. The Wald test was applied to calculate p-values obtained from the Cox multiple regression analysis. Relative risk (RR) estimates were calculated and presented with 95% CI.

In study III, continuous variables were characterized by means and standard deviations (SD) or medians and range of values. In case of categorical variables, frequencies and percentages were presented. Differences in relation to normally distributed continuous variables were tested with Student's t-test for using independent samples. For non-normally distributed variables, Mann- Whitney's *U*-test was used. Categorical variables were analyzed using the X^2 (chi-square) test or Fisher's exact test. Kaplan-Meyer survival analysis was used to calculate survival percentages

In study IV, potential risk factors were analyzed by univariate multinomial logistic regression on three variables. The results were expressed as odds ratios (OR) with 95% CI. A multivariable logistic model was obtained by backward elimination.

5. RESULTS

5.1. Studies based on the Turku University Hospital medical records (I, III and IV)

5.1.1. Structural onlay allografts in periprosthetic fractures

In study I, the average age of the donor was 41.1 years and the age of the recipient 75.7 years. The average follow-up time was 943 days (range 90 – 3428 days). 3 patients were lost during follow-up. The overall union rate was 91%. 20 patients died during follow-up, 6 of them during the first six months after operation. 8 patients (12%) had an infection during follow-up. All of these patients were reoperated. Extensive debridement with antibiotic added power lavage and a new fixation, if necessary, was performed. In five cases the fracture healed and patients did/do not have any symptoms. In 3 cases treatment was not successful. Two infected fractures were later reoperated with one-stage revision with debridement and reconstruction with a megaprosthesis. The other patient has still an infection within the megaprosthesis but is able to walk with canes. 1 patient was operated 3 times because of infection and bleeding and died. The fracture of 6 patients was not united properly. 3 nonunions were due to the infections mentioned above. In two cases the non-union was associated with fracture malposition. In both cases the patients were old low demand patients with multiple comorbidities, and since they were painless, a new operation was contradicted. One patient with non- union and plate fracture was reoperated with plate and strut graft fixation and healed in a malposition after delayed fracture healing. Two more fractures were united in malposition but the patients declined a reoperation. In two fractures around the knee, the fracture united but the TC 3 type prosthesis became luxated.

1 patient had a cerebral infarction as a complication of the operation. The total complication rate including all infections, non-unions, malunions, dislocation and death within 6 month of the operation was 23.9%.

Infections, non-unions and malunions around hip and knee in study I are presented in table 2.

Table 2. Infections, non-unions and malunions around hip and knee. (Original publication I).

Infections, nonunions and unions around hip and knee. (non-union defined as patients with pain and clinical instability).

Fracture site	Infection	Malunion	Nonunion	Union
Knee	2	1	0	17
Hip	6	2	6	44

5.1.2. Structural onlay allografts in revision surgery

In study III, the mean age of the patients was 76 years (range 47– 93 years). The proportion of women was 33 of 40 (82.5%). The reason for the revision was aseptic loosening in 33 of 40 (82.5% of all revisions), dislocation in 2 of 40 (5.0%), pseudoarthrosis in 3 of 40 (7.5%) and infection in 2 of 40 (5.0%) patients. A strut allograft was needed to treat a perioperative perforation, which occurred when bone cement was removed in 7 of 40 (17.5%) cases, to treat a perioperative periprosthetic fracture in 14 of 40 (35.0%) cases, to treat bone deficiency in 11 of 40 (27.5%) cases and to strengthen an extended trochanter osteotomy in 8 of 40 (20.0%) cases. The initial diagnoses were osteoarthritis (OA) in 27 of 40 (67.5%) cases, rheumatoid arthritis (RA) in 7 of 40 (17.5%) cases, fracture in 3 of 40 (7.5%) cases, avascular necrosis in 2 of 40 (5.0%) cases and Legg–Perthes–Calve's disease in 1 of 40 (2.5%) cases. A cemented stem had been used in 31 of 40 cases (77.5%) and a cementless stem in 9 of 40 cases (22.5%). The index revision was the first revision of the hip in 24 of 40 (60.0%) cases, the second revision in 10 of 40 (25.0%) cases, the third revision in 3 of 40 (7.5%) cases, the fourth revision in 2 of 40 (5.0%) cases and the fifth revision in 1 of 40 (2.5%) cases. In all, 36 of 40 (90.0%) revision stems eventually healed with bony union. The strut allograft was incorporated into the bone tissue of 37 of 40 (92.5%) patients. There was one patient with RA whose revision stem and strut allograft did not ossify. Overall, 14 of 40 (35.0%) patients had at least one surgical complication during follow-up. The mean age of the patients without any complications was 76 years (range 55–93 years) and with at least one complication 76 years (range 47–88 years). The mean follow-up time of the patients without complications was 51 months (range 12–122 months) and of those with at least one complication 54 months (range 12–125 months). In all, 12 of 33 female patients (36.4%) and 2 of 7 male patients (28.6%) had at least one complication. The number of study patients was too small to allow statistical comparison between gender and the occurrence of complications.

Femoral bone deficiency grading (according to Paprosky) could be made for 30 patients. There were 5 Type I, 8 Type II, 8 Type IIIA, 6 Type IIIB and 3 Type IV deficiencies. The number of study patients was too small to allow statistical comparison between Paprosky grading and the occurrence of complications or osteointegration of the strut. When bone loss was further divided into two (mild bone loss, including Paprosky I and II, and severe bone loss, including Paprosky IIIA, IIIB, and IV), there were 3 of 13 (23.1%) complications in the mild bone loss group and 9 of 17 (52.9%) complications in the severe bone loss group. The association between the severity of bone loss (two- class) and the occurrence of complications was not statistically significant ($p = 0.14$). Mild bone loss was not associated with the occurrence of osteointegration of the strut, either ($p = 0.24$).

Both the strut graft and the cementless revision stem osteointegrated in 26 of 31 (83.9%) patients after a revision of a cemented stem and in 8 of 9 (88.9%) patients after a revision of a cementless stem.

The number of complications by diagnosis is presented in table 3, the number of complications by cause for revision is presented in table 4 and the number of complications by stem design is presented in table 5. Infection occurred in 4 of 40 (10.0%) patients during the follow-up, all among female patients. Of the 4 infections, 3 were deep (3 of 40, 7.5%) and 1 superficial (1 of 40, 2.5%). One patient with deep infection was treated by one-stage revision surgery and parenteral antibiotics. The strut graft was removed. The re-revision stem subsided, but the hip was still painful and antibiotic treatment continued. Two patients with a deep infection were treated only with parenteral antimicrobial agents and no surgery. During follow-up, the strut grafts and the revision stems became incorporated and the infections healed. The patient with a superficial wound infection was treated with superficial lavage. The strut graft and the stem became incorporated, and the infection healed during follow-up. In all, 4 of 40 (10.0%) stems subsided and did not become incorporated, but all needed revision. However, the strut graft united in three of these patients despite the stem being loose. Overall, 6 of 40 (15.0%) stems became dislocated at least once. These dislocated hips were treated by closed reduction, open reduction or revision of the cup (constrained liner). No stems were revised because of dislocation. There were 3 of 40 (7.5%) PPFs, all among women. The strut graft did not heal in one of these; the stem osteointegrated in all three cases. There was a lesion in the distal part of the femoral artery in one patient who needed vascular reconstruction. The extremity leg and the strut healed. There were 19 of 31 (61.3%) patients without any complications in the cemented stem group and 7 of 9 (77.8%) patients in the cementless group. There were 20 of 31 (64.5%) patients without any complications in the long porous-coated revision stem group and 6 of 9 (66.7%) patients in the distal fixation revision stem group.

Table 3. Complications of revision surgery and diagnosis of primary operation (Original publication III) .

The number of complications in the revision operation and the diagnosis of the primary operation (percentage in parenthesis). Infection was the main complication, if there were more than one complication in the same patient. One patient had both subsidence of the stem and dislocation. Here, subsidence of the stem was considered as the main complication. One patient had a fracture and an arterial lesion. Fracture was considered here as the main complication.

	OA (N = 27) n (%)	RA (N = 7) n (%)	Fracture (N = 3) n (%)	Other (N = 3) n (%)	Total (N = 40) n (%)
No complications	20 (74.1)	3 (42.9)	2 (66.7)	1 (33.3)	26 (65.0)
Infection	2 (7.4)	1 (14.3)	0 (0)	1 (33.3)	4 (10.0)
Fracture	0 (0)	3 (42.9)	0 (0)	0 (0)	3 (7.5)
Subsidence of the stem	2 (7.4)	0 (0)	0 (0)	1 (33.3)	3 (7.5)
Dislocation	3 (11.1)	0 (0)	1 (33.3)	0 (0)	4 (10.0)

OA: osteoarthritis; RA: rheumatoid arthritis.

Table 4. Complications and indication for revision (Original publication III).

The number of complications and the revision indication (percentage in parenthesis). Infection was the main complication, if there were more than one complication in the same patient. One patient had both subsidence of the stem and dislocation. Here, subsidence of the stem was considered as the main complication. One patient had a fracture and an arterial lesion. Fracture was considered here as the main complication.

	Revision indication: loosening (N = 33) n (%)	Revision indication: infection (N = 2) n (%)	Revision indication: pseudoarthrosis (N = 3) n (%)	Revision indication: dislocation (N = 2) n (%)	Total (N = 40) n (%)
No complications	23 (69.7)	1 (50.0)	0 (0)	2 (100.0)	26 (65.0)
Infection	2 (6.1)	1 (50.0)	1 (33.3)	0 (0)	4 (10.0)
Fracture	3 (9.1)	0 (0)	0 (0)	0 (0)	3 (7.5)
Subsidence of the stem	2 (6.1)	0 (0)	1 (33.3)	0 (0)	3 (7.5)
Dislocation	3 (9.1)	0 (0)	1 (33.3)	0 (0)	4 (10.0)

Table 5. Complications and revision implant design (Original publication III).

The number of complications and the revision implant design (percentage in parenthesis). Infection was the main complication, if there were more than one complication in the same patient. One patient had both subsidence of the stem and dislocation. Here, subsidence of the stem was considered as the main complication. One patient had a fracture and an arterial lesion. Fracture was considered here as the main complication.

	Integral (N = 14) n (%)	Link MP (N = 8) n (%)	Biomet 300 (N = 2) n (%)	Reach (N = 14) n (%)	Zimmer (N = 1) n (%)	Mallory-Head (N = 1) n (%)	Total (N = 40) n (%)
No complications	9 (64.3)	6 (75.0)	0 (0)	10 (71.4)	0/1 (0)	1 (100)	26 (65.0)
Infection	1 (7.1)	0 (0)	2 (100)	1 (7.1)	0 (0)	0 (0)	4 (10.0)
Fracture	0 (0)	1 (12.5)	0 (0)	2 (14.3)	0 (0)	0 (0)	3 (7.5)
Subsidence of the stem	1 (7.1)	1 (12.5)	0 (0)	1 (7.1)	0 (0)	0 (0)	3 (7.5)
Dislocation	3 (21.4)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	4 (10.0)

5.1.3. Adverse reaction to metal debris after LDM MoM

In study IV, 3 patients (3 hips, Table 6) required revision due to ARMD. ARMD was verified during the revision operation in all of these cases.

8 patients (8 hips, table 7) were considered to have definite ARMD, but a revision operation had not been performed (11 of 80 hips altogether). 29 patients (32 hips) were considered to have a probable or possible ARMD. Altogether, there were 43 out of 80 hips with a definite, probable or possible ARMD and 34 patients (37 hips) with no ARMD. A soft tissue mass or a collection of fluid of any size was found in 46 of 78 hips with MRI (table 7). Univarite associations assessed with multinomial logistic regression analysis between certain risk variables and ARMD are presented in table 8. A sensation of subluxation, clicking, swelling and a poor OHS score were associated with ARMD. In the multivariate model, clicking and swelling remained statistically significant factors when patients with ARMD were compared to patients with no ARMD (OR = 7, CI: 1.5–38; p = 0.02 and OR = 10, CI: 1.3–76; p = 0.03, respectively). Age was significant when patients with probable or possible ARMD were compared with patients with no ARMD (OR = 1, CI: 1.0–1.2; p = 0.02).

Table 6. Data on three patients who required revision (original publication IV).

A	B	C	D	E	F	G	H	I	J	K	L	M	N
58 F	33	M	No	Yes	Yes	2.5	3.8	41	Solid mass and fluid 60 × 30 × 30 mm	Pseudotumor	Cold-welded	ETO + revision of stem and cup	Neg
71 M	29	M	Yes	No	Yes	4.9	6.6	57	Fluid 29 × 76 × 62 mm	Milk-like yellowish fluid	Cold-welded	Revision of the stem + Avantage	Neg
65 F	32	M	Yes	Yes	No	13.5	24.0	45	Fluid 90 × 130 × 70 mm	Milk-like yellowish fluid, pseudotumor, gluteus medius muscle necrosis	Corrosion of trunnion and adapter	Avantage	Neg

A Age and gender
B OHS, See Table 1
C Pain
M = Moderate
D Clicking
E Subluxation sensation
F Swelling
G Serum chromium level µg/L
H serum cobalt level µg/L
I Cup inclination angle in degrees
J Magnetic resonance imaging
K Status of the hip at revision (all had ARMD)
L Status of the trunnion/head at revision
Cold-welded = the Magnum head could not be detached from the adapter and trunnion
M The procedure performed in revision
ETO = extended trochanter osteotomy to revise the stem
Avantage = the Biomet Dual-Mobility E1 mobile polyethylene liner.
N Bacterial culture

Table 7. Data on 8 patients who were considered to have ARMD but had not undergone revision surgery. See table 6 for abbreviations (original publication IV).

A	B	C	D	E	F	G	H	I	J	K
70 M	47	No	No	No	No	49.1	11.3	41	Fluid 60 × 70 × 20 mm	Revision scheduled
60 F	37	Mild	No	Yes	No	7.8	10.0	53	Fluid 25 × 35 × 40 mm	Strict follow-up
61 M	32	Moderate	Yes	No	No	26.1	42.5	62	Fluid 60 × 70 × 22 mm	Revision scheduled
66 F	48	No	Yes	No	No	2.9	2.9	37	Solid and fluid 76 × 30 × 1 mm and 30 × 20 × 20 mm	Strict follow-up
66 F	45	Mild	Yes	Yes	No	10.2	6.7	50	No findings	Strict follow-up
63 M	47	Mild	No	No	Yes	9.1	8.4	40	Solid 60 × 60 × 90 mm	Revision scheduled
75 F	27	Moderate	Yes	Yes	No	5.4	14.1	39	Fluid 47 × 13 × 70 mm	Patient did not want revision
71 F	13	Hard	No	No	Yes	4.8	10.0	42	No findings	Strict follow-up

A–J: See Table 2
K Status of the patient

Table 8 Associations between certain risk factors and ARMD (original publication IV).

	ARMD vs. ARMD not found		ARMD probable or possible vs. ARMD not found	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.0 (0.95–1.1)	0.5	1.1 (1.0–1.2)	0.02
Gender (female vs. male)	0.6 (0.1–2.4)	0.4	0.4 (0.1–1.0)	0.05
Side	4.4 (1.0–19)	0.05	0.8 (0.3–2.0)	0.6
Subluxation sensation	5.0 (1.1–23)	0.04	0.9 (0.2–3.7)	0.9
Clicking	7.2 (1.6–33)	0.01	1.2 (0.3–4.4)	0.8
Swelling	9.4 (1.4–62)	0.02	1.8 (0.3–11)	0.5
Inclination angle of the cup	1.0 (0.95–1.1)	0.4	1.0 (0.97–1.1)	0.2
OHS score	1.1 (1.0–1.2)	0.03	1.0 (0.95–1.1)	0.7
OHS poor and fair vs. good and excellent	7.2 (1.6–33)	0.01	0.9 (0.2–3.7)	0.9
Bilateral ReCap-M2a-Magnum	0.4 (0.05–3.9)	0.5	0.6 (0.2–2.3)	0.5
Bilateral MoM THA	0.6 (0.1–2.4)	0.4	0.6 (0.2–1.6)	0.3
Bilateral THA	0.4 (0.1–1.8)	0.2	0.7 (0.3–1.7)	0.4

5.2. Studies based on the Finnish arthroplasty register

5.2.1. Short time survivorship of large diameter MoM head THA's from Finnish arthroplasty register

In study II, the main reasons for the revision of LDH MoM THA were aseptic loosening and fracture, whereas cemented THAs were revised most often because of aseptic loosening and dislocation. Unspecified ("other") reasons for revision were recorded in 4% of the LDH MoM THA revisions, as compared to 3% in THA revisions (table 9).

The 7-year unadjusted Kaplan–Meier survival was 96% (95% CI = 95–97) for the LDH MoM THA and 95% (95% CI = 95–96) for the cemented THA (table 9). By Cox's regression analysis, there was no difference in the revision risk between LDH MoM THAs and cemented THA (RR = 0.90, CI = 0.74–1.10, p = 0.3) (table 10, Figs 4 and 5).

For both male and female patients younger than 55 years, the revision risk of the cementless LDH MoM THA was lower than that of the cemented THAs (RR = 0.38, CI = 0.17–0.87, p = 0.02 and RR = 0.46, CI = 0.22–0.93, p = 0.03, respectively). However, female patients with LDH MoM THA aged 55 years or more had an increased revision risk compared to those with a cemented THA (RR = 1.33, CI = 1.04–1.70, p = 0.02).

When we compared different LDH MoM THA designs using the BHR/Synergy as a reference implant, the Durom/CLS carried a higher risk of revision than the BHR/Synergy (RR = 2.82, CI = 1.16–6.82, p = 0.02) (table 7). CI for the other designs showed considerable overlap, and the analysis does not permit any ranking between them. The femoral head diameter, age (<55 or ≥55 years), gender, diagnosis or hospital volume (<100/≥100 procedures) did not have a statistically significant influence on the revision rate (table 11).

The main indications for the revision (202) of LDH MoM THA were aseptic loosening (93), fracture (41) and infection (31). 8 were classified as other. The main indication for revision of cemented THAs (555) was aseptic loosening (213) followed by dislocation (175) and infection (81).

The 7-year unadjusted Kaplan-Meier survival was 96% (95% CI 95-97) for the cementless LDH MoM THA and 95% (95% CI 95-96) for cemented MoP THA.

There was no difference in the revision risk between LDH MoM THA and cemented MoP THA, according to Cox's regression analysis.

In the age group <55 the revision risk for LDH MoM THA was less than for cemented MoP THA, regardless of gender (RR=0,38, (CI 0.17-0.87, p=0.02) and RR=0.46 (CI 0.22-

0.93, p=0.03), fig. 2). Females in the ≥55 age group had a greater revision risk if they had a LDH MoM THA than a cemented MoP THA (RR=1.33 (CI 1.04-1.70, p=0.02)).

5.2.2. Designs

When different LDH MoM THAs were compared, the Durom/CLS was associated with a statistically significant higher risk for revision than the BHR/Summit, the reference implant (fig. 5). Femoral head diameter, age group (<55 or ≥55 years), gender, diagnosis or hospital volume did not have a statistically significant influence on the revision rate (table 11).

Table 9. Indications for revision (original publication II).

Hip device	N	Aseptic loosening of both components	Aseptic loosening of the cup	Aseptic loosening of the stem	Infection	Dislocation	Malposition	Fracture	Fracture of the prosthesis	Other reason[a]	All
LDH MoM THA	8059	42 (20.8)	34 (16.8)	17 (8.4)	31 (15.3)	11 (5.4)	17 (8.4)	41 (20.3)	1 (0.5)	8 (4.0)	202 (100)
Conventional cemented THA	16,978	119 (21.4)	81 (14.6)	18 (3.2)	81 (14.6)	175 (31.5)	25 (4.5)	33 (5.9)	4 (0.7)	19 (3.4)	555 (100)
Total	25,037	161	115	35	112	186	42	74	5	27	757

LDH MoM THA: large diameter head metal-on-metal total hip arthroplasty.
Percentage of cases is given in parenthesis.
[a]Including local periprosthetic reactions like metallosis associated with the metal-on-metal articulation.

Table 10. Survival of LDH MoM and conventional cemented THA, reference group (original publication II).

	N	Mean follow-up years (range)	AR of 3 years	3-year survival (95% CI)	AR of 5 years	5-year survival (95% CI)	AR 7 year	7-year survival (95% CI)	Adjusted RR for revision (95% CI)	p value
BHR/Synergy	432	2.5 (0.0–5.6)	208	98 (96–99)	37	98 (96–99)	—	—	0.68 (0.34–1.33)	0.3
ASR/Summit	495	2.2 (0.0–5.7)	196	97 (95–99)	24	97 (95–99)	—	—	1.00 (0.58–1.74)	1.0
ReCap/Bi-Metric	4202	1.8 (0.0–5.0)	1190	97 (97–98)	59	97 (96–98)	—	—	0.93 (0.73–1.20)	0.6
Durom/CLS	154	3.5 (0.5–4.8)	134	94 (90–98)	25	89 (81–97)	—	—	2.13 (1.17–3.90)	0.01
M2a38/Bi-Metric	2459	3.6 (0.0–7.8)	1776	97 (97–98)	823	97 (96–98)	85	96 (95–97)	0.78 (0.59–1.02)	0.07
ASR/Corail	120	2.0 (0.0–4.6)	47	97 (93–100)	—	—	—	—	1.01 (0.32–3.16)	1.0
Durom/ML-Taper	197	1.3 (0.0–3.6)	19	—	—	—	—	—	1.31 (0.54–3.17)	0.6
All LDH MoM THAs	8059	2.4 (0.0–7.8)	3568	97 (97–98)	968	96 (96–97)	85	96 (95–97)	0.90 (0.74–1.10)	0.3
Conventional cemented THAs	16,978	4.1 (0.0–8.0)	12,409	97 (97–98)	7574	96 (96–97)	3034	95 (95–96)	1.0	—

CI: confidence interval; LDH MoM THA: large diameter head metal-on-metal total hip arthroplasty; N: number of operations; AR: at risk; RR: risk ratio from the Cox regression analysis (LDH MoM THAs compared to conventional cemented THAs; adjustment made for age, gender, diagnosis, and implant type).
End point is defined as revision of any component due to any reason. Survival rates were obtained from the Kaplan–Meier analysis.

Table 11 Relative risk of revision in 8059 LDH MoM THAs (original publication II).

	RR	95% CI	p value
BHR/Synergy (reference)	1.0	—	—
Durom/CLS	2.82	1.16–6.82	0.02
Durom/ML-Taper	1.61	0.54–4.83	0.4
ASR/Summit	1.42	0.61–3.31	0.4
ASR/Corail	1.30	0.35–4.82	0.7
ReCap/Bi-Metric	1.23	0.62–2.44	0.6
M2a38/Bi-Metric	0.99	0.45–2.19	1.0
Female/male	1.22	0.89–1.67	0.2
Age (<55 or ≥55 years)	0.89	0.61–1.31	0.6
Secondary/primary OA	1.08	0.65–1.79	0.8
Hospital production volume <100/≥100 procedures	1.23	0.83–1.81	0.3
Femoral head diameter			
<44 mm (reference)	1.0	—	—
45–49 mm	0.94	0.39–2.27	0.9
50–54 mm	0.88	0.39–1.98	0.8
≥55 mm	0.84	0.38–1.87	0.7

LDH MoM THA: large diameter head metal-on-metal total hip arthroplasty; OA: osteoarthritis; CI: confidence interval; RR: risk ratio.
Data are based on a Cox regression model including age (<55 or ≥55 years), gender, diagnosis, femoral head diameter (categorized as ≤44 mm, 45–49 mm, 50–54 mm, and ≥55 mm), hospital volume (<100/≥100 procedures), and the seven most common LDH MoM THA designs with BHR/Synergy as reference.

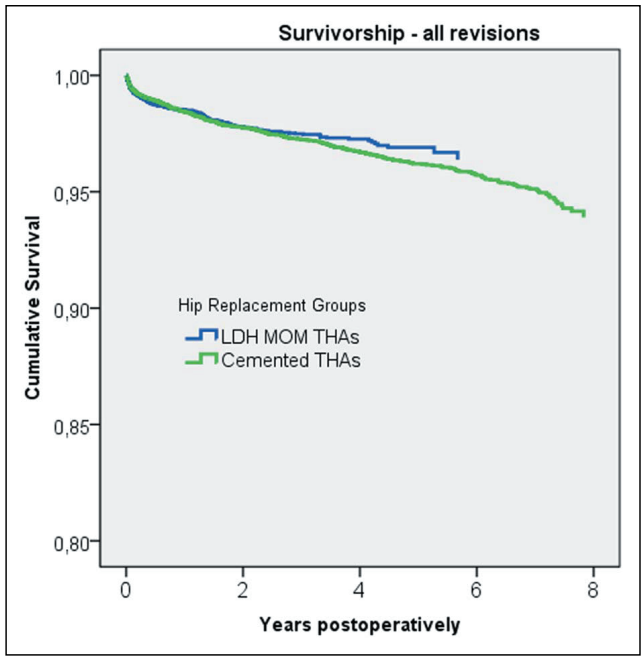

Figure 4. Cox-adjusted survival curves of 8,059 cementless LDH MoM THAs and 16,978 cemented THAs (III). The endpoint was defined as revision for any reason. Adjustment was made for gender, age and diagnosis (original publication II).

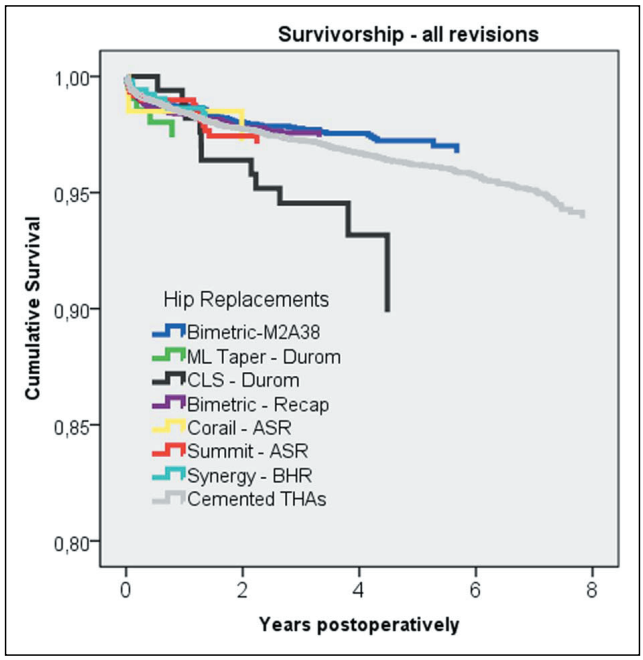

Figure 5. Cox-adjusted survival curves for 7 different cementless LDH MoM THAs (III). The endpoint was defined as revision for any reason. Adjustments were made for gender, age, diagnosis and implant(original publication II).

6. DISCUSSION

Strut grafting proved to be a reliable and safe fixation method. However, the complication rate was quite high. The vast majority of patients were pleased with the functioning and painless limb. The PPF patients are a very challenging patient group. They have often numerous comorbidities and the fracture site is very often located in an area of osteolysis. Bone quality and soft tissue healing are compromised and therefore the operative strategy should be carefully planned. All catastrophic failures were associated with poor bone quality and infection at the fracture site at the time of grafting. Results also showed that eradication of an infection is very difficult, apparently due to the poor vascularity of the grafted area. Placing the graft on the fracture site demands some kind of stripping, but should be avoided as much as possible.

In fractures around the knee implant, fractures of the distal femur that occur adjacent to a femoral component are the most difficult to treat. Fixation options are compromised by poor osteolytic bone quality, short articular segment, frequent fracture comminution and the presence of the implant itself. It is very difficult to secure the fixation. Our results showed that, in some cases, although the fracture eventually did unite, the functionality of the knee was less satisfactory. Component malposition after fracture healing may cause problems, especially to elderly people. We recommend that a distal replacement prosthesis should be considered, although strut grafting with plate fixation is a possible alternative for the fixation of distal supracondylar fractures. Although relatively good results have been achieved with the use of intramedullary nails and distal locking plates (Gliatis et al 2007, Herrera et al 2008), we believe that such procedures are not feasible if the patient has a distal, poor bone quality fractures. The more distal the fracture is, the more likely it is for complications to occur.

The specific strategy chosen to treat a PPF should depend on the quality of the remaining bone stock, type of implant, location and classification of the fracture and patient related factors, e.g., age and comorbidities. Use of cortical bone struts is a good option in fractures associated with poor bone quality. Haddad has suggested that a cortical onlay strut allograft acts as biological bone plates, serving both a mechanical and a biological function (Haddad et al. 2012). The use of cortical struts, either alone or in conjunction with a plate, led to a very high rate of fracture union, satisfactory alignment and an increase in femoral bone stock within a short follow-up. Using an allograft strut combined with a nonlocking plate, which offers the highest stiffness known, may provide superior biomechanical stability compared

with other methods (Zdero et al. 2008). Unicortical screw fixation with cables is recommended proximally in hip fractures. The cable provides bending resistance and screws maintain the length and provide torsional strength. However, this method is valuable only if the implant is securely fixed. Otherwise, a revision arthroplasty is needed.

We acknowledge that the study on structural onlay allografts for the treatment of bone deficiency in revision total hip arthroplasty has some methodological shortcomings. Our database does not include systematic data on the classification of femoral bone defects; we made the classification according to Paprosky retrospectively based on preoperative radiographs, and we had not assessed the validity of the available radiographs for interpreting graft incorporation. It is difficult to assess graft incorporation, given the amount of metal that is present, which includes not only the stem itself but also cerclage wires or Dall-Miles® cables, which cover the femur (Kim and Kim 2005). However, the assessment of the available radiographs was performed systematically by two experienced physicians (H.K. and K.M.). Union of the grafts was defined as complete trabecular bridging between the graft and host bone (Gross et al. 2003, Kim and Kim 2005). We excluded patients with a follow-up of less than 1 year. A mechanical failure rate of 4% has been reported for cementless fully porous-coated stems used with cortical strut allografts for revision THA (Paprosky et al. 1999, Kim and Kim 2005). However, the published series are small and they are not strictly comparable, since the revision methods and patient characteristics differ.

The revision methods in our clinic during the study period involved the use of long, extensively porous-coated cementless stems and the use of fluted distal fixation stems. The mechanical failure rate (aseptic loosening) in our study was 10.0%. The failed stems were all downsized and they had subsided soon after the index revision. Three stems were extensively porous-coated, and one was a distal fixation stem. Since THA revision with structural allografts is a demanding procedure, the operation should be performed by surgeons who have sufficient experience. The radiographic union rate of the strut allograft varies reportedly from 92% to 100% (Emerson et al. 1992, Gross et al. 2003, Otte et al. 2006). The grafts pass the phases of union, revascularization, remodeling and maturation. The entire sequence takes 3–5 years (Head et al. 2000). In this study, 92.5% of the allografts were incorporated into the osseous structure. The three graft nonunions were associated with one failed revision stem and one PPF. Partial resorption of the strut during the follow-up of one patient did not lead to malpositioning of the femoral stem or to reoperation. The union and complication rates of the strut graft were similar regardless of the fixation method of the revised stem (whether cemented or cementless). The potential problems associated with excessive use of allografts are devascularization of the

proximal femur, increased risk of infection, increased time in surgery and increased cost (Kim and Kim 2005). The postoperative infection rate after revision THA with strut allografts varies from 6% to 11% (Kim and Kim 2005,). The infection rate in this study was 10.0%. Our patients were old, had several medical problems and needed multiple surgical interventions. Strut graft fixation with cables is currently a relatively fast operation compared to the total operation time of a revision THA. However, in contrast to patients with PPFs, these patients are prepared for surgery on an elective basis. The infection risk may be increased with massive strut allografts.

Seven of the 40 patients had RA. Four of 7 (57.1%) of the rheumatoid patients experienced at least one complication; the corresponding rate among the patients with OA was only 25.9%. The overall bone quality of RA patients is usually weaker than of OA patients due to the disease itself and chronic medication with glucocorticosteroids. The total number of patients was small, and statistical comparisons between the OA and RA groups were not possible.

The strut grafts are removed from the femur or tibia in connection with other organ banking procedures of cadaver donators soon after death. Strictly aseptic conditions are maintained. The method involves ethics and economics. Since usually other organs of the cadaver are also removed simultaneously for recipient use (heart, lungs, liver, kidneys, corneas), the ethical issues are manageable. Having said this, we nevertheless need to be reassured that the use of transplanted organs is in full agreement with the donor's lifetime wish and with the family of the departed. Allografting is expensive. Still, organ transplants and tissue banking are an important part of the modern treatment of severe diseases.

There are publications reporting good long-term results of femoral impaction bone grafting in the treatment of bone deficiency in connection with revision THA (Schreus et al. 2006, Ornstein et al. 2009, Kerboull et al. 2009, Lamberton et al. 2011). However, these reports are often generated by clinics involved in developing the techniques (Schreus et al. 2006, Lamberton et al. 2011). On the other hand, there are several reports of complications due to femoral impaction bone grafting, especially of fractures and of massive subsidence of the stem (Elderidge et al. 1997, Masterson et al. 1997, Pekkarinen et al. 2000). Our own experience is similar to the latter. The use of modular proximal femoral reconstruction prostheses ("megaprostheses") is an option for treating massive metadiaphyseal bone loss, and recent reports claim quite good results. However, infections and dislocations still constitute a problem (Sewell et al. 2010, Gebert et al. 2010). Our experience is that the indications for using these reconstruction prostheses are not identical with those for revision with strut grafts or impaction bone grafting. In our hands, reconstruction prostheses are best used as salvage implants under nonneoplastic conditions.

In conclusion, the use of cortical onlay allografts provides a feasible option for restoring the integrity of the proximal femur in revision THA. However, our retrospective results show a high percentage of complications, especially among female patients with RA. Since the operative procedure is rather demanding, the surgeon performing these operations should be appropriately experienced. We believe that the early mechanical stabilizing effect of the strut grafts contributes crucially to a satisfactory outcome for most patients.

We found that cementless LDH MoM THA had comparable short-term survivorship as cemented THA at a nationwide level. However, in female patients aged 55 years or above, cementless LDH MoM THA performed inferiorly. Furthermore, implant design affected the revision rates. The dislocation tendency was much higher (over sevenfold) in the conventional THA group than in the LDH MoM THA group. This may explain most of the differences in revision rates between cemented and cementless implants. The fracture risk was prominent (twofold) when cementless implants were used.

We acknowledge that this study has some methodological shortcomings. We were not able to perform radiological analyses, which could have detected silent osteolysis or adverse biological reactions linked to MoM articulation (Grammatopoulos et al. 2009, Ollivere et al. 2009)). Furthermore, we are not aware of the blood chromium or cobalt values of the MoM patients. Patients in the LDH MoM THA group had a lower mean age than patients in the conventional THA group. There were also more male patients in the LDH MoM THA group. These matters were adjusted for as far as possible by the use of regression models.

The follow-up time was short. With longer follow-up, other reasons for revision—and especially those related to wear and ARMD—might certainly change the relative distribution of revisions. The total number of revisions was also relatively low, permitting only a minimum of stratified analysis and increasing the sensitivity to random effects of single revision cases.

Recent reports from national joint replacement registers have shown that revision rates are higher for the LDH MoM THAs compared to conventional arthroplasty (Lie et al. 2004, AOANJRR 2013). According to the Australian arthroplasty register, the cumulative revision rate of LDH MoM THAs (head size >40 mm) in 5 years was 6.4% (CI = 5.5–7.4) (11). In our study, the 5-year survival of LDH MoM THAs was 96% (CI = 96–97), which is slightly higher than that published from Australia. The adjusted risk ratio for revision between LDH MoM THAs and conventional cemented THA did not differ significantly in our study. However, implant design did influence revision rates. Two designs, namely, M2a38/ Bi-Metric and ReCap/Bi-Metric, were

used in 82% of all cases. At present, the LDH MoM M2a38/Bi-Metric and ReCap/ Bi-Metric implants have performed well in Finland. This is in accordance with the findings from the Australian register of the Recap-cup with M2a head surface.

Register data from Australia have revealed an increased revision rate for women compared to men when LDH MoM THA is used (AOANJRR 2013). In our analysis, female patients aged 55 years or more who have undergone cementless LDH MoM THA had a higher risk of revision compared to cemented THA. In the short term, elderly women with compromised bone quality are prone to PPFs and early subsidence of the cementless stem. The supposed advantage of cementless implants is indeed the long-term durability of implant fixation. Femoral head size was not independently associated with the revision risk in our study. In the Australian register data, a larger metal/ metal head size (>32 mm) was associated with a higher risk of revision than a smaller metal/metal head size (≤32 mm) (AOANJRR 2013). However, the most often used cup in Australia was ASR, and the third most often used cup was the Durom. In our opinion, these LDH MoM THAs yield, as is known, poor results (Langton et al. 2010, Long et al. 2010) and this makes the results of the whole group of larger head size worse.

With respect to experience, we used a limit of 100 LDH MoM THAs to separate low-volume hospitals from high-volume hospitals. There was a tendency that the risk of revision was reduced in high- volume hospitals, but this finding was not statistically significant.

Survival rates of 95% – 100% for 5 – 15 years of use have been reported for the Bi-Metric stem (Marshall et al. 2004). The amount of ARMD related to M2a38 or Recap acetabular components is currently low in Finland. This is in accordance with Australian findings (AOANJRR 2013). Our data is the largest series we are aware of concerning M2a38 and Recap LDH MoM THAs. However, it is common that wear takes its toll by 7 – 10 years and sets the limit to THA survival (Mäkelä et al. 2008). A longer follow-up is needed to estimate the true value of Biomet metal-on-metal bearings.

Survival rates of 98% – 99% for follow-ups between 13 and 17 years have been reported for the CLS stem (Müller et al. 2010, Biemond et al. 2011). The evidence of the ML-Taper stem is scarce, although excellent long-term results have been published for similar cementless tapered titanium stems (McLaughlin et al. 2010). According to current data, the ML-Taper stem may perform better with the Durom cup than the CLS stem. However, the follow-up time for the Durom/ML-Taper has been shorter than for Durom/CLS. Early fixation failure of the Durom cup with a smooth porous coating and Metasul MoM bearing surfaces has been reported (Long

et al. 2010), although not all the results have been that poor (Mertl et al. 2010). We have experienced fixation failure of the Durom cup.

Survival rates of 97% for follow-up times of 5 – 20 years have been reported for the Corail stem (Vidalain 2011). The short-term results of the Summit stem have been satisfactory (Garcia-Cimberlo et al. 2010). The short-term results of the ASR cup have been poor due to ARMD, although most of these results are related to hip resurfacing arthroplasty (Johanson et al. 2010). Most of the ASR cups (both cementless LDH MoM THAs and HRAs) in Finland have been used by the Coxa Hospital in Tampere, which is one of the largest hip arthroplasty centers in Europe. Although the ASR cups have been implanted by high-volume surgeons in Finland, the outcome has not been satisfactory (Seppänen et al. 2012). In the present study, the short-term survival of the cementless ASR LDH MoM THA with Corail and Summit stems was satisfactory. However, ARMD problems related to ASR LDH MoM THA surgery may well be expected.

The mid-term survival of the cementless Synergy stem has been 100% for an average follow-up time of 75 months (Nishino et al. 2008)). The literature presents mainly results on the use of the BHR cup as a hip resurfacing device. Medium-term survival of the BHR device has been 91% – 97% for a follow- up time of 6 – 10 years (Reito et al.2011, Treacy et al. 2011, Baker et al. 2011). In the present study, the short-term population-based survival of the BHR/Synergy was comparable to that of the conventional cemented THA.

The most common reason for LDH MoM THA revision in Australia was aseptic loosening followed by infection and dislocation (AOANJRR 2013). In our study, the most common reason for revision was aseptic loosening of both components (21% of all cases, 42 out of 202 revisions). Furthermore, there were 41 revisions for PPF (20%) and 34 cases of aseptic loosening of the cup only (17%). Totally, 93 out of 202 cementless LDH MoM THA revisions (46%) recorded in the Finnish register were performed for aseptic loosening. Many of the early problems of aseptic loosening in Finland are due to early instable cups due to technical failures or smooth porous coating. Perioperative and postoperative periprosthetic femoral fractures are a major problem with cementless press-fit stems. Nevertheless, the revision risk of the best cementless implant (the M2a38/Bi-Metric) was lower than that of the conventional cemented implants. The purported benefit of cementless fixation is avoidance of late aseptic loosenings.

There were 11 revisions due to dislocation in the LDH MoM THA group (0.1% of all LDH MoM THAs) and 175 in the THA group (1.0% of all THAs). The relatively high dislocation rate of THA must not be forgotten when comparing different devices.

ARMD is a notorious disadvantage associated with MoM articulations (Grammatopoulos et al. 2009, Ollivere et al. 2009). The Finnish Arthroplasty Register notification form does not at this stage ask specifically about these bearing surface complications. Some of these LDH MoM THAs metal bearing complications are probably coded in the Finnish register as revisions performed for "other reason." However, there were only eight LDH MoM THA revisions performed for "other reason." It may be that over the past couple of years, surgeons have not yet been as familiar with this metal bearing problem as today and some of these complications may have been coded falsely as loosening or malposition. Although the short-term results of the LDH MoM THA were comparable to those of conventional cemented THAs, a longer follow-up time is needed to detect the true incidence of revisions for ARMD. There is a lag time before register-based analyses detect early problems of new implants.

In our hospital register based study, 3 of 74 patients (3 of 80 hips) had undergone a revision operation because of ARMD. 8 additional patients (8 hips) were considered to have definite ARMD during a mean follow-up time of 6 years. Furthermore, 29 patients (32 hips) had probable or possible ARMD. Thus, 43 of 80 hips had a definite, probable or possible ARMD. Based on these data, the continued use of the ReCap-M2a-Magnum device cannot be encouraged. Clicking, swelling, a sensation of subluxation and a poor or fair Oxford hip score were associated with definite ARMD but not with probable or possible ARMD. Asymptomatic patients with a small fluid collection in MRI and slightly elevated serum metal ion levels may not need immediate revision surgery. A systematic follow-up of these patients including metal ion levels, MRI and symptom questionnaires is advisable.

Concern has been raised recently about the high failure rate of LDH MoM THA due to ARMD. In April 2010, the British Orthopaedic Association issued an alert to its members concerning LDH MoM THA (MHRA 2010). In May 2011, the American Food and Drug Administration ordered 21 companies to introduce and uphold post-marketing surveillance of MoM THA (FDA 2011).In May 2012, the Finnish Arthroplasty Association recommended that LDH MoM THAs should be discontinued (FAA 2012).

The first reports of early clinical success of ReCap-M2a-Magnum THA (Kostensalo et al. 2012, Meding et al. 2012) and ReCap-Magnum hip resurfacing arthroplasty (HRA) (Gross and Liu 2012, van der Weegen et al. 2012) were promising. The short-term survival of the ReCap-M2a-Magnum THA was comparable to that of conventional cemented THA based on data from the Finnish Arthroplasty Register. The cumulative revision percent after ReCap-M2a-Magnum THA at 5 years (3.6, CI: 2.4–5.3) is significantly lower than that of ASR THA (DePuy) (22, CI: 21–24) according to Australian registry data (AOANJRR 2012). Cormet THA (Corin) and BHR

THA (Smith and Nephew) do not have a lower revision risk than ReCap-M2a-Magnum THA at 5 years (6.0, CI: 4.1–8.7 and 5.5, CI: 4.5–6.7, respectively) (AOANJRR 2012). However, registry studies are not able to detect effectively early implant failures, since radiological data on osteolysis and ARMD emerge late. Early clinical trials may focus solely on radiographic findings.

Bosker et al. (2012) reported an incidence of CT/MRI-verified pseudotumors of 39% in 109 unilateral M2a-Magnum-ReCap THAs and a subsequent revision rate of 12%. These results are in accordance with our findings. We based the radiological diagnosis of fluid collections and soft tissue masses solely on MRI, except in 3 cases. 1 patient had a loose stem by radiography and a poor OHS score (24 points). She was revised with a Biomet Reach revision stem before the MRI was done. Her serum chromium and cobalt levels were 0.8 µg/L and 1.0 µg/L, respectively. There were no peroperative signs of ARMD at the stem revision. 1 patient underwent a bilateral CT scan rather than MRI because of a pacemaker and there was no evidence of ARMD. Her serum chromium and cobalt levels were 2.1 µg/L and 2.1 µg/L. MRI-verified fluid collections and soft tissue masses were more common in our study than CT-verified fluid collections and soft tissue masses in the study of Bosker et al. (2012). Of note, we based our ARMD diagnosis not only on MRI findings but also on serum metal ion levels, although elevated serum metal ion levels may not be considered to be a true reaction per se. The clinical relevance of asymptomatic fluid collections detected by MRI in patients with normal metal ion levels is unclear. The prevalence of MRI-verified pseudotumors in hip resurfacing arthroplasty (HRA) patients with a painful hip is similar to that of asymptomatic HRA patients (Hart et al. 2012).

The high rate of fluid collections seen on MRI and the soft tissue destruction at the time of revision found in our patients is a cause for great concern. The indications and timing for revision surgery are not clear. Revision surgery should be performed under all circumstances before necrosis of the gluteal muscles ensues.

A limitation of our study was that the unrevised ARMD hips were not clearly defined and stated. Persistent pain after LDH MoM THA is associated with higher serum metal ion levels than 8 µg/L (Lardanchet et al. 2012). There were 2 hips in our study that we considered to have ARMD due to high serum ion levels despite normal MRI findings (table 7). These 2 patients had symptoms, and strict follow-up was scheduled. Another limitation was that we included patients with bilateral metal-on-metal implants. Bilateral metal-on-metal implants may introduce bias to metal ion analyses. However, the cutoff level was raised from 8 µg/L – the level suggested by Lardanchet et al. (2012) – to 10 µg/L because we included bilateral MoM hips. We used a metal ion level of ≥ 5 µg/L as a criterion for probable or possible ARMD. The risk of a radiological pseudotumor in unilateral ReCap-M2a-Magnum THA patients with

serum cobalt levels > 5 µg/L is 4-fold compared to patients with serum cobalt levels < 5 µg/L (Bosker et al. 2012). Due to potential bias caused by inclusion of bilateral MoM devices, we performed further analyses to assess bilaterality. Bilaterality was not associated with ARMD (table 8). 2 of our 11 definite ARMD patients had, in fact, normal serum ion levels (< 5 µg/L). 1 of these 2 patients needed revision and ARMD was verified at surgery (tables 6 and 7). Normal metal ion levels may thus be misleading when ARMD is diagnosed, and metal ion measurements alone should not be used for ARMD screening (Macnair et al. 2013). Another limitation of the present study was that the approximate size of the fluid collections by MRI was used to define definite ARMD but not probable or possible ARMD. All fluid collections with a solid component and other soft tissue masses were considered to be definite ARMD. The differentiation between MRI findings of ≥ 50 mm in any dimension and < 50 mm is artificial. We therefore hypothesize that a fluid collection of ≥ 50 mm in any dimension is a clinically significant amount of fluid with regard to a diagnosis of AMRD. This study was also limited by a lack of CT-based evaluation of implant position. It is also possible that the fluid detected by MRI may have collected for reasons other than ARMD.

The association of the risk factors with ARMD was analyzed using multinomial logistic regression, because ARMD consisted of 3 groups (definite cases, probable or possible cases, and no ARMD). The results were expressed by odds ratios (ORs). When interpreting these results, one must keep in mind OR is not equivalent to relative risk (RR) (Schmidt and Kohlmann 2008). There were more female patients in the possible/probable ARMD group than in the group with no ARMD, and the patients in the former group were also older (table 8). This is probably a chance finding, but it may need to be re-addressed in other studies. Likewise, the finding of an effect of laterality on ARMD occurrence was probably a chance finding.

Metal ion release differs between the various models of LDH MoM THA. An adapter sleeve made of titanium, such as the one used with the ReCap-M2a-Magnum THA, probably does not contribute to the release of cobalt ions. Of 4 LDH MoM THAs (Biomet, DePuy, Smith and Nephew, Zimmer), the Biomet implant releases least cobalt (Lavigne et al. 2011). However, extensive corrosion on the taper and trunnion, contributing to the formation of metal debris, has been encountered in ReCap-M2a-Magnum THA revisions (Bosker et al. 2012). Well-positioned ReCap-M2a-Magnum components may be associated with increased production of debris from this junction. There is no association between pseudotumors detected with CT/MRI and the CT-detected position of ReCap-M2a-Magnum components (Bosker et al. 2012), or between pseudotumors detected with MRI and the CT-detected HRA cup position (Hart et al. 2012). These results are in accordance with our findings. In 2 of the 3 ARMD revisions that we performed in this study, the cold-welded Magnum head

could not be detached from the adapter and trunnion. Our experience supports the assumption that extensive corrosion on the taper and trunnion of the ReCap-M2a-Magnum device contributes to metal debris. Incidentally, there was a patient with sepsis and a deep prosthetic infection caused by Staphylococcus aureus. The cold-welded Magnum head could not be detached from the adapter and trunnion in this case either, but there were no other signs of ARMD. The chromium and cobalt levels were 6.3 µg/L and 7.7 µg/L, respectively. After 2 years, the sepsis relapsed. At surgery, the finding of a cold-welded Magnum head was the same. This patient was considered to have a possible or probable ARMD.

Although the systematic follow-up carried out at our institution did not reveal any clinical signs of cobalt poisoning, it seems reasonable to assume that elevated systemic concentrations of Co-ions due to wear debris pose a health issue for patients with MoM bearings.

7. CONCLUSIONS

Our study leads to following conclusions:

I. The overall union rate was 91%. Use of cortical bone struts is a good option in surgery of fractures associated with poor bone quality.

II. The use of the cortical onlay allografts provides a feasible option for restoring the integrity of the proximal femur in revision total hip arthroplasty, but the complication rate is high, particularly in female patients with rheumatoid arthritis.

III. Overall, cementless large diameter head metal-on-metal total hip arthroplasty had a short- term survivorship comparable with cemented total hip arthroplasty. However, in female patients aged 55 years or above, cementless large diameter head metal-on-metal total hip arthroplasty showed inferior results. The implant design impacted also on revision rates. Longer follow-up is needed to assess the success of large diameter head metal-on-metal total hip arthroplasty.

IV. ARMD is common after ReCAp-M2a-Magnum total hip arthroplasty, and I discourage the use of this device. Asymptomatic patients with a small fluid collection on MRI may not need immediate revision surgery but must be followed up closely.

8. ACKNOWLEDGEMENTS

This study was carried out in Department of Orthopedics and Traumatology of Turku University Hospital. This study was partly financially supported by Research Grant of Turku University Hospital (EVO).

I owe my deepest and most humble gratitude to my supervisor Adjunct Professor Keijo Mäkelä. This thesis project would not have been possible to carry out without his inspiring guidance. Keijo has done an enormous amount of work to renovate the Finnish Arthroplasty Register. His knowledge of arthroplasty registers is unparalleled. He has an admirable amount of expertise for doing orthopedic research and still he has enough time for answering any questions. His suggestions have always been very focused and clear minded.

I also wish my most sincere gratitude and appreciation to my other supervisor Adjunct Professor and former chief of the Department of Orthopedics and Traumatology of Turku University Hospital, Petri Virolainen. He has always encouraged me throughout the whole long lasting project, even in despair. His attitude for creating an open atmosphere, where ideas and skills are shared amongst all in our department is admirable.

I also thank Adjunct Professor and the new chief of the Department of Orthopedics and Traumatology of Turku University Hospital, Ville Äärimaa for his support over the years that we have collaborated.

I am grateful to the reviewers of this thesis, Adjunct Professor Jorma Pajamäki and Adjunct Professor Hannu Miettinen. Your criticism and constructive suggestions have been excellent. Without them this thesis would not have been as coherent as it is now. I am privileged to get feedback from such esteemed and clinically skillful colleagues.

The co-workers of original studies, Matti Seppänen, Mika Junnila, Hannes Keemu, Juho Rantakokko, Ville Äärimaa, Juha Kukkonen, Ville Remes and Antti Eskelinen have all contributed and encouraged this work. Without their support this thesis would not have been possible. In my absence from clinical work, Mika Junnila, Matti Seppänen, Hannes Keemu and Mikko Karvonen, have shared my clinical burden on their shoulders.

BCB-Medical team and Joni Hirviniemi have had an important role in gathering data from Implant DB and Tissue DB. I thank you for that.

My deepest gratitude for accurate statistical analysis for the thesis goes to Tero Vahlberg, Pekka Pulkkinen, Mari Koivisto, Tuukka Pölönen and Teija Stormi. Adjuct Professor

Robert Paul is credited for his linguistic expertise. I also thank Adjunct Professor Kimmo Mattila and Esa Tuominen for their excellent radiological analyses.

I would like to express my deepest gratitude to all colleagues working in Turku University Surgical Hospital. Thank you for your collaboration, numerous intriguing discussion sessions and for your friendship. This hospital would not have been the same without you.

I equally would like to express my gratitude to the ward and OA nurses from Turku University Surgical Hospital for your warm friendship and collaboration over the years.

I also want to express my special gratitude to Adjunct Professor Eero Gullichsen, Niko Strandberg and Jani Toukosalo for numerous hearth warming discussions, scientific or not, during the Solbacken fishing sessions in Porvoo, Jedi-knights forever. My Achilles tendon thanks especially Niko Strandberg and Kari Isotalo for their skillful hands.

I also want to thank my family: Miia, Miisa, Mimi and Miska for your patience. I want to thank my parents, Risto and Terttu for your love and support. I also want to thank my brother Jussi and his family.

This thesis would have been more difficult without abundant household help from my parents-in-law Jussi and Maija. I am more than grateful for that. I also want to express my gratitude for Marko and Tuuli for their friendship.

9. REFERENCES

AJRR American Joint Replacement Registry. 2014. http://teamwork.aaos.org/ajrr/default.aspx

AOANJRR Australian Orthopaedic Assosiation. National Joint Replasement Registry. 2013 *https://aoanjrr.dmac.adelaide.edu.au/annual-reports-2013*

NJR National Joint Registry 2014 Uk *http://www.njrreports.org.uk/Portals/0/PDFdownloads/NJR%2011th%20Annual%20Report% 202014.pdf*

NAR Norvegian Arthroplasty Register 2014. *http://nrlweb.ihelse.net/Rapporter/Rapport2014.pdf*

SAY Suomen artroplastiayhdistys 2012 *www.suomenartroplastiayhdistys.fi*

Suomen tekonvelrekisteri 2011 *http://www.julkari.fi/bitstream/handle/10024/104402/Tr09_13.pdf?sequence=1* SHAR Svenska Höftregistertet 2013. *http://www.shpr.se/sv/Publications/DocumentsReports.aspx*

Ahmad, Z. 2006., Principles of Corrosion Engineering and Corrosion Contol. *Butterworth- Heineman.* p 2.

Aho, A.1973., Allogenic joint transplantation in the dog. *Annales chirurgiae et gynaecologiae Fenniae*. 62 226-33.

Alberton, G.M., High, W., A, anf Morrey, B.F., 2002. Dislocation after Revision Total Hip Arthroplasty: An Analysis of Risk Factors and Treatment Options. *The Journal of Bone and Joint Surgery.* 84A, 10, pp1788-92

Althuizen, M.N., v Hoof,M.L., v.d. Berg –v.Erp, S.H., v. Limbeek, J., and Nijhof, M.W. 2012. Early failures in large head metal-on-metal total hip arthroplasty. *Hip International.* 22, 6, pp 585-691

Amstutz, H.C., Beaule, P.E., Dorey. F.J., Le Duff, M.I., Cambell, P.A., Gruen, T.A., 2004. Metal-on- Metal Hybrid Surface Arthroplasty: Two to Six-Year Follow-up Study. *Journal of Joint and Bone Surgery. 86A, pp 28-39*

Amstutz, H.C., Grigoris, P., Dorey, J. 1998. Evolution and future of surface replacement of the hip. *Journal of Orthopeadic Science, 3, pp 169-186*

Archibeck, M.J., Jacobs, J.J., Roebuck, K.A., and Glant, T., 2000. The basic Science of Periprosthetic wear. *The Journal of Bone and Joint Surgery.* 82A, 10, pp 1478-89.

August, A.C., Aldham, C.H., and Pynset, P.B., 1986. The McKee-Farrar hip arthroplasty. A long-term study. *The Journal of Bone and Joint Surgery. British volume.* 68B, 4, pp520-527

Azuma, T., Yasuda, H., Okagi, K., and Sakai, K., 1994. Compressed allograft chips for acetabular reconstruction in revision hip arthroplasty. *The Journal of bone and joint surgery. British volume*, 76B, pp.740–744.

Baer, W.S. 1926 Arthroplasty of the Hip, *AAOS, Atlanta April 27 1926*

Baker, R.P., Pollard, T.C.B., Estaugh-Waring, S.J., and Bannister, G.C., 2011. A medium-term comparison of hybrid hip replacement and Birmingham hip resurfacing in active young patients. *The Journal of Bone and Joint Surgery.* 93B, 2, pp158-163

Beaulé, P.E., Kim, P.R., Hamdi, A. and Fazekas, A. 2011. A Prospective Metal Iion Study of Large Head Metal-on-Metal Bearing: A Matched-Pair Analysis of Hip Resurfacing Versus Total Hip Replacement. *Orthopaedic Clinics of North America. 42, pp 251-257*

Berry, J.D., 1999. Epidemiology. Hip and Knee. *Orthopaedic Clinics of North America.* 30, Pp 183-190

Berry, J.D., 2003. Periprosthetic Fractures Associated with Osteolysis. A problem on the Rise. *The Journal of Arthroplasty.* 18, 3, supp 1, pp 107-111

Berry, D.J., Abdel, M.P. and Callaghan, J.J. 2014. What Are the Current Clinical Issues in Wear and Tribocorrosion. *Clinical Orthopaedics and Related Research.* [Epub ahead of print]

Berry, J.D., Lewallen, D.G., Hanssen,A.D., and Cabanela, M.E., 1999. Pelvic discontinuity in Revision Total Hip Arthroplsaty. *The Journal of Bone and Joint Surgery.* 81A, 12, pp 1692-1702.

Biemond, E.J., Pakvis, D.F.M., van Hellemond, G.G., and Buma, P., 2011. Long term survivorship analysis of the cementless Spotorno femoral component in patients less than 50 years in age. *The Journal of Arthroplasty.* 26, 3, pp 386-390.

Bisschop, R., Boomsma, M.F., and Van Raay, J., 2013. High prevalence of pseudotumors in patients with a Birmingham Hip Resurfacing prosthesis. *The Journal of Bone and Joint Surgery.* 95A, pp.1554–1560.

Bolland, B., Gardner, E., Rogues, A., Maul, C., Culliford, D., Zeineh, N., and O'Hara, L., 2013. High Taper Sleeve Wear and and Failure Associated with Synergy/BHR Large Diameter Metal on Metal Total Hip Replacement. *Orthopaedic Proceedings, Supp 434, 17*

Bosker, B.H., Ettema, H.B., Boomsma, M.F., Kollen,B.J., Maas, M., and Verheyen, C.C.P.M., 2012. High

incidence of pseudotumour formation after large-diameter metal-on-metal total hip replacement: A prospective cohort study. *Journal of Bone and Joint Surgery. British Volume*. 94B, pp.755–761.

Boutin, P., 2000. Total Hip Arthroplasty using a ceramic prosthesis. *Clinical Orthopaedics and Related Research, 379, pp 3-11.*

Bozic, K.J., Kurtz, S.M., Lau,E., Omn, K., Vail, T.P., and Berry, D., J., 2009., The Epidemiology of Reviosin Total Hip Arthroplasty in the United States. *Journal of Bone and Joint Surgery.* 91A, 1, pp 128-133

Brady, O.H., Garbuz, S.D., Masri, B.A., and Duncan C.P., 2000. The reliability and Validity of the Vancouver Classification of Femoral Fractures After Hip Replacement. *The Journal of Arthroplasty. 15, pp 59-62*

Breuch, S, and Malchau H., 2005. The Well-Cemented Total Hip Arthroplasty. Theory and Practise, *Springer, pp 52-59.*

Brown, N.M., Foran, J.R.H., Della Valle, G.J., Moric, M., Sporer, S.M., Levine, B.R., and Paprosky, W.G., 2014. The Inter-Observer and Intra-Observer Reliability of the Paprosky Femoral Bone Loss Classification System. *The Journal of Arthroplasty.* 29, pp 1482-84

Canadian Hip Resurfacing Study Group. 2011. A Survey on the prevalence of Psudotumours with Metal-on-Metal Hip Resurfacing in Canadian Academic Centers. *Journal on Bone and Joint Surgery.* 93 Suppl 2, pp 118-120

Chandler, H., Lopez, C., Murphy, S., and van Eenenaam, D.P., 1995. Acetabular reconstruction using structural grafts in total hip replacement: a 12 ½ year follow-up. *Seminars in Arthroplasty.* 6, 2, pp 118-130

Chang, E.Y., McAnally, J.L., Van Horne, J.R., Statum, S., Wolfson, T., Gamst, A., and Chung C.B., 2012. Metal-on-Metal Total Hip Arthroplasty: Do Symptoms Correlate with MR Imaging Findings? *Radiology*. 265, 3, pp

Charnley, J.,1960. Anchorage of the femoralprothesis to the saft of the femur. *The Journal of bone and joint surgery. British volume, 42B, pp 28-30.*

Charnley, J.1960, Surgery of the hip-joint: present and future developments. *British Medical Journal. 1, 5176, pp 821-826*

Charnley, J., 1961. Arthroplasty of the hip:a new operation. *Lancet. 1, pp 1129-32.*

Chitre,A., Wynn Jones, H., Shah, N., and Clayson A., 2013 Complications of total hip arthroplasty: periprosthetic fractures of the acetabulum. *Current Reviews in Musculosceletal Medicine.* 6, pp 357-363

Chung, K-Y., Chiu, K-H, Cand Cheung K-W., 2012. Osteoradionecrosis of the acetabulum in a total hip arthroplasty: a case report. *Journal of Orthopaedic Surgery.* 18, 1, pp110-112

Cook, R.E., Jenkins, P.J., Walmsley, P.J., Patton, J.T., and Robinson, C.M. 2008. Risk factors for Periprosthetic Fractures of the Hip: A survivorship Analysis. *Clinical Orthopaedics and Related Research.* 466, 7, pp 1652-1656

Corradi, M., Daniels, J., Ziaee, H., Alinovi, R., Mutti, A., and McMinn D.J.W., 2011. Early markers of nephrotoxicity in patients with metal-on-metal hip arthroplasty. *Clinical Orthopaedics and Related Research*, 469, pp.1651–1659.

CRC Handbook of Chemistry and Physics 2014, 95th edition. Taylor & Francis pp 7-48.

Cuckler, J.M., 2005. The rationale for Metal-on-metal Total Hip Arthroplasty. *Clinical Orthopaedics and Related Research. 441, pp 132-136*

Cumming, R.G., Nevitt, M.C., and Cummings S.R., 1997. Epidemiology of Hip Fractures. *Epidemiologic Reviews.* 19, 2, pp 244-256

D'Antonio, J.A., McCarthy, J.C., Bargar, W.L., Borden, L.S., Capello, W.N., Collis, D.K., Steinberg, M.E., and Wedge, J. H.,1993. Classification of femoral abnormalities in total hip arthroplasty. *Clinical Orthopaedics.* 293, pp 133-139.

D'Antonio, J.A., Capello, W.N., Borden, L.S., Bargar, W.L., Bierbaum, B.F., Boettcher, W.G., Steinberg, M.E., Stulberg, S.D., and Wedge, J., 1989. Classification and Management of Acetabular Abnormalities in Total Hip Arthroplasty. *Clinical Orthopaedics and Related Research.* 244, pp 126-137.

Daras M., 2009. Total Hip Arthroplasty in Young Patients With Osteoarthritis. *American Journal of Orthopedics, 38, pp 125-129.*

Davidson, D., Pike, J., Garbuz, D., Duncan, C.P., and Masri B.A., 2008. Intraoperative Periprosthetic Fractures During Total Hip Arthroplasty. Evaluation and Management. *The Journal of Bone and Joint Surgery.* 90A, 9, pp 2000-12

Davies, A.P., Willert, H.G, CAmbell P.A., Learmonth, I.D., and Case C.P., 2005. An Unusual Lympholytic Perivascular Infiltration in Tissues Around Contemporary Metal-on-Metal Joint Repalcements. *The Journal of Bone and Joint Surgery, 87A, pp 18-27*

Della Valle, G.J., Berger,R.A., Rosenberg, A.G., Galante, J.O., Cementless acetabulars reconstruction in revision total hip arthroplasty. *Clinical Orthjopedics and Related Research.* 420, pp 96-100

Della Valle, C.J., Momberger, N.G., and Paprosky, W.G., 2003. Periprosthetic Fractures of the Acetabulum

Associated with Total Hip Arthroplasty. *Instructional Course Lectures.* 2003, 52, pp 281-290.

Della Valle, G.J., and Paprosky W.G., 2003. Classification and an Algorithmic Approach to the Reconstruction of Femoral Deficiency in Revision Total Hip Arthroplasty. *The Journal of Bone and Joint Surgery.* 85A, supp 4. pp 1-6.

De Smet, K.A., De Haan, R., Calistri, A., Cambell, P.A., Ebramzadeh, E., Pattym, C., and Gill, H.S., 2008. Metal Ion Measurement as a Diagnostic Tool to Identify Problems with Metal-on-Metal Hip Resurfacing. *The Journal of Bone and Joint Surgery.* 90, supp 4., pp 202-208

De Smet, K.A., Van Der Straen, C. Van Orsouw, M., Doubi R.,Backers, K. and Grammatopoulos G. 2011. Revisions of Metal-on-Metal Hip Resurfacing: Lessons Learned and Improved Outcome. *Orthopaedic Clinics of North America.* 42, pp 259-269

Dorr, L.D., Zhinian, W., Longjohn, D.B., Dubois, B., and Murken, R. 2000. Total Hip Arthroplasty with Use of the Metasul Metal-on-Metal Articulation. *Journal of bone and Joint Surgery. 82A, pp 789-797,*

Dumbleton, J.H., and Manley, M., 2005. Metal-on-metal Total Hip Replacement. What Does the Literature Say? *The Journal of Arthroplasty, 20, pp 174-188.*

Duncan, C.P., Haddad, F.S., 2014. The Unified Classification System (UCS): improving our understanding of preiprosthetic fractures. *The Journal of Bone and Joint Surgery. British volume.* 96B, 6, 713-716

Duncan, C.P., and Masri, B.A., 1995. Fractures of the Femur after Hip Replacement. *Instructional Corse Lectures.* 45, pp 293-303

Drexler, M., Dwyer, T., Chakravertty, R., Backstein, D. Gross, A.E., and Safir, O., 2014. The outcome of Modified Extended Trochanteric Osteotomy in Revision THA for Vancouver B2/B3 Periprosthetic Fractures of the femur. *The Journal of Arthroplasty.* Article in press

Ebramzade, E., Campell, P.A., Takamura, K.M., Lu, Z., Sangiorgio, S.N., Kalma, J.J., Smet, K.A., and Amstutz, H.C., 2011. Failure Modes of 433 Metal-on-Metal Hip Implants: How, Why and Wear.*The Orthopaedics Clinics of North America.*42, pp 241-250

Elderidge, D.J., Smith, E.J., Hubble, M.J., Whitehouse, S.L., and Learmonth, I.D., 1997. Massive early subsidence following femoral impaction grafting. *The Journal of Arthroplasty.* 12, 5, pp 535-540

Emerson, R.H., Malinin, T.I., Cuellar, A.D., Head, W.C., and Peters, P.C., 1992. Cortical strut allografts in the reconstruction of the femur in revision total hip arthroplasty. A basic science and clinical study. *Clinical Orthopaedics and Related Research.* 285, pp 35-44.

Engelbrecht, E., Heinert, K., 1987. Klassifikation und Behandlungsrichtlinien von Knochensubstanz-verlusten bei Revisionsoperationen am Knochen-substanzverlusten bei Revisionsoperationen am Huftgelenkmittelfristige Ergebnisse. Primare und Revisionsalloarthroplastik Endo-Klinik. Berlin, Springer-Verlag.

Eskelinen A., Remes, V., Helenius, I., Pulkkinen, P., Nevalainen, J., and Paavolainen, P., 2006. Uncemented total hip arthroplasty for primary osteoarthritis in young patients. A mid- to long-term follow-up study from the Finnish Arthroplasty Register. *Acta Orthopaedica, 77, pp 57-77.*

Eustace, S., Goldberg, R., Williamson, D., Melhem,E.R., Oladipo, O., Ycel E.K., and Jara, H., 1997. MR imaging of soft tissues adjacent to orthopaedic hardware: techniques to minimize suspectibility artefact. *Clinical Radiology.* 52, pp 589-594

Fehring, T.K., Odum, S.M., Fehring, K., Springer, D.B., Griffin, L.W. and Dennos, A. 2010. Mortality Following Revision Joint Arthroplasty: Is Age a Factor? *Orthopedics. 33, 10*

Fetzer, g.B., CAllaghan, J.J., Templeton, J.E., Goetz, D.D., Sullivan, P.M., and Johnston, R.C., 2001. Impaction Allografting With Cement for Extensive Femoral Bone Loss in Revision Hip Surgery. *The Journal of Arthroplasty.* 16, 8, supp1,pp 195-202

Fink, B., Gtossman, A.,and Singer J., 2012. Hip revision Arthroplasty in Periprosthetic Fractures of Vancouver Type B2 and B3. *Journal of Orthopaedic Trauma.* 26, 4, pp 206-211.

Fitzek, O.S., Wedemyer, C., Löer, F., con Knoch, M., and Saxler G., 2006. Reinforcement of deficient femur with inlay strut grasfts in revision hip arthroplasty: a small series. *Archives of Orthopaedic and Trauma Surgery.* 126, pp 649-653

Fletcher, X., Sporer, S., and Paprosky, W., 2008. Management of Severe Bone Loss in Acetabular Revision Using a Trabecular Metal Shell. *The Journal of Arthroplasty.* 23, 7, pp 949-955

Garbuz, D.S., Tanzer, M., Greidanus, N.V., Masri B.A., Duncan, C.P., 2010. Metal-on-Metal Resurfacing versus Large-diameter Head Metal-on-Metal Total Hip Arthroplasty. *Clinical Orthopaedic and Related Research, 468, pp 318-325.*

Garcia-Cimberlo, E., Bru-Pomer, A., Garecia-Benitez, B., Hernandes-Blanco, M., and Varquero, J., 2010. Multicentric and prospective study of the Summit cementless stem. *Hip International.* Suppl. 7, 20, pp 63-69.

Garcia-Cimberlo, E., Cruz-Pardos, A., and Sanches-Sotelo, J., 2000. Low-Friction Arthroplasty in

Patients Younger Than 40 Years Old. 20- to 25- Year Results. *The Journal of Arthroplasty,* 15, pp 825-31

Gebert, G., Wessling, M., Götze, C., Gosheger, G., and Hardes, J., 2010. The Modular Universal Tumour and Revision System (MUTARS) in endoprosthetic revision surgery. *International Orthopaedics (SICOT).* 34, pp 1261-63.

Gie, G.A., Linder, L., Ling, R.S.M., Simon, J-P., Slooff, T.J.J.H., and Timperley, A.J., 1993. Impacted cancellous allografts and cement for revision total hip arthroplasty. *The Journal of Bone and Joint Surgery. British volume.* 75B, pp 14-21

Gililland, J.M., Anderson, L., Heninger, H.B., Kubiak, E.N., and Peters, C.L., 2013. Biomechanical Analysis of Acetabular Revision Constructs. Is Pelvic Discontinuity Best Treated With Bicolumnar or Traditional Unicolumnal Fixation. *The Journal of Arthroplasty.* 28, 1, pp 178-1867

Gliatis, J., Megas,P., Panagiatopoulos, E., and Lambiris, E., 2005. Midterm Results of Treatment With a Retrograde Nail for Supracodylar Periprosthetic Fractures of the Femur Following Total Knee Arthroplasty. *Journal of Orthopedic Trauma.* 19, 3, pp 164-170

Gozzard, C., Blom, A.,Taylor,A., Smith,E., and Learmonth, I. 2003. A comparison of the Reliability and Validity of Bone Stock Loss Classification Systems Used for Revision Hip Surgery. *The Journal of Arthroplasty.* 18, 5, pp 638-642

Grammatopoulos, G., Pandit, H., Kwon, Y-M., Gundle, R., McLardy-Smith, P., Beard, D.J., Murray, D.W., and Gill H.S., 2009. Hip resurfacings revised for inflammatory pseudotumor have poor outcome. *The Journal of Bone and Joint Surgery. British volume.* 91B, 8, pp 1019-24

Grammatopoulos, G., Pandit, H., Glyn-Jones, S., McLardy-Smith, P., Gundle, R., Whitwell, D., Gill, H.S., and Murray, D.W. 2010. Optimal acetabular orientation hip resurfacing. *The Journal of Bone and Joint Surgery. Br.* 92B, 8, pp 1072-1078

Greenwald, E.S., Hill, D.P., Garino, J.P. 2001. Alternative Bearing Surfaces: The Good, The Bad, and The Ugly. *The Journal of Bone and Joint Surgery. 83A, pp 68-72.*

Gross, A.E., Hutchison, C, R., 1998. Proximal Femoral Allografts for Reconstruction of Bone Stock in Revision Arthroplasty of the Hip. *Orthopaedic Clinics of North America.* 29, 2, pp 313-317

Gross, A.E., Wong, P.K.C., Hutchison, C.R., and King, A., E., 2003. Onlay Cortical Strut Grafting in Revision Arthroplasty of the Hip. *The Journal of Arthroplasty.* 18, 3, supp 1, pp 104 - 106

Gross, T.P., and Liu, F., 2012. Hip resurfacing with the Biomet hybrid ReCap-Magnum system. 7- year results. *The Journal of Arthroplsty.* 27,9, pp 1683-89.

Grübl, A.,Marker,M., Brodner, W., Giurae, A., Melsinger, V., Zehetgruber, H., and Kotz,R., 2006. Long-Term Follow-Up of Metal-on-Metal Total Hip Replacement. *The Journal of Orthopaedic Research, 25, 7, pp 841-848.*

van Haaren, E.H., Heyligers, I.C., Alexander, F.G.M., and Wuisman P.I.J.M., 2007. High rate of failure of impaction grafting in large acetabular defects. *The Journal of Bone and Joint Surgery. British volume*, 89B, 3, pp 296–300.

Haddad, F.S., Duncan, C.P., Berry, D.J., Lewallen, D.G., Gross, A.E., and Chandler, H.P., 2002. Periprosthetic Femoral Fractures Around Well-Fixed Implants: Use of Cortical Onlay Allografts with or without a Plate. *The Journal of Bone and Joint Surgery.* 84A, 6, pp 945-950

Haddad, F.S., Masri, B.A., Garbuz, D.S., and Duncan, C.P., 1999. Femoral Bone Loss in Total Hip Arthroplasty: Classification and Preoperative Planning. *The Journal of Bone and Joint Surgery.* 81A, 10, pp 1483-97

Haddad, F.S., and Rayan, F., 2009. The role of Impaction Grafting: The When and How. *Orthopedics.* 32, 9,pp 1-7

Haidukewych, J.G., Jacofsky, D.J., Hanssen, A.D., and Lewallen, D.G. 2006. Intraoperative Fractures of the Acetabulum During Primary Total Hip Arthroplasty. *The journal of Bone and Joint Surgery.* 88A, 9, pp 1952-1956.

Hargreaves, B.A., Worters, P.W., PAuly, K.B., Pauly, J.M., Koch, K.M., and Gold, G.E., 2011, Metal- Induced Artifacts in MRI. *American Journal of Roentgenology.* 197, 3, pp 547-555

Harris W.H., 2004. Conquest of a worldwide human disease: particle-induced periprosthetic osteolysis. *Clinical Orthopaedics and Related Research, 429, pp 39-42.*

Harris, W.H., 1995. The problem is osteolysis. *Clinical orthopaedics.* 311, pp 46-53

Hart, A.J., Sabah, S., Henckel, J., Cobb, J., Sampson, B., Mitchell, A. and Skinner J.A. 2009. The painful metal-on-metal hip resurfacing. *The Journal of Bone and Joit Surgery. British edition. 91B, pp 738-744*

Hart, A.J., Satchithananda, K., Liddle, A.D., Sabah, S.A., McRobbie, D., Henckel, J., Cobb, J.P., Skinner, J.A., and Mitchell, A.; w., 2012. Pseudotumors in Association with Well-Functioning Metal-on-Metal Hip Prosthesis. A Case-Control Study Using Three-Dimensional Computed tomography and Magnetic Resonance Imaging. *The Journal of Bone and Joint Surgery.* 94, 3, pp 317-325

Hartman, A., Hannemann, F., Lützner, J., Drexler, H. Günther, P. and Schmitt, J. 2013. Metal Ion Concentrations in Body Fluids after Implantation

of Hip Replacements with Meral-on-Metal Bearing . Systematic Review of Clinical and Epidemiological Studies. *PLoS One.- 8, pp 1-25*

Hauptfleisch, J., Pandir, H., Grammatopoulos, G., Gill, H.S., Murray, D., and Ostlere,S., 2012. A MRI classification of periprosthetic soft tissue masses (pseudotumours) associated with metal-on- metal resurfacing hip arthroplasty, *Skeletal Radiology.* 41, pp 149-155

Havelin, L.I., Engesaeter, L.B., Espehaug, B., Fornes, O., Lie, S.A., and Vollset, S.E., 2000. The Norwegian Arthroplasty Register. 11 years and 73 000 arthroplasties. *Acta Orthopaedica, 71, pp 337-353.*

Hayashi, A. 2008. Building a national joint replacement registry. *AAOS Now.*

Head, W.C., Malinin, T.I., Emerson, R.H., and Mallory, T.H., 2000. Restoration of bone stock in revision surgery of the femur. *International Orthopaedics (SICOT) 24, pp 9-14*

Herrera, D.A., Kregor, P.J., Cole, P.A., Levy, B.A., Jönsson, A., and Zlowodski, M., 2008. Treatment of acute distal femur fractures above a knee arthroplasty. Systematic review of 415 cases (1981-2006). *Acta Orthopaedica.* 79,1,pp 22-27.

Heyligers, I.C., Schreurs. B.W., and van Haaren E.H., 2014. Femoral revision with impaction bone grafting and a cemented polished tapered stem. *Operative Orthopädie und Traumatolgie.* 26, pp 156-161

Holley K., Zelken, J., Padgett, BD.B.A., Chimento, G., Yun, A., and Buly R., 2007. Periprosthetic Fractures of the Femur After Hip Arthroplasty: An Analysis of 99 Patients. *HSS Journal The Musculosceletal Journal of Hospital for Special Surgery.* 3, pp 190-197

Jacobs, J.J., 2010, Commentary on an article by Stephen S. Tower, "Arthroprosthetic Cobaltism: Neurological and Cardiac Manifestations in Two Patients with Metal-on-Metal Arthroplasty. A Case Report". *The Journal of Bone and Joint Surgery.* 95A, pp1-2

Jacobs, J.J., Skipor, A.K., Cambell, P.A., Hallab, N.J., Urban, R.M., and Amstutz, H.C., 2004. Can metal levels be used to monitor metal-on-metal hip arthroplasties? *The Journal of Arthroplasty.* 9, suppl 3, pp 59-65

Jasty, M., Haire, T., and Tenzer, M., 1991, Femoral osteolysis: a generic problem with cementless and cemented femoral components. *Orthopaedic Transactions.* 15, pp 758-759

Johanson, P-E., Fenstad, A.M., Furnes, O., Garellick, G., Havelin, L., Overgaard, S., Pedersen, A.B., and Kärrholm, J., 2010. Inferior outcome after hip resurfacing arthroplasty than after conventional arthropalsty. Evidence from the Nordic Arthroplasty Association (NARA) database, 1995 to 2007. *Acta Orthopaedica.* 81, 5, pp 535-541

Jones, L.C., Park, S.H., Chiesa, R., Doorn, P., Lu, B., Normand, P., Gigoris, P., and Amstutz, H., 1987. Cement Disease. *Clinical Orthopaedics.* 225, pp 192-206

Judet, J. and R., 1950. The use of an artificial femoral head for arthroplasty of the hip joint. *The Journal of Bone and Joint Surgery. British volume, 32B, pp 166-173.*

Junnila, M., Kostensalo, I., Virolainen, P., Remes, V. Natilainen, M., Vahlberg, T., Pulkkinen, P., Eskelinen, A., Itälä, A., and Mäkelä K.T., 2013. Hip resurfacing arthroplasty versus large- diameter head metal-on-metal total hip arthroplasty: comparison of three designs from the Finniash Artroplasty Register. *Scandinavian Journal of Surgery.* 103, pp 54-59

Junnila, M., Seppänen, M., Mokka, J., Virolainen, P., Pölönen, T., Vahlberg, T., Mattila, K., Tuominen, E.K.J., Rantakokko, J., Äärimaa, V., Itälä, A., and Mäkelä, K. 2015. Adverse reaction to metal debris after Birmingham hip resurfacing arthroplasty. *Acta Orthopaedica.* 86, 3, pp 345-360

Kamath, F.A., Prieto, H., and LeWallen D-G., 2013. Alternative Bearings in Total Hip Arthroplasty in the Young Patient. *Orthopaedic Clinics of North America.* 44, pp 451-462

Kashan, M., Amar, E., Drexler, M. Chechic, O., Cohen, Z., and Steinberg,E., L., 2013. Superior outcome of strut allograft-augmented plate fixation for the treatment of periprosthetic fractures around a stable femoral stem. *Injury. International Journal of the Care of the Injured.* 44, pp 1556-60.

Keegan, G.M., Learmonth, I.D, and Case, C. 2008. A Systematic Comparison of the Actual, Potential, and Theoretical Health Effects of Cobalt and Chromium Exposures from Industry and Surgical Implants. *Critical Reviews in Toxicology, 38, 8, pp 645-647.*

Kerboull, L., Hamadouche, M., and Kerboull M., 2009. Impaction grafting in association with the Charnley-Kerboull cemented femoral component. Operative technique and two- to 16-year follow-up results. *The Journal of Bone and Joint Surgery. British Volume.* 91B, 3, pp 304309.Kim, Y.H., and Kim, J.S., 2005. Revision hip arthroplasty using strut allografts and fully porous- coated stems. *The Journal of Arthroplasty.* 18, supp 1, pp 104-106.

Korim, M.T., Esler, C.N.A., and Ashford, R.U., 2014. Systematic review of Proximal Femoral Arthropaslty for Non-Neoplastic Conditions. *The Journal of Arthroplasty.* Article in press.

Kostensalo, I., Junnila, M., Virolainen, P., Remes, V., Matilainen, M., Vahlberg,T., Pulkkinen, P., Eskelinen, A., and Mäkelä,K. 2013. Effect of the femoral head size on revision risk for dislocation after total hip arthroplasty. A population-based analysis of 42,379

primary procedures fro, the Finnish Arthroplasty Register. *Acta Orthopaedica.* 84, 4, ppo 342-347.

Kostensalo, I., Seppänen, M., Mäkelä, K., Mokka, J., Viorolainen, P., and Hirviniemi, J., 2012. Early results of large head metal-on-metal hip arthroplasties. *Scandinavian Journal of Surgery.* 101, pp 62-65.

Kremers, M.H., Howard, J.L., Loechler, Y., Schleck, C.D., Harmsen, W.S., Berry, D.J., Cabanela, M.E., Hanssen, A.D., Pagnano, m.W., Trousdale, R.T., and Lewallen, D.G., 2012. Comparative Long- Term Survivorship of Uncemented Acetabular Components in Revision Total Hip Arthropplasty. *The Journal of Bone and Joint Surgery.* 94A, pp 82-90.

Kumar, C.N., Arora, G.N.C., and Datta, B., 2014. Bearing surfaces in hip replacement - Evolution and likely future. *Medical journal armed forces India, article in press.*

Kurtz, S., Lau, E., Mowat, F. and Halpern. M. 2007. Projections of Primary and Revision Hip and Knee Arthroplasty in the United States from 2005 to 2030. *Journal of Bone and Joint Surgery.* 89, pp 780-785.

Kurtz, S., Mowat, F., Ong,K., Chan, N. Lau, E., and Halpern, M. 2005. Prevalence of Primary and Revision Total Hip and Knee Arthroplasty in the United States from 1990 through 2002. *The Journal of Bone and Joint Surgery.* 87A, 7, pp 1487-97.

Kwon, Y-M., Ostlere, S.J., McLardy-Smith, P., Athanasou, N.A., Gill, H.S., and Murray, D. 2011. "Asymptomatic" Pseudotumors After Metal-on-Metal Hip Resurfacing Arthroplasty. *The Journal of Arthroplasty. 26, pp 511-518.*

Lakstein, D., Kosasvili, Y., Backstein, D, Safir, O., Lee, P., and Gross, A.E., 2011. The long modified extended sliding trochanteric osteotomy. *International Orthopaedics.* 35, pp 13-17.

Lamberton, T.D., Kenny, P.J., Whitehouse, S.L., Timperley, A.J., and Gie G.A., 2011. Femoral impaction grafting in revision total hip replacement - a follow-up of 540 hips. *The Journal of Arthroplasty.* 28, 8, pp 1154-60.

Langton, D.J., Jameson, S.S., Joyce, T.J., Hallab, N.J., Natu, S. and Nargol A., V., F. The effect of component size and orientation on the concentrations of metal ions after resurfacing arthroplasty of the hip. 2008. *The Journal of Bone and Joins surgery. Br.* 90B, 9, pp 1143-1151.

Langton, D.J., Jameson, S.S., Joyce, T.J., Hallab, N.J., Natu, S. and Nargol A., V., F. 2009. Early failure of metal-on-metal bearings in hip resurfacing and large-diameter total hip replacement. *The Journal of bone and joint surgery, British volume. 92B, pp38-46.*

Lardanchet, J-F., Taviaux, J., Arnalsteen, D., Gabrion, A., and Mertl, P., 2012. One-year prospective comparative study of three large-diameter metal-on-metal total hip prostheses: serum metal ion levels and clinical outcomes. *Orthopaedics and Traumatology, Surgery and Research.* 98, pp 265-274.

Lavigne, M., Belzilw E-. L., Roy, A., Morin, F., Amzica, T., and Vendittoli, P-A., 2011, Comparison of Whole-Blood Metal Ion Levels in Four Types of Metal-on-metal Large-Diameter Femoral Head Total Hip Arthroplasty: The potential iInfluence of the Adapter Sleeve. *The Journal of Bone and Joint Surgery.* 93A, Supp 2, pp 128-136.

Learmonth, I., 2007. The operation of the Century: total hip replacement. *Lancet, 370, pp 1508-19.*

Lewinnek, G.E., Lewis, J.L., Tarr, R., Compere, C.L., and Zimmerman, J.R. 1978, Dislocations after Total Hip-Replacement arthtoplasties. *The Journal of Bone and Joint Surgery.* 60A, 2, pp 217-220.

Lie, S.A., Engesaeter, L.B., Havelin, L.I., Gjessing,H.K., and Vollset, S.E., 2004. Dependency issues in survival analyses of 55 782 primary hip replacements from 47 355 patients. *Statistics in Medicine.* 23, 20, pp 3227-40.

Lindahl, H. Epidemiology of periprosthetic femur fractures around a total hip arthroplasty. 2007. *Injury. Internationlan Journal of the Care of the Injiured.* 38, 6, pp 651-654.

Lindahl, H., Garellick, G., Regnér H., Herberts P., and MAlchau H., 2006. Three Hundred and Twenty-one Periprosthetic Femoral Fractures. *The Journal of Bone and Joint Surgery.* 86A, 6, pp 1215-22.

Lindahl, H., Regnér H., Malchau H., Herberts P., and Garellick, G., 2005 Periprosthetic Femoral Fractures. Classification and Demographics of 1049 Periprosthetic Femoral Fractures from the Swedish National Hip Arthroplasty Register, *The Journal of Arthroplasty.* 20, 7,pp 857865I.

Lombardi, A.V., Mallory, T.H., Alexiades, M.M., Cuckler, J.M., Farios, P.M., Jaffe, K.A., Keating, M.E., Melson, C.L., Ranawat, C.S., Williams, J., Wixon, R., Hartman, J.F., Capps, S.G., and Kefauver, J.A., 2001. Short-term results of the M2a-taper metal-on-metal articulation. *The Journal of Arthroplasty.* 16, 8, Supp 1, pp122-128.

Lombardi, A.V., Mallory, T.H., Cuckler, J.M., Williams, J., Berend, K.R., and Smith, T.M., 2004. Mid- term results of a polyethylene-Free Metal-on-Metal Articulation. *The Journal of Arthroplasty.* 19, 7, supp 7, pp 42.-47.

Long, W.T., Dastane, M., Harris, M.J, and Wan, Z., 2010. Failure of the Durom Metasul Acetabular Component. *Clinical Orthopaedics and Related Research.* 468, pp 400-405.

Macnair, R.D., Wynn-Jones, H., Wimhurst, J.A., Toms, A., and Cahir, J., 2013. Metal Ion Levels Not Sufficient Screening Measure for Adverse Reactions in Metal-on-Metal Hip Arthroplasties. *The Journal of Arthroplasty.* 29, 1, pp 78-83.

Maloney, W.J., Jasty, M., Harris, W.H., Galante, J., and Callaghan, J, 1990. Endosteal Erosion in Association with Stable Uncemented Femoral Components. *The Journal of Bone and Joint Surgery.* 72A, 7, pp 1025-34.

Malchau, H., Herberts, P., Eisler, T., Garellick, G., and Söderman P., 2002. The Swedish Total Hip Replacement Register. *The Journal of Bone and Joint Surgery, 84A, pp 2-20.*

Marshall, A.D., Mokris, J.G., Reitman, R.D., Dandar, A., And Mauerhan, D.R., 2004. Cementless titanium tapered-wedge femoral stem. 10 to 15 year follow-up. *The Journal of Arthroplasty.* 19, 5, pp 546-552.

Masri, B.A., Meek, D.R.M., and Duncan, C.P., 2004. Periprosthetic Fractures Evaluation and Treatment. *Clinical Orthopaedics.* 420, pp80-95.

Masterson, E.L., Masri, B.A., and Duncan,C.P., 1997. The Cement Mantle in the Exeter Impaction Allograft Technique. A Cause for Concern. *The Journal of Arthroplasty.* 12, 7, pp 759-764.

McKee, G.K. and Watson-Farrar, J., 1966. Replacement of arthritic hips by the McKee-Farrar Prothresis. *Journal of Bone and Joint Surgery. British Volume.* 48B, 2, pp 245-259.

McLaughlin, J.R., and Kyla, L.R., Uncemented total hip arthroplasty with tapered femoral component: a 22- to 26-year follow-up study. *Orthopedics*. 33, 9.

McMinn, D,. Treacy, R., Lin, K., and Pynset, P., 1996. Metal on metal surface replacement of the hip:experience of the McMinn prosthesis. *Clinical Orthopaedics and Related Research, 329, pp 89-98.*

Meding, J.B., Meding, L.K., Keating, M.E., and Berend, M.E., 2012. Low incidence of groin pain and early failure with large metal articulation total hip arthroplasty. *Clinical Orthopaedics and Related Research.* 470, pp 388-394.

Meek, R.M.D., Norwood, T., Smith, R., Brenkel, I.J., and Howie, C.R., 2010. The risk of peri- prosthetic fracture after primary and revision total hip and knee replacement. *The Journal of Bone and Joint Surgery. British edition.* 93B, 1, pp 96-101.

Mertl, P., Boughebri, O., Havet, E., Tricot, P., Lardanchet, J.-F, and Gabrion A., 2009. Large diameter head metal-on-metal bearings total hip arthroplasty: Preliminary results. *Orthopaedics & Traumatology: Surgery & Research. 96, pp 14-20.*

Miner, T.M., Momberger, N., G., Chong, D., and Paprosky, W.G., 2001. The extended Trochanteric Osteotomy in Revision Hip Arthroplasty. A Critical Review of 166 Cases at Mena 3-year, 9 Month Follow-Up. *The Journal of Arthroplasty.* 16, 8, supp 1, pp 188-194.

Moore, A.,T and Bohlman, H., R, 1943. Metal Hip Join. A Case Report. *The Journal of Bone and Joint Surgery, 3, pp 688-692.*

Morin, Y.L., Foley, A.R., Martinneau,A.R., and Roussel G., 1967. Quebec beer-drinkers cardiomyopathy: forty-eight cases. *Canadian Medical Association Journal.* 97, pp 881-883.

MRHA 2010. Medical Device Alert: all metal-on-metal (MoM) hip replacements (MDA/2010/033) http://mhra.gov.uk/publications/safetywarnings/medicaldevicealerts/CON79157.

Müller, A.L., Wenger, N., Schramm, M., Hohmann, D., Forst, R., and Carl, H-D., 2010. Seventeen- year survival of the cementless CLS Spotorno stem. *Archives of Orthopaedic and Trauma Surgery.* 130, pp 269-275.

Müller, M.E., 1970. Total Hip Prosthesis. *Clinical Orthopaedics and Related Research. 72, pp 46-48.*

Mäkelä, KL.T., Eskelinen, A., Pulkkinen, P., Paavolainen, P., and Remes, V., 2008. Total hip arthroplasty for primary osteoarthritis in patients fifty-five years of age and older. An analysis of the Finnish Arthoplasty Registry. *The Journal of Bone and Joint Surgery.* 90A, 10, pp 2160-70.

Mäkelä, K.T., Matilainen, M., Pulkkinen, P., Fenstad, A.M., Havelin, L.I., Engesaeter, L., Furnes, O., Overgaard, S, Pedersen, A.B., Kärrholm, J., Malchau, H., Garellick, G., Ranstam, J. and Eskelinen, A., 2014. Countrywise results of total hip replacement. An analysis of 438,77 hips based on the Nordic Arthroplasty Register Association database. *Acta Orthopaedica.* 85, 2, pp 107-116.

Mäkelä, K.T., Visuri, T., Pulkkinen, P., Eskelinen, A., Remes, V., Virolainen, P., Junnila M., and Pukkala, E. 2012. Risk of cancer with metal-on-metal hip replacements: population based study. *British Medical Journal*- 345,4646.

Mäkelä, K.T., Visuri, T., Pulkkinen, P., Eskelinen, A., Remes, V., Virolainen, P., Junnila, M., and Pukkala E., 2014. Cancer incidense and cause-specific mortality in patients with metal-on- metal hip replacements in Finland. A population-based study with mean follow-up of 466 (1-11) years. *Acta Orthopaedica.* 85, 1, pp 32-38.

Naal, F.D., pilz, R., Munziger, U. Hersche, O. Leunig, M. 2011. High revision rate at 5 years after hip resurfacing with the Durom implant. *Clinical Orthopaedics and Related Research*, 469, pp.2598–2604.

Naudie, D., Roeder, C.P., Parevizi, J., Berry, D.J., Eggli, S., Busato, A., 2004. Metal-on-Metal Versus Metal-on-

Polyethylene Bearings in Total Hip Arthroplasty. A Matched Case-Control Study. *The Journal of Arthroplasty.* 19, suppl 2, pp 35-41.

Nelisse, B.H.H., Bauer, T.W., Weidenheilm,L.R.A., LeGollvan, D.P., and Mikhail, M.W.E., 1995. Revision Hip Arthroplasty with Use of Cement and Impaction Grafting. *The Bone and Joint Surgery.* 77A, 3, 412-422.

Neuerburg C., Impellizzeri, F., Frey, P., Naal, F.D., von Knoch, M, and von Knoch F., 2012. Survivorship of second-generation metal-on-metal primary total hip. *Archives of Orthopaedic and Trauma Surgery, 132, pp 527-533.*

Ollivere, B., Darrah, C., Barker, T., and Porteous J., 2009. Early clinical failure of the Birmingham metal-on-metal hip resurfacing is associated with metallosis and soft tissue necrosis. *The Journal of Bone and Joint Surgery. British volume.* 91B, 8, pp 1025-30.

Ornstein, E., Linder, L., Ranstam, J., Lewold, S., Eisler, T., and Torper, M., 2009. Femoral impaction bone grafting with the Exeter stem - the Swedish experience. *The Journal of Bone and Joint Surgery. British volume.* 91B, 4, pp 441-446.

Otte, S., Fitzek, J., Wedemeyer, C., Löer, F., von Knoch, M., and Saxler, G., 2006. Reinforcement of deficient femur with inlay strut grafts in revision hip arthroplasty. A small series. *Archives of Orthopaedic and Trauma Surgery.* 126, pp 649-653.

Paavolainen P., Hämäläinen, M., Mustonen, H., and Slätis, P. 1991. Registration of arthroplasties in Finland. A nationwide prospective project. *Acta Orthopaedica Scandinavica.* 62, supp 241, pp 27-30.

Palm, L., JAcobsson, S-A., Kvist, J., Lindholm, A., Öjersjö,A., and Ivarsson, I. 2006., Acetabular Revision With Extensive Allograft Impaction and Uncemented Hydroxyapatite-Coated Implants. Results After 9 (7-11) Years Follow-Up. *The Journal of Arthroplasty.* 22, 8, pp 1083-91.

Pandit, H., Glyn-Jones, S., McLardy-Smith, P., Gundle, R., Whitwell, D., Gibbons, C-L-M., Oslere, S., Athanasou, N., Gill, H.S., and Murray D.W., 2008. Pseudotumours associated with metal-on- metal hip resurfacings. *The Journal of bone and joint surgery.* British volume, 90B, pp847-851.

Paprosky, W.G., and Aribindi, R. 2000. Hip replacement: Treatment of Femoral Bone Los Using Distal Bypass Fixation. *Instructional Course Lectures.* 49.pp 119-130.

Paprosky, W.G., Greidanus, N.V., and Antoniu, J., 1999. Minimum 10-year result of extensively porous-coated stems in revision hip arthroplasty. *Clinical Orthopaedics and Related Research.* 369, pp 230-242.

Paprosky, W.G., Lawrence, J.M., and Cameron H.U., 1990, Femoral defect classification: A clinical application. *Orthopedic Reviews. 19,9, pp.*

Paprosky,W.G., Perona, P.G., and Lawrence J.M., 1994. Acetabulars Defect Classification and Surgical Reconstruction in Revision Arthroplasty. A 6-year Follow-up Evaluation. *The Journal of Arthroplasty.* 9, 1, pp 33-44.

Parvizi, J. and Vegari, N.D., 2011. Periprosthetic Proximal Femur Fractures: Current Concepts. *Journal of Orthpedic Trauma.* 6, supp, pp 77-81.

Pastides, P.S., Dodd, M., Saraf, K.M., Willis-Owen, C.A. 2013. Trunnionosis: A pain in the neck. *World Journal of Orthpedics. 18, pp 161-166.*

Pedersen, A.B., Mehnert, F., Havelin, L.I., Furnes, O., Herberts, P., Kärrholm, J., Gallerick, G., Mäkelä, K., Eskelinen, A., and Overgaard, S., 2014. Association between fixation technique and revision risk in total hip arthroplasty patients younger than 55 years of age. Results from the Nordic Arthroplasty Register Association. *Osteoarthritis and Cartillage.* 22, pp 659-667.

Pekkarinen, J., Alho, A., Lepistö, J., Ylinen,P., and Paavilainen T., 2000. Impaction bone grafting in revision hip surgery. *Journal of Bone and Joint Surgery. British volume.* 82B, pp 103-107.

Posada, M.O., Gilmour, D., Tate, R., J, and Grant, H.M., 2014. CoCr wear particles generated from CoCr alloy metal-on-metal hip replacements, and cobalt ions stimulate apoptosis and expression of general toxicology-related genes in monocyte-like U937 cells. *Toxicology and Applied Pharmacology.* Article in press.

Pulido, L., Rachala, S.R., and Cabanela, M., 2011., Cementless acetabular revision: past, present and the future. Revision total hip arthroplasty: the acetabular side using cementless implants. *International Orthopaedics.* SICOT 35, pp 289-298.

Puolakka, J.S., Pajamäki, J.J., Halonen, P.J., Pulkkinen P.O., Paavolainen, P., and Nevalainen, J.K., 2001. The Finnish Arthroplasty Register. Report of the hip register. *Acta Orthopedica, 72, pp 433-441.*

Rayan, F., Dodd, M., and Haddad, F.S., 2008. European validation of the Vancouver classification of peri-prosthetic proximal femoral fracture. *The Journal of Bone and Joint Surgery. British volume.* 90B, pp 1576-9.

Reito, A., Puolakka, T. and Pajamaki, J. 2011. Birmingham hip resurfacing: Five to eight year results. *International Orthopaedics (SICOT). 35, pp 1119-24.*

Reito, A., Puolakka, T., Elo, P., PAjamäki, J., Eskelinen, A. 2013. High prevalence of Adverse Reactions to

Metal Debris is Small-headed ASR Hips. *Clinical Orthopaedics and Related Research. 471, pp 2954-61.*

Reito, A., Puolakka, T., Elo, P., PAjamäki, J., and Eskelinen, A., 2014. Outcome of Birmingham hip resurfacing at ten years: role of routine whole blood metal ion measurements in screening for pseudotumours. *International Orthopaedics. SICOT.*

Richards, J.C., Duncan, P.C., and Crawford, R.W., 2011. Cement-in-Cement Femoral Revision for the Treatment of Highly Selected Vancouver B2 Periprosthetic Fractures. *The Journal of Arthroplasty.* 22,2, pp 335-337.

Rieker, C.B., Schön, R., and Köttig, P., 2004. Development and Validation of a Second-Generation Metal-on-metal Bearing. Laboratory Studies and Analysis of Retrievals. *The Journal of Arthrplasty 8 Suppl, pp 5-11.*

Ring, P.A. 1968. Complete replacement arthroplasty of the hip by the Ring prosthesis. *The Journal of bone and joint surgery. British volume, 50B, pp 720-731.*

Rizetti, M.C., Liberini, P., Zarattini, G., CAtalani, S., Pazzaglia,U., Apostolio, P. and Padovani, A. 2009. Loss of sight and sound. Could it be the hip? *Lancet.* 373, p 1052.

Rogers, B.A., Sternheim, A., De Iorio, M., Backstein, D., Safit, O., and Gross, A., E., 2012. Proximal Femoral Allograft in Revision Hip Surgery With Severe Femoral Bone Loss. A Systematic Review and Meta-Analysis. *The Journal of Arthroplasty.* 27, 6, pp 829-836.

Roshan, P.S., Christy, J.M., Sporer, M.S., and Paprosky, W.G., 2014. Pelvic discontinuity: Where are we today? *Seminars in Arthroplasty* (Article in press).

Santavirta, S., Hoikka, V., Eskola, A., Konttinen, Y.T., Paavilainen, T., and Tallroth K. 1990. Aggressive granulomatous lesions in cementless total hip arthroplasty. *The Journal of Bone and Joint Surgery. British volume.* 72B, pp 980-4.

Santavirta, S., Konttinen, Y.T., Bergroth, V., Eskola, A., Tallroth, A., and Lindholm, S.T. 1990. Aggressive Granulomatous Lesions Associated with Hip Arthroplasty. *The Journal of Bone and Joint Surgery.* 72A, 2, pp 252-258.

Sariali, E., Lazennec, J.Y., Khiami, F, and Catonne, Y. 2009. Mathematical evaluation of jumping distance in total hip arthroplasty. Influence of abduction angle, femoral head offset and head diameter- *Acta Orthopaedica, 80, pp 277-282.*

Schreurs, W.B., Arts, C.J.J., Verdonschot, N., Buma, P., Slooff, T.J.J.H., and Gardeniers, J.W.M., 2005. Femoral Component Revision with Use of Impaction Bone-Grafting and a Cemented Polished Stem. *The Journal of Bone and Joint Surgery.* 87A, 11, pp 2499-507.

Schmalzried, T. 2011. The future of Hip Resurfacing. *Orthopaedic Clinics of North America. 42, pp 271-273.*

Schmalzried, T.P., Jasty, M., and Harris, W.H., 1992. Periprosthetic Bone Loss in Total Hip Arthroplasty. Polyethylene wear debris and the concept of the effective joint space. *The Journal of Bone and Joint Surgery, 74A, pp 849-863.*

Schmalzried, T.P., Peters, P.C., Mauler, B.T., Bragdon, C.R., and Harris, W.H., 1996. Long-duration Metal-on-metal Total Hip Arthroplasties With Low Wear on the Articulating Surfaces. *The Journal of Arthroplasty, 11, pp 322-331.*

Schmidt, C.O., and Kohlmann, T., 2008., When to use the odds ratio or the relative risk? *International Journal of Public Health.* 53, pp 165-167.

Sedel, L., Kerboull, L., Christel, P, Meunier, A, and Witvoet, J., 1990. Alumina-on-alumina hip replacement. Result and survivorhip in young patients. *The Journal of Bone and Joint Surgery. British volume, 72B, pp 658-63.*

Seppänen, M., Mäkelä, K, Viorolainen, P., Remes, V., Pulkkinen, P., and Eskelinen, A. 2013. Hip resurfacing arthroplasty: Short-term survivorship of 4401 hips from the Finnish Arthroplasty Register. *Acta Orthopaedica. 83, pp 207-213.*

Sewell, D.M., Hanna, A.S., Carrington, R.W., Pollock,R.C., Skinner, J.A., Cannon, S.R., and Briggs, T.W.R., 2010, Modular proximal femoral replacement in salvage hip surgery for non- neoplastic conditions. *Acta Orthopedica Belgica.* 76, pp 493-502.

Shimmin, A.J., Bare, J., Black, D.L., 2005. Complications Associated with Hip Resurfacing Arthroplasty. *The Orthopaedic Clinics of North America, 36, pp 187-193.*

Shinar, A.A., and Harris, W.H., 1995. Bulk Structural Autogenous Grafts and Allografts for Reconstruction of the Acetabulum in Total Hip Arthroplasty. Sixteen-Year-Average-Follow-up. *Journal of Bone and Joint Surgery.* 79A, 2, pp 159-168.

Sieber, H.P., Rieker C.B., Köttig, B. 1998. Analysis of 118 second-generation metal-on-metal retrieved hip implants. *The Journal of Bone and Joint Surgery. British volume, 80B, pp 46-50.*

Sivash K., M. 1969. The development of total metal prosthesis for the hip joint from a partial joint replacement. *Reconstructive Surgery and Traumatology, 11, pp 53-58*

Skinner, J., and Kay, P., 2011. Commentary: Metal on metal hips. *British Medical Journal.* 342:d3009.

Sloof, T.J.J.H., Huiskes, R., van Horn, J., and Lemmens,A.J., 1984. Bone grafting in total hip replacement

for acetabular protrusion. *Acta Orthopaedica Scandinavica.* 55, pp 593-596.

Sporer, C.M. and Poprosky W.G., 2006. The use of a Trabecular Metal Acetabular Component and Trabecular Metal Augments for severe Acetabular Defects. *The Journal of Arthroplasty.* 21, 6, supp 2, pp 83-86.

Sporer, C.M. and Poprosky W.G., 2006. Acetabular Revision Using a Trabecular Metal Acetabular Component for Severe Acetabular Bone Loss Associated With a Pelvic Discontinuity. *The Journal of Arthroplasty.* 21, 6, supp 2, pp 87-90.

Steen, W., von Foerster, G and Kayzer, A., 2006. Severe cobalt poisoning with loss of sight after ceramic-metal pairing in a hip - a case report. *Acta Orthopaedica.* 77, 5, 830-832.

Steffen, R.T., Pandit, H.P., Palan, J., Beard, D.J., Gundle, R., McLardy-Smith, P., Murray, D.W., and Gills, H.S., 2008. The five-year results of the Birmingham Hip Resurfacing arthroplasty: an independent series. *The Journal of bone and joint surgery. British volume*, 90, pp.436–441.

Söderman, P., Malchau, H., and Herberts, P. Outcome after total hip arthroplasty. Part I General health evaluation in relation to definition of failure in the Swedish National Total Hip Arthroplasty Register. *Acta Scandinavica.* 71, 4, pp 354-359

Söderman, P., Malchau, H., Herberts, P., Züner, R., Regnér, H., and Garellick, G. 2000. Outcome after total hip arthroplasty. Part II Disease specific follow-up and the Swedish National Total Hip Arthroplasty Register. *Acta Orthopaedica.* 72, 2, pp 113-119.

Talmo, C.T, and Bono, J.V., 2008. Treatment of Intertrochanteric Non-union of the Proximal Femur Using the S-ROM Prostheis. *Orthopaedics.* 31, pp 125.

Thien, T.M., Chatziagorou, G., Garellick, G., Furnes, O., Havelin, L.I., Mäkelä, K.T., Overgaard, S., Pedersen, A., Eskelinen, A., Pulkkinen, P., and Kärrholm, J., 2014. Periprosthetic Femoral Fracture within Two Years After Total Hip Replacement. Analysis of 437,629 Operations in the Nordic Arthroplasty Register Association Database. *The Journal of Bone and Joint Surgery.* 96A, pp 167-174.

Thomas, M.S., Wimhurdt, J.A., Nolan, J.F., and Toms, A.P., 2013. Imaging Metal-on-Metal Hip Replacements: the Norwich Experience. 2013. *Hospital for Special Surgery.* 9, pp 247-256.

Thompson, F.R., 1952. *Vitallium intramedullary hip prosthesis - preliminary report. N.Y. State Journal of Medicine, 52, pp 3011-20.*

Tomford, W.W., Thongphasuk, J., Mankin,H.J., and Ferraro, M.J., 1995. Transmission of disease through transplantation of musculoskeletal allografts. *The Journal of bone and joint surgery. American volume*, 77, pp.1742–1754.

Toms, A.P., Marshall, T.J., Cahir J., Darrah, C., Donell, S.T., Barker, T., and Tucker, J.K., 2008. MRI of early symptomatic metal-on-metal total hip arthroplasty: a retrospective review of radiological findings in 20 hips. *Clinical Radiology.* 2008; 63:49–58.

Tower, S.S., 2010. Arthroprosthetic cobaltism: neurological and cardiac manifestations in two patients with metal-on-metal Arthroplasty. A case report. *The Journal of Bone and Joint Surgery.* 92A, pp 2847-51.

Treacy, R.B.C., McBryde, C.W., Shears, E., and Pynset, P.B., 2011. Birmingham hip resurfacing. A minimum follow-up of then years. *The Journal of Bone and Joint Surgery. British volume.* 93B, 1, pp 27-32.

Ollivere, B., Darrah, C., Barker, T., Nolan, J., and Porteous M.J., 2009. Early clinical failure of the Birmingham metal-on-metal hip resurfacing is associated with metallosis and soft-tissue necrosis. *The Journal of Bone and Joint Surgery. British volume, 91B, pp1025-30.*

Walsh, A.J., Nikolaou, V.S. & Antoniou, J., 2012. Inflammatory pseudotumor complicating metal-on-highly cross-linked polyethylene total hip arthroplasty. *Journal of Arthroplasty, 27, pp 324-328*.

Ward, C. 2009. History of self-experimentation in orthopaedics. *Iowa Orthopedic Journal, 29, pp 127-139.*

Wassef, A.J., and Schmalzried, T.P., Femoral taperosis. An Accident Waiting to Happen. *The Journal of Bone and Joint Surgery.* 95B, 11, pp 3-6.

van der Weegen, W., Hoekstra, H-J., Sijbesma, T., Austen, S., and Poolman R., 2012. Hip resurfacing in a district general hospital: 6-year clinical results using the ReCap hip resurfacing system. *BMC Musculosceletal Disorders.* 13,247-260.

Vidalain, J-P., 2011, Twenty-year results of the cementless Corail stem. *International Orthopaedics (SICOT).* 35, pp 189-194.

Wiles, P., 1957. The surgery of the osteo-arthritic hip. *British Journal of Surgery, 45, pp 488-497.*

Wiley, K.F., Ding, K., Stoner, J.A., Teaque, D.C., and Yousuf, K.M., 2013. Incidence of pseudotumor and acute lymphocytic vasculitis associated lesion (ALVAL) reactions in metal-on-metal hip articulations: A meta-analysis. *Journal of Arthroplasty*, 28, pp.1238–1245.

Willert, H.G., Buchhorn, G.H., Fayyazi,A., Flury, R. Windler M., Köster, G., and Lohman, C.H., 2005. Metal-on-metal bearings and hypersensitivity in patients with artificial hip joints. A clinical and

histomorphological study. *The Journal of Bone and Joint Surgery.* 87, 1, pp 28-36.

Willert, H.G., Bucchorn, G.H., Göbel, D., Käster, G., Schaffner, S., and Schenk R., 1996. Wear Behaviour and Histopathology of classic cemented metal on metal hip endoprotheses. *Clinical Orthopaedics and Related Research.* 329, 7, pp 160-186.

Virolainen, P., Heikkilä, J., Hirn, M., Aro, H.T., and Aho, A.J., 2003. 30 years of bone banking at Turku bone bank. *Cell and Tissue Banking, 4, pp 43-48.*

Younger, T.I., Bradford, M., S., Magnus, R., E., and Paprosky, W.G., 1995. Extended Proximal Femoral Osteotomy. *The Journal of Arthroplasty. 10, 3, pp 329-338.*

Yu, T., Hofstaeder, J.G., Sullivan, T., Costi, K., Howie, D.W., and Solomon, L.B., 2013. Validity and Reliability of the Paprosky Acetabular Defect Classification. *Clinical Orthopaedics and Related Research.* 471, 7, pp 2259-65.

Zdero, R., Waalker, R., Waddell, J.P., and Schemitsch, E.H., 2008. Biomechanical Evaluation of Periprosthetic Femoral Fracture Fixation. *The Journal of Bone and Joint Surgery.* 90A, 3, pp 1068-77-

Zuurmond,R.G., van Wijhe, W., van Raay, J.J.A.M, and Bulstra, S.K., 2010, High incidence of complications and poor clinical outcome in the operative treatment of periprosthetic femoral fractures: An analysis of 71 cases. *Injury. International Journal of the Care of the Injured.* 41, pp 629-633.

Zywiel, M.G., Brandt, J-M., Overgaard, C.B., Cheung, A.C., Turgeon, T.R., and Syed, K.A. (2013). Fatal cardiomyopathy after revision total hip replacement for fracture of a ceramic liner. *The Journal of Bone and Joint Surgery.* 95B, 1, pp 31-37.