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REGISTERS IN ASSESSING COMPLICATION AND REVISION RATE AFTER HIP ARTHROPLASTY

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To my godmother Eila

ABSTRACT

Mika Junnila: Registers in assessing complication and revision rate after hip arthroplasty

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Annales Universitatis Turkuensis

Cemented low-friction arthroplasty, pioneered by Sir John Charnley, is the basis for modern total hip arthroplasty (THA). The Charnley THA is still considered as the gold standard against which new devices are compared. However, aseptic loosening was a relatively common cause for the failure of cemented THAs. Therefore, new fixation methods and bearing surfaces were developed, *e.g.,* uncemented THAs, resurfacing arthroplasty (HRA), and metal-on-metal THAs.

National arthroplasty registers were established to assess new THA devices and to detect outlier products as early as possible. The Swedish Hip Arthroplasty Register was established in 1979, the Finnish Arthroplasty Register (FAR) in 1980, the Norwegian Arthroplasty Register in 1987, and the Danish Hip Arthroplasty Register in 1995. A combined Nordic arthroplasty register (Nordic Arthroplasty Register Association, NARA) was established in 2007 with the overall aim of improving the quality of joint replacement surgery by registry-based research collaboration.

The aim of this thesis was to assess risk factors and prevalence of adverse reaction to metal debris (ARMD) associated with two metal-on-metal hip devices – the Birmingham Hip Resurfacing (BHR) HRA and the Biomet ReCap Magnum THA – based on data of the joint replacement register of the Turku University Hospital. Another aim was to compare the differences in survivorship of three HRA designs with their analogous uncemented, large-diameter head metal-on-metal THAs based on FAR data. Further, survival of the most common cemented THA brands was assessed by data of the NARA.

We found that hip resurfacing arthroplasty with the BHR HRA may be more dangerous than previously thought. Systematic follow-up of these patients is advised. There was a high prevalence of ARMD among ReCap-M2a-Magnum THA patients. The short-term revision risk of large diameter head MoM hip replacements was not increased compared to similar HRAs (FAR data), but implant-related factors may contribute to this success. Several brands of cemented THAs performed well in the long term, but there are significant differences in implant survival between the best and the worst performers.

Keywords: Finnish Arthroplasty Register (FAR), Nordic Arthroplasty Register Association (NARA), total hip arthroplasty (THA), implant survival, metal-on-metal, large-diameter-head, hip resurfacing arthroplasty (HRA), adverse reaction to metal debris (ARMD), revision rate, cemented total hip arthroplasty.

TIIVISTELMÄ

Mika Junnila: Registers in assessing complication and revision rate after hip arthroplasty

Turun Yliopisto, Lääketieteellinen tiedekunta, Kliinisen lääketieteen laitos, Ortopedian ja traumatologian klinikka, Turun kliininen tohtoriohjelma.

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Sementtikiinnitteinen lonkan tekonivelleikkaus on modernin lonkkaproteesikirurgian perusta. Muiden leikkausmenetelmien pysyvyystuloksia verrataan edelleen sementtikiinnitteisen Charnleyn proteesiin (DePuy; Johnson and Johnson, New Brunswick, NJ). Sementtikiinnitteisen proteesin uusintaleikkauksen yleisin syy on sementtikiinnityksen pettäminen, eli aseptinen irtoaminen. Uusia kiinnitysmenetelmiä ja liukupintaratkaisuja kehitettiinkin sementtiproteesien verrattain tavallisen irtoamisongelman takia. Sementitön lonkan tekonivel kiinnittyy luutumisen kautta. Perinteisen muovi-metalli liukuparin lisäksi on käytetty keraami-keraami sekä keraami-muovi liukupintavaihtoehtoja. 2000-luvulla liukupintamateriaaleina yleistyivät metalli-metalli-liukupinnat.

Kansalliset tekonivelrekisterit on perustettu tuottamaan tietoa tekonivelten uusintaleikkauksista. Tavoitteena on havaita huonot proteesimallit mahdollisimman aikaisin, jotta uusintaleikkauksien määrä saataisiin pidettyä vähäsenä. Pohjoismaisista tekonivelrekistereistä Ruotsin lonkkaproteesirekisteri perustettiin 1979, Suomen Tekonivelrekisteri 1980, Norjan tekonivelrekisteri 1987, ja Tanskan lonkkaproteesirekisteri 1995. Yhdistetty pohjoismainen tekonivelrekisteri (The Nordic Arthroplasty Register Association, NARA) perustettiin 2007 parantamaan tekonivelkirurgian laatua Pohjoismaissa havainnoivan rekisteritutkimuksen avulla.

Tämän väitöskirjatutkimuksemme tarkoituksena oli arvioida metalli-metalli-liukupintaisiin lonkan tekoniveliin liittyvien metallihierrekomplikaatioiden yleisyyttä ja riskitekijöitä käytettäessä BHR- ja ReCap Magnum-lonkkaproteeseja Turun yliopistollisen sairaalan proteesirekisteriin perustuen. Tarkoituksenamme oli myös arvioida lonkan pinnoiteproteesien ja vastaavien kokotekonivelmallien pysyvyyttä

lyhyen aikavälin seurannassa Suomen Tekonivelrekisteriin perustuen. Tutkimme myös sementtikiinnitteisten lonkan tekonivelten mallikohtaista pysyvyyttä Pohjoismaisessa NARA-rekisterissä.

Totesimme tutkimuksessamme että BHR-pinnoitetekonivelleikkaukseen saattaa liittyä aiempaa luultua enemmän ongelmia. Suosittelemmekin näiden potilaiden systemaattista seurantaa. Metallihierrekomplikaatioiden määrä ReCap Magnum-proteesia käytettäessä oli varsin korkea. Lyhyen aikavälin uusintaleikkausriski käytettäessä pinnoiteproteesia tai vastaavaa isonuppista, metalli-metalli-liukupintaista kokotekoniveltä oli samaa suuruusluokkaa. Havaitsimme lisäksi että monet sementtikiinnitteiset kokotekonivelmallit toimivat hyvin pitkällä aikavälillä. Mallien pitkäaikaispysyvyydessä oli kuitenkin merkitseviä eroja.

Avainsanat: Suomen tekonivelrekisteri, Nordic Arthroplasty Register Association (NARA), lonkan tekonivelleikkaus, implantin pysyvyys, komplikaatio, metalli-metalli liukupinta, isonuppinen tekonivel, pinnoiteproteesi, metallihierrekomplikaatio, sementtikiinnitteinen proteesi.

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ABBREVIATIONS

AAOS	American Academy of Orthopedic Surgeons
ALVAL	Aseptic lymphocyte-dominant vasculitis-associated lesion
AOANJRR	Australian Orthopedic 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
CI	Confidence interval
Co	Cobolt
CoC	Ceramic-on-ceramic
Cr	Chrome
CT	Computed tomography
DHAR	Danish Hip Arthroplasty Register
DKAR	Danish Knee Arthroplasty Register
EQ-5D	EuroQol-5D
FAA	Finnish Arthroplasty Association
FAR	Finnish Arthroplasty Register
FINAS	Finnish Accreditation Service
GEE	Generalized estimation equation
HA	Hydroxy Apatite
HHS	Harris hip score
HMWP	High molecular weight polyethylene
HR	Hazard ratio
HRA	Hip resurfacing arthroplasty
HRQoL	Health-related quality of life
HXLPE	Highly cross-linked polyethylene

ICD	International Classification of Diseases
ICOR	International Consortium of Orthopaedic Registries
IN	Indiana USA
ISAR	International Society of Arthroplasty Registries
LDH MoM THA	Large-diameter head metal-on-metal total hip arthroplasty
MARS MRI	Metal artifact reduction sequence magnetic resonance imaging
MHRA	Medicines and Healthcare Products Regulatory Agency (UK)
MoM	Metal-on-metal
MoP	Metal-on-polyethylene
NAR	Norwegian Arthroplasty Register
NARA	Nordic Arthroplasty Register Association
NC	North Carolina USA
NHP	Nottingham Health Profile
NHS	National Health Service (UK)
NJ	New Jersey USA
NJR	National Joint Registry of England and Wales
NORE	Network Orthopaedic Registries of Europe
OA	Osteoarthrosis
OHS	Oxford Hip Score
OR	Odds ratio
PMMA	Polymethylmetacrylate
PROM	Patient Reported Outcome Measure
PPF	Periprosthetic fracture
PVR	Pulmonary vascular resistance
RCT	Randomized Controlled Trial
RR	Risk ratio
SAY	Suomen Artroplastiayhdistys
SDM	Shared Decision-Making
SF-36	36-Item Short Form Survey
SHAR	Swedish Hip Arthroplasty Register
SKAR	Swedish Knee Arthroplasty Register

SVR	Systemic vascular resistance
THA	Total hip arthroplasty
THL	Terveyden ja Hyvinvoinnin laitos
TKA	Total knee arthroplasty
VAS	Visual Analoque Scale
WOMAC	The Western Ontario & McMaster Universities Osteoarthritis Index

LIST OF ORIGINAL PUBLICATIONS

The present thesis is based on the following papers, which will be referred in the text by their Roman numerals. The original publications have been reproduced with the permission of the copyright holders.

I Junnila M, Seppänen M, Mokka J, Virolainen P, Pölönen T, Vahlberg T, Mattila K, Tuominen E, Rantakokko J, Äärimaa V, Itälä A, Mäkelä K. Adverse reaction to metal debris after Birmingham hip resurfacing arthroplasty. Acta Orthop 2015;86(3):345-50.

II Mäntymäki H, Junnila M, Lankinen P, Seppänen M, Vahlberg T, Mäkelä KT. Systematic screening of adverse reaction to metal debris after ReCap-Magnum metal-on-metal total hip arthroplasty. Scand J Surg 2017 Mar 1 [Epub ahead of print].

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

IV Junnila M, Laaksonen I, Eskelinen A, Pulkkinen P, Havelin L, Furnes O, Fenstad AM, Pedersen AB, Overgaard S, Kärrholm J, Garellick G, Malchau H, Mäkelä KT. Implant survival of the most common cemented total hip devices from the Nordic Arthroplasty Register Association database. Acta Orthop 2016;87(6):546-553.

1. INTRODUCTION

Cemented total hip arthroplasty (THA) with metal-on-polyethylene bearing surfaces has been the gold standard for the treatment of hip arthrosis for decades. It was introduced by Sir John Charnley in the 1960's (Charnley 1960). The treatment was originally reserved for patients above 65 years with end-stage osteoarthrosis (OA). Later, national register datas have shown that cemented THA is indeed the method of choice for treating the osteoarthritic hip in elderly patients (Swedish Hip Arthroplasty Register; SHAR, Finnish Arthroplasty Register; FAR, National Joint Registry; NJR, Australian Orthopaedic Association National Joint Replacement Registry; AOANJRR). However, survival of the THA implant among young and active patients is inferior compared to elderly (FAR, AOANJRR). The most common reason for failure of cemented THA is aseptic loosening of the components (FAR, SHAR, AOANJRR). Aseptic loosening may be associated with osteolysis generated by biologically active polyethylene wear particles (Mirra et al. 1982, Cooper et al. 1992). Therefore, alternative bearing couples were developed to minimize wear and osteolysis. Perfect articulating surfaces should have minimal wear and any wear debris should not evoke a host immune response. The bearing materials should exhibit low friction to reduce forces on implants. The material properties of the head and liner/acetabular components should be chemically stable *in vivo*, tough enough to minimize the risk of fracture, and hard and non-ductile to reduce the susceptibility to scratching and third-body wear (Raipura et al. 2014).

Several manufacturers were encouraged to produce new hip resurfacing arthroplasty (HRA) devices after publication of the wear rates of the metal-on-metal bearing surfaces of the McKee-Farrar THA (McKellop et al. 1996, Schmalzried et al. 1996*)* and the good experiences of cemented fixation of the femoral resurfacing components (Hungerford et al. 1998). HRA consists of an uncemented acetabular component, a cemented femoral component, and a cobalt chromium–cobalt chromium articulation. HRA became a popular treatment of hip arthrosis worldwide during the first decade of this millennium. In Finland, this trends was followed rapidly (AOANJRR, NJR, Seppänen et al. 2012).

Restoring limb length and minimizing joint reactive forces are important goals of any hip arthroplasty (McGrory et al.1995, Sakalkale et al. 2001). HRA had potential benefits compared to conventional THA, *e.g.,* more accurate restoration of leg length, femoral

offset and femoral anteversion. HRA may provide a more natural feeling for the patient and it was recommended for younger and more active patients (National Institute for Clinical Excellence 2002). Good short term results (Daniel et al. 2004, Treacy et al. 2005) encouraged clinicians and patients further and the clinical use of HRA became widespread.

Large-diameter head metal-on-metal (LDH MoM) THA was introduced soon after HRA. The perceived benefits over the conventional metal-on-polyethylene (MoP) THA were a reduced risk of dislocation (Herrlin et al. 1988, Cuckler et al. 2004) and improved articular wear (Jantsch et al. 1991). However, from early on there was some concern 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 raised also questions (Savarino et al. 2002, Dumbleton and Manley 2005). Scientific evidence of local complications of metal-on-metal (MoM) bearing surfaces started to accumulate (Shimmin et al. 2005, Davies et al. 2005, Pandit et al. 2008) and there was an increasing number of patients with pain and swelling in the groin due after MoM hip arthroplasty (Macpherson and Breusch 2011). The finding of substantial sterile effusions of the hip and/or of macroscopic necrosis/metallosis associated with MoM joint failure became known as adverse reactions to metal debris (ARMD) (Langton et al. 2010). The first population-based evidence of inferiority of MoM hips due to ARMD came in 2007 when AOANJRR identified HRAs as requiring a higher than anticipated rate of revisions (AOANJRR 2007). It took some time before MoM bearings were largely abandoned due to early and mid-term failures (MHRA 2010, SAY 2012). Although local soft tissue damage associated with HRA and LDH MoM THA are relatively common, the theoretical risk of mutagenicity and carcinogenicity of MoM hip devices has fortunately not actualized. The risk of cancer is not increased after MoM hip replacements during mid-term follow-up. However, longer follow-up is still needed before MoM bearings may be declared safe in terms of cancer (Brewster et al. 2013, Mäkelä et al. 2014).

There are several failed innovations in the history of orthopedic surgery. Individual products as well as entire categories of devices, like MoM hips, are sometimes found to be faulty and must be recalled. Common to these incidents are insufficient preclinical data, lack of long-term studies and limited multicenter cohort studies before the general

release of devices. Post-marketing surveillance exploiting national arthroplasty registers has proven to be an effective method for detection of outlier implants. Without register monitoring identification of many of the failed innovations would have been delayed (Malchau et al. 2015). Further, there is evidence that operative outcomes using even established methods like cemented fixation in THA surgery may vary between devices used (AOANJRR, FAR).

The aim of this thesis was to assess the complication rates of two MoM hip devices – the Birmingham Hip Resurfacing (BHR) HRA (Smith & Nephew, Warwick, UK) and the Biomet ReCap Magnum THA (Biomet, Warsaw IN, USA). For this assessment, the joint replacement register of the Tyks Turku University Hospital was used. Another aim was to compare the differences of early survival rates of the most common HRA brands and analogous LDH MoM THAs and here the FAR was used. A further aim was to assess implant survival of the most common conventional cemented THA brands as recorded in the Nordic Arthroplasty Register Association (NARA) database.

2. REVIEW OF THE LITERATURE

2.1 National Arthroplasty Registers

2.1.1 Finnish Arthroplasty Register (FAR)

FAR was founded in 1980 by the Finnish Orthopedic Association to collect information on orthopaedic endoprosthetic surgery. Of the national registers, only the Swedish Knee Arthroplasty Register (SKAR) (1975) and the SHAR (1979) are older than the FAR. In 1993, FAR was integrated with the National Agency for Medicines. A major data contents revision of the FAR was performed on 1996. FAR data were published systematically in yearbooks published in 1997, 1998-1999, 2002-2003, 2004, 2006, and 2007. In November, 2009, FAR was transferred for hosting by the National Institute for Health and Welfare (THL). THL has published annually descriptive data on hip and knee arthroplasty in the internet (in Finnish).

In the recent years, it became obvious that the data content of the FAR from the 1990's is no longer appropriate. For example the same data notification form was used for all types of arthroplasty like hip, knee and shoulder. Advanced in IT-technology allow electrical data collection instead of collecting data on paper notification forms. Further, new implants were introduced to the market rapidly. Although FAR data had been the basis for numerous scientific publications, it was time to move on and the need to produce more systematic information rapidly became pressing.

In 2012, the Finnish Arthroplasty Society made an initiative to the THL of revising FAR data contents, data collection, and reporting. An Advisory Board of the FAR was established with representatives from the THL, the 5 University Hospital Districts of Finland, the National Supervisory Authority for Welfare and Health (Valvira), and from BCB Medical Ltd, which has developed health information systems in Finland, with a special impact on electrical barcode reading of overseas products.

The data on hip and knee arthroplasties was revised by May 2014 and includes now data on the bearing surfaces of devices used for THA. Electronical barcode reading of the implants in operative theaters has been widely used in Finland since 2005.

However, until May 2014, about 20 per cent of all hip and knee arthroplasty notifications to the THL were made on papers. IT-managers of the THL developed a user interface for those hospitals that did not have a commercial implant data collection system. The fully electronic national FAR started on May 19th 2014.

Combining old and new register data contents was not straightforward. A library of ref-codes of all available hip and knee implants was created in collaboration with manufacturers, the International Society of Arthroplasty Registries (ISAR), and the International Consortium of Orthopaedic Registries (ICOR). Barcodes of archived implant notification form stickers of the old register were read to examine the types of bearing surfaces used for THAs implanted since 2000. The new FAR data contents include also new variables, *e.g.*, surgical approach, American Society of Anaestetisiolgy- grade (ASA-grade), and duration of the operation. The ENDOnet (www.thl.fi/far) is a new open-access reporting system developed by the THL and the Advisory Board. The ENDOnet includes joint data from the old and new registers, *e.g.,* data on the cumulative fraction of revisions of implanted brands and implant survival. However, the ultimate goal of FAR has remained constant, to detect outlier implants and methods as early as possible.

Implant-specific survival data based on the FAR was not published in an annual yearbook-format for several years before establishment of the ENDOnet in 2014. Research activity, however, based on FAR material has always been high. A good example of the ability of a register to capture outlier devices is the study of Puolakka et al. (1999). They reported poor implant survival of cementless Biomet total hips (Puolakka et al. 1999). The 9-year survival was only 65% (95% CI 61-69). The poor survival was due to the inferiority of the cup and the polyethylene liner. This finding was common to all metal-shell designs using polyethylene liners with a Hexloc locking mechanism. The authors recommended that Biomet cups with Hexloc liners be abandoned.

There are several publications based on FAR data focusing on the success of the fixation method of the THA. Eskelinen et al. (2005) evaluated the population-based survival of THA fixation methods in OA patients under 55 years old and the factors affecting survival. Their statement was that, for younger patients, uncemented

proximally circumferentially porous- and hydroxyl apatite (HA)-coated stems are the implants of choice. Regarding the cup side, when all revisions were taken into account, the survival of uncemented cups was no better that of all-poly cemented cups. The results for patients under 55 years of age with rheumatoid arthritis (RA) were similar (Eskelinen et al. 2006).

FAR data has also been used to evaluate implant survival of THA devices brandwise. Mäkelä et al. (2008) published the results of the 12 most common cemented implants in patients aged 55 years and above. They found that only two stem designs, the Exeter Universal (Stryker Howmedica, Mahwah NJ, USA) and the Müller Straight stem (Zimmer Winterthur, Switzerland), had a survivorship of over 95% at 10 years; revision for aseptic loosening was their study endpoint. In the subgroup of patients aged 55 to 64 years, overall survivorship for all cemented prostheses was less than 90% at 10 years.

There are several national medical registers in Finland which can be linked for retrieval of data for research purposes. Several linkage studies have been published using the FAR and other nationwide register data, *e.g.*, the Finnish Cancer Register and other nationwide Finnish health and quality registers. Jämsen et al. (2014) published data on the early failure rate after cementless THA in patients aged 80 years or older and found the rate to be high. They combined FAR data and comorbidity data from the National Discharge Register. Cementless hip replacement was associated with a higher rate of early revision than cemented hip replacement, particularly among female patients (hazard ratio 2.9). The difference was not explained by comorbidity or provider-related factors.

FAR and the Finnish Cancer Register data have been combined in several studies during the past decades to assess the cancer risk of THA devices. Paavolainen et al. (1999) found that the overall cancer risk after total knee arthroplasty (TKA) is not increased. Mäkelä et al. (2012) concluded that MoM hip replacements were not associated with an increased overall risk of cancer during a mean follow-up of four years. Two years after that, the data was updated and findings were similar (Mäkelä et al. 2014).

FAR data has also been used to assess the risk of revision after THA and TKA for specific disease groups. Jämsen et al. (2014) assessed the duration of hospitalization, occurrence of infections, dislocations, revisions, and mortality following THA and TKA in patients with Parkinson's disease. It turned out that they had a longer mean duration of hospital stay and an increased risk of hip dislocation during the first postoperative year. There was no difference in infection or revision rates, or one-year mortality.

2.1.1.2. Turku University Hospital Implant database

Ref-codes of all total hip and knee devices are read electronically using bar code reader in the operative theatre during operation in Turku University Hospital. Operative data like diagnosis or reason for revision are also entered into the database during operation by nurses, although surgeons are responsible for that missing data does not exist. Turku University Hospital data are then delivered to National Institute for Health and Welfare for FAR purposes. Patient reported outcome measures (PROM) are not included in the data contents. Unfortunately there is mainly advertizing litterature concerning Turku University Hospital Implant Database, which is managed by BCB Medical. BCB Medical databases overall are under rapid national development, and validation process is therefore going on separately for each database.

2.1.2. Swedish Hip Arthroplasty Register

The Swedish Hip Arthroplasty Register (SHAR) was established in 1979 and is the oldest nationwide hip arthroplasty register in the world. Since 1999, the SHAR has reported implant survival and hospital level data publicly in annual reports. SHAR is governed by the Sahlgrenska University Hospital, Gothenburg, *i.e.*, by the orthopedic profession. It seems obvious now in 2017 that the leadership of clinicians has played a very important role in the success of the SHAR. In Finland, FAR was managed a long time by the Finish Medical Agency, and more recently by THL. Knowledge of surgical details and a clinical interest of the fate and prognosis of the patients is crucial in producing data of clinical significance (SHAR).

The annual reports and feedback from the SHAR has led to a continuous improvement in the national results of THA. Stepwise introduction of hip implant innovations was

introduced already in 1995 (Malchau H. Thesis. Göteborg University 1995). Therefore, the SHAR has guided implant policy in Sweden to a great extent over several decades. Total hip devices without long-term survival data and unproven clinical performance have not been introduced into common practice. The prophylactic role of the SHAR in avoiding large-scale use of inferior implants has been remarkable in Sweden compared to the FAR in Finland. For instance, MoM THAs were not introduced almost at all in Sweden, although they became popular in Finland very rapidly. During 2013-2014 only 37 hip resurfacings were implanted in Sweden, and the proportion of MoM bearing surfaces of all bearing surfaces used was minor from 2005 to 2014 (SHAR). At the same time more than 20,000 MoM THAs were inserted in Finland with, as we now know, poor survivorship and poor clinical results (www.thl.fi/far). Continuous improvement of implant survival in Sweden is evidenced by the SHAR annual reports, where the 10-year survival of total hips operated in the late 1970's was less than 90%, after 1992 it was 90.3% and after 2005 it has been 93.8%. This improvement was reported also by Herberts and Malchau (2000).

Besides annual reports numerous scientific, peer reviewed papers have been published based on SHAR data and these have played an important role in changing clinical practice. For example, there is a tradition in Sweden to use cemented fixation in elderly patients in primary THA to avoid early post-operative fractures and late osteolysis. Cemented primary THA has yielded high implant survival of elderly patients in Sweden (Hailer et al. 2010).

Despite improvement, however, revision hip arthroplasty remains a challenge, especially in younger patients. Cement for fixation is often not an option in revision surgery where patients often have major bone deficiency. Strömberg et al. (1988) found that revision hip arthroplasty with cement in young and middle-aged patients with cemented primary arthroplasty is associated with a high rate of failure due to aseptic loosening. They suggested alternative methods and techniques for revision surgery in younger patients. Later the same group reported outcomes of revision THAs with a second-generation cementing technique in young patients and reported a 14% failure rate at 7 years, predominantly for aseptic loosening (Strömberg and Herberts 1996). Adelani et al. (2014) stated that the overall survival after revision THA in younger patients was 69% at the mean follow-up of 6.7 years despite the use of modern

cementless implants and techniques. It is obvious that the optimal fixation method in THA has still not been established.

SHAR was one of the first national registries to include patient-reported outcome measures (PROM). Since 2008, all clinics have reported patient-reported variables where a current response frequency of 85% preoperatively and almost 90% at one year of follow-up (SHAR Annual Report 2014). PROMs enable patients to assess their own condition in the pre- and postoperative periods. Implant survivorship information from registries do not give the surgeon a sense of how patients feel about their surgery and identification of protective factors associated with better and worse outcomes is important (Greene et al. 2016). PROMs are not, as yet, included in the FAR data base, although the Finnish Arthroplasty Society is preparing introduction of PROM data.

Peer reviewed PROM studies based on SHAR data have been published already at late 1990's. Garellick et al. (1998) compared Harris hip score (HHS) to the Nottingham Health Profile (NHP) in the evaluation of THA. After five years, both measures reflected the function of the implant and the general state of the patient, but a higher degree of sensitivity was needed to show differences in implant performance. Söderman et al. (2000) compared the validity and reliability of the Swedish Western Ontario and McMaster Universities Ostearthritis Index (WOMAC) to generic instruments (SF-36 and NHP). Initially, they preferred the Swedish WOMAC to be used in association with THA surgery. Later, however, as the importance of PROMs grew, the WOMAC was superseded by the health-related quality of life (HRQoL) measure EQ-5D and visual analogue scales (VAS) for pain and satisfaction (Rolfson et al. 2011). The same authors also tested internet-based follow-up questionnaires for PROMs. The results have been promising, and the authors hope that register work may someday become less resource-consuming and that results could be analyzed in real time.

The Nordic possibility to identify persons with personal identification number enables database linkage studies between registers. SHAR data has been frequently combined with data from other Swedish medical registries. For example, Greene et al. (2014) evaluated the effect of the level of education of the patient on PROMs after THA. They merged data on all THAs with complete PROM data from national databases containing education attainment, marital status, and comorbidities. High

education attainment was associated with higher HRQoL after THA, whereas those with low and medium education were at risk of lower HRQoL. The same study group assessed the association between antidepressants and PROMs after THA. Using antidepressants was related with a poorer HRQoL, higher levels of pain before and after surgery, and less satisfaction. Preoperative antidepressant use was independently associated with poorer PROMs 1 year after THA, regardless of patient-reported anxiety/depression (Greene et al. 2016).

One of the next aims of SHAR is to integrate patient wishes and expectations with the expertise of surgeons in the form of a Shared Decision-Making (SDM) instrument. This is done by linking the SHARs database with databases of Statistics Sweden and the National Board of Health and Welfare (Cnudde et al. 2016). The aim is to establish a tool to provide individualized multidimensional outcome predictions based on information provided by patients (demography, baseline PROMs, and comorbidities) and by clinicians (diagnosis and technical details about appropriate methods and implants). It could inform and educate patients about the possible risks and expected outcomes in an effort to set realistic expectations after THA. It could also recognize risk factors, *e.g.*, smoking and alcoholism that could identified and managed properly before surgery. For the orthopedic surgeon the SDM could also be an instrument, based on the individual characteristics of the patient, that could facilitate recommendations about the implant, *e.g.*, type of fixation and bearing surface (Cnudde et al. 2016).

2.1.3. Norwegian Arthroplasty Register

The Norwegian Arthroplasty Register (NAR) was established in 1987. NAR publishes annual reports with demographic data, operating volumes, use of different types of prostheses and cements, and other characteristics of the procedure. Implant survival data is published mainly by peer-reviewed journals. NAR works under government sponsorship in the Haukeland University Hospital, Bergen. NAR includes, besides THA, TKA, and total shoulder replacement data, also data on the Norwegian Cruciate Ligament Register established in 2004 and the Norwegian Hip Fracture Register established in 2005 (NAR 1016).

During the first 15 years, 26 scientific papers were published based on NAR data, but after that the volume of papers has expanded markedly. In the last 15 years, over 120 peer-reviewed papers have been published (NAR 2016). NAR has been very systematic in its search for outlier devices. Havelin et al. (1994) assessed early failures among THA devices on the brand level. The BIO-FIT cementless stem had high failure rates, as did the Harris/Galante stem without circumferential coating. The results of the Femora cementless stem, which had spiral throughout the stem, differed by which side it was implanted. In the same paper, high early failure rates were reported in some smooth, uncemented cups without porous coating. Havelin et al (1995) also observed that the Boneloc cement, introduced in Europe only four years earlier accompanied by substantial marketing efforts, had poor survivorship. After only three years of use, it became clear that the two-year survival rate of prostheses cemented with Boneloc was 95.5 per cent – significantly inferior compared to other bone cements on the market. A poor performance of two HA-coated acetabular cups was also implied by NAR data (Havelin et al. 2002). The Tropic cup in combination with an aluminum ceramic femoral head had a survivorship comparable to that of the Charnley cup. However, when used in combination with a stainless-steel head, the need for revision beyond four years was 3.4-fold for the Tropic cup compared to the Charnley cup. Over the same period, the Atoll cup had to be revised 3.8 times more often when used with an aluminum head and 6.1 times more often when used with stainless-steel heads (Havelin et al. 2002). It soon emerged that the reason for the high failure rates was excessive thickness of the HA coating; this coating was quickly resorbed especially if the implant was smooth under the HA-layer (Overgaard et al. 1998). Espehaug et al. (2009) demonstrated the importance of long-term follow-up in their report of clinically important differences between cemented prosthesis brands. They identified inferior results for prostheses, some in common use, which had been introduced to the market efficacy and safety largely undocumented. Several prostheses with low revision rates in the short term did not perform well as follow-up times grew, *e.g.*, the Reflection All-Poly/Spectron-EF combination.

Identification of outlying implants based on NAR data has been very successful during several decades. However, the amount of arthroplasty devices on the market has increased rapidly during the latest years. The peer review process in scientific papers may be very slow. It seems obvious, in view of the current overwhelming surge of data

on devices and the need for robust and quick data, that all information included in the national registers cannot be published by the peer review process. Some information on surgical methods and devices should be available almost in real time. Currently, it seems that the ability of arthroplasty registers to detect outliers is most effective, if Kaplan-Meier (KM) survival estimates are presented implantwise as raw, unadjusted open-access data in the internet, not only in published scientific papers. The role of scientific, peer reviewed studies is to deepen our understanding of the open access data after adjustments and analyses of the reasons for the need for revisions. FAR has been developed lately with the NAR experiences in mind. In Finland, open access implantwise survival estimates are available in the internet in the ENDOnet arthroplasty register (www.thl.fi/far).

2.1.4. Australian Orthopaedic Association National Joint Replacement Registry

The Australian Orthopaedic Association Nation Joint Replacement Registry (AOANJRR) was established in 1998 to fulfill the need for information on joint replacement surgery outcomes in Australia. This was, in part, kindled by the documented success of a number of arthroplasty registries in other countries, in particular the Swedish Arthroplasty Registries. Data collection started in 1999 and became fully national in 2002. In June 2009, the Federal Parliament passed legislation to enable the government to recover funding costs from the orthopedic industry. Currently, more than 85,000 hip and knee replacements are undertaken each year in Australia and data coverage by the registry exceeds 98%. The strength of AOANJRR is the large number of registered patients. It gives very detailed information on patterns of implant usage and surveillance of implants performance nationwide across all surgeons. Understandably, then, the registry has already by now had a major impact on clinical practice. Large numbers of patients combined with active authors of the registry ensures fast screening of outlier devices. Like many other national registries, the AOANJRR does not collect assessment scores, PROM data, nor radiographic data (https://aoanjrr.sahmri.com)

Since 2004, the AOANJRR has developed a standardized process for identifying outlier devices. It is based on a 3-stage process consisting of an automated algorithm, on an extensive analysis of individual prostheses or combinations by registry staff, and,

finally, a on a meeting involving a panel of experts from the Australian Orthopaedic Association Arthroplasty Society (de Steiger et al. 2013). Thus, in the 2007 Annual Report, the AOANJRR identified the Acetabular Hip System (ASR), Cormet 2000 HAP, and the Durom as having a higher than anticipated rate of revision (AOANJRR Annual Report 2007). Problems associated with the MoM issue became evident from the AOANJRR Annual Reports and led to a worldwide recall of large head MoM devices (de Steiger et al. 2011).

Three years later, femoral stems with exchangeable femoral necks had reportedly twice the risk of revision compared to all other femoral stems (AOANJRR 2010). Since then exchangeable femoral necks have been abandoned worldwide largely due to such observational register reports, not to randomized controlled studies (RCT). The ability of RCTs to detect outlier devices is limited since the number of observations is small, and there is a high risk of selection bias.

De Steiger et al. (2015) have also stated AOANJRR data indicates that there is still a growing learning curve for the direct anterior approach for THA even when prosthesis combinations specifically marketed for that approach are used.

Only few register reports have assessed re-revision rates after revised HRAs. More than 15,000 primary HRAs have been recorded in the AOANJRR. De Steiger et al. (2015) evaluated the cumulative rate of re-revision for failed HRA. Revision of a primary HRA was associated with a high risk of re-revision. The cumulative re-revision rate was 26% at 10 years. There was no difference in the rate of revision when the different types of initial revision and different bearing surfaces in the first revision were assessed.

Linkage studies between AOANJRR and other Australian quality register data have not been as frequent as in the Nordic countries due to relatively young register tradition in Australia. However, comorbidity data has been recently combined with AOANJRR data (Geeske Peeters et al. 2016). The effect of mental health before surgery on the long-term outcome of TKA and THA among female patients was assessed and it was found that in middle-aged and older women, THA improved physical function and reduced bodily pain, with improvements sustained up to 10 years after surgery, regardless of the state om mental health of the patients.

2.1.5. National Joint Registry for England, Wales, Northern Ireland and the Isle of Man

The National Joint Registry (NJR) for England, Wales, Northern Ireland and the Isle of Man was established in 2002. It was set up by the Department of Health and the Welsh Government. Northern Ireland joined in 2013 and the Isle of Man in July 2015. NJR is managed by a Steering Committee which is responsible for the work and progress of the NJR. The Steering Committee consists of orthopedic surgeons, epidemiologists, representatives, and range of stakeholders (www.njrcentre.org.uk).

NJR is the largest joint replacement register in the world with a record of more than 2 million procedures. Over 200,000 procedures are added yearly. It is obvious that high data quality and coverage are difficult to reach in such a large set up. After continuous monitoring of data and auditing, compliance has grown over the lifetime of the registry. In 2016 over 95% of all primary operations and over 90% of all revisions were recorded (NJR Annual Report 2016). However, Sabah et al. (2015) have recently expressed some concern about the reliability of the NJR data, and their study suggested that NJR reports may underestimate the true rates of revision. They recommended a system for continuous independent evaluation of the quality and validity of NJR data. Some concerns about data inaccuracy concerning identification of the operating surgeon were also published earlier by Kosy et al. (2013), who compared hospital computer systems and operation notes to the data extracted from the NJR.

The key aim of the NJR is to identify any brand of devices showing high failure rates and to allow prompt removal from the market. For example, in 2010 the higher than expected revision rate for the MoM THA implants was identified based on NJR data (NJR Annual Report 2010, Smith et al. 2012). Information about implant performance is reported every six months to the NJR's Implant Performance Group. If the monitoring results show that the performance of an individual implant does not meet expectations, the Implant Performance Group notifies the Medicines and Healthcare Products Regulatory Agency (MHRA). The MHRA then undertakes an investigation in collaboration with the device manufacturer (NJR).

One of the main goals of the NJR is to inform clinicians of outcomes achieved by joint replacement surgery. NJR gives clinical feedback to orthopedic surgeons who have

submitted data to the NJR and are registered as NJR users. Surgeons can view NJR reports and indicators about procedures that have been recorded in their name and analyze this within the context of hospital, sector (NHS and independent sector healthcare), and national benchmarks. The feedback to clinicians is designed to support assessment of clinical practice by enabling surgeons to understand and interpret NJR data in a wider context than is currently possible through NJR Reports online (NJR).

NJR data has been used in several recent peer reviewed scientific studies. Palan et al. (2016) studied the influence of the kind of cemented femoral stem used on the incidence of revision indicated by a periprosthetic fracture (PF) in 257,202 primary THAs. Compared with the Exeter V40, the revision ratio adjusted for age, gender, and ASA grade was 3.9 for the cemented Collarless Polished Tapered (CPT) stem (Zimmer, Warsaw IN, USA), 0.9 for the C-Stem (DePuy; Johnson & Johnson, New Brunswick NJ, USA), and 0.4 for the Charnley stem (DePuy; Johnson & Johnson, New Brunswick NJ, USA). NJR data has also been utilized in national linkage studies. The clinical impact has been substantial. Smith et al. (2012) assessed the cancer risk of metal-on-metal THAs using linkage of NJR data and hospital episode statistics. 40,576 patients with hip replacement with MoM bearing surfaces and 248,995 with alternative bearings were analyzed. Compared with alternative bearings, there was no evidence that MoM bearing surfaces were associated with an increased risk of any cancer diagnosis at least for seven years after surgery. These findings have had a high impact on revision surgery indications of MoM THA worldwide.

Data based on large observational registry studies may be difficult to interpret, especially when assessing variables registers are not designed for. Hunt el al. (2013) studied the 90-day mortality after 409,096 THAs performed for OA based on NJR data. 1,743 patients had died within 90 days of surgery during 8 years. There was a substantial secular decrease in mortality: from 0.56% in 2003 to 0.29% in 2011 even after adjustment for age, gender, and comorbidity. They concluded that widespread adoption of four simple clinical management strategies (posterior surgical approach, mechanical prophylaxis, chemical prophylaxis, and spinal anesthesia) could, if causally related, reduce mortality further. However, Whitehouse et al. (2014) disputed this conclusion and claimed that it is inappropriate to use NJR data to study an outcome

affected by a multitude of confounding variables when these cannot be adequately accounted for in the available data set. Their Schemper's statistic showed that only 19% of the variation in mortality was explained by the variables available in the NJR data set.

2.2. International collaboration of arthroplasty registers

2.2.1. Nordic Arthroplasty Register Association

The Nordic countries (Denmark, Sweden, Finland, and Norway), have all had a long and successful tradition of arthroplasty registries. In Sweden, there is the Swedish Hip Arthroplasty Register (SHAR) and the Swedish Knee Arthroplasty Register (SKAR), in Norway the Norwegian Arthroplasty Register (NAR), in Finland the Finnish Arthroplasty Register (FAR), and in Denmark the Danish Hip Arthroplasty Register (DHAR) and the Danish Knee Arthroplasty Register (DKAR). There is no arthroplasty register in Iceland. Registries are characterized by a high research activity aiming to improve the quality of treatment of patients undergoing joint replacement surgery. However, results presented by the Nordic registries have suggested differences among the countries. These differences are related to the data collection system, the data/variables being collected, the definition of the data, and statistical methods. Reports from the Nordic registries have, further, shown differences regarding indication for surgery, characteristics of the joint replacement populations, fixation methods used, and implant survival. Due to these differences, the results from the different Nordic registries have not been fully comparable. Furthermore, although the Nordic registries are population-based and cover approximately 25 million inhabitans, the numbers of patients included in specific populations (*e.g.*, patients that undergo joint replacement due to RA or patients operated on for osteonecrosis) or the number of patients developing specific adverse events after surgery (*e.g.*, revision due to infection or periprosthetic fracture) are relatively small. This naturally limits the statistical precision of risk estimates and may affect the validity of conclusions.

The Nordic registries have acknowledged these limitations and the need for collaboration across national borders. Thus, the Nordic Arthroplasty Register Association (NARA) was established in 2007 with the overall aim to improve the quality

of research and our understanding of the clinical course of patients undergoing joint replacement surgery. The goal is to provide data to improve the treatment quality in this field of surgery. NARA set several specific aims for its work. A common dataset has been created to compare demographics and results regarding total joint replacement surgery among countries, and to study outcomes in patient groups which are too small to be studied in each separate country. An important aim of the NARA is to promote joint Nordic research where it is of common interest and to improve data quality. NARA aims also to co-operate on methods to develop research and quality in register studies, and to coordinate a joint Nordic standpoint towards other international register associations like the ISAR (International Society of Arthroplasty Registries), ICOR (International Consortium of Orthopaedic Registries), and NORE (Network Orthopaedic Registries of Europe) (NARA).

These aims have been largely reached in 2016. Through collaboration with regular meetings and networking the data quality in respective national registries has improved and a more valid basis for quality monitoring and research has been achieved. The misunderstandings about how to define the pertinent research variables have been discussed and a common understanding has been achieved. Thus, for example, before NARA, different calculation methods on how to assess the completeness of registration and of revision burden were used. Through the internal collaboration, initiatives have been taken to improve the registration systems in the Danish and Finnish registers using the experience from Sweden and Norway. The Finnish registration system was restructured and the register has been transformed from paper to electronic (www.thl.fi/far). Currently, implant data are gathered electronically using reference code reading from all hospitals in Finland. A similar system is under reconstruction in Denmark, initially funded by a NordForsk NTA Grant 2014-2016. Thus, much work on harmonization of implant reporting and data collection in general has been done and is still being done at high priority.

The NARA dataset includes only variables all countries can deliver. It is a dynamic minimal dataset with 25 variables for the hip and 20 for the knee. Each year a new dataset is agreed upon and there is also an ongoing discussion on the values of the variables and on the best set of variables. The NARA dataset includes all primary hip and knee replacement procedures performed in Norway, Denmark, Sweden, and

Finland since 1995 (for hip procedures) or 1997 (for knee procedures). These years were chosen because registration in Danish registries started in 1995/1997. Primary procedures are linked to revision procedures, if revisions have been made, and are registered in the respective national registries. Data are afterwards anonymized and transferred to the common NARA dataset. All countries define a revision procedure as a surgical procedure including removal, exchange, or insertion of any component(s) (NARA).

The projects performed using the NARA dataset have, to a large extent, used statistical methods presented by the NARA group itself (Ranstam et al. 2011a, Ranstam et al. 2011b). The group is continuously working on improving statistical methods and applying new ones, including the propensity score matching method to reduce confounding, the multiple imputation method to deal with missing data, and the Pseudo Value Approach which includes death as a competing risk to assess the relative risk (NARA).

The NARA group has contributed to quality improvement through research projects designed to answer clinically important questions of importance in the current setting. Scientific publications based on NARA data have led to significant changes in treatment policies. For example, MoM THA and resurfacing arthroplasty have been abandoned due to an increased revision risk (Johanson et al. 2010, Varnum et al. 2015). Further, the use of uncemented THA for elderly patients has decreased significantly, at least in Finland (Mäkelä et al. 2014). Projects have also contributed to the education of young researchers and have increased the awareness of evidence-based decision-making. Currently there are 25 peer reviewed NARA papers either published or accepted for publication (Havelin et al. 2009, Robertsson et al. 2010, Johanson et al. 2010, Jämsen et al. 2010, Ranstam et al. 2011a, Ranstam et al. 2011b, Havelin et al. 2011, Engesaeter et al. 2012, Dale et al. 2012, Rogmark et al. 2014, Bergh et al. 2014, Thien et al. 2014, Mäkelä et al. 2014a, Mäkelä et al. 2014b, Pedersen et al. 2014, Hailer et al. 2015, Gjertsen et al. 2014, Schrama et al. 2015, Varnum et al. 2015, Glassou et al. 2015, Rasmussen et al. 2016, Junnila et al. 2016, Wangen et al. 2016, Niemeläinen et al. 2016, Ackerman et al. 2016). Further, 6 papers have been submitted to high quality journals, and 5 manuscripts are being authored.

As an example of NARA research, Robertsson et al. (2010) published the first study based on NARA- data related to the knee. They compared the national knee registries in terms of patient characteristics, diagnosis for knee procedure, and surgical techniques. The study showed considerable differences between the countries and suggested that further classification and standardization work is needed before more elaborate studies become possible. Further, Dale et al. (2012) reported an increased relative risk of revision and increased cumulative 5-year revision rates due to infection after primary THA during the period 2005–2009 compared to earlier years. There was no change in risk factors in the NARA dataset that could explain this increase. The authors stated that there has been an actual increase in the incidence of prosthetic joint infections after THA. Pedersen et al. (2014) reported that uncemented implants perform better than cemented implants as concerns the long-term risk of aseptic loosening. Patients below the age of 55 years, fitted with either uncemented and hybrid THAs, were subject to more revisions in the short term due to problems of dislocation, periprosthetic fracture, and infection compared to patients of similar age with cemented THAs.

Thien et al. (2014) reported that the risk of revision due to early periprosthetic fracture increased during the 2003 to 2009 period compared with the 1995 to 2002 period; the difference persisted even after adjustment for demographic factors and fixation. Ther results showed that uncemented implants led more often to periproshethic fracture than cemented implants, especially in the old age groups. Schrama et al. (2015) found a slightly higher overall risk of revision for infection among RA patients than OA patients, but the difference was evident only after 2001. In THRs with antibiotic-loaded cement, the risk of very early and late infections leading to revision was higher among RA patients than OA patients. Bergh et al. (2014) reported that patients with femoral head necrosis had an overall increased risk of revision. This increased risk persisted over the entire period of observation (1995–2011) and covers largely all of the 4 most common reasons for revision. Glassou et al. (2015) examined if the volume of THAs hospital-wise was associated with the risk of revision after primary THA in the Nordic countries from 1995 to 2011. This study showed a consistent and strong association between hospital procedure volume and long-term risk of revision after primary THA – primarily due to this association prevailing in the large group of cemented THAs.

2.3 Adverse reaction to metal debris (ARMD) and reasons for revision of THA

ARMD is a common term, which describes soft-tissue reactions after MoM THA and HRA (Pandit et al. 2008, Glyn-Jones et al. 2009). These soft tissue reactions may include sterile effusions of the hip and/or macroscopic necrosis/metallosis associated with joint failure and pain (Langton et al. 2010). The symptoms of ARMD patients often include pain, swelling, clicking, and a sensation of subluxation (Langton et al. 2010, Kwon et al. 2011, Reito et al, 2013). Furthermore, there may exist asymptomatic pseudotumors (Kwon et al. 2011, Matthies et al. 2012). The reaction to excess metal wear debris is often associated with increased serum metal ion levels (Langton et al. 2010, Kwon et al. 2010). Magnetic resonance imaging (MRI) optimized to reduce image artifacts and distorsions caused by metallic implants is an important tool in diagnosing local softtissue abnormalities and mass lesions (Haddad et al. 2011). MRI analysis is useful in delineating soft-tissue abnormalities and mass lesions even when radiographs are normal (Hart et al. 2012).

The most common reasons for THA revision in 2016 in Finland were ARMD (16.7%), infection (16.5%), and dislocation (15.4%) (FAR). 10-year revision rate of large-head metal-on-metal THAs overall is higher than that of conventional THA. According to FAR ENDOnet reporting pages (available open access www.thl.fi/far), 10-year revision rate of ASR/Summit MoM THA is as high as 56.9%, whereas that of ReCap/Bimetric MoM THA is 12.1%. The 10-year revision rate of ASR HRA in Finland is 32.5, whereas that of ReCap HRA 14.2%. These revision rates are remarkably higher than those of cemented THA. For example, 10-year revision rate of Link IP/Lubinus SP II is 8.5%, and that of Exeter All Poly/Exeter Universal 7.4%.

2.4. Weaknesses of register research

We acknowledge that register studies overall have several limitations. First, implant survival is the only outcome we are able to assess. For example, patient reported outcome measures (PROM) are not included in the FAR data contents. It is possible that some of the patients may be symptomatic even though they have not been revised. Secondly, data regarding patients' medical history, comorbidities, or hip radiographs

are not available. It is possible that there is selection bias towards using some implant type in more severe cases that could have been detected from the radiographs.

Overall completeness of primary and revision THA data in FAR is high, meaning that almost all primary THAs and most revision THAs are reported to FAR when compared to the National Discharge Register. Overall completeness of primary THA from 2005 to 2015 was 95%, and that of revision surgery 85% (FAR). However, completeness of reporting revision surgery to FAR varies between hospitals, which may cause bias. For example, in 2015 THA revision completeness varied from 60% to 100% at hospital level (FAR). Overall coverage of FAR is good, meaning that every hospital performing THA delivers data into FAR. However, accuracy concerning reasons for revision prior to FAR data contents revision in May 2014 is incomplete. Since the data contents revision of FAR in May 2014, however, the accuracy of reporting reason for revision data has significantly improved, and quality checkups are currently systematically performed. The degree of coverage and completeness in the Scandinavian registries is high (Pedersen et al. 2004, Arthursson et al. 2005, Espehaug et al. 2006, SHAR 2014).

Further, arthroplasty survival studies are prone to the selection bias because revision indication may vary. For example, elderly patients are less likely to be revised compared with younger ones, because of shorter life expectancy or poor medical condition, even if the implant fails and functional result is poor. Similarly, implants with easier or less invasive revision are probably more likely to be revised.

3. AIMS OF THE PRESENT STUDY

The aim of this thesis was to investigate the prevalence and risk factors of adverse reaction to metal debris (ARMD) related to two MoM hip devices - BHR HRA and Biomet ReCap Magnum THA – based on the joint replacement ImplantDB database of the Turku University Hospital. Another aim was to compare the differences in survivorship of three HRA designs with their analogous cementless LDH MoM THAs based on the FAR. Also, the aim was to assess implant survival of the most common cemented THA brands as assessed by data in the NARA database.

The specific aims of the studies were:

1) to evaluate the prevalence and risk factors of ARMD with BHR HRA at our institution (I),

2) to evaluate the prevalence, risk factors and symptoms of ARMD associated with the ReCap-M2a-Magnum LDH MoM THA at our institution (II),

3) to compare survivorship of three HRA designs with their analogous cementless large-diameter head MoM THAs based on the FAR (III), and

4) to compare the survivorship of cemented THAs on a brand level as assessed by data in the NARA database (IV).

4. PATIENTS AND METHODS

4.1. Patients

4.1.1. Studies I and II

In study I, patient data were retrospectively collected from the Turku University Hospital ImplantDB database (BCB Medical). From 2003 to 2011, the BHR was the most commonly used HRA device at our institution, with 249 implantations. In study I, 32 patients (42 hips) who had undergone a BHR HRA between April 2004 and March 2007 were included (Table 1). The total number of hips with a BHR inserted in our unit between April 2004 to March 2007 was 116 (of which 42 were included in the study).

Table 1. Characteristics of 32 patients and results for 42 corresponding hips. Data on swelling, clicking, and subluxation sensation are given hipwise for 41 hips (the data on 1 hip are missing). Data on mean OHS (range) and the OHS classification are given

[a] Mean (range) ARMD: adverse reaction to metal debris; OHS: Oxford hip score (42–48 = excellent, 34–41 = good, 27–33 = fair, and 0–26 = poor).

	Total	ARMD	Probable ARMD	ARMD not found
Patients, n	32	6	8	18
Males, n	24	6	7	11
Serum cobalt, µg/L[a]	2.5 (0.8–14.9)	6.9 (1.2–14.9)	1.5 (0.8–2.6)	1.5 (0.8–2.6)
Serum chromium, µg/L[a]	2.1 (0.6–7.6)	4.4 (1.1–7.6)	1.5 (1.0–2.4)	1.6 (0.6–2.5)
Hips, n	42	8	8	24
Age, years [a]	59 (26–77)	63 (49–70)	58 (26–76)	58 (38–77)
Follow-up, years [a]	6.7 (2.4–8.8)	6.0 (2.4–7.0)	6.8 (6.3–7.3)	7.0 (6.2–8.8)
Swelling, n	2	2	0	0
Clicking, n	2	2	0	0
Subluxation sensation, n	6	2	1	3
Inclination angle of the cup, degrees [a]	47 (37–64)	47 (42–61)	50 (39–64)	46 (37–60)
OHS [a]	44 (21–48)	40 (33–48)	45 (32–48)	44 (21–48)
OHS excellent, n	30	3	7	20
OHS good, n	6	4	0	2
OHS fair, n	2	1	1	0
OHS poor, n	2	0	0	2

The mean age of the patients was 59 (26–77) years. None of the patients had undergone BHR HRA of both hips in 1 session. 10 patients had both hips operated during study period with BHR HRA, but in separate sessions. 1 patient had a BHR HRA in the contralateral hip, but it was operated outside the study period (2010). 1 patient had a Synergy-BHR large-head MoM THA in the contralateral hip and 1 patient had a cemented Müller THA in the contralateral hip. The posterior approach was used in all cases. 1 hip had recurrent dislocations. There were no femoral neck fractures, infections, nerve damages, or other complications in a mean follow-up of N years.

The BHR cup has a hemispherical design and a cast-in POROCAST ingrowth surface. This HA-coated ingrowth surface does not require heat treatment to attach beads and therefore preserves the carbide structure. This surface is integral to the cup and is not a spray-on coating. The BHR femoral component is cemented to the femoral bone. The BHR HRA uses an as-cast cobalt chrome MoM bearing surface with a highly polished finish. In theory, cobalt chrome in the as-cast form has superior wear resistance to other forms of the alloy (BHR product manual).

In study II, patient data were also collected from the ImplantDB database (BCB Medical). 1,188 patients (1,329 hips) had undergone a ReCap-M2a-Magnum LDH MoM THA at our institution between August 2005 and April 2012. 28 patients had undergone a simultaneous bilateral procedure and 113 patients had both hips operated but in separate sessions. 74% (989/1329 hips) of the patients required surgery because of primary OA 7% because of hip dysplasia, 5% because of RA, 5% because of post-traumatic arthrosis, 3% because of avascular necrosis, and 3% because of fracture. A modified Hardinge approach was used in all study cases and the Bi Metric or Reach stem (Biomet, Warsaw IN, USA) was used.

The ReCap-M2a-Magnum (Biomet, Warsaw IN, USA) components are made from an 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).

4.1.2. Study III

Study III is based on data retrieved from the FAR. Since 1980, the FAR has been collecting information on THAs. Healthcare authorities, institutions and orthopedic units are obliged to provide the National Institute for Health and Welfare with information essential for maintenance of the registry. Currently some 95% of all implantations are registered (www.thl.fi/far/).

During the study period 2001–2011 5464 Bi Metric/ReCap THAs (Biomet), 698 ReCap HRAs (Biomet), 475 Synergy/BHR THAs (Smith&Nephew), 1902 BHR HRAs

(Smith&Nephew), 632 Corail and Summit/ASR THAs (Depuy; Johnson & Johnson, New Brunswick NJ, USA)), and 979 ASR HRAs (Depuy) were implanted in Finland.

To reduce the distortion in the demographic distribution between patients operated with HRA and those operated with THA, patients older than 85 years were excluded (the oldest patient operated with HRA was 85 years old). In addition, patients diagnosed with other reasons than OA (including fractures and avascular necrosis of the femoral head) or RA were excluded. Demographic data are given in Table 2.

Table 2. Demographic data relating to HRAs and THAs in 10,150 hips.

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

4.1.3. Study IV

The THA registers of Sweden, Denmark, Norway, and Finland were used. From 1995 to 2013, the 4 registries used the individual registration of THA and patients. A minimum NARA dataset was created containing data that all registers could provide (Havelin et al. 2009). The degree of coverage and completeness of the Nordic registers is high (Pedersen et al. 2004, Arthursson et al. 2005, Espehaug et al. 2006, DHAR

2014, SHAR 2014, FAR 2015). Selection and transformation of the respective datasets and patient de-identification, including deletion of the patient's national social security number, were carried out in each national register. The anonymized data was then merged into a common database.

From 1995 to 2013, there were 360,584 all-cemented primary THAs in the NARA database. The most common cemented THAs were evaluated: Lubinus (Link), Exeter (Stryker), Charnley (Depuy), Spectron (Smith and Nephew), MS-30 (Zimmer), CPT (Zimmer), Elite (DePuy), Müller THA (Zimmer), and C-stem THA (Depuy) (Table 3).

Table 3. Number and proportion of study implants, and demographic data.

		Proportion	Mean	Female	POA	Mean follow-up
THA	n	%	age	%	%	years
Charnley	43,849	15	72	69	78	9.6
Lubinus	116,186	41	72	61	81	6.9
Exeter	7,588	26	72	64	84	7
Spectron EF	25,214	8,8	73	69	80	7.2
Müller	3,192	1,1	71	66	88	8.9
MS-30	8,674	3	71	64	89	4.3
CPT	6,222	2,2	73	66	85	8.8
Elite	5,647	2	70	66	74	10.1
C-stem	2,082	0,7	71	63	86	7.8
Total	286,946	100	72	64	82	7.4

4.2. Methods and statistical analyses

4.2.1. Study I

Patients were examined between March 2012 and June 2012 with MRI, measurement of serum metal ion concentrations, the Oxford Hip Score (OHS) questionnaire, and by physical examination. The mean follow-up time was 6.7 (range 2.4–8.8) years. MRI was used to identify collections of fluids and soft tissue masses (Toms et al. 2008, Hart et al. 2012). MRI was performed on 40 hips, regardless of patient symptoms. 1 patient

refused MRI due to claustrophobia. For 1 patient, a revision operation had been performed earlier for ARMD without MRI.

We used 3 1.5T MR imagers (Philips Ingenia (2012); Philips Medical Systems, Best, the Netherlands; Siemens Avanto (2008) and Siemens Aera (2012); Siemens, Erlangen, Germany). The pulse sequences were optimized to reduce metal-induced artifacts (Hargreaves et al. 2011). MARS (metal artifact reduction sequence) MRI is a recently developed technique that provides good metal artifact suppression while minimizing image blurring and scanning time (Eustace et al. 1997, Hart et al. 2012). One imager (Siemens Aera) was equipped with an advanced metal artifact reduction technique—Slice Encoding for Metal Artifact Correction—with view angle tilting (SEMAC-VAT) (Sutter et al. 2012). At least 2 sequences covering the whole pelvic area were obtained in the coronal and axial planes (STIR and T2 or T1) followed by smaller field-of-view images in 3 planes centralized in the joint with implant (STIR, T1, and T2).

Images were examined by radiologists experienced in ARMD-related MRI diagnostics. ARMD is the finding of large sterile fluid effusions of the hip and sometimes macroscopic necrosis/metallosis associated with joint failure and pain. In MRI imaging special attention was paid to detection of periarticular fluid collections and soft-tissue masses. Pathological changes were measured in 3 planes and stored for analysis. 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 conventional pelvic and hip radiography; radiographs were used to measure the angle of inclination of the cup. Radiographs were taken in a vertical position. The angles of inclination of the cup were analyzed from digital pelvic radiographs using digital angle measurement. There were no instances of osteolysis or heterotopic ossification in the hips. In one patient, a partial radiolucent line under the cup in Gruen Zone I was seen, but the position of the cup was not changed and was considered stable.

Serum metal ion concentrations (cobalt and chromium) were measured during follow-up. The Finnish Institute of Occupational Health performed all measurements of cobalt and chromium ions using inductively coupled plasma mass spectrometry. The analysis methods have been accredited (FINAS T013).

The OHS questionnaire was completed by 31 patients at follow-up (40 hips). Clicking, a sensation of subluxation, and swelling of the hip were considered separately. The OHS questionnaire was not completed preoperatively or during routine outpatient visits. All patients were evaluated clinically by 1 of the 5 orthopedic surgeons who does revision surgery at the Turku University Hospital.

The prevalence of ARMD after the BHR HRA and the risk factors of ARMD were assessed: age, gender, device head size (≥ 54 mm versus ≤ 50 mm), diagnosis (secondary OA vs. primary OA), cup inclination, and bilaterality. The association of the patient's symptoms with the ARMD was analyzed separately. The symptoms evaluated were clicking, subluxation sensation, swelling, total OHS score, and relation of poor / fair versus good / excellent OHS score.

ARMD was considered definite, if the patient required revision because of ARMD and 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 where there was a solid mass or a fluid collection of ≥ 50 mm in MRI (in any plane). In patients who had not undergone surgery, ARMD was defined as being probable either if the serum chromium or cobalt concentration was ≥ 5 µg/L and/or if there was a fluid collection of any size by MRI.

A radiograph and an MRI image of a BHR hip with a pseudotumor are presented in Figure 1. By pseudotumor we mean a fluid collection which may alsocontain soft tissue debris.

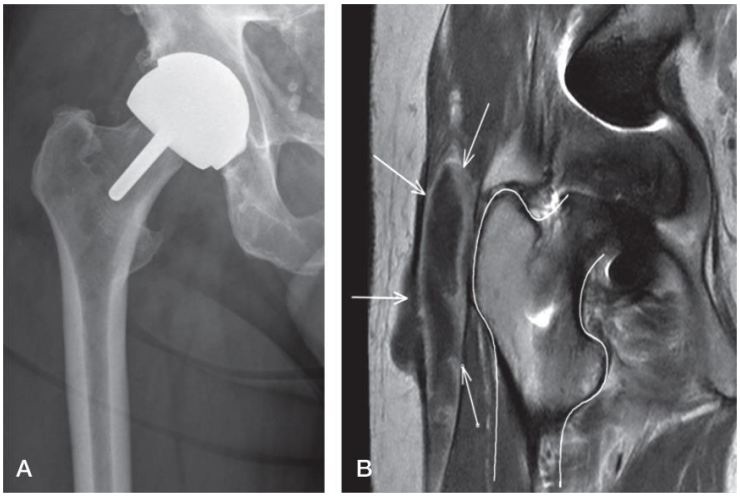


Figure 1. A radiograph (panel A) and an MRI image (panel B) of a BHR hip with a pseudotumor.

Potential risk factors for ARMD were analyzed by binary logistic regression with random interception for the patient. The ARMD-dependent variable consisted of 2 groups (definite or probable cases and no ARMDs), with no ARMD as a reference group. The results are expressed as crude odds ratios (OR) with confidence intervals (CI) of 95%. Multiple binary logistic regression including risk factors with $p < 0.40$ in a bivariate model, direct selection and retrospective elimination methods (inclusion criteria, $p < 0.20$) were used to investigate the potential confounding effect of other risk variables. An exact χ^2-test was used to analyze clicking and swelling due to 0 cell counts. Statistical analysis was performed using SAS for Windows version 9.3.

4.2.2. Study II

Routine screening for ARMD consisted of an OHS questionnaire, radiographs of the hip and pelvis, and measurements of serum chromium and cobalt ion levels by the end of September 2014. The mean follow-up time was 5.2 (range 0.003–9.1) years; 8.1% (96/1188) of the patients died during the follow-up period. MRI was performed on patients with symptoms and / or increased metal ion levels (≥ 5 µg/L). An experienced orthopedic surgeon also evaluated all patients. MARS-MRI was used to identify ARMD as a collection of fluids and soft tissue masses (also called pseudotumors) around the

prostheses (Hart et al. 2012, Hargreaves et al. 2011). MRI was performed on 352 hips (Hargreaves et al. 2011).

The inclination of the cup and the anteversion angle were measured by examination of pelvic and hip radiographs. As the measurement of the anteversion angle is relatively inaccurate in lateral hip radiographs, cups were categorized into two subgroups for regression analysis: retroversion and non-retroversion. Pelvic radiographs were available for all 1199 hips for measurement the angle of inclination, and hip radiographs were available for all patients.

The serum levels of cobalt and chromium ions were measured in 87.7 % (959/1094) of the patients (SAY 2012), but not in patients with loosening, fractures, or infections of their prostheses.

The OHS questionnaire was not completed preoperatively and the total score in the follow-up was available for 67.8% (742 /1094) patients. Separate questions about clicking, a sense of subluxation, and swelling of the hip were also asked. Patients with bilateral Recap-M2a-Magnum THAs had only one OHS questionnaire available, and we could not pinpoint which hip the questionnaire referred to. Therefore, patients with bilateral Recap-M2a-Magnum procedures were left out of the regression analyses..

The following risk factors were assessed for ARMD: age, gender, laterality, cup angle of inclination (categorical variables <30 degrees, 30-50 degrees and> 50 degrees), anteversion angle of the cup (categorical variables> 0 degrees and ≤ 0 degrees), and device head size (categorical variables ≤ 44 mm, 46-50 mm and ≥ 52 mm). The relation between the OHS score (poor, fair, or good vs. excellent), pain (no, mild, moderate, or severe), symptoms (clicking, subluxation, and / or swelling), and ARMD were also examined. We further assessed the same risk factors and symptoms when there was revision surgery due to ARMD.

Table 4. Demographic data of the 1329 study hips presented hip wise.

Demographic data of the 1329 study hips presented hipwise (Study II).

	Total hips (n=1329)	ARMD (n=190)	Probable ARMD (n=114)	No ARMD (n=1025)
Mean age (years)	64.2	64.3	64.5	64.1
Mean follow-up years (range)	5.2 (0.003-9.1)	5.8 (0.3-8.8)	5.5 (0.2-8.8)	5.0 (0.003-9.1)
Mean head size (mm)	49.2	48.8	48.8	49.4
Head size ≤ 44mm (n, %)	170 (13%)	31 (16%)	19 (17%)	120 (12%)
Head size 46-50mm (n, %)	744 (56%)	109 (57%)	62 (54%)	573 (56%)
Head size ≥ 52mm (n, %)	415 (31%)	50 (26%)	33 (29%)	332 (32%)
Mean inclination angle of the cup (degrees)¤	42.8	44.5	44	42.4
Inclination angle of the cup <30 degrees (n, %)¤	29 (2%)	2 (1%)	2 (2%)	25 (3%)
Inclination angle of the cup 30-50 degrees (n, %)¤	1013 (84%)	146 (82%)	86 (80%)	781 (85%)
Inclination angle of the cup >50 degrees (n, %)¤	157 (13%)	29 (16%)	19 (18%)	109 (12%)
Anteversion angle of the cup ≤0 degrees (n, %)	30 (2%)	6 (3%)	1 (1%)	23 (2%)
Anteversion angle of the cup >0 degrees (n, %)	1299 (98%)	184 (97%)	113 (99%)	1002 (98%)
Mean serum cobalt (µg/l) (range)*	4.4 (0.3-196.2)	16.4 (0.6-196.2)	4.3 (0.5-9.5)	1.7 (0.3-4.9)
Mean serum chromium (µg/l) (range)*	3.0 (0.5-44.7)	7.8 (0.5-44.7)	3.6 (0.8-7.4)	1.8 (0.6-4.8)

¤ *Data of cup inclination angle based on pelvic radiographs were available for 1199 hips.*

* *Metal ion data was available for 1094 hips: 802 hips in no ARMD group, 107 in probable ARMD group, and 185 in definite ARMD group.*

Demographic data are presented hip-wise in Table 4 and patient-wise for patients with a unilateral study device in Table 5.

Table 5. Patient characteristics for those with a unilateral arthroplasty.

Patient characteristics for those with a unilateral arthroplasty.

	No of patients with an unilateral study device (n=1047)	ARMD (n=143)	Probable ARMD (n=70)	No ARMD (n=834)
Males (n, %)	469 (45%)	45 (31%)	29 (41%)	395 (47%)
Mean OHS*	40.4	36	41.3	41.1
OHS excellent (n, %)*	464 (63%)	44 (42%)	31 (63%)	389 (66%)
OHS good (n, %)*	135 (18%)	22 (21%)	11 (22%)	102 (17%)
OHS fair (n, %)*	60 (8%)	17 (16%)	5 (10%)	38 (6%)
OHS poor (n, %)*	83 (11%)	23 (22%)	2 (4%)	58 (10%)
No pain (n, %)#	377 (51%)	38 (36%)	22 (45%)	317 (54%)
Mild pain (n, %)#	280 (38%)	42 (40%)	20 (41%)	218 (37%)
Moderate or severe pain (n, %)#	82 (11%)	26 (25%)	7 (14%)	49 (8%)
Swelling yes (n, %)**	39 (5%)	11 (11%)	3 (6%)	25 (4%)
Swelling no (n, %)**	681 (95%)	89 (89%)	46 (94%)	546 (96%)
Clicking yes (n, %)***	62 (9%)	21 (21%)	6 (12%)	35 (6%)
Clicking no (n, %)***	655 (91%)	79 (79%)	43 (88%)	533 (94%)
Subluxation sensation yes (n, %)¤	106 (15%)	23 (22%)	6 (12%)	77 (13%)
Subluxation sensation no (n, %)¤	620 (85%)	80 (78%)	43 (88%)	497 (87%)
Mean serum cobalt (µg/l) (range)****	3.6 (0.3-71.5)	12.9 (0.6-71.5)	4.2 (0.5-9.5)	1.5 (0.3-4.8)
Mean serum chromium (µg/l) (range)****	2.6 (0.5-34.2)	6.5 (0.5-34.2)	3.2 (0.8-7.4)	1.7 (0.6-4.8)

OHS=Oxford hip score, 42-48=excellent, 34-41=good, 27-33=fair, 0-26=poor.

* OHS data available for 742 patients with a unilateral study device.
\# Data available for 739 patients with a unilateral study device.
** Data available for 720 patients with a unilateral study device.
*** Data available for 717 patients with a unilateral study device.
¤ Data available for 726 patients with a unilateral study
**** Data available for 844 patients with a unilateral study device.

The potential risk factors associated with ARMD were analyzed by univariate multinomial logistic regression. The dependent variable consisted of 3 groups (definite

ARMD, probable ARMD, and no ARMD), with no ARMD being used as the reference group. The results were expressed in odds ratios (OR) with a 95% confidence interval (CI). The logistic regression model was evaluated with a deviance test, while the multivariate logistic model was obtained by retrograde elimination (inclusion criteria, $p < 0.10$) to examine any confounding effects of other risk variables. The generalized estimation equation (GEE) was used for hip-wise data to assess the correlation between the hips of the same patient. Kaplan-Meier estimates for revision operations (for any reason) and for ARMD were calculated. Cox regression analysis was used to analyze the association between risk factors and symptoms and the revision of ARMD. Hip-wise survival data were analyzed with a log-normal fragility model to account for the correlation between the hips of the same patient, and the results of the Cox regression were expressed using HR with a 95% CI. The proportional risk assumptions were assessed using a log-cumulative risk diagram and the assumptions were met. Values of $P < 0.05$ were considered statistically significant and the statistical analysis was performed using SAS for Windows, version 9. 4 (SAS Institute Inc., Cary, NC, USA).

4.2.3. Study III

The risk of revision of ReCap HRA was compared to that of Bimetric / ReCap THA, the risk of revision of the BHR HRA was compared to that of Synergy / BHR THA, and the risk of revision of the BHR- ASR HRA was compared to that of Corail and Summit / performed over the same period. This data was adjusted for age at time of surgery, gender, operated side, device head size <50 or ≥ 50 mm, and diagnosis, using Cox multiple regression analysis. In addition, stratified analysis was performed for males and females <55 or ≥55 years of age. In these subanalyses by age and gender, the risk of revision of LDH MoM THAs was compared with the risk of revision of analogous HRAs performed for similar patients during the same period of time.

The revisions were linked to the primary operation using a personal identification number. The endpoint for survival was defined as first revision when one of the components (including the femoral head) or the entire implant was removed or exchanged. Each of the reasons for revision (aseptic loosening, dislocation, infection, and periprosthetic fracture) served as a separate endpoint. In 41 revisions, the

indication recorded for the revision was "other reason". KM survival data were used to construct the survival probabilities of implants. These survival data were compared using the log-rank test. Patients who died or were relocated outside Finland during the follow-up period were censored. The Cox multiple regression model was used to study differences between groups and to adjust for potential confounders. The factors studied with the Cox model were: age, gender, diagnosis, and implant design. The effect of age on survival was also analyzed by dividing the patients into two age groups: those under 55 and those 55 years and older. Cox regression analyses provided estimates of survival probabilities and adjusted revision risk ratios (RR). Estimates of Cox analyses were used to construct survival curves adjusted to the mean values of the risk factors. The Wald test was applied to calculate the p-values for the data obtained from the Cox multiple regression analysis. Differences between groups were considered statistically significant if the two-tailed p-value was less than 0.05.

4.2.4. Study IV

We evaluated the survival of implant families consisting of all versions of the same device, as several versions of the study implants were introduced during the study period. The different versions of the study implants were not necessarily the same in the 4 countries. In addition, the study devices were not necessarily coded similarly in the 4 registers. Only cup / stem combinations with at least 100 implantations in one country were included. Elite, MS 30, C-stem, CPT, and Müller THA were created by combining the study stem with a cemented acetabular component by the same manufacturer. Introduction of similar coding of the cup component in the 4 national registers provided a sufficient number for separate analyses of Exeter X3 Rimfit, Exeter Contemporary, Exeter All-Poly, and Exeter Duration (Table 6).

Table 6. Number and proportion of Exeter-subgroup devices, and demographic data.

		Proportion	Mean	Female	Primary OA	Mean follow-up
Exeter THA	**n**	**%**	**age**	**%**	**%**	**years**
X3 Rimfit	7,189	9,5	73	65	84	1.4
Contemporary	19,889	26	74	67	85	6.1
All-poly	25,032	33	72	65	81	9.3
Duration	23,770	31	71	61	86	7
Total	75,880	100	72	64	83	7

We used Kaplan-Meier analysis with 95% CI to assess implant survival at 10 and 15 years, until there were at least 100 THAs at risk. Patients were censored at death or on December 31, 2013, whichever came first. The outcome variable was revision for any reason. Kaplan-Meier survival was also evaluated separately for each device for 2 periods of time, 1995–2004 and 2005–2013, using any reason for revision as the endpoint. In addition, Kaplan-Meier survival for aseptic loosening of the cup, the stem, or both components were evaluated by the type of cement used (Palacos type, Simplex type, or other) (Espehaug et al. 2009).

We used Cox multiple regression to determine survival rates and risk ratios (HR), with revision for any reason as endpoint and with adjustment for age (<60, 60-64, 65 -69, 70-74, ≥ 75), diagnosis (primary osteoarthritis, hip fracture, non-traumatic femoral head necrosis, inflammatory disease, childhood hip, or other illness / unknown), and material of the femoral head (metal, ceramic, or other). The hypothesis of proportional hazards was fulfilled, as assessed by visual inspection of log-minus-log plots.

The Kaplan-Meier and Cox analyses are based on the hypothesis of non-informative censoring, which is not fulfilled when estimating the risk of revision and censoring for death. Thus, a competing risk assessment was also carried out using the statistical software Stata 14.

Patients with bilateral procedures were included, since previous research has shown that this does not distort the results (Lie et al. 2004, Ranstam and Robertsson 2010). We considered that any p-value less than 0.05 was statistically significant. For most statistical analyses, we used SPSS version 22.0.

5. RESULTS

5.1. Studies based on the Turku University Hospital register

5.1.1. ARMD after BHR arthroplasty

Six patients (9 of 42 hips) were considered to have a definite ARMD. 4 of these hips had been revised for ARMD (Table 7). 8 patients (8 hips) were considered to have probable ARMD. In total, there were 17 hips with a definite or probable ARMD. 18 patients were considered not to have ARMD.

Table 7. Data on the 6 patients (9 hips) with a definite adverse reaction to metal debris (ARMD). None of the patients had major muscle destruction. The 64 M, 69 M, and 62 M patients had both hips with ARMD. The ARMD diagnosis of the right hip of 64 M was based on operative findings in a revision operation in 2009.

Age	Sex	Side	OHS	Pain	Clicking	Sublux.	Swelling	s-Cr, µg/L	s-Co, µg/L	Cup incl. (°)	MRI	Revision or follow-up
64	M	Right	NA	Moderate	No	Yes	No	NA	NA	48	NA	Revised
64	M	Left	35	Moderate	Yes	Yes	Yes	3.9	4.5	43	Solid and fluid	Revised 55 × 35 × 110 mm
69	M	Right	44	Mild	No	No	No	7.6	13.5	61	Fluid 30 × 40 × 65 mm	Revised and 85 × 80 × 30 and solid 20 × 20 × 50
69	M	Left	44	No	No	No	No	7.6	13.5	47	Fluid 57 × 46 × 10 mm	Follow-up
49	M	Right	33	Hard	Yes	Yes	Yes	4.3	4.5	42	Fluid 70 × 26 × 23 mm	Follow-up
62	M	Right	39	No	No	No	No	7.6	14.9	48	No findings	Follow-up
62	M	Left	39	No	No	No	No	7.6	14.9	43	Some fluid	Revised
59	M	Right	41	Moderate	No	No	No	1.6	2.9	47	Fluid 50 × 5 × 5 mm	Follow-up
67	M	Right	48	No	No	No	No	1.1	1.2	47	Fluid 13 × 19 × 50 mm	Follow-up

OHS: See Table 1. Sublux.: subluxation sensation; s-Cr: serum chromium level; s-Co: serum cobalt level; Cup incl.: cup inclination angle; MRI: magnetic resonance imaging; NA: not available.

Male gender was associated with a definite ARMD, although not statistically significantly so (OR = 11, 95% CI: 0.7-165, p = 0.08). Gender (p = 0.2), bilateral MoM (p = 0.3), and head size of the device (p = 0.7) were not statistically significant in the multiple logistic regression model (Tables 8 and 9). Gender was the only risk factor included in the final model using direct selection and retrograde elimination methods.

Table 8. Results of testing of associations between risk factors and ARMD using logistic regression with random intercept for patient, with crude odds ratios (ORs) and 95% confidence intervals (CIs). ARMD: adverse reaction to metal debris; MoM: metal-on-metal implant; THR: total hip arthroplasty; OA: osteoarthritis; For 1 unit increase (continuous variable).

ARMD definite or probable (n = 17) vs. ARMD not found (n = 25)

	Risk factor	OR (95% CI)	p-value
Age at follow-up	1.03 [a]	(0.93–1.13)	0.5
Sex (male vs. female)	10.8	(0.7–165)	0.08
Inclination angle of the cup	1.05 [a]	(0.93–1.2)	0.4
Bilateral MoM	0.33	(0.05–2.1)	0.2
Bilateral THA	0.55	(0.09–3.4)	0.5
Diagnosis secondary vs. primary OA	2	(0.27–14)	0.5
Head size (≥ 54 vs. ≤ 50 mm)	4.1	(0.66–25)	0.1

The OHS score (crude OR = 0.97, 95% CI: 0.85-1.1, p = 0.7 for an increase of 1 unit in this continuous variable) or poor/fair OHS versus good /excellent OHS (crude OR= 1.6, 95% CI: 0.09-27, P = 0.7) was not associated with ARMD. Nor was the sensation of subluxation (crude OR = 1.7, 95% CI: 0.16-18, p = 0.6) or clicking and swelling associated with ARMD (p = 0.07 for both, chi-square test).

Table 9. Results of testing of associations between risk factors and ARMD using a multiple logistic regression model with random intercept for patient, with adjusted odds ratios (ORs) (including risk factors with p < 0.40 in bivariable model) and 95% confidence intervals (CIs). For abbreviations: See Table 8.

ARMD definite or probable (n = 17) vs. ARMD not found (n = 25)

	Risk factor	OR (95% CI)	p-value
Sex (male vs. female)	7.6	(0.29–204)	0.2
Bilateral MoM	0.4	(0.05–3.2)	0.3
Head size (≥ 54 vs. ≤ 50 mm)	1.6	(0.16–16)	0.7

5.1.2. Systematic screening for ARMD after ReCap-M2a-Magnum MoM THA

104 patients (106 hips, 8.0% of all hips) required a revision operation for any reason by the end of follow-up. 33 patients (33 hips, 2.5% of all hips) required a revision operation due to ARMD. The Kaplan-Meier survival estimate of ReCap-Magnum THA at 5 years was 93.3% for any reason (95% CI: 91.9-94.8) and 98.6% (95% CI: 97.8-99.3) for ARMD revision. There was definite ARMD in 157 hips which did not undergo a revision operation during the follow-up period (157 of 1,329 hips, 11.8% of all hips). Probable ARMD was present in 114 hips (8.6%). In total, 190 out of 1,329 (14.3%) hips had definite ARMD, and 1,025 (77.1%) hips did not have ARMD.

Table 10. Crude odds ratios (ORs) and 95% confidence intervals (CIs) of associations between risk factors and symptoms with ARMD.

	ARMD versus no ARMD		**Probable ARMD versus no ARMD**	
	Crude OR (95% CI)	p-value	Crude OR (95% CI)	p-value
Age*	1.00 (0.99-1.01)	0.9	1.00 (0.99-1.02)	0.7
Gender (female vs. male)**	1.96 (1.34-2.86)	0.0005	1.27 (0.78-2.09)	0.3
Side (left vs. right)*	0.91 (0.68-1.21)	0.5	1.12 (0.80-1.57)	0.5
Pain (mild vs. no pain)**	1.61 (1.00-2.58)	0.05	1.32 (0.70-2.48)	0.4
Pain (moderate or severe vs. no pain)**	4.43 (2.47-7.93)	<0.001	2.06 (0.84-5.07)	0.1
Subluxation sensation**	1.86 (1.10-3.13)	0.02	0.90 (0.37-2.19)	0.8
Clicking**	4.05 (2.24-7.31)	<0.001	2.13 (0.85-5.33)	0.1
Swelling**	2.70 (1.28-5.68)	0.009	1.42 (0.41-4.90)	0.6
Head size ≤ 44mm vs. ≥ 52mm*	1.72 (1.02-2.87)	0.04	1.59 (0.84-3.03)	0.2
Head size 46-50mm vs. ≥ 52mm*	1.26 (0.86-1.86)	0.2	1.09 (0.68-1.74)	0.7
Inclination angle of the cup, <30 vs. 30-50 deg***	0.43 (0.10-1.82)	0.3	0.73 (0.17-3.08)	0.7
Inclination angle of the cup, >50 vs. 30-50 degrees***	1.42 (0.90-2.24)	0.1	1.58 (0.91-2.76)	0.1
Anteversion angle of the cup, >0 vs ≤0 degrees*	0.70 (0.28-1.76)	0.5	2.59 (0.35-19.43)	0.4
OHS poor vs. excellent**	3.51 (1.97-6.23)	0.04	0.43 (0.10-1.86)	0.1
OHS fair vs. excellent**	3.96 (2.06-7.59)	0.02	1.65 (0.61-4.50)	0.2
OHS good vs. excellent**	1.91 (1.09-3.33)	0.4	1.35 (0.66-2.79)	0.3

*** Multinomial logistic regression using GEE-estimation based on data of all hips and *** all pelvic radiographs (1199).**
**** Multinomial logistic regression based on data of patients with an unilateral study device.**

Table 11. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of associations between risk factors and symptoms with ARMD using multiple multinomial logistic regression based on data of 714 patients with an unilateral arthroplasty.

	ARMD versus no ARMD		Probable ARMD versus no ARMD	
	Adjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Gender (female vs. male)	2.22 (1.19-4.15)	0.01	0.88 (0.41-1.85)	0.7
Pain (mild vs. no pain)	1.06 (0.58-1.94)	0.9	1.40 (0.68-2.89)	0.4
Pain (moderate or severe vs. no pain)	2.67 (0.97-7.34)	0.06	8.57 (2.08-35.34)	0.003
Clicking	2.85 (1.49-5.45)	0.002	2.31 (0.87-6.16)	0.09
Head size ≤ 44mm vs. ≥ 52mm	1.12 (0.49-2.55)	0.8	2.32 (0.78-6.96)	0.1
Head size 46-50mm vs. ≥ 52mm	0.49 (0.26-0.94)	0.03	0.98 (0.44-2.20)	1
OHS poor vs. excellent	1.35 (0.50-3.67)	0.6	0.07 (0.01-0.51)	0.008
OHS fair vs. excellent	2.14 (0.92-4.95)	0.08	0.59 (0.16-2.24)	0.4
OHS good vs. excellent	1.38 (0.69-2.74)	0.4	0.96 (0.41-2.24)	0.9

Table 12. Crude hazard ratios (HRs) and 95% confidence intervals (CIs) of associations between risk factors and ARMD revisions.

.

Risk factors of ARMD revisions

	Crude HR (95% CI)	p-value
Age*	1.00 (0.97-1.04)	1
Gender (female vs. male)**	1.87 (0.79-4.40)	0.2
Side (left vs. right)*	1.66 (0.84-3.32)	0.1
Pain (mild vs. no pain)**	0.46 (0.09-2.27)	0.3
Pain (moderate or severe vs. no pain)**	2.37 (0.59-9.46)	0.2
Subluxation sensation**	0.57 (0.07-4.43)	0.6
Clicking**	3.97 (1.05-14.99)	0.04
Swelling**	1.94 (0.25-15.21)	0.5
Head size ≤ 44mm vs. ≥ 52mm*	3.35 (1.08-10.38)	0.04
Head size 46-50mm vs. ≥ 52mm*	2.06 (0.77-5.51)	0.2
Inclination angle of the cup, <30 vs. 30-50 deg*	0.01 (0.000-34081149)	0.7
Inclination angle of the cup, >50 vs. 30-50 degrees*	1.28 (0.55-2.99)	0.6
Anteversion angle of the cup, ≤0 vs. >0 degrees*	7.63 (2.19-26.6)	0.001
OHS poor vs. excellent**	3.26 (0.78-13.64)	0.1
OHS fair vs. excellent**	1.24 (0.14-10.59)	0.8
OHS good vs. excellent**	1.67 (0.32-8.62)	0.5

* Cox regression with random intercept for patient (frailty model) based on data of all hips.

** Cox regression based on data of patients with an unilateral study device.

The univariable associations assessed using the multinomial logistic regression analysis between the risk variables/symptoms and ARMD are presented in Table 10. Pain, subluxation sensation, clicking, small head size of the device (≤ 44 mm vs. ≥ 52 mm), and fair/poor OHS scores were associated with definite ARMD. In the multivariable model, female gender, clicking, large head size of the device (≥ 52 mm vs. 46-50 mm), and pain (moderate/severe vs. no pain) were associated with ARMD

(Table 11). The results of the univariable associations between the risk factors and symptoms and ARMD revision assessed via the Cox regression analysis are presented in Table 12. Retroversion of the cup, small head size of the device (≤ 44 mm vs. ≥ 52 mm) and clicking were associated with the occurrence of ARMD revision.

For bilateral arthroplasties, the whole blood level Co and Cr values were available for 125 patients. The mean concentration of Co ions was 7.2 µg/L (range 0.6–196.2) and of Cr 4.3 ions µg/L (range 0.7–44.7).

5.2. Study based on the Finnish Arthroplasty Register

According to the register, the most common reason for THA revision was aseptic loosening of both components. By Cox regression analysis, there was no statistically significant difference in the revision risk between ReCap HRA and Bimetric / ReCap THA (RR = 1.43, 95% CI = 0.95–2.14, p = 0.09) or between BHR HRA and Synergy / BHR THA (RR = 1.35, 95% CI = 0.75–2.43, p = 0.31). The risk of revision of Summit and Corail / ASR THA was, however, significantly increased compared to that of the ASR HRA (RR = 0.73, 95% CI = 0.54–0.98, p = 0.04) (Table 13, Figures 2 to 4).

Table 13. Survival of HRA and THA, the reference group. HRAs compared to THAs; adjustment made for age, gender, operated side, head size, diagnosis, and implant.

	N	MF yr	AR 4 yr	4-yr survival (95% CI)	AR 6 yr	6-year survival (95% CI)	AR 8 yr	8-yr survival (95% CI)	Adjusted RR for revision (95% CI)	p-value
Bimetric/ReCap THA	5,464	3,1 (0-7,0)	1612	97 (96-97)	109	-	-	-	1	
ReCap resurfacing	698	4,1 (0-7,7)	364	96 (94-97)	118	-	-	-	1.43 (0.95-2.14)	0.09
Synergy/BHR THA	475	4,0 (0-7,6)	257	97 (95-98)	49	97 (94-98)	-	-	1	
BHR resurfacing	1,902	6,0 (0-10,7)	1459	97 (96-97)	1078	95 (94-96)	464	94 (93-95)	1.35 (0.75-2.43)	0.31
Summit & Corail/ASR THA	632	3,9 (0-7,7)	301	90 (88-93)	39	72 (64-79)	-	-	1	
ASR resurfacing	979	5,0 (0-7,8)	752	92 (90-94)	267	83 (80-86)	-	-	0.73 (0.54-0.98)	0.04
Total	10,150	4,0 (0-10,7)	4745	95 (95-96)	1660	92 (91-93)	464	90 (88-91)		

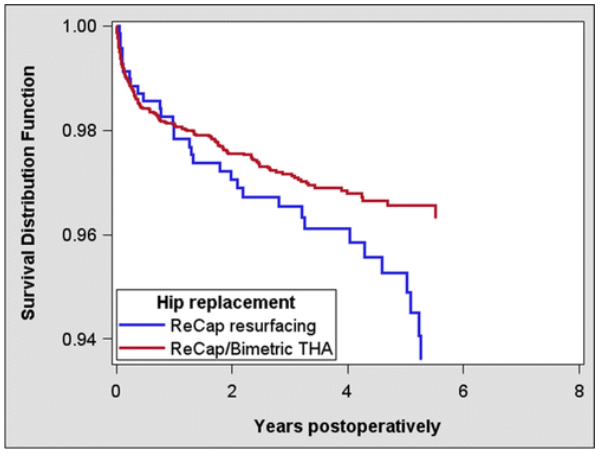


Figure 2.Cox-adjusted survival curves of 698 ReCap resurfacings and 5464 ReCap/Bimetric THAs. The end point was defined as revision for any reason. Adjustment was made for age at surgery, gender, operated side, head size, and diagnosis. THA: total hip anthroplasty.

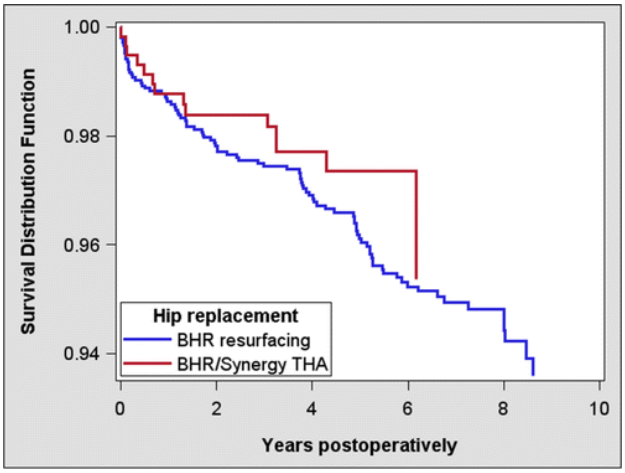


Figure 3. Cox-adjusted survival curves of 1902 BHRs and 475 BHR/Synergy THAs. The end point was defined as revision for any reason. Adjustment was made for age at surgery, gender, operated side, head size, and diagnosis. BHR: Birmingham hip resurfacing; THA: total hip anthroplasty.

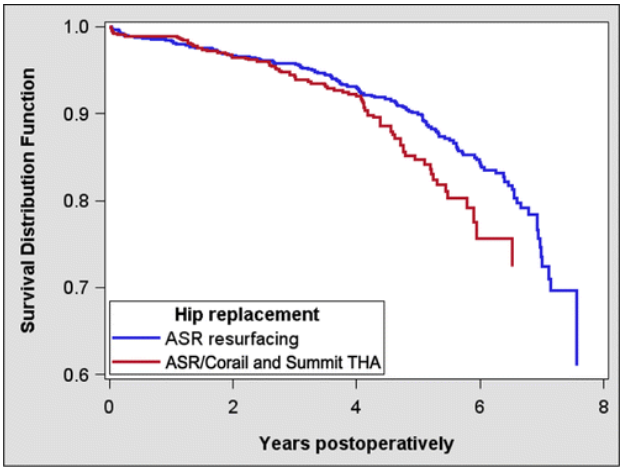


Figure 4. Cox-adjusted survival curves of 979 ASR resurfacings and 632 ASR/Corail and Summit THAs.The end point was defined as revision for any reason. Adjustment was made for age at surgery, gender, operated side, head size, and diagnosis. ASR: articular surface replacement; THAs: total hip anthroplasty.

There was no statistically significant difference of the risk of revision risk of aseptic loosening between ReCap HRA and Bimetric / ReCap THA ($p = 0.8$) or between BHR HRA and Synergy / BHR THA ($p = 0.2$). The revision risk of ASR HRA for aseptic loosening of both components was significantly lower ($p < 0.001$) compared to Corail and Summit / ASR THA.

There was no difference in the risk of revision for dislocation between the pairs of implants compared (ASR HRA vs. THA p = 0.4, BHR HRA vs THA p = 0.5; ReCap HRA vs. THA ReCap p = 0.7).

There were no differences in fracture revision risk between the pairs of implants compared (ASR HRA vs. THA p = 0.2, BHR HRA vs. THA p = 0.5, ReCap HRA vs. THA p = 0.2).

No difference was found in the risk of infection between the implants in comparison pairs (ASR HRA vs. THA p = 0.2, BHR HRA vs. THA p = 0.95, Recap HRA and THA p = 0.1).

Table 14. Age- and gender-stratified relative risk of revision. HRAs were compared to analogous LDH MoM THAs during the same period 2001–2011. Data are based on a Cox regression model adjusted for age, operated side, head size, diagnosis, and type of implant.

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

The subgroup analysis by age and gender is presented in Table 14. Elderly male patients with Corail and Summit / ASR THA has an increased risk of revision compared to those with ASR HRA (RR = 0.48, 95% CI = 0.28–0.84, p = 0.01). Elderly female patients with ReCap HRA had an increased risk of revision compared with those with Bimetric / ReCap THA (RR = 3.52, 95% CI = 1.87–6.60, p <0.001).

5.3. Study based on Nordic Arthroplasty Register Association database

The Lubinus THA was the most common study device; it was used in 41% of all implantations. Mean age at the time of surgery was highest for the CPT THA (73 years). The proportion of female patients was highest for the Charnley THA (69%) (Figure 5).

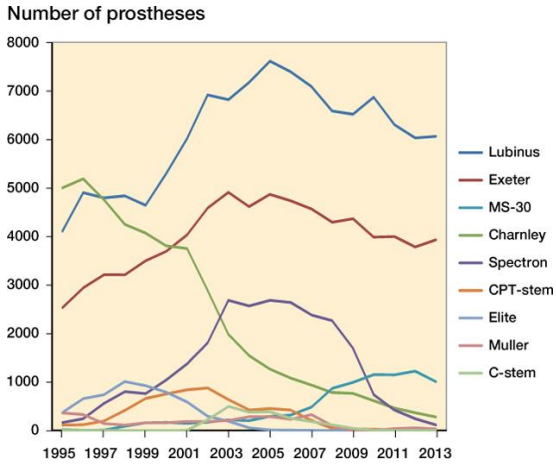


Figure 5. Time trends in using the study devices during the period 1995–2013.

Several THAs had a 10-year survival rate of 95% or more, including the Lubinus (95.7%, 95% CI: 95.5–95.9), MS 30 (96.6%, 95% CI: 95.8% 97.4), and C-stem (95.8%, 95% CI: 94.8–96.8). The lowest survival at 10 years occurred in patients implanted with Spectron EF THA (89.9%, 95% CI: 89.3–90.5) and Elite THA (89.8%, 95% CI: 89.0–90.6) (Tables 15 and 16, and Figures 6 and 7).

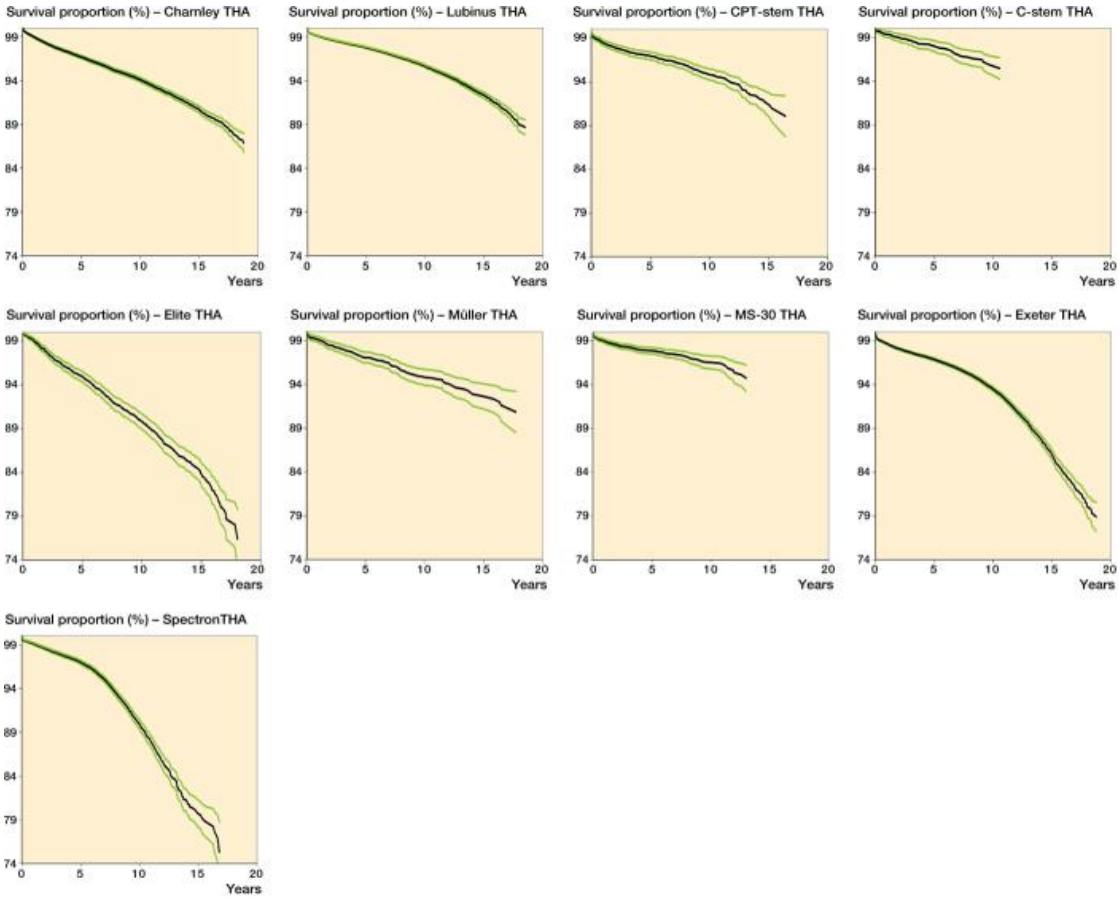
Table 15. Implant survival at 7 years for the time periods 1995–2004 and 2005–2013, with any reason for revision as the endpoint.

		7-year survival for 1995–2004		7-year survival for 2005–2013
THA	**At risk**	**% (95% CI)**	**At risk**	**% (95% CI)**
Charnley	27,686	95.7 (95.5–95.9)	1,953	95.7 (95.1–96.3)
Lubinus	40,948	97.1 (96.9–97.3)	11,662	96.9 (96.7–97.1)
Exeter	27,748	95.8 (95.6–96.0)	7,411	96.1 (95.9–96.3)
Spectron	8,783	95.2 (94.8–95.6)	4	95.1 (94.7–95.5)
Müller	1,656	96.6 (95.8–97.4)	437	95.9 (94.5–97.3)
MS-30	1,005	97.3 (96.3–98.3)	493	97.5 (96.9–98.1)
CPT	3,609	96.6 (96.0–97.2)	719	95.1 (93.7–96.5)
Elite	3,959	92.7 (91.9–93.5)	13	–
C-stem	929	97.5 (96.5–98.5)	496	96.4 (95.0–97.8)

Table 16. Kaplan-Meier survivorship of the study devices at 10 and 15 years with revision for any reason as the endpoint, and adjusted revision rate (RR) (age, sex, diagnosis, femoral head material) for revision using Cox regression.

	At risk at	10-year survival	At risk at	15-year survival	Adjusted RR	
THA	**10 years**	**(95% CI), %**	**15 years**	**(95% CI), %**	**(95% CI), %**	**p-value**
Charnley	21,794	94.1 (93.9–94.3)	7,199	90.7 (90.3–91.1)	1	–
Lubinus	29,016	95.7 (95.5–95.9)	6,685	92.4 (92.0–92.8)	0.77 (0.73–0.81)	< 0.001
Exeter	19,606	93.5 (93.3–93.7)	4,066	86.0 (85.4–86.6)	1.25 (1.18–1.31)	< 0.001
Spectron EF	5,311	89.9 (89.3–90.5)	512	79.8 (78.2–81.4)	1.73 (1.62–1.84)	< 0.001
Müller	1,225	94.9 (93.9–95.9)	372	92.6 (91.2–94.0)	0.83 (0.70–0.99)	0.03
MS-30	834	96.6 (95.8–97.4)	–	–	0.73 (0.63–0.86)	< 0.001
CPT	2,756	94.9 (94.3–95.5)	391	91.6 (90.4–92.8)	0.94 (0.84–1.06)	0.3
Elite	3,201	89.8 (89.0–90.6)	986	83.9 (82.5–85.3)	1.65 (1.51–1.80)	< 0.001
C-stem	550	95.8 (94.8–96.8)	–	–	0.70 (0.55–0.90)	0.005

Figure 6. Kaplan-Meier implant survival. Green lines are upper and lower 95% confidence limits



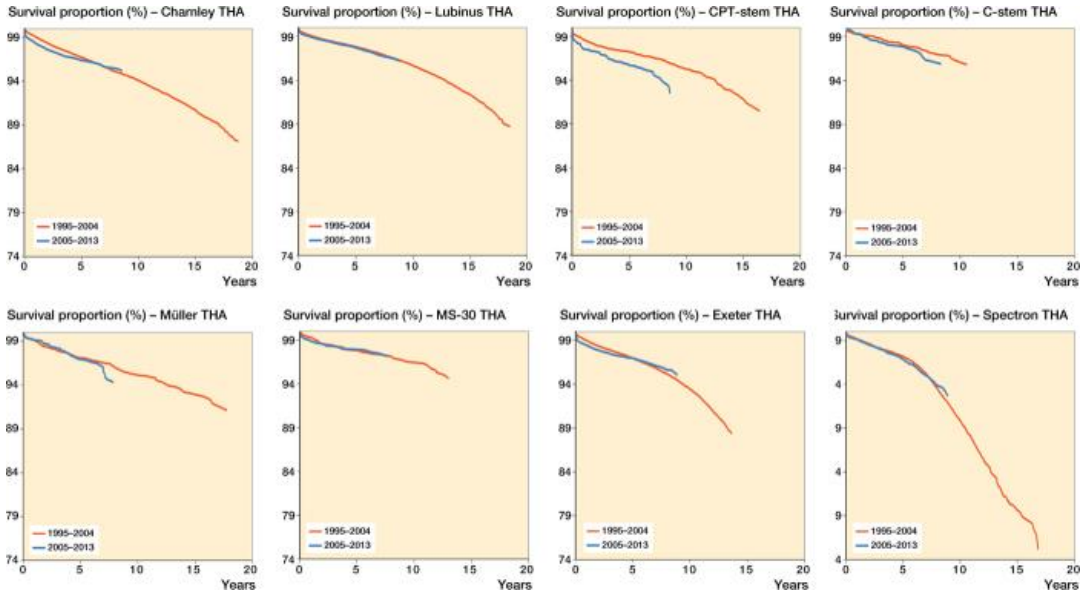


Figure 7. Implant survival of THAs for the time periods 1995–2004 and 2005–2013, with revision for any reason as the endpoint.

Implant survival of Charnley, Exeter, and Elite THAs with the Palacos-type of cement was higher than the survival of the same implants with other types of cement. Survival of Lubinus, Spectron, and Müller THAs with the Palacos- and Simplex-type of cement was higher than the survival of the same implants with other types of cement (Table 17).

Table 17. Kaplan-Meier survivorship of the study devices with either Palacos-type, Simplex-type, or other bone cement at 10 years with aseptic loosening as the endpoint.

		At risk at	10-year survival
THA	**n**	**10 years**	**(95% CI), %**
Charnley + Palacos	38,925	18,95	97.2 (97.0–97.4)
Charnley + Simplex	411	242	92.4 (89.5–95.3)
Charnley + other	4,335	2,542	91.7 (90.7–92.7)
Lubinus + Palacos	93,393	24,918	98.1 (97.9–98.3)
Lubinus + Simplex	2,430	1,483	97.4 (96.6–98.2)
Lubinus + other	20,224	2,724	95.6 (95.0–96.2)
Exeter + Palacos	51,729	12,2	97.2 (97.0–97.4)
Exeter + Simplex	13,366	4,148	96.2 (95.8–96.6)
Exeter + other	10,31	3,057	96.1 (95.5–96.7)
Spectron + Palacos	22,152	5,031	92.6 (92.0–93.2)
Spectron + Simplex	1,523	144	92.8 (90.1–95.5)
Spectron + other	1,497	141	85.0 (80.5–89.5)
Müller + Palacos	2,108	888	97.7 (96.9–98.5)
Müller + Simplex	234	140	97.9 (95.5–100)
Müller + other	850	233	92.9 (90.5–95.3)
MS-30 + Palacos	4,250	898	98.8 (98.2–99.4)
CPT + Palacos	5,630	2,610	98.7 (98.3–99.1)
CPT + other	469	116	97.3 (94.8–99.8)
Elite + Palacos	4,222	2,450	94.4 (93.6–95.2)
Elite + Simplex	166	98	87.8 (82.5–93.1)
Elite + other	1,254	668	88.2 (86.2–90.2)
C-stem + Palacos	1,599	683	99.0 (98.4–99.6)

Lubinus (revision risk (RR) = 0.77, 95% CI: 0.73–0.81), Müller (RR =0.83, 95% CI: 0.70–0.99), MS 30 (RR =0.73, 95% CI: 0.63–0.86), and C-stem THAs (RR =0.70, 95% CI: 0.55–0.90) were associated with a lower revision risk than Charnley THA. Spectron EF (RR= 1.73, 95% CI: 1.62–1.84), Exeter (RR =1.25, 95% CI: 1.18–1.31), and Elite THAs (RR =1.65, 95% CI: 1.51–1.80) had a higher revision risk than Charnley THA after adjustment for age, gender, and diagnosis (Table 15).

Subgroup analysis of the Exeter devices showed that the Exeter X3 Rimfit THA had a similar risk of revision as the reference implant (Charnley) THA (RR = 1.13, 95% CI: 0.91–1.39). The Exeter Duration THA had a lower risk of revision of the reference implant (RR = 0.84, 95% CI: 0.77–0.90) (Table 18).

Table 18. Adjusted revision risk (age, sex, diagnosis, femoral head material) for revision of the Exeter-subgroup devices.

THA	**Adjusted revision risk (95% CI)**	**p-value**
Charnley	1	–
Exeter X3 Rimfit/Exeter	1.13 (0.91–1.39)	0.3
Exeter Contemporary/Exeter	1.41 (1.31–1.52)	< 0.001
Exeter All-poly/Exeter	1.47 (1.39–1.56)	< 0.001
Exeter Duration/Exeter	0.84 (0.77–0.90)	< 0.001

6. DISCUSSION

The main result of the Study I of this thesis was that 9 of the 42 BHR hips assessed had a definite ARMD. It was concluded that BHR may be more problematic than previously thought. Systematic follow-up of these patients was recommended. The main result in Study II was that 14% of ReCap-M2A-Magnum MoM THAs had definite ARMD. We concluded that although the prevalence of ARMD is high, most of the patients did not require revision operation. Further, our main finding from Study III was, that revision risk of ASR THA was significantly increased compared to ASR HRA, although that was not the case concerning analogous THA/HRA devices studied. The main finding in the Study IV was that the Spectron EF THA and the Elite THA had a lower implant survival than the reference THA. Implant survival of the Müller, MS 30, CPT, and C-stem THAs was above the acceptable limit for 10-year survival.

The four studies were included in this thesis because they all had the aim to assess complications and revision operations of THA surgery with the same observational method.

We acknowledge that register studies overall have several limitations. First, implant survival is often the only outcome we are able to assess based on national registers. However, in local registers like Turku University Hospital Database the data contents are understandably more diverse, including for example data on metal ion levels in MoM THA patients.

Further, register studies are prone to selection bias because revision indication may vary. For example, elderly patients are less likely to be revised compared with younger ones, because of shorter life expectancy or poor medical condition, even if the implant fails and functional result is poor. Similarly, implants with easier or less invasive revision are probably more likely to be revised.

Overall completeness of primary and revision THA data in FAR is high, meaning that almost all primary THAs and most revision THAs are reported to FAR when compared to the National Discharge Register. Overall completeness of primary THA from 2005 to 2015 was 95%, and that of revision surgery 85% (FAR). However, completeness of

reporting revision surgery to FAR varies between hospitals, which may cause bias. For example, in 2015 revision completeness varied from 60% to 100% at hospital level (FAR). Overall coverage of FAR is good, meaning that every hospital performing THA delivers data into FAR. However, accuracy concerning reasons for revision prior to FAR data contents revision in May 2014 is incomplete. Since the data contents revision of FAR in May 2014, however, the accuracy of reporting reason for revision data has significantly improved, and quality checkups are currently systematically performed. The degree of coverage and completeness in the Scandinavian registries is high (Pedersen et al. 2004, Arthursson et al. 2005, Espehaug et al. 2006, SHAR 2014).

6.1. ARMD after BHR arthroplasty

We found that the BHR HRA may be more problematic than previously thought. 4 of 42 hips were revised for ARMD in mean follow-up of 6.7 years. There was a tendency of the male gender being associated with definite ARMD.

One limitation of the BHR HRA study is that the definition of unrevised ARMD was unclear. Persistent pain after insertion of MoM hip prostheses is associated with higher serum metal ion concentrations (above 8 µg/L) (Lardanchet et al. 2012). A cut-off level of 10 µg/L has previously been used in the evaluation of ARMD in patients with a MoM hip prosthesis (Mokka et al. 2013). There was 1 hip in our study considered as having ARMD due to high serum ion levels without MRI findings. Another limitation is that we included patients with bilateral MoM implants, which may have biased metal ion analyses.

However, we increased the cutoff level from 8 µg/L suggested by Lardanchet et al. (2012) to 10 µg/L due to the inclusion of bilateral HRAs. We used a metal ion level ≥ 5 µg/L as a criterion for probable ARMD. Due to the possible bias caused by the inclusion of bilateral HRAs, we conducted a more in-depth analysis to assess bilaterality and found that it was not associated with ARMD. 4 of our 6 patients with ARMD had a normal serum metal ion level (<5 µg/L). 1 of these patients was revised, and ARMD was verified at the operation. Normal levels of serum metal ions may be misleading in detecting ARMD and metal ion measurements alone should not be used for screening for ARMD (Macnair et al. 2013).

Another limitation of this study is that the approximate size of fluid collections by MRI was used to define definite ARMD and to differentiate it from probable ARMD. All collections of fluid with a solid component were considered to signify definite ARMD. The dichotomy between MRI ≥ 50 mm in any dimension and <50 mm is artificial, and we must assume that a liquid collection ≥ 50 mm in any dimension is a clinically significant amount of fluid relative to the diagnosis of ARMD. A further limitation of the present study is the lack of evaluation of the position of the implant by computed tomography. However, a previous study showed no association between pseudotumor formation by MRI and HRA cup position by CT (Hart et al. 2012), which is consistent with our results.

Another limitation of our study is that not all patients who were operated in our hospital from April 2004 to March 2007 were included. At first, we wanted to track patients who had been operated on in 2004–2005, but the contralateral hip of many of these patients were operated with a BHR implant later, by 2007. We decided to include these patients with bilateral hips (although one was operated later). On the other hand, there were many BHR operations in 2006 and 2007 that were not included in this screening study due to lack of resources. The total number of hips with a BHR inserted in our unit between April 2004 to March 2007 was 116 (of which 42 were included in the study). Thus, unintentional bias is possible, although it is unlikely that this would have undermined our results.

The risk factors associated with ARMD were identified with binary logistic regression (definite or probable case vs. no ARMD). The results were expressed as ORs. It is of note the OR is not equivalent to relative risk (RR) (Schmidt and Kohlmann 2008). The risk factors evaluated were not statistically significantly associated with ARMD, probably due to the relatively low number of hips in the study. Thus, it is still possible that some patient symptoms are associated with ARMD (score OHS, OHS relationship between poor / fair compared to good / excellent, sense of subluxation, clicking, swelling).

Concern was recently raised about the high failure rate of HRA due to ARMD. In May 2012, the Finnish Arthroplasty Association recommended that the HRAs should no longer be performed (FAA 2012). However, the first reports on the clinical success of the BHR were promising (Treacy et al. 2005, Steffen et al. 2008, Heilpern et al. 2008):

the short-term survival of the BHR was comparable to that of the conventional cemented THR, according to data from the Finnish Arthroplasty Register (Seppänen et al. 2012) and the cumulative revision rate of BHR at 5 years (3.5%, 95% CI: 3.2–3.9) and 10 years (7.0%, 95% CI: 6.6–7.6) was relatively low according to Australian registry data (AOANJRR 2016). However, registry data identify early implant failure poorly, since radiological data on osteolysis and ARMD appear late. Indeed, early clinical studies can focus exclusively on radiological findings. Bisschop et al. (2013) reported a 28% prevalence of CT-verified pseudotumors in 149 BHR HRAs after an average follow-up of 3 years. These results are consistent with our findings. In contrast to that study, we used exclusively MRI to diagnose radiologically fluid collections and soft tissue masses (except in 2 cases) and the prevalence of fluid collections confirmed by MRI in our study was higher. The follow-up period in our study was longer, which is probably related to the high prevalence of ARMD. However, our goal was to detect the prevalence of ARMD based on MRI findings, serum metal ion levels, and surgical findings, and not just the prevalence of radiologically detected pseudotumors. The clinical relevance of asymptomatic fluid collections detected by MRI in patients with normal metal ion content is unclear. The prevalence of MRI-verified pseudotumors in HRA patients with a painful hip is similar to that of asymptomatic HRA patients (Hart et al. 2012). Nevertheless, the high rate of fluid collections seen by MRI and the soft tissue destruction at the time of revision found in our patients is a cause of great concern.

6.2. Systematic screening of ARMD after ReCap-M2a-Magnum MoM THA

We found that 33 of 1188 patients (33 hips of 1329, 2.5%) had revision operations due to ARMD. In addition, 157 hips (11.8%) were considered to have definite ARMD at a mean follow-up of 5.2 years, but had not had revision surgery by the end of September 2014. Thus the prevalence of ARMD in this cohort was 14.3% (190/1,329), which is similar to that of the preliminary study by Mokka et al. (2013).

There are some limitations in our study. We concluded that patients with high ion levels (≥ 10 µg/L) have definite ARMD. ARMD is generally related to soft tissue changes around the prosthesis (Langton et al. 2010). The Medicines and Health Products Regulatory Agency (MHRA) (MHRA 2012) recommended a threshold of blood cobalt

and chromium of 7 µg/L. Although this shows good specificity, it shows a relatively low sensitivity with regard to the presence of a pseudotumor (Hart et al. 2011). The risk of developing a pseudotumor is four times higher with blood levels of metal ions above 5 µg /L (Bosker et al. 2012) and a threshold of 10 µg/L was previously used to evaluate ARMD in combination with MoM hip implants (Mokka et al. 2013).

Another limitation is that we included patients with bilateral MOM implants, which may have biased metal ion analyses. However, we raised the cut-off threshold from 8 µg/L as suggested by Lardanchet et al. (2012) to 10 µg/L due to the inclusion of bilateral THAs. We used a level of metal ions ≥ 5 µg /L as a criterion for possible ARMD.

Dividing the "definite" and "probable" groups by the amount of fluid collections in MRI is problematic. The dichotomy between MRI findings ≥ 50 mm and <50 mm is artificial and we hypothesized that a collection of fluid ≥ 50 mm in any dimension is a clinically significant amount of fluid with respect to the diagnosis of ARMD. The same cut-off has been used in a previous study conducted in our hospital (Mokka et al. 2013).

Another limitation of our study is that we selected to perform MRI based on symptoms of the patient and the amount of ion levels, and hence not all patients were examined by MRI. Additionally, the assessment of some cases of ARMD was based on the surgical findings at operations described in the medical reports, and some revision operations were made before the surgeons were familiar with the concept of ARMD.

A strength of our study is that all ReCap-M2a-Magnum implantations were performed in a single center ans standardized surgical protocol was used. The BiMetric stem and Hardinge approach was used in every operation, so the stem or the surgical approach did not introduce bias. In addition, to improve the assessment of complications, we used MARS-MRI. Cases present with adverse local tissue reactions and periprosthetic fluid collection or soft tissue masses are typically not detectable by radiography nor, in many cases, by computed tomography. MRI is the best method for assessing patients with MOM hip resurfacing arthroplasty, because of its high soft tissue contrast and lack of ionizing radiation (Robinson et al. 2014).

The short-term survival of the ReCap-M2a-Magnum THA is comparable to that of the conventional cemented THA, according to FAR data (Mokka et al. 2013). The

cumulative revision percentage of ReCap-M2a-Magnum THAs at 7 years was 6.4% (95% CI: 4.8–8.4) according to the Australian register (AOANJRR 2008) and 7% (CI 95%: 4.7–8.0) according to the FAR Register (thl.fi/far/). Overall, the revision rate of the ReCap-M2a-Magnum THA is higher than that of conventional THAs but lower than that of ASR THAs (www.thl.fi/far, AOANJRR 2008, Varnum et al. 2015). A hazard warning for MoM Biomet M2a devices (38 mm and Magnum) was published in Australia in February, 2015 (tga.gov.au).

Bosker et al. (2012) reported an incidence of pseudotumors of 39% and a revision rate of 12% at 3.6 years after the ReCap-M2a-Magnum THA procedure. In our preliminary study of 80 ReCap-M2a-Magnum THA, we found 11 definitive cases of ARMD, 3 of which were revised at that stage (Mokka et al. 2013). Recently, Bosker et al. (2015) examined 706 ReCap-M2a-Magnum hips in 626 patients by computed tomography and found 228 pseudotumors (32%) in 219 patients (35%). In addition, 76 hips (11%) were revised in 73 patients (12%) after a median of 5.3 (1.0–8.3) years. Pseudotumor formation detected by CT was markedly more common in that study than the prevalence of ARMD based on MRI / ion levels in our study. The difference between the results of these two studies is explained by our selective use of MRI.

There might have been asymptomatic patients in our study with low levels of metal ions, fluid collection, or masses of soft tissue in their hips. However, we believe that the clinical significance of imaging findings in asymptomatic patients with normal ionic levels is low. The overall revision rate in our study was somewhat lower than in the study by Bosker et al. (2015). Most of our revisions were made for reasons other than ARMD, *e.g.,* periprosthetic fractures, lack of osteointegration of uncemented implants, and infections. The reasons for the revisions were not evaluated in the study of Bosker et al. (2015). We agree that early detection of pseudotumors is important because if revision surgery is performed before substantial soft tissue damage, the result is likely to be better than in surgery comes late. In addition, many of the ReCap-M2A-Magnum THA revisions have been complicated in our clinic by cold-welded femoral heads and adapters, which is a unique feature of this device (Mäntymäki et al. 2016).

ARMD may occur in asymptomatic hips fitted with a LDH MoM device (Kwon et al. 2011). Still, pain, a sense of subluxation, clicking, and fair or poor OHS scores were associated with ARMD in our study. Pain was also associated with ARMD in the study

by Bosker et al. (2015). In addition, females and devices with small diameter heads (≤ 44 mm) are reported to be risk factors for ARMD (Reito et al. 2013). We found, by multivariate modeling, that larger head sizes were associated with ARMD compared to medium sizes. Theoretically, it is possible that the lubrication between the bearing surfaces works better with medium sized heads. In our study, retroverted cups were rare, but they were significantly associated with ARMD revision. The probability of strain to the edge of the cup is increased if the cup is incorrectly positioned.

Systemic symptoms of poisoning are among the theoretical health risks related to chronically elevated blood metal ion concentrations induced by abnormal wear and corrosion of the MoM implants (Steens et al. 2006, Lombardi et al. 2015), but such toxicity is rare, but there are several recent reports on the systemic toxicity of cobalt, including symptoms such as fatigue, weakness, hypothyroidism, cardiomyopathy, polycythemia, visual and hearing disorders, cognitive dysfunction, and neuropathy (Zywiel et al. 2013). We do not know of any of our patients with severe systemic symptoms of cobalt poisoning, although these symptoms were not systematically scrutinized.

We found a high prevalence of ARMD when we screened systematically all ReCap-M2a-Magnum THA patients in our hospital, but most of these patients did not require revision and 77% of the hips showed no signs of ARMD. Time course analysis estimates have been presented suggesting that pseudotumor development continues in ReCap-M2a-Magnum THA patients (Bosker et al. 2015). Therefore, annual follow-up of all patients subjected to LDH MoM THA has been suggested for the duration of the time the prosthesis is *in situ* (Bosker et al. 2015). The Finnish Arthroplasty Society recommended that patients should be monitored every other year by patient questionnaires, metal ion level measurements, and imaging with MRI, CT, or ultrasound. Based on our results, follow-up is still warranted (FAS 2015).

6.3. HRA vs. analogous LDH MoM THA

The short-term risk of revision of LDH MoM THAs was not increased compared to their analogous HRAs concerning two of the three devices studied on a nationwide level.

However, the risk of revision of ASR THA was significantly increased compared to that of the ASR HRA. Longer follow-ups and further information on the incidence of adverse soft tissue reactions in these cohorts are needed.

LDH MoM THAs can produce more metal ions than HRA due to wear and corrosion at the junction between the femoral neck and the adapter sleeve and the open femoral head design. Lavigne et al. (2011) reported that the cobalt-chromium adapter sleeve of the ASR THA system appears to possess better design characteristics than, for example, the Zimmer device. The cumulative 5-year revision rate in Australia for ASR THA was comparable to that of ASR HRA (10.3%, 95% CI = 9.0–11.6 and 10.5%, 95% CI = 8.6–12.7, respectively) (AOANJRR 2011). In England and Wales, the ASR HRA had slightly better survival than the Corail and Summit / ASR THAs (9.6%, 95% CI = 8.3–11.2 and 11.3%, 95% CI = 9.1–14.2, respectively) (NJR 2011). Our data corroborates the view that the ASR THA performs worse than the ASR HRA.

The main reason for ASR HRA and ASR THA revisions in the current data was aseptic loosening of both components. However, ARMD as a reason for revision in the old data collection form of the FAR was not asked specifically. Therefore, ARMDs may have been falsely encoded as aseptic loosening in the register. ARMD is not always coded as "other reason", because there were only 12 ASR HRA and 4 ASR THA revisions recorded as "other reason". The Finnish data collection form has been updated since then in collaboration with the Nordic Arthroplasty Register Association (NARA).

The cumulative 5-year revision rate of BHR THA was higher than that of BHR HRA in Australia (4.9%, 95% CI = 3.8–6.3 and 3.5%, 95% CI = 3.1–3.9, respectively). In addition, the cumulative 7-year revision rate of BHR THA was higher than that of BHR resurfacing (6.7%, 95% CI = 4.8–9.4 and 5.0%, 95% CI = 4.4–5.5, respectively) (AOANJRR 2011). The stem designs used for BHR THA were not mentioned. In England and Wales, BHR resurfacing had a 5-year revision rate of 3.4% (95% CI = 3.1–3.8). Equivalent figures for BHR THA are not available (NJR 2011). There was no statistical significant difference in the short-term revision rate between BHR resurfacing and BHR THA in our study. However, the total number of Synergy/BHR combinations was small (430) compared with BHR resurfacings (1636). It is possible that the stems used in Australia not specified in the register did not manage as well as the Synergy

stem seems to manage in Finland. The short-term survival of BHR resurfacing in Finland is worse than in Australia and in England and Wales. Despite this, the BHR has been one of the best performing resurfacing designs in Finland (Seppänen et al. 2012).

In Australia, the cumulative 3-year revision rate of ReCap HRA was higher than that of ReCap THA (6.0%, 95% CI = 3.4–10.7 and 1.9%, 95% CI = 1.1–3.1, respectively). The cumulative 5-year revision rate of ReCap THA was 3.4% (95% CI = 2.1–5.5) in Australia (AOANJRR 2011) and of the ReCap HRA 6.4% (95% CI = 4.1–9.8) in England and Wales. Corresponding figures for ReCap THA were not available (NJR 2011). There was no statistically significant difference in short-term revision rate between ReCap resurfacing and Bimetric/ReCap in our study. The total number of Bimetric/ReCap combinations was high (5,464). The short-term survival of the Bimetric/ReCap with a Magnum bearing surface has been promising also in previous studies (Meding et al. 2012, Kostensalo et al. 2012, Mokka et al. 2013). These data support the Australian finding of a low short-term revision rate of the ReCap THA.

There was no difference in the risk of revision for dislocation between the pairs of implants compared. A large size of the device head seems to protect against dislocation, whether the head of the prosthesis is connected to the femoral neck or to the femoral component. Nor was there any difference in the risk of revision of the peri-prosthetic fracture between the implanted pairs compared. In the short-term, the incidence of calcar fractures after cementless THA and femoral neck fractures after HRA appears to be similar. There was no difference in the risk of revision due to infection between the three LDH MoM THAs and the analogous HRAs. The assumed protective effect of the antibiotic cement of the HRA designs was not supported by our data. LDH MoM THAs are probably performed by a higher number of surgeons than HRAs in Finland. HRA has a reputation for being a relatively difficult procedure, and, wisely, it was centralized to the hands of the most experienced surgeons in many hospitals. The total number of ASR THA and BHR THA in this study was nevertheless low.

Various studies have shown that more than a 60° abduction angle could be a significant risk factor for increased metal ion levels and ARMD (Langton et al. 2009, Reito et al.

2011). In a registry-based study with a high number of patients, it is not possible to assess radiographs and thus this assumption cannot be addressed.

In this study, elderly females had an increased risk of revision with ReCap HRA compared to ReCap THA, probably due to a high number of fractures of the femoral neck. Elderly males had an increased risk of revision with ASR THA compared to ASR HRA. There was also a tendency for elderly females of an increased risk of revision related to ASR THA compared to ASR HRA. ASR THAs may perform worse than ASR HRA due to wear of the adapter sleeve.

In conclusion, there is no difference in the risk of revision between BHR HRAs and THAs or between ReCap HRAs and THAs in the short- to medium-term on a nationwide level. The ReCap LDH MoM adapter sleeve is made of titanium, not cobalt chrome as the other two models (Lavigne et al. 2011), which may affect the development of ARMD. However, the risk of revision of ASR THAs is much higher than that of ASR HRAs (AOANJRR). The actual prevalence of ARMD in patients who have undergone MoM arthroplasty is not yet known and longer annual follow-ups are needed to establish if there are differences between HRAs and THAs as well as between designs of different manufacturers in the incidence of ARMD.

6.4. Implant survival of the most common cemented total hip devices

The Spectron EF and Elite THAs had poorer survival than the Charnley THA, the reference implant. The survival of the Müller, MS 30, CPT, and C-stem implants (94.9–96.6% at 10 years) was well above the acceptable 10-year survival limit. However, the total quantity of these devices was low compared to Charnley, Lubinus, and Exeter THAs, although all were implanted in more than 2000 hips. When a certain implant model becomes more widespread and used by a growing number of surgeons, the results will be more representative as they can be assumed to reflect a wider range of differences in the surgical technique.

One of the main strengths of this study is the unique collaboration among 4 national registries with the goal to create a multinational database with a large number of patients and a long follow-up time. The main weakness of the study is that we could

not evaluate each updated version of each device separately. The study devices were recorded as families of implants, made up of several versions of the devices. Another weakness is that we could not evaluate cup and stem survival separately with revision for any reason as the endpoint, since these data are not available in the FAR and cannot therefore be included in the 4-country minimum data set. In addition, our data do not include information on parameters such as surgeon volume, hospital volume, ASA grade, or preoperative patient-reported outcome measures (PROMs).

The survival of Charnley THA implants was high (94.1% at 10 years), but slightly lower than that reported by the NJR (10-year survival of 95.1% for Charnley Ogee/Charnley and 97.0% for Charnley/Charnley) (NJR 2015). In Australia, the 10-year survival of Charnley Ogee/Charnley was 91.6%, whereas that of Charnley/Charnley was 93.0% (AOANJRR 2015). The total quantity of Charnley THAs in Australia was low (1,300), which could explain the results being slightly poorer than those in Finland. The Charnley THAs studied included several versions of the Charnley stem, *e.g.,* Charnley flanged, Charnley heavy flanged, and Charnle flat and round-backed stems. It has been previously reported that the survival of the Charnley THA implant after 1995 has been good, and differences in implant survival between the Charnley stems are minor (Espehaug et al. 2009). Similarly, the cup designs of the Charnley THA varied. The use of Charnley's THA decreased drastically towards the end of the study period.

The Elite Plus THA was introduced in 1994 as the second modular evolution of the original Charnley THA. Several modifications were made to the shape and dimensions of the femoral component to improve the proximal transfer of the load and to reduce contact stress. The design also incorporated a sub-section of the collar flange (DePuy 1993). The overall survival of Elite THAs in our study was lower than that of the reference implant. The Elite Plus has been withdrawn from the market due to divergent clinical findings (Hauptfleisch et al. 2006, Kim et al. 2007, von Schewelov et al. 2010). Our findings support the earlier findings. One weakness of our Charnley vs. Elite THA analysis is that Elite cups were sometimes - albeit rarely - used with Charnley stems, and vice versa, which may have introduced some bias.

The survival of the third device of DePuy which was evaluated, the C-stem THA (95.8% at 10 years), was higher than that of the Charnley THA and comparable to previous reports (a 10-year survival of 94.6% for C-stem/Elite Plus in AOANJRR and a 10-year

survival of 98% for C-stem / Elite Plus Ogee in the NJR). The triple-tapered, polished C-stem introduced in 1993 was based on the original Charnley concept of polished flat-back stem (Purbach et al. 2013). However, the total number of C-stem THAs that have been implanted to date in the Nordic countries - and worldwide - is low compared to the original Charnley THA.

Long-term survival of the Lubinus THA in our study was higher than that of the reference implant. Most of the study stems were SP II models with a high degree of documentation (Annaratone et al. 2000, Wierer et al. 2013, Prins et al. 2014, SHAR 2014). However, most of the Lubinus THAs (79%) in our study were implanted in Sweden, which has twice the population of each of the other 3 countries. In general, survival of cemented THA implants in Sweden is significantly higher than in the other 3 countries (Mäkelä et al. 2014). The SHAR has provided feedback to the profession and has provided continued training on cementing techniques for more than 30 years. Thus, the excellent survival of Lubinus THA implants in the present study may have been biased by the "Swedish factor". The threshold for carrying out a revision operation is also culture-dependent and may vary between the Nordic countries. X-linked Lubinus cups were coded separately in the NARA hip database only in Sweden, so that we could not evaluate the X-linked Lubinus THA separately. However, these devices may be detected in the future by NARA data, once the catalog number-based registry is ready.

The long-term survival of the Exeter THA was satisfactory, although lower than of the reference device. The overall survival of Exeter THA implants (93.5%) was slightly lower than that reported by the NJR (10-year survival 97.1% for Exeter V40 / Contemporary, and 96.3% for Exeter V40 / Exeter Duration), but similar to that reported by AOANJRR (10 years survival for Exeter V40 / Contemporary 94.1%). In this study, Exeter's THA family consisted almost exclusively of Exeter Universal stems. The Exeter V40 stem was coded separately only in Denmark in the NARA database, and the number of THA Exeter V40 defined in the present study was low. However, we did perform subgroup analyses for Exeter THAs by acetabular component (Table 18). The Exeter X3 Rimfit THA (X3-stabilized UHMWPE, the latest version of the high crosslinking) was separately encoded in each of the 4 registers. The survival of this implant was comparable to that of the reference implant. The total number of Exeter

X3 Rimfit THAs was, however, low compared to Exeter Contemporary THAs and Exeter THAs All-poly, and the follow-up time was shorter. The long-term survival of Exeter Contemporary THA and Exeter All-poly THA implants was good, although not as good as the best implants. According to Swedish datasurvival of the Lubinus THA and Exeter THA implants is similar (SHAR 2014). The "Swedish factor" seems to have a substantial influence on the survival of the Exeter THA, as well. The most common device used in Sweden was the Exeter Duration THA, with excellent survival. In England and Wales, the survival of Exeter / Contemporary THA implants was slightly longer than that of Exeter / Exeter Duration THAs, which was contrary to our results. In Australia, the Exeter / Duration THA is not evaluated separately. However, the 15-year survival of the Exeter THA in our study was lower than that of the best performers. The 15-year survival data for Exeter THAs are not yet available from the NJR or AOANJRR.

The Exeter stem is easy to revise and the method of revision of the cementing of a new, smaller stem without removing the old bone cement is a well-established procedure (te Stroet et al. 2014). The ease of revision of the Exeter stem may have biased the survival of Exeter THAs in our study. However, the risk of revision of the Exeter stem for periprosthetic fracture is higher than for the Lubinus SP II stem (Thien et al. 2014).

Implant survival of the Spectron EF THA in our study (89.9% at 10 years and 79.8% at 15 years) was inferior to that of the other THAs, and also lower compared to previous reports (with 10-year survival of 92.1% for Spectron EF / Reflection in AOANJRR and in Norway (Espehaug et al. 2009)). In our study, the Spectron THA consisted mainly of Spectron EF stems and Reflection cups. RSA studies have shown that cups with ethylene oxide-sterilized polyethylene (such as the Reflection cup) have higher wear rates than those with gamma irradiation-sterilized polyethylene (Digas 2005, Kadar et al. 2011a, Jonsson et al. 2015). The Spectron EF modular stem was introduced in 1988, and in 1989 the roughness of the proximal part of the stem was increased. 5 years later, other stem changes were introduced and the brand name changed to Spectron EF Primary. The collar was polished and smaller sizes were introduced. This design performed worse than its predecessor, especially the smaller sizes (Thien and Kärrholm 2010, SHAR 2014). Maybe the addition of a rough surface to the Spectron

stem was detrimental with respect to the long-term success of the implant (Della Valle et al. 2006, Grose et al. 2006, Espehaug et al. 2009, Kadar et al. 2011b). Our results support these findings.

Implant survival of Müller THAs (94.9% at 10 years and 92.6% at 15 years) was higher than that of the reference implant, and comparable to that of previous reports (Mäkelä et al. 2008, Clauss et al. 2013). The Müller THAs consisted mainly of straight Müller stems and Müller all-polyethylene cups. Müller stems of titanium alloy with a rough surface finish were excluded due to previous reports of an increased risk of revision compared to cobalt-polished chrome Müller stems (Clauss et al. 2013, FAR 2015). The survival of the implants of another Zimmer device, the MS-30 THA (96.6% at 10 years) was also high and comparable to that of previous reports (10-year survival of 97.5% for MS-30/Low Profile in the AOANJRR, and 10-year survival of 99% for MS-30/Low Profile in the NJR). However, survival of the stem was poor – 80% at 12 years, a figure reported also for the MS-30 (Witte et al. 2009). The original MS-30 (Morscher-Sportorno) stem was made of stainless steel and it was straight, three-dimensionally tapered, collarless, and matt-surfaced (Berli et al. 2005, Brigstocke et al. 2014). However, most MS-30 stems inserted in Sweden were polished. The MS-30 stem was used in combination with Zimmer all-polyethylene cups, such as ZCA and highly crosslinked ZCA XLPE. A weakness of the Müller and MS-30 THA analyses was that all Müller THAs in the study were implanted in Finland and Sweden, and all THA MS-30s were implanted in Sweden and Norway.

Survival of the third Zimmer device studied, the CPT THA (94.9% at 10 years and 91.6% at 15 years), was comparable to that of the reference THA, and to those of previous reports: 10-year survival of 95.4% for CPT / ZCA in AOANJRR, and a 10-year survival of 96.4% for CPT / ZCA in the NJR. The CPT (collarless polished tapered) stem was originally developed as a collarless, highly polished, double-tapered prosthesis for distribution in the United States. Like the Exeter stem, from which the principles of its design were taken, the CPT also uses the concept of the taper slip. The CPT differs from the Exeter Universal Stem in its broad lateral shoulder, more complete lateral taper, and more rectangular proximal geometry (Burston et al. 2012). CPT stems made of stainless steel and chrome-cobalt were included in the current

study, which may have introduced some bias. Although they were implanted in all 4 countries, the total number of CPT THAs was low.

The long-term performance of cemented THAs depends on many non-implant related factors, *e.g.,* patient characteristics, surgical and cementing technique, and properties of the bone cement. Although all current bone cements are based on methylmethacrylate, their performance may vary. Poor results have been reported for some low-viscosity cements (Havelin et al. 1995, Furnes et al. 1997, Espehaug et al. 2002). We also determined the survival of the implants by type of cement (Palacos-type, Simplex-type or other) (Espehaug et al. 2009). The survival of the Charnley, Elite, and Exeter THA implants was higher when used with high-viscosity Palacos-type cement. Our results support previous results (Havelin et al.1995, Espehaug et al. 2002). The survival of implants was similar between 1995 and 2004 and between 2005 and 2013. Cementing techniques seem to have become standardized in the Nordic countries over the past two decades.

In summary, several brands of cemented THAs behave well in the long run. However, there are significant differences in implant survival between high and low performers.

7. CONCLUSIONS

Our study leads to the following conclusions:

1) Hip resurfacing arthroplasty with the Birmingham Hip Resurfacing may be more problematic than previously thought. Systematic follow-up of these patients is recommended.

2) The prevalence of ARMD in patients fitted with the ReCap-M2a-Magnum THA is high.

3) The need for revision in the short term of large diameter head MoM hip replacements has not increased compared to similar hip resurfacing arthroplasties. There may be implant-related factors involved.

4) Several brands of cemented THAs perform well in the long term. There are significant differences in the survival of implants between the best and worst performers.

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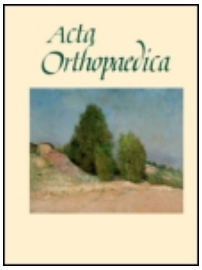
10. ORIGINAL PUBLICATIONS



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Adverse reaction to metal debris after Birmingham hip resurfacing arthroplasty

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Background and purpose — Concern has emerged about local soft-tissue reactions after hip resurfacing arthroplasty (HRA). The Birmingham Hip Resurfacing (BHR) was the most commonly used HRA device at our institution. We assessed the prevalence and risk factors for adverse reaction to metal debris (ARMD) with this device.

Patients and methods — From 2003 to 2011, BHR was the most commonly used HRA device at our institution, with 249 implantations. We included 32 patients (24 of them men) who were operated with a BHR HRA during the period April 2004 to March 2007 (42 hips; 31 in men). The mean age of the patients was 59 (26–77) years. These patients underwent magnetic resonance imaging (MRI), serum metal ion measurements, the Oxford hip score questionnaire, and physical examination. The prevalence of ARMD was recorded, and risk factors for ARMD were assessed using logistic regression models. The mean follow-up time was 6.7 (2.4–8.8) years.

Results — 6 patients had a definite ARMD (involving 9 of the 42 hips). 8 other patients (8 hips) had a probable ARMD. Thus, there was definite or probable ARMD in 17 of the 42 hips. 4 of 42 hips were revised for ARMD. Gender, bilateral metal-on-metal hip replacement and head size were not factors associated with ARMD.

Interpretation — We found that HRA with the Birmingham Hip Resurfacing may be more dangerous than previously believed. We advise systematic follow-up of these patients using metal ion levels, MRI/ultrasound, and patient-reported outcome measures.

The medium-term revision risk of many hip resurfacing arthroplasty (HRA) devices is high (AOA 2012, NJR 2012). Concern has emerged about soft-tissue reactions after HRA (Pandit et al. 2008, Glyn-Jones et al. 2009). Patients whose devices are failing often experience pain and swelling in the groin (Macpherson and Breusch 2011). The finding of large sterile effusions of the hip and/or macroscopic necrosis/metallosis associated with joint failure and pain may be referred to as adverse reactions to metal debris (ARMD) (Langton et al. 2010). Furthermore, asymptomatic pseudotumors are common after HRA (Kwon et al. 2011, Matthies et al. 2012). The reaction to excess metal wear debris is often associated with increased serum metal ion levels (Langton et al. 2010, Kwon et al. 2010). Magnetic resonance imaging (MRI) optimized to reduce image artifacts and distorsions caused by metallic implants is an important tool in diagnosing local soft-tissue abnormalities and mass lesions (Haddad et al. 2011). MRI analysis is useful in delineating soft-tissue abnormalities and mass lesions even when radiographs are normal (Hart et al. 2012).

HRA has been popular in Finland during the last 10 years (Seppänen et al. 2012). From 2003 to 2011, the BHR HRA (Smith and Nephew, Warwick, UK) was the most commonly used HRA device at our institution, with 249 implantations. We analyzed the prevalence of ARMD in an early BHR cohort consisting of 42 BHR HRA implantations performed from April 2004 to March 2007. BHR HRA is considered to be the best-performing HRA, with 10-year registry follow-up (AOA 2012). For the assessment, in addition to a physical examination, we used radiographs and MRI of the hip, serum metal ion concentrations, and the Oxford hip score (OHS) questionnaire. On the basis of these results, we tried to identify risk factors for ARMD.

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Patients and methods

32 patients (42 hips) had undergone a BHR HRA between April 2004 and the end of March 2007 (Table 1). There were 24 male patients (31 study hips). The mean age of the patients was 59 (26–77) years. The patients were examined between March 2012 and June 2012 with MRI, assessment of serum metal ion measurements, the Oxford hip score (OHS) questionnaire, and physical examination. The mean follow-up time was 6.7 (2.4–8.8) years. None of the patients had undergone BHR HRA of both hips in 1 session; 10 patients had had both hips operated during the study period with BHR HRA, but in separate sessions (20 hips). 1 patient with a study implant also had a BHR HRA in the contralateral hip, but it was inserted outside the study period (2010). 1 patient had a Synergy-BHR (Smith and Nephew) large-head metal-on-metal (MoM) replacement (THR) in the contralateral hip; 1 patient had a cemented Muller THR (Zimmer, Warsaw, IN) in the contralateral hip. Posterior approach was used in all cases. 1 hip had recurrent dislocations. There were no femoral neck fractures, infections, nerve damage, or other complications.

The BHR cup has a hemispherical design with the cast-in POROCAST ingrowth surface. This HA-coated ingrowth surface does not require heat treatment to attach beads, and therefore preserves the carbide structure. This surface is integral to the cup and is not a spray-on coating. The BHR femoral component is cemented to femoral bone. The BHR HRA uses an as-cast cobalt chrome metal-on metal-bearing surface with a highly polished finish. In theory, cobalt chrome in its as-cast form has superior wear resistance to other forms of the alloy (BHR Product Manual).

MRI was used to identify fluid collections and soft-tissue masses (Toms et al. 2008, Hart et al. 2012). MRI was performed on 40 hips regardless of the patient's symptoms. 1 patient refused MRI examination due to claustrophobia. For 1 patient, a revision operation had been performed earlier for ARMD without MRI imaging. We used 3 1.5T MR imagers (Philips Ingenia (2012); Philips Medical Systems, Best, the Netherlands; Siemens Avanto (2008) and Siemens Aera (2012); Siemens, Erlangen, Germany). The pulse sequences used were optimized to reduce metal-induced artifacts (Hargreaves et al. 2011). MARS (metal artifact reduction sequence) MRI is a recently developed technique that provides good metal artifact suppression while minimizing image blurring and scanning time (Eustace et al. 1998, Hart et al. 2012). One imager (Siemens Aera) was equipped with an advanced metal artifact reduction technique—Slice Encoding for Metal Artifact Correction—with view angle tilting (SEMAC-VAT) (Sutter et al. 2012). At least 2 sequences covering the whole pelvic area were obtained in the coronal and axial planes (STIR and T2 or T1) followed by smaller field-of-view images in 3 planes centralized in the joint with implant (STIR, T1, and T2).

Images were examined by radiologists experienced in ARMD-related MRI diagnostics. Special attention was paid to detection of periarticular fluid collections and soft-tissue masses. Pathology was measured in 3 planes and stored for analysis. 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 conventional radiography of the pelvis and hip; the radiographs were used to measure the inclination angle of the cup. Radiographs were taken in upright position. Cup inclination angles were analyzed from digital pelvic radiographs using digital angle measurement. There was no osteolysis or heterotopic ossification in any of the hips. In 1 patient, there was a partial radiolucent line under the cup in Gruen zone I, but the cup position was not changed and it was considered stable.

Serum metal ion measurements (cobalt and chromium) were performed at follow-up. For ion measurements, 5–7 mL of whole blood was taken in a test tube containing heparin (for example, Venosafe or Vacuette trace elements). The Finnish Institute of Occupational Health performs all the cobalt and chromium ion measurements in Finland using inductively coupled plasma mass spectrometry. The analyses have been accredited (FINAS T013).

The OHS questionnaire was completed by 31 patients at the time of follow-up (40 hips). Clicking, a sensation of subluxation, and swelling of the hip were considered separately. 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 who performed revision surgery at the Turku University Hospital.

The prevalence of ARMD after the BHR HRA was assessed and risk factors for ARMD were evaluated: age, sex, head size (≥ 54 mm vs. ≤ 50 mm), diagnosis (secondary vs. primary OA), inclination of the cup, and bilaterality. The association of patient symptoms with ARMD was analyzed separately. The symptoms assessed were clicking, subluxation sensation, swelling, OHS total score, and relation of poor/fair versus good/excellent OHS score. OHS group 1 was considered excellent, group 2 good, group 3 fair, and group 4 poor.

ARMD was considered definite if the patient was revised for ARMD and 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 where there was a solid mass or a fluid collection of ≥ 50 mm in MRI (in any plane). In patients who had not undergone surgery, ARMD was considered to be probable either if the serum chromium or cobalt concentration was ≥ 5 µg/L and/or if there was a fluid collection of any size by MRI.

A radiograph and an MRI image of a BHR hip with a pseudotumor are presented in Figure 1.

Statistics

Potential risk factors for ARMD were analyzed by binary logistic regression with random intercept for patient. The

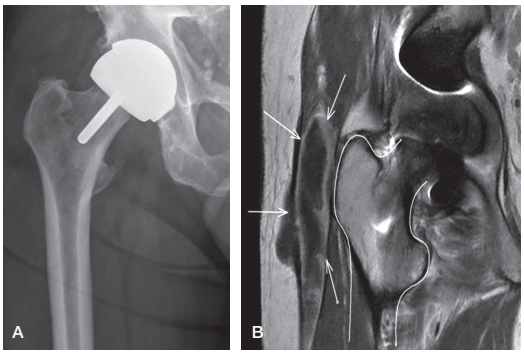

Figure 1. A radiograph (panel A) and an MRI image (panel B) of a BHR hip with a pseudotumor.

dependent variable ARMD consisted of 2 groups (definite or probable cases and no ARMD), with no ARMD being used as the reference group. Results are expressed as crude odds ratios (ORs) with 95% confidence intervals (CIs). Multiple binary logistic regression including risk factors with $p < 0.40$ in a bivariable model, forward selection, and backward elimination methods (inclusion criteria, $p < 0.20$) were used to investigate the potential confounding effect of other risk variables. Exact chi-square test was used to analyze clicking and swelling due to 0 cell counts. were considered statistically significant. Statistical analysis was carried out using SAS for Windows version 9.3.

Ethics

Ethical approval was not required due to adherence to national guidelines on the follow-up of metal-on-metal hip arthroplasty patients. The study was performed according to the ethical standards of Turku University Hospital and the Helsinki Declaration.

Results

6 patients (9 of 42 hips) were considered to have a definite ARMD. 4 of these hips were revised for ARMD (Tables 1 and 2). 8 patients (8 hips) were considered to have a probable ARMD. Altogether, there were 17 hips with a definite or probable ARMD. 18 patients were considered not to have ARMD.

Male sex was associated with definite ARMD, although not statistically significantly so (OR = 11, CI: 0.7–165; p = 0.08). However, sex (p = 0.2), bilateral MoM (p = 0.3), and head size (p = 0.7) were not statistically significant in the multiple logistic regression model (Tables 3 and 4). Sex was the only risk factor included in the final model using forward selection and backward elimination methods.

OHS score (crude OR = 0.97, CI: 0.85–1.1; p = 0.7, for 1 unit increase in this continuous variable) or OHS poor/fair vs. good/excellent relation (crude OR = 1.6, CI: 0.09–27; p = 0.7) were not associated with ARMD. Furthermore, subluxation sensation (crude OR = 1.7, CI: 0.16–18; p = 0.6) was not associated with ARMD. Clicking and swelling were not associated with ARMD either (p = 0.07 for both; Fisher's exact test).

Table 1. Characteristics of 32 patients and results for 42 corresponding hips. Data on swelling, clicking, and subluxation sensation are given hipwise for 41 hips (the data on 1 hip are missing). Data on mean OHS (range) and the OHS classification are given hipwise for 40 hips (the data on 2 hips are missing). Data on mean (range) age, follow-up, and inclination angle of the cup are given hipwise for 42 hips

	Total	ARMD	Probable ARMD	ARMD not found
Patients, n	32	6	8	18
Males, n	24	6	7	11
Serum cobalt, µg/L[a]	2.5 (0.8–14.9)	6.9 (1.2–14.9)	1.5 (0.8–2.6)	1.5 (0.8–2.6)
Serum chromium, µg/L[a]	2.1 (0.6–7.6)	4.4 (1.1–7.6)	1.5 (1.0–2.4)	1.6 (0.6–2.5)
Hips, n	42	8	8	24
Age, years [a]	59 (26–77)	63 (49–70)	58 (26–76)	58 (38–77)
Follow-up, years [a]	6.7 (2.4–8.8)	6.0 (2.4–7.0)	6.8 (6.3–7.3)	7.0 (6.2–8.8)
Swelling, n	2	2	0	0
Clicking, n	2	2	0	0
Subluxation sensation, n	6	2	1	3
Inclination angle of the cup, degrees [a]	47 (37–64)	47 (42–61)	50 (39–64)	46 (37–60)
OHS [a]	44 (21–48)	40 (33–48)	45 (32–48)	44 (21–48)
OHS excellent, n	30	3	7	20
OHS good, n	6	4	0	2
OHS fair, n	2	1	1	0
OHS poor, n	2	0	0	2

[a] Mean (range)
ARMD: adverse reaction to metal debris;
OHS: Oxford hip score (42–48 = excellent, 34–41 = good, 27–33 = fair, and 0–26 = poor).

Discussion

We found that BHR HRA may be more dangerous than previously thought. 4 of 42 hips were revised for ARMD. There was a trend of male sex being associated with definite ARMD.

One limitation of the present study was that the definition of a non-revised ARMD was not clear. Persistent pain after metal-on-metal hip implants has been shown to be associated with higher serum metal ion levels with a probable cutoff of 8 µg/L (Lardanchet et al. 2012). A cutoff level of 10 µg/L has been used previously in assessing ARMD in association with metal-on-metal hip implants (Mokka et al. 2013). There was 1 hip in our study that we considered to have ARMD due to high serum ion levels, without MRI findings. Another limitation was that we included patients with bilateral metal-on-metal implants, which may have biased

Table 2. Data on the 6 patients (9 hips) with a definite adverse reaction to metal debris (ARMD). None of the patients had major muscle destruction. The 64 M, 69 M, and 62 M patients had both hips with ARMD. The ARMD diagnosis of the right hip of 64 M was based on operative findings in a revision operation in 2009

Age	Sex	Side	OHS	Pain	Clicking	Sublux.	Swelling	s-Cr, µg/L	s-Co, µg/L	Cup incl. (°)	MRI	Revision or follow-up
64	M	Right	NA	Moderate	No	Yes	No	NA	NA	48	NA	Revised
64	M	Left	35	Moderate	Yes	Yes	Yes	3.9	4.5	43	Solid and fluid 55 × 35 × 110 mm	Revised
69	M	Right	44	Mild	No	No	No	7.6	13.5	61	Fluid 30 × 40 × 65 mm and 85 × 80 × 30 and solid 20 × 20 × 50	Revised
69	M	Left	44	No	No	No	No	7.6	13.5	47	Fluid 57 × 46 × 10 mm	Follow-up
49	M	Right	33	Hard	Yes	Yes	Yes	4.3	4.5	42	Fluid 70 × 26 × 23 mm	Follow-up
62	M	Right	39	No	No	No	No	7.6	14.9	48	No findings	Follow-up
62	M	Left	39	No	No	No	No	7.6	14.9	43	Some fluid	Revised
59	M	Right	41	Moderate	No	No	No	1.6	2.9	47	Fluid 50 × 5 × 5 mm	Follow-up
67	M	Right	48	No	No	No	No	1.1	1.2	47	Fluid 13 × 19 × 50 mm	Follow-up

OHS: See Table 1. Sublux.: subluxation sensation; s-Cr: serum chromium level; s-Co: serum cobalt level; Cup incl.: cup inclination angle; MRI: magnetic resonance imaging; NA: not available.

Table 3. Results of testing of associations between risk factors and ARMD using logistic regression with random intercept for patient, with crude odds ratios (ORs) and 95% confidence intervals (CIs)

Risk factor	ARMD definite or probable (n = 17) vs. ARMD not found (n = 25) OR	(95% CI)	p-value
Age at follow-up	1.03 [a]	(0.93–1.13)	0.5
Sex (male vs. female)	10.8	(0.7–165)	0.08
Inclination angle of the cup	1.05 [a]	(0.93–1.2)	0.4
Bilateral MoM	0.33	(0.05–2.1)	0.2
Bilateral THA	0.55	(0.09–3.4)	0.5
Diagnosis secondary vs. primary OA	2.0	(0.27–14)	0.5
Head size (≥ 54 vs. ≤ 50 mm)	4.1	(0.66–25)	0.1

ARMD: adverse reaction to metal debris;
MoM: metal-on-metal implant; THR: total hip arthroplasty
OA: osteoarthritis.
[a] For 1 unit increase (continuous variable).

Table 4. Results of testing of associations between risk factors and ARMD using a multiple logistic regression model with random intercept for patient, with adjusted odds ratios (ORs) (including risk factors with p < 0.40 in bivariable model) and 95% confidence intervals (CIs)

Risk factor	ARMD definite or probable (n = 17) vs. ARMD not found (n = 25) OR	(95% CI)	p-value
Sex (male vs. female)	7.6	(0.29–204)	0.2
Bilateral MoM	0.40	(0.05–3.2)	0.3
Head size (≥ 54 vs. ≤ 50 mm)	1.6	(0.16–16)	0.7

For abbreviations: See Table 3.

metal ion analyses. However, we increased the cutoff level from 8 µg/L suggested by Lardanchet et al. (2012) to 10 µg/L due to the inclusion of bilateral HRAs. We used a metal ion level of ≥ 5 µg/L as a criterion for probable ARMD. Due to the possible bias caused by inclusion of bilateral HRAs, we performed further analysis to assess bilaterality and found that it was not associated with ARMD. 4 of our 6 definite ARMD patients had normal serum metal ion levels (< 5 µg/L). 1 of these patients was revised, and ARMD was verified at the operation. Normal serum metal ion levels may be misleading in detecting ARMD, 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 and to differentiate it from probable ARMD. All fluid collections with a solid component were considered to be definite ARMDs. The dichotomy between MRI findings ≥ 50 mm in any dimension and < 50 mm is artificial. We thus hypothesize that a fluid collection ≥ 50 mm in any dimension is a clinically significant amount of fluid with regard to a diagnosis of AMRD. Furthermore, 1 of the limitations of the present study was the lack of CT-based evaluation of implant position. However, no association has been found between MRI-detected pseudotumor formation and CT-detected HRA cup position (Hart et al. 2012), which is in accordance with our findings.

Another limitation of our study was that not all patients who were operated in our unit during the period April 2004 to March 2007 were included. At the start, we wanted to follow up patients who had been operated 2004–2005. However, the contralateral hips of many of these patients were operated with a BHR implant later, up to 2007. We decided to include these patients with bilateral hips (although one was operated later). However, there were many BHR operations in 2006 and 2007 that were not included in this screening study due to lack of resources. The total number of BHR hips inserted at our unit

during the period April 2004 through March 2007 was 116 (42 of which were included in the study). We understand that there may have been selection bias, although it was not intentional. However, we believe that this did not undermine our results. ARMD was common, and several revisions for ARMD were performed.

Possible association of the risk factors with ARMD was determined using binary logistic regression (definite or probable cases vs. no ARMD). Results were expressed using ORs. When interpreting these results, the reader should be aware that OR is not equivalent to relative risk (RR) (Schmidt and Kohlmann 2008). The risk factors assessed were not statistically significantly associated with ARMD, probably due to the relatively small number of hips in the study. The same was true of possible associations between symptoms of the patients and ARMD (OHS score, relation of OHS poor/fair versus good/excellent, subluxation sensation, clicking, swelling).

Concern has been raised recently about the high failure rate of HRA due to ARMD. In May 2012, the Finnish Arthroplasty Association recommended that performance of HRAs should not be continued (FAA 2012). However, the first reports of the clinical success of BHR were promising (Treacy et al. 2005, Steffen et al. 2008, Heilpern et al. 2008). The short-term survival of the BHR was found to be comparable to that of conventional cemented THR, based on data from the Finnish Arthroplasty Register (Seppänen et al. 2012). The cumulative revision percentage of BHR at 5 years (3.6%, 95% CI: 3.2–4.0) and at 10 years (6.7%, 95% CI: 6.0–7.5) is relatively low, based on Australian registry data (AOA 2012). However, registry studies are poor at detecting early implant failure, since radiological data on osteolysis and ARMD emerge late. Early clinical trials may focus solely on radiographic findings. Bisschop et al. (2013) reported a 28% prevalence of CT-verified pseudotumors in 149 BHR HRAs after an average follow-up of 3 years. These results are in accordance with our findings. However, we based the radiological diagnosis of fluid collections and soft-tissue masses solely on MRI, except in 2 cases. The prevalence of fluid collections verified by MRI in our study was higher than that of CT-verified pseudotumor in the study by Bisschop et al. (2013). The follow-up time in the present study was longer, which is probably related to the high prevalence of ARMD. However, our aim was to detect the prevalence of ARMD based on MRI findings, serum metal ion levels, and surgical findingsand not only the prevalence of radiologically detected pseudotumors. 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 HRA patients with a painful hip is similar to that in asymptomatic HRA patients (Hart et al. 2012). However, the high rate of fluid collections seen by MRI and the soft-tissue destruction at the time of revision found in our patients is a cause for great concern. A systematic follow-up of these patients using metal ion levels, MRI/ultrasound, and symptom-based questionnaires is advisable.

MJ, JM, MS, PV, and KTM designed the study protocol. MJ, JM, MS, PV, JR, VÄ, AI, and KTM performed the surgery, recorded the intraoperative data, and wrote the manuscript. TP, TV, and KTM analyzed the data. KM and ET designed the MRI protocol and participated in image interpretation and revision of the manuscript for intellectual content.

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Original Research Article

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SYSTEMATIC SCREENING OF ADVERSE REACTIONS TO METAL DEBRIS AFTER RECAP-M2A-MAGNUM METAL-ON-METAL TOTAL HIP ARTHROPLASTY

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ABSTRACT

Background and Aims: **An adverse reaction to metal debris is a known complication after large diameter head metal-on-metal total hip arthroplasty. However, the failure rate varies depending on the implant design. Therefore, we investigated the prevalence of adverse reaction to metal debris, as well as the symptoms and risk factors after undergoing a ReCap-M2a-Magnum large diameter head metal-on-metal total hip arthroplasty.**

Materials and Methods: **Between 2005 and 2012, 1188 patients (1329 hips) underwent ReCap-M2a-Magnum total hip arthroplasty at our institution. Systematic screening for adverse reaction to metal debris was arranged using the Oxford Hip Score questionnaire, hip and pelvic radiographs, and assessments of the serum chromium and cobalt ion levels. Clinical evaluation and magnetic resonance imaging were performed for the symptomatic patients, as well as those with either chromium or cobalt ion levels $\geqslant$5 µg/L. The prevalence of adverse reaction to metal debris after ReCap-M2a-Magnum total hip arthroplasty was assessed, and the risk factors for adverse reaction to metal debris were evaluated using logistic regression. The mean follow-up time was 5.2 (0.003–9.1) years. This study was an extension of a previous study conducted at our institution with 80 patients.**

Results: **In total, 33 patients (33 hips, 2.5% of all hips) required a revision operation due to adverse reaction to metal debris. Moreover, 157 hips exhibited definitive adverse reaction to metal debris, but a revision operation was not performed (157 of 1329 hips, 11.8% of all hips). Overall, 190 out of 1329 (14.3%) hips had definitive adverse reaction to metal debris. Pain, subluxation sensation, clicking, swelling, a small head size, and a fair/poor Oxford Hip Score were associated with definitive adverse reaction to metal debris.**

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Conclusion: **We found a high prevalence of adverse reaction to metal debris in the ReCap-M2a-Magnum total hip arthroplasty patients in this study; however, most of the patients did not require revision operations.**

Key words: Hip; metal-on-metal total hip arthroplasty; adverse reaction to metal debris; Recap-M2a-Magnum; chromium ion; cobalt ion; metal artifact reduction sequence magnetic resonance imaging

INTRODUCTION

The large diameter head metal-on-metal total hip arthroplasty (LDH MOM THA) was introduced to decrease the wear induced osteolysis associated with metal on polyethylene bearings, increase the range of motion, and decrease the dislocation rate (1). Some of the short-term results have been encouraging (2, 3). The popularity of LDH MOM THA has grown rapidly, with more than one million metal-on-metal (MOM) hip implants being performed worldwide (4). In Finland, approximately 15,000 LDH MOM THA have been performed, according to the Finnish Arthroplasty Register (5).

It soon became obvious that the Articular Surface Replacement (ASR) total hip arthroplasty (THA) (Johnson & Johnson) was a poor performer, with an increased risk of early revision (6–8). In addition, recent evidence has suggested that other LDH MOM designs may have increased revision risks due to the collection of periarticular fluid, soft tissue masses, and gluteal muscle necrosis. The symptoms of these patients often include pain, swelling, clicking, and a sensation of subluxation (8–10). This condition has been called an adverse reaction to metal debris (ARMD) or adverse local tissue reaction (ALTR) (9). Some designs have been recalled by the manufacturers due to the increased risk of revision caused by ARMD (11).

The ReCap-M2a-Magnum THA (Biomet, Warsaw, IN, USA) was the most commonly used LDH MOM device in Finland from 2005 until 2012, with 6655 implantations performed (5). It was also the most commonly used total hip implant at our institution during the same time period, with a total of 1329 implantations performed. Mokka et al. (12) have previously reported the preliminary results of 80 ReCap-M2a-Magnum THA performed at our institution, in which 11 (14%) of the patients had definitive ARMD and 29 had probable ARMD. Recently, Bosker et al. (13) evaluated 626 patients (706 hips) who had undergone THA with ReCap-M2a-Magnum implants. In their study, the incidence of pseudotumors was 35%, and it increased significantly during the prolonged follow-up. The aim of this study was to assess the prevalence of ARMD using a systematic screening of the total ReCap-M2a-Magnum cohort of 1329 hips at our institution. Our hypothesis was that the prevalence of ARMD was 14%, based on our preliminary study (12).

MATERIALS AND METHODS

PATIENT POPULATION/STUDY POPULATION

At our institution, 1188 patients (1329 hips) underwent ReCap-M2a-Magnum LDH MOM THA, and the surgeries were performed between August 2005 and April 2012. The systematic screening for ARMD consisted of an Oxford Hip Score (OHS) questionnaire, hip and pelvic radiographs, and measurements of the serum chromium and cobalt ion levels, before the end of September 2014.

Magnetic resonance imaging (MRI) was performed on those patients exhibiting symptoms and/or increased ion levels ($\geqslant$5 µg/L). An experienced orthopedic surgeon also assessed all these patients. The study population included a subset of 74 patients (80 hips) which we have described in a previous publication (12).

Overall, 989 (74%) of the patients had primary arthrosis as an indication for THA, while the other indications included hip dysplasia (7%), rheumatoid arthritis (5%), post-traumatic arthrosis (2%), secondary arthrosis (5%), avascular necrosis (3%), and fracture (3%).

Altogether, 74 hips (74 patients) were revised for reasons other than ARMD during the follow-up: 25 for periprosthetic fractures, 12 for infections, and 28 for early loosening. Dislocation was the reason for revision in three patients, and one of those had ARMD. The mean follow-up time was 5.2 (0.003–9.1) years, and 96 of the patients died during the follow-up period. In addition, 28 patients had undergone simultaneous bilateral ReCap-M2a-Magnum THA, and 113 patients had both hips operated on in separate sessions. The Biomet Bi-Metric or Reach stem and Hardinge approach were used in all of the study cases.

The ReCap-M2a-Magnum is an metal-on-metal (MOM) articulation. The bearing articulation consists of a cobalt chrome molybdenum cup (ReCap) and a cobalt chrome molybdenum head (Magnum). The head size varies from 38 to 60 mm and is considered to be a large diameter head (14).

STUDY DESIGN

Metal artifact reduction sequence magnetic resonance imaging (MARS-MRI) was used to identify the ARMD changes as fluid collection and soft tissue masses around the prostheses (15, 16). MRI was performed on 352 hips (16).

The cup inclination and anteversion angle were measured using pelvic and hip x-rays. Because the measurement of the anteversion angle is relatively inaccurate in lateral hip x-rays, we categorized the cups into two subgroups for regression analysis purposes: retroverted and not retroverted. The pelvic radiographs were available for all 1199 of the hips to measure the inclination angle, and hip radiographs were available for all of the patients.

The serum cobalt and chromium ion levels were measured in 959 patients (1094 hips) (17, 18). However, the metal ion concentrations were not measured in those patients with loosening, fractures, or infections in their prostheses.

An OHS of 42–48 points was considered to be excellent, 34–41 was good, 27–33 was fair, and 0–26 was poor. Separate questions about clicking, subluxation sensation, and swelling of the hip were also asked. The OHS questionnaire was not filled out preoperatively, and the total points were available for 742 patients. Generally, those patients with bilateral Recap-M2a-Magnum THA had only one OHS questionnaire available, and we could not pinpoint which hip was of concern. Therefore, those patients with bilateral Recap-M2a-Magnum procedures were left out of the regression analyses, including their OHS data.

Definitive ARMD was established in three ways:

1. It was diagnosed in revision surgery.
2. There was a solid mass or fluid collection ⩾50 mm in the MRI.
3. The serum chromium or cobalt level was ⩾10 μg/L.

Probable ARMD was established with either of the following:

1. A collection of fluid <50 mm in the MRI.
2. The serum chromium or cobalt concentration was ⩾5 but <10 μg/L.

ARMD was confirmed intraoperatively if there was milky fluid, a solid pseudotumor mass, or muscle necrosis. The revision surgery was comprised of several different operations: head exchange with or without acetabular revision and stem revision with or without acetabular revision. Those patients with clearly elevated metal ion levels or pseudotumor findings did not undergo surgery if the patient refused on the basis of an asymptomatic hip or poor overall health.

The following risk factors for ARMD were assessed: age, sex, laterality, inclination angle of the cup (categorical variables: <30°, 30°–50°, and >50°), anteversion angle of the cup (categorical variables: >0° and ⩽0°), and head size (categorical variables: ⩽44, 46–50, and ⩾52 mm). The associations between the OHS score (poor, fair, or good vs excellent), pain (no, mild, moderate, or severe), symptoms (clicking, subluxation sensation, and/or swelling), and ARMD were also examined. We further assessed the same risk factors and symptoms for the occurrence of an ARMD revision.

The demographic data are presented hipwise in Table 1 and patientwise for those having a unilateral study device in Table 2.

ETHICS

This study was based on the national recommendations for the systematic screening of all LDH MOM THA patients provided by the Finnish Arthroplasty Society (18).

STATISTICAL ANALYSIS

The potential risk factors for ARMD were analyzed via univariable multinomial logistic regression. The dependent variable consisted of three groups (definitive ARMD, probable ARMD, and no ARMD), with no ARMD being used as the reference group. The results were expressed using odds ratios (ORs) with a 95% confidence interval (CI). The goodness-of-fit for the logistic regression models was evaluated with a deviance test, while the multivariable logistic model was obtained using backward elimination (inclusion criteria, $p < 0.10$) to examine the potential confounding effect of the other risk variables. The generalized estimating equation (GEE) was used for the hipwise data to account for the correlation between the hips from the same patient. Kaplan–Meier estimates for the revision operations (for any reason) and for the ARMD were calculated. The Cox regression analysis was used to analyze the association between the risk factors and symptoms and ARMD revision. The hipwise survival data were analyzed with a lognormal frailty model to account for the correlation between the hips from the same patient, and the results of the Cox regression were expressed using hazard ratios (HRs) with a 95% CI. The proportional hazard assumptions were evaluated with a log-cumulative hazard plot, and the assumptions were met. p-values < 0.05 were considered to be statistically significant, and the statistical analyses were carried out using SAS for Windows, version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Throughout the follow-up period, 104 patients (106 hips, 8.0% of all hips) required revision operations, while 33 patients (33 hips, 2.5% of all hips) required revision operations due to ARMD. The Kaplan–Meier survival estimate of the ReCap-M2a-Magnum THA at 5 years was 93.3% for any reason (95% CI: 91.9%–94.8%), and 98.6% (95% CI: 97.8%–99.3%) for those patients with ARMD revisions.

There was definitive ARMD in 157 hips, in which revision operations were not performed (157 of 1329 hips, 11.8% of all hips). Probable ARMD was determined in 114 hips (8.6%). In total, 190 out of 1329 (14.3%) hips had definitive ARMD, and 1025 (77.1%) hips did not have ARMD.

The univariable associations assessed using the multinomial logistic regression analysis between the risk variables/symptoms and ARMD are presented in Table 3. Pain, subluxation sensation, clicking, small head size (⩽44 vs ⩾52 mm), and fair/poor OHS scores

TABLE 1
Demographic data of the 1329 study hips presented hipwise.

	Total hips (n = 1329)	ARMD (n = 190)	Probable ARMD (n = 114)	No ARMD (n = 1025)
Mean age (years)	64.2	64.3	64.5	64.1
Mean follow-up years (range)	5.2 (0.003–9.1)	5.8 (0.3–8.8)	5.5 (0.2–8.8)	5.0 (0.003–9.1)
Mean head size (mm)	49.2	48.8	48.8	49.4
Head size: ⩽44 mm (n, %)	170 (13%)	31 (16%)	19 (17%)	120 (12%)
Head size: 46–50 mm (n, %)	744 (56%)	109 (57%)	62 (54%)	573 (56%)
Head size: ⩾52 mm (n, %)	415 (31%)	50 (26%)	33 (29%)	332 (32%)
Mean inclination angle of the cup (°)[a]	42.8	44.5	44.0	42.4
Inclination angle of the cup: <30° (n, %)[a]	29 (2%)	2 (1%)	2 (2%)	25 (3%)
Inclination angle of the cup: 30°–50° (n, %)[a]	1013 (84%)	146 (82%)	86 (80%)	781 (85%)
Inclination angle of the cup: >50° (n, %)[a]	157 (13%)	29 (16%)	19 (18%)	109 (12%)
Anteversion angle of the cup: ⩽0° (n, %)	30 (2%)	6 (3%)	1 (1%)	23 (2%)
Anteversion angle of the cup: >0° (n, %)	1299 (98%)	184 (97%)	113 (99%)	1002 (98%)
Mean serum cobalt (µg/L) (range)[b]	4.4 (0.3–196.2)	16.4 (0.6–196.2)	4.3 (0.5–9.5)	1.7 (0.3–4.9)
Mean serum chromium (µg/L) (range)[b]	3.0 (0.5–44.7)	7.8 (0.5–44.7)	3.6 (0.8–7.4)	1.8 (0.6–4.8)

ARMD: adverse reaction to metal debris.
[a]Data of cup inclination angle based on pelvic radiographs were available for 1199 hips.
[b]Metal ion data were available for 1094 hips: 802 hips in no ARMD group, 107 in probable ARMD group, and 185 in definite ARMD group.

TABLE 2
Patient characteristics for those with a unilateral arthroplasty.

	No of patients with a unilateral study device (n = 1047)	ARMD (n = 143)	Probable ARMD (n = 70)	No ARMD (n = 834)
Males (n, %)	469 (45%)	45 (31%)	29 (41%)	395 (47%)
Mean OHS[a]	40.4	36.0	41.3	41.1
OHS: excellent (n, %)[a]	464 (63%)	44 (42%)	31 (63%)	389 (66%)
OHS: good (n, %)[a]	135 (18%)	22 (21%)	11 (22%)	102 (17%)
OHS: fair (n, %)[a]	60 (8%)	17 (16%)	5 (10%)	38 (6%)
OHS: poor (n, %)[a]	83 (11%)	23 (22%)	2 (4%)	58 (10%)
No pain (n, %)[b]	377 (51%)	38 (36%)	22 (45%)	317 (54%)
Mild pain (n, %)[b]	280 (38%)	42 (40%)	20 (41%)	218 (37%)
Moderate or severe pain (n, %)[b]	82 (11%)	26 (25%)	7 (14%)	49 (8%)
Swelling yes (n, %)[c]	39 (5%)	11 (11%)	3 (6%)	25 (4%)
Swelling no (n, %)[c]	681 (95%)	89 (89%)	46 (94%)	546 (96%)
Clicking yes (n, %)[d]	62 (9%)	21 (21%)	6 (12%)	35 (6%)
Clicking no (n, %)[d]	655 (91%)	79 (79%)	43 (88%)	533 (94%)
Subluxation sensation yes (n, %)[e]	106 (15%)	23 (22%)	6 (12%)	77 (13%)
Subluxation sensation no (n, %)[e]	620 (85%)	80 (78%)	43 (88%)	497 (87%)
Mean serum cobalt (µg/L) (range)[f]	3.6 (0.3–71.5)	12.9 (0.6–71.5)	4.2 (0.5–9.5)	1.5 (0.3–4.8)
Mean serum chromium (µg/L) (range)[f]	2.6 (0.5–34.2)	6.5 (0.5–34.2)	3.2 (0.8–7.4)	1.7 (0.6–4.8)

OHS: Oxford Hip Score: 42–48 = excellent, 34–41 = good, 27–33 = fair, 0–26 = poor; ARMD: adverse reaction to metal debris.
[a]OHS data available for 742 patients with a unilateral study device.
[b]Data available for 739 patients with a unilateral study device.
[c]Data available for 720 patients with a unilateral study device.
[d]Data available for 717 patients with a unilateral study device.
[e]Data available for 726 patients with a unilateral study device.
[f]Data available for 844 patients with a unilateral study device.

were associated with definitive ARMD. In the multivariable model, female gender, clicking, large head size (⩾52 vs 46–50 mm), and pain (moderate/severe vs no pain) were associated with ARMD (Table 4). The results of the univariable associations between the risk factors and symptoms and ARMD revision assessed via the Cox regression analysis are presented in Table 5. Retroversion of the cup, small head size (head size: ⩽44 vs ⩾52 mm), and clicking were associated with the occurrence of ARMD revision.

For bilateral arthroplasty, the Co and Cr values were available for 125 patients. Mean Co was 7.2 µg/L (0.6–196.2), and mean Cr was 4.3 µg/L (0.7–44.7).

DISCUSSION

In this study, we determined that 33 of the 1188 patients (33 of 1329 hips, 2.5%) had undergone revision operations due to ARMD. In addition, 157 hips (11.8%) were considered to have definitive ARMD

TABLE 3

Crude odds ratios (ORs) and 95% confidence intervals (CIs) of associations between risk factors and symptoms with ARMD.

	ARMD versus no ARMD		Probable ARMD versus no ARMD	
	Crude OR (95% CI)	p-value	Crude OR (95% CI)	p-value
Age[a]	1.00 (0.99–1.01)	0.9	1.00 (0.99–1.02)	0.7
Gender (female vs male)[b]	1.96 (1.34–2.86)	0.0005	1.27 (0.78–2.09)	0.3
Side (left vs right)[a]	0.91 (0.68–1.21)	0.5	1.12 (0.80–1.57)	0.5
Pain (mild vs no pain)[b]	1.61 (1.00–2.58)	0.05	1.32 (0.70–2.48)	0.4
Pain (moderate or severe vs no pain)[b]	4.43 (2.47–7.93)	<0.001	2.06 (0.84–5.07)	0.1
Subluxation sensation[b]	1.86 (1.10–3.13)	0.02	0.90 (0.37–2.19)	0.8
Clicking[b]	4.05 (2.24–7.31)	<0.001	2.13 (0.85–5.33)	0.1
Swelling[b]	2.70 (1.28–5.68)	0.009	1.42 (0.41–4.90)	0.6
Head size: ⩽44 versus ⩾52 mm[a]	1.72 (1.02–2.87)	0.04	1.59 (0.84–3.03)	0.2
Head size: 46–50 versus ⩾52 mm[a]	1.26 (0.86–1.86)	0.2	1.09 (0.68–1.74)	0.7
Inclination angle of the cup, <30° versus 30°–50°[c]	0.43 (0.10–1.82)	0.3	0.73 (0.17–3.08)	0.7
Inclination angle of the cup, >50° versus 30°–50°[c]	1.42 (0.90–2.24)	0.1	1.58 (0.91–2.76)	0.1
Anteversion angle of the cup, >0° versus ⩽0°[a]	0.70 (0.28–1.76)	0.5	2.59 (0.35–19.43)	0.4
OHS: poor versus excellent[b]	3.51 (1.97–6.23)	0.04	0.43 (0.10–1.86)	0.1
OHS: fair versus excellent[b]	3.96 (2.06–7.59)	0.02	1.65 (0.61–4.50)	0.2
OHS: good versus excellent[b]	1.91 (1.09–3.33)	0.4	1.35 (0.66–2.79)	0.3

OHS: Oxford Hip Score; ARMD: adverse reaction to metal debris.
[a]Multinomial logistic regression using GEE-estimation based on data of all hips and (1199).
[b]Multinomial logistic regression based on data of patients with a unilateral study device.
[c]Multinomial logistic regression using GEE-estimation based on data of all pelvic radiographs (1199).

TABLE 4

Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of associations between risk factors and symptoms with ARMD using multiple multinomial logistic regression based on data of 714 patients with a unilateral arthroplasty.

	ARMD versus no ARMD		Probable ARMD versus no ARMD	
	Adjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Gender (female vs male)	2.22 (1.19–4.15)	0.01	0.88 (0.41–1.85)	0.7
Pain (mild vs no pain)	1.06 (0.58–1.94)	0.9	1.40 (0.68–2.89)	0.4
Pain (moderate or severe vs no pain)	2.67 (0.97–7.34)	0.06	8.57 (2.08–35.34)	0.003
Clicking	2.85 (1.49–5.45)	0.002	2.31 (0.87–6.16)	0.09
Head size: ⩽44 versus ⩾52 mm	1.12 (0.49–2.55)	0.8	2.32 (0.78–6.96)	0.1
Head size: 46–50 versus ⩾52 mm	0.49 (0.26–0.94)	0.03	0.98 (0.44–2.20)	1.0
OHS: poor versus excellent	1.35 (0.50–3.67)	0.6	0.07 (0.01–0.51)	0.008
OHS: fair versus excellent	2.14 (0.92–4.95)	0.08	0.59 (0.16–2.24)	0.4
OHS: good versus excellent	1.38 (0.69–2.74)	0.4	0.96 (0.41–2.24)	0.9

OHS: Oxford Hip Score; ARMD: adverse reaction to metal debris.

during a mean follow-up time of 5.2 years but had not been revised by the end of September 2014. The prevalence of ARMD in our cohort was 14.3% (190/1329), which was similar to that of our preliminary study (12).

There were some limitations in our study that may have biased the results. For example, we concluded that patients with high ion levels (⩾10 µg/L) had definitive ARMD. ARMD is generally related to soft tissue changes around the prosthesis (9). The Medicines and Healthcare products Regulatory Agency (MHRA) (19) has recommended a cutoff level of serum cobalt and chromium of 7 µg/L. Although this shows good specificity, it shows relatively low sensitivity (20). The risk of developing a pseudotumor is four times higher with serum metal ion levels >5µg/L (21), and a cutoff level of 10 µg/L has been used previously in assessing ARMD in association with MOM hip implants (12, 22).

Another limitation was that we included patients with bilateral MOM implants, which may have biased the metal ion analyses. However, we increased the cutoff level from 8 µg/L, as suggested by Lardanchet et al. (23), to 10 µg/L due to the inclusion of the bilateral THA. We used a metal ion level of ⩾5 µg/L as a criterion for possible ARMD.

Moreover, dividing the "definite" and "probable" groups by the amount of fluid collection in the MRI is problematic. The dichotomy between MRI findings ⩾50 and <50 mm is artificial; thus, we hypothesized that a fluid collection ⩾50 mm in any dimension was a clinically significant amount of fluid with regard to

TABLE 5
Crude hazard ratios (HRs) and 95% confidence intervals (CIs) of associations between risk factors and ARMD revisions.

	Risk factors of ARMD revisions	
	Crude HR (95% CI)	p-value
Age[a]	1.00 (0.97–1.04)	1.0
Gender (female vs male)[b]	1.87 (0.79–4.40)	0.2
Side (left vs right)[a]	1.66 (0.84–3.32)	0.1
Pain (mild vs no pain)[b]	0.46 (0.09–2.27)	0.3
Pain (moderate or severe vs no pain)[b]	2.37 (0.59–9.46)	0.2
Subluxation sensation[b]	0.57 (0.07–4.43)	0.6
Clicking[b]	3.97 (1.05–14.99)	0.04
Swelling[b]	1.94 (0.25–15.21)	0.5
Head size: ⩽44 versus ⩾52 mm[a]	3.35 (1.08–10.38)	0.04
Head size: 46–50 versus ⩾52 mm[a]	2.06 (0.77–5.51)	0.2
Inclination angle of the cup, <30° versus 30°–50°[a]	0.01 (0.000–34081149)	0.7
Inclination angle of the cup, >50° versus 30°–50°[a]	1.28 (0.55–2.99)	0.6
Anteversion angle of the cup, ⩽0° versus >0°[a]	7.63 (2.19–26.6)	0.001
OHS: poor versus excellent[b]	3.26 (0.78–13.64)	0.1
OHS: fair versus excellent[b]	1.24 (0.14–10.59)	0.8
OHS: good versus excellent[b]	1.67 (0.32–8.62)	0.5

OHS: Oxford Hip Score; ARMD: adverse reaction to metal debris.
[a]Cox regression with random intercept for patient (frailty model) based on data of all hips.
[b]Cox regression based on data of patients with a unilateral study device.

the diagnosis of ARMD. This was also the way the patients were divided into the categories in the previous research conducted at our institute (12).

A further limitation of our study was that we selected MRI based on the patients' symptoms and ion levels, and not all of the patients were scrutinized using MRI. Furthermore, the assessment of some ARMD cases was made based on the surgical findings in the medical reports, and some revisions were performed before the surgeons were familiar with the concept of ARMD.

The strengths of our study included the fact that all of the ReCap-M2a-Magnum implantations were performed at our institution. The Bi-Metric stem and Hardinge approach were used in every operation, so the stem or approach did not cause bias. In addition, to improve the assessment of the complications, we used MARS-MRI. Those cases presenting with ALTRs and periprosthetic fluid collection or soft tissue masses are not typically detectable in radiographs, or in most cases, computed tomography (CT). MRI is the best method for the evaluation of patients with MOM hip resurfacing arthroplasty because of its high soft tissue contrast and lack of ionizing radiation (24).

Concern has been raised about the high failure rate of LDH MOM THA due to ARMD. The Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) (6) first reported increased failure rates with MOM implants in 2008, while the MHRA issued a medical device alert about MOM implants in April 2010 (20). In May 2011, the American Food and Drug Administration (FDA) (25) ordered post-marketing surveillance of MOM THA from 21 companies. Furthermore, the Finnish Arthroplasty Society (18) recommended that physicians discontinue the use of LDH MOM THA in May 2012.

The short-term survival of the ReCap-M2a-Magnum THA was shown to be comparable to that of the conventional cemented THA, based on data from the Finnish Arthroplasty Register (3). The cumulative revision percentage of ReCap-M2a-Magnum THA at 7 years was 6.4% (95% CI: 4.8–8.4) according to the Australian registry data (6) and 7% (95% CI: 4.7–8.0) according to the Finnish Arthroplasty Register (5). Overall, the revision rate of ReCap-M2a-Magnum THA is higher than that of conventional THA, but lower than that of ASR THA (5, 6, 26). A hazard alert for the Biomet M2a (38 mm and Magnum) MOM devices was issued in Australia in February 2015 (27).

Bosker et al. (21) reported a pseudotumor incidence of 39% and revision rate of 12% 3.6 years after the ReCap-M2a-Magnum THA procedure. In our preliminary study of 80 ReCap-M2a-Magnum THA, we found 11 definitive ARMD cases, of which 3 had been revised at that stage (12). Recently, Bosker et al. (13) screened 706 ReCap-M2a-Magnum hips in 626 patients using CT and found 228 pseudotumors (32%) in 219 patients (35%). In addition, 76 hips (11%) were revised in 73 patients (12%) after a median of 5.3 (1.0–8.3) years. The CT-detected pseudotumor formation in their study was remarkably more common than the MRI/ion measurement–based ARMD prevalence in our study, which was based only on selective imaging. The difference between the outcomes of these two studies is understandable due to the selective MRI use in our study.

It is possible that there were asymptomatic patients in our study with low ion levels, fluid collection, or soft tissue masses in their hips. However, we believe that the clinical importance of the imaging findings of asymptomatic patients with normal ion levels may be diminutive. The overall revision rate in our study was slightly lower than that in the study by Bosker et al.

(13). Most of our revisions were performed for reasons other than ARMD, such as periprosthetic fractures, lack of osteointegration of uncemented implants, and infection. The reasons for revision were not assessed in the study by Bosker et al. (13); however, we agree that the early detection of pseudotumors is important because if revision surgery is performed in patients before substantial soft tissue damage has occurred, the outcome is likely to be better. Furthermore, many of the ReCap-M2a-Magnum THA revisions in our clinic were complicated by cold-welded femoral heads and adapters, which is a unique feature of this device (28).

ARMD may occur in asymptomatic LDH MOM hips (10); however, pain, subluxation sensation, clicking, and fair/poor OHS scores were significantly associated with ARMD in our study. Pain was also associated with ARMD in the study by Bosker et al. (13). In addition, female gender and small diameter head sizes ($\leqslant$44) have been reported as risk factors for ARMD in previous studies (8); but in one multivariable model, larger head sizes were associated with ARMD when compared to medium sizes. Theoretically, it is possible that the lubrication between the bearing surfaces works best with medium sized heads. In our study, retroverted cups were scarce, but they were significantly associated with the ARMD revisions. The probability of edge loading is increased with malpositioned cups.

The theoretical health risks related to chronically elevated blood metal ion concentrations induced by abnormal wear and corrosion of MOM implants include systemic symptoms of poisoning (29). Systemic metal ion toxicity cases due to a failed hip replacement are rare; however, there have been several recent reports of systemic cobalt toxicity, including symptoms like fatigue, weakness, hypothyroidism, cardiomyopathy, polycythemia, visual and hearing impairment, cognitive dysfunction, and neuropathy (30). We are not aware of any of our patients having severe systemic symptoms of cobalt poisoning, although these symptoms were not systematically scrutinized.

We found a high prevalence of ARMD in a systematic screening of all of the ReCap-M2a-Magnum THA patients at our institution, but most of these patients did not require a revision operation. Moreover, 77% of the hips did not present with ARMD findings. Time course analysis estimates have been presented, suggesting that the development of pseudotumors continues in ReCap-M2a-Magnum THA patients (13). Therefore, annual follow-ups of all patients subjected to LDH MOM THA have been suggested for as long as the prosthesis is in situ (13). The Finnish Arthroplasty Society (31) has recommended following these patients biannually using patient questionnaires, metal ion level measurements, and imaging techniques like MRI, CT, or ultrasound when needed. Based on these results, the follow-ups should not be discontinued.

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DECLARATION OF CONFLICTING INTERESTS

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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HIP RESURFACING ARTHROPLASTY VERSUS LARGE-DIAMETER HEAD METAL-ON-METAL TOTAL HIP ARTHROPLASTY: COMPARISON OF THREE DESIGNS FROM THE FINNISH ARTHROPLASTY REGISTER

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ABSTRACT

Background and Aims: **Large headed metal-on-metal total hip arthroplasty may produce more metal ions than hip resurfacing arthroplasty. Increased metal-ion levels may be associated with higher revision rates due to adverse reaction to metal debris. The purpose of our study was to compare the survivorship of three hip resurfacing arthroplasty designs with their analogous cementless large-diameter head metal-on-metal total hip arthroplasties.**

Material and Methods: **Based on data obtained from the Finnish Arthroplasty Register, the revision risks of three metal-on-metal hip resurfacing arthroplasty/total hip arthroplasty design couples performed during 2001–2011 were analyzed using the Cox regression model.**

Results: **In the Cox regression analysis for compared design pairs adjusted for age, gender, operated side, head size, diagnosis, and implant, there was no statistically significant difference in revision risk between ReCap hip resurfacing arthroplasty and Bimetric/ReCap total hip arthroplasty (risk ratio = 1.43, confidence interval = 0.95–2.14, p = 0.09) or between Birmingham hip resurfacing arthroplasty and Synergy/Birmingham hip resurfacing total hip arthroplasty (risk ratio = 1.35, confidence interval = 0.75–2.43, p = 0.31). However, the revision risk of Corail and Summit/articular surface replacement total hip arthroplasty (ASR HRA) was significantly increased compared to ASR HRA. (risk ratio = 0.73, confidence interval = 0.54–0.98, p = 0.04).**

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Conclusion: **We conclude that the short-term revision risk of large headed metal-on-metal total hip arthroplasties was not increased compared to analogous hip resurfacing arthroplasties in two out of three devices studied at a nationwide level. There may be implant-related factors having an effect on the success of single manufacturer devices. However, more information on the incidence of adverse soft-tissue reactions in these patient cohorts is needed.**

Key words: Total hip arthroplasty, hip resurfacing arthroplasty, metal-on-metal hip arthroplasty, adverse reaction to metal debris, revision, register study

INTRODUCTION

Hip resurfacing arthroplasty (HRA) and large-diameter head metal-on-metal total hip arthroplasty (LDH MoM THA) have gained popularity during the last decade in hip surgery (1–4). Recently, increased numbers of MoM bearing surface wear complications have been detected (5–7). Concerns exist regarding the consequences of prolonged exposure to increased metal-ion levels, such as adverse reaction to metal debris (ARMD) (8, 9). It has been stated that although HRAs and LDH MoM THAs have the same bearing characteristics, wear and corrosion at the junction between the femoral neck and the adapter sleeve, as well as the open femoral head design, are suspected to be responsible for the additional load of metal-ion release (10). The revision risk of LDH MoM THAs as a group has been increased compared with that of HRAs according to register data (11, 12). The aim of our study was to analyze the early outcome of three HRA designs and compare it with that of analogous LDH MoM THAs from the data of the Finnish Arthroplasty Register.

MATERIAL AND METHODS

THE FINNISH ARTHROPLASTY REGISTER

Since 1980, the Finnish Arthroplasty Register has been collecting information on total hip replacements (13). Health-care authorities, institutions, and orthopedic units are obliged to provide the National Institute for Health and Welfare with information essential for maintenance of the registry. Since 1995, the data of the registry have been compared with those of hospital discharge registries at regular intervals. Currently, 98% of implantations are recorded. An English translation of the notification form used by the Finnish Arthroplasty Register has been discussed previously (14).

STUDY POPULATION AND INCLUSION CRITERIA

During the study period 2001–2011, 5464 Bimetric/ReCap THAs (Biomet, Warsaw, IN, USA), 698 ReCap HRAs (Biomet), 475 Synergy/Birmingham hip resurfacing (BHR) THAs (Smith & Nephew, Memphis, TN, USA), 1902 BHR HRAs (Smith & Nephew), 632 Corail and Summit/articular surface replacement (ASR) THAs (DePuy, Warsaw, IN, USA), and 979 ASR HRAs (DePuy) were performed in Finland. To reduce the skew in the demographic distribution between patients operated with HRA and those operated with THA, patients older than 85 years of age were excluded (the oldest patient operated with HRA was 85 years old). In addition, those patients with a diagnosis of other reasons (including fractures and avascular necroses of femoral head) or rheumatoid arthritis were excluded. Demographic data are given in Table 1.

HIP RESURFACING VERSUS LDH MOM THA

The revision risk of ReCap HRA was compared with that of Bimetric/ReCap THA, the revision risk of BHR HRA was compared with that of Synergy/BHR THA, and the revision risk of ASR HRA was compared with that of Corail and Summit/ASR THA performed during the same time period with adjustment for age at surgery, gender, operated side, head size <50 or ≥50 mm, and diagnosis, using Cox multiple regression analysis. In addition, stratified analyses were performed for males and females aged <55 or ≥55 years. In these sub-analyses by age and gender, the revision risk of LDH MoM THAs was compared with the revision risk of analogous HRAs performed for similar patients during the same time period.

STATISTICAL ANALYSIS

Revisions were linked to the primary operation by using a personal identification number. The end point for survival was defined as revision when either one component (including the femoral head) or the whole implant was removed or exchanged. Revision for any reason, revision for aseptic loosening, revision for dislocation, revision for infection, and revision for periprosthetic fracture each served separately as an end point. In 41 revisions, the recorded indication for revision was "other reason." Kaplan–Meier survival data were used to construct the survival probabilities of implants. These survival data were compared using the log-rank test. Patients who died or left Finland during the follow-up period were censored at that point. The Cox multiple regression model was used to study differences between groups and to adjust for potential confounding factors. The factors studied with the Cox model were age, gender, diagnosis, and implant design. The effect of age on survivorship was also analyzed by dividing the patients into two age groups: those under 55 years and those

TABLE 1
Demographic data relating to HRAs and THAs in 10,150 hips.

Hip device	n	Mean follow-up (range)	Mean age (range)	Males (%)	Implanting period	Operated side, % right	Diagnosis, % primary osteoarthritis
Bimetric/ReCap THA	5464	3,1 (0–7,0)	63 (21–85)	54	2005–2011	56	93
ReCap resurfacing	698	4,1 (0–7,7)	56 (25–77)	65	2004–2011	52	96
Synergy/BHR THA	475	4,0 (0–7,6)	58 (18–82)	55	2004–2011	54	92
BHR resurfacing	1902	6,0 (0–10,7)	54 (18–83)	69	2001–2011	53	91
Corail and Summit/ ASR THA	632	3,9 (0–7,7)	60 (21–78)	58	2004–2010	54	91
ASR resurfacing	979	5,0 (0–7,8)	56 (25–79)	64	2004–2010	56	96
Total	10,150	4,0 (0–10,7)	60 (18–85)	59	2001–2011	55	93

HRA: hip resurfacing anthroplasty; THA: total hip anthroplasty; BHR: Birmingham hip resurfacing; ASR: articular surface replacement.

TABLE 2
Survival of HRA and THA, the reference group. HRAs compared to THAs; adjustment made for age, gender, operated side, head size, diagnosis, and implant.

	N	MF (years)	AR—4 years	4-year survival (95% CI)	AR—6 years	6-year survival (95% CI)	AR—8 years	8-year survival (95% CI)	Adjusted RR for revision (95% CI)	p-value
Bimetric/ReCap THA	5464	3,1 (0–7,0)	1612	97 (96–97)	109	—	—	—	1	
ReCap resurfacing	698	4,1 (0–7,7)	364	96 (94–97)	118	—	—	—	1.43 (0.95–2.14)	0.09
Synergy/BHR THA	475	4,0 (0–7,6)	257	97 (95–98)	49	97 (94–98)	—	—	1	
BHR resurfacing	1902	6,0 (0–10,7)	1459	97 (96–97)	1078	95 (94–96)	464	94 (93–95)	1.35 (0.75–2.43)	0.31
Corail and Summit/ ASR THA	632	3,9 (0–7,7)	301	90 (88–93)	39	72 (64–79)	—	—	1	
ASR resurfacing	979	5,0 (0–7,8)	752	92 (90–94)	267	83 (80–86)	—	—	0.73 (0.54–0.98)	0.04
Total	10,150	4,0 (0–10,7)	4745	95 (95–96)	1660	92 (91–93)	464	90 (88–91)		

HRA: hip resurfacing anthroplasty; THA: total hip anthroplasty; BHR: Birmingham hip resurfacing; ASR: articular surface replacement; N: number of operations; MF: mean follow-up; AR: at risk; RR: risk ratio from the Cox regression analysis; CI: confidence interval.
End point is defined as revision of any component due to any reason. Survival rates were obtained from the Kaplan–Meier analysis.

55 years and older. Cox regression analyses provided estimates of survival probabilities and adjusted risk ratios (RRs) for revision. Estimates from the Cox analyses were used to construct adjusted survival curves at mean values of the risk factors. The Wald test was applied to calculate p-values for data obtained from the Cox multiple regression analysis. Differences between groups were considered to be statistically significant if the p-value was less than 0.05 in a two-tailed test.

RESULTS

According to the revision reasons recorded in the register, the most common reason for revision was aseptic loosening of both components. In the Cox regression analysis, there was no statistically significant difference in revision risk between ReCap HRA and Bimetric/ReCap THA (RR = 1.43, confidence interval (CI) = 0.95–2.14, p = 0.09) or between BHR HRA and Synergy/BHR THA (RR = 1.35, CI = 0.75–2.43, p = 0.31). However, the revision risk of Corail and Summit/ASR THA was significantly increased compared with that of ASR HRA (RR = 0.73, CI = 0.54–0.98, p = 0.04) (Table 2, Figs 1 to 3).

The revision risk of ASR HRA for aseptic loosening of both components was significantly decreased compared with that of Corail and Summit/ASR THA ($p < 0.001$). There was no statistically significant difference in revision risk for aseptic loosening between ReCap HRA and Bimetric/ReCap THA (p = 0.8) or between BHR HRA and Synergy/BHR THA (p = 0.2)

No difference was found in dislocation revision risk between the implant pairs compared. (ASR HRA vs ASR THA p = 0.4; BHR HRA vs BHR THA p = 0.5; ReCap HRA vs ReCap THA p = 0.7).

No difference was found in fracture revision risk between the implant pairs compared (ASR HRA vs ASR THA p = 0.2; BHR HRA vs BHR THA p = 0.5; ReCap HRA vs ReCap THA p = 0.2).

There was no difference in infection revision risk between implant pairs compared (ASR HRA vs ASR THA p = 0.2; BHR HRA vs BHR THA p = 0.95; ReCap HRA and ReCap THA p = 0.1).

The subgroup analysis by age and gender is provided in Table 3. Elderly male patients with Corail and Summit/ASR THA had an increased risk of revision compared to those with ASR HRA (RR = 0.48, 95% CI = 0.28–0.84, p = 0.01). Elderly female patients with ReCap HRA had an increased risk of revision

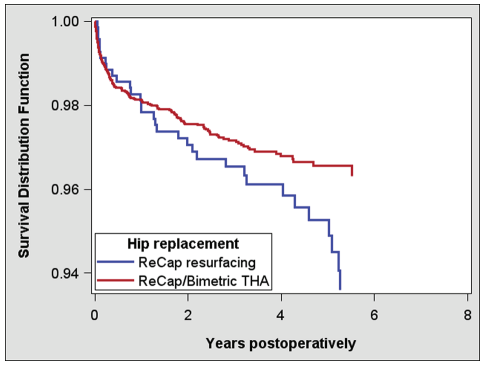

Fig. 1. Cox-adjusted survival curves of 698 ReCap resurfacings and 5464 ReCap/Bimetric THAs.
The end point was defined as revision for any reason. Adjustment was made for age at surgery, gender, operated side, head size, and diagnosis.
THA: total hip anthroplasty.

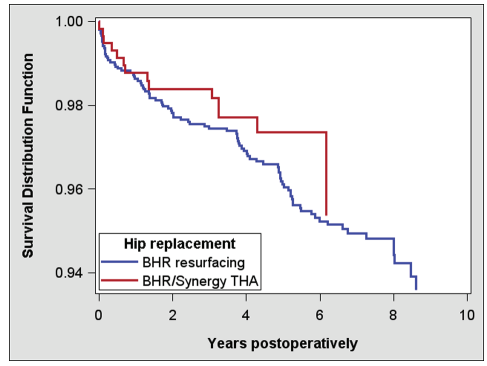

Fig. 2. Cox-adjusted survival curves of 1902 BHRs and 475 BHR/Synergy THAs.
The end point was defined as revision for any reason. Adjustment was made for age at surgery, gender, operated side, head size, and diagnosis.
BHR: Birmingham hip resurfacing; THA: total hip anthroplasty.

compared to those with Bimetric/ReCap THA (RR = 3.52, 95% CI = 1.87–6.60, $p < 0.001$).

DISCUSSION

We found out that the short-term revision risk of LDH MoM THAs was not increased compared to analogous HRAs in two out of three devices studied at a nationwide level. However, the revision risk of ASR THA was significantly increased compared to that of ASR HRA. Longer follow-up and more information on the incidence of adverse soft-tissue reactions in these patient cohorts are needed.

ASR and BHR cups and analogous HRA femoral components are all made of cast high-carbon-content cobalt–chromium alloy (10, 11). ReCap cup's inner surface (bearing surface) is made of high-carbon-content cobalt–chromium alloy as well. The outer surface of the shell is covered with titanium alloy. The analogous Biomet HRA femoral component is made of cobalt–chromium alloy (12). The outer surface of BHR cup is covered with hydroxyapatite (10). The radial clearance levels for the cups are 75–150 µm for ReCap, 50 µm for ASR, and 100 µm for BHR. Cup wall thickness at rim is 3.0 mm for ReCap, 3.1 mm for ASR, and 3.6/4.6 mm for BHR depending on component diameter (15). Synergy, ReCap, and Corail and Summit stems used in THA are all made of titanium alloy (16, 17).

LDH MoM THAs may produce more metal ions than HRA due to wear and corrosion at the junction between the femoral neck and the adapter sleeve and open femoral head design. In the study of Lavigne et al. (10), it was concluded that the cobalt–chromium adapter sleeve of the ASR THA system seems to possess better design characteristics than, for example, the Zimmer device. The cumulative 5-year revision rate in Australia for ASR THA was comparable to that of ASR resurfacing (10.3%, 95% CI = 9.0–11.6 and 10.5%, 95% CI = 8.6–12.7, respectively) (18). In England

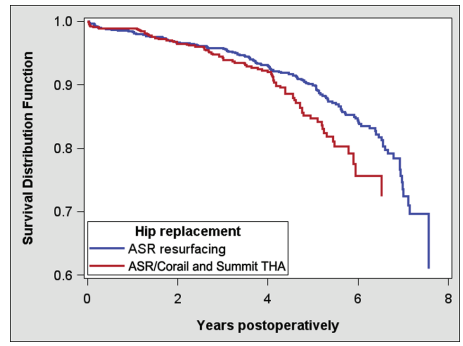

Fig. 3 Cox-adjusted survival curves of 979 ASR resurfacings and 632 ASR/Corail and Summit THAs.
The end point was defined as revision for any reason. Adjustment was made for age at surgery, gender, operated side, head size, and diagnosis.
ASR: articular surface replacement; THAs: total hip anthroplasty.

and Wales, the ASR resurfacing had slightly better 5-year survival than the Corail and Summit/ASR THA (9.6%, 95% CI = 8.3–11.2 and 11.3%, 95% CI = 9.1–14.2, respectively) (19). Our data support the view that ASR THA performs worse than ASR HRA.

The main reason for ASR HRA and ASR THA revision in the current data was aseptic loosening of both components. However, there is no specific question for ARMD as a reason for revision in the Finnish Arthroplasty Register data collection form. Therefore, ARMDs may be falsely coded as aseptic loosenings in the register. ARMD is not always coded as "other reason" either, because there were only 12 ASR HRA revision and 4 ASR THA revisions recorded as "other reason." The Finnish data collection form is currently

TABLE 3

Age- and gender-stratified relative risk of revision. HRAs were compared to analogous LDH MoM THAs during the same period 2001–2011. Data are based on a Cox regression model adjusted for age, operated side, head size, diagnosis, and type of implant.

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

HRA: hip resurfacing anthroplasty; LDH MoM THA: large-diameter head metal-on-metal total hip arthroplasty; BHR: Birmingham hip resurfacing; ASR: articular surface replacement; RR: risk ratio; CI: confidence interval.

being updated in collaboration with the Nordic Arthroplasty Register Association (NARA).

The cumulative 5-year revision rate of BHR THA was higher than that of BHR HRA in Australia (4.9%, 95% CI = 3.8–6.3 and 3.5%, 95% CI = 3.1–3.9, respectively). In addition, the cumulative 7-year revision rate of BHR THA was higher than that of BHR resurfacing (6.7%, 95% CI = 4.8–9.4 and 5.0%, 95% CI = 4.4–5.5, respectively) (18). The stem designs used when performing BHR THA were not set out. In England and Wales, the BHR resurfacing had a 5-year revision rate of 3.4% (95% CI = 3.1–3.8). Equivalent figures for BHR THA were not available (19). There was no statistical significant difference in short-term revision rate between BHR resurfacing and BHR THA in our study. However, the total amount of Synergy/BHR combinations was small (430) compared with BHR resurfacings (1636). It is possible that in Australia, the stems used, but not specified in the register, did not manage as well as the Synergy stem seems to manage in Finland. The short-term survival of the BHR resurfacing in Finland is worse than in Australia and in England and Wales. Despite this, the BHR has been one of the best performing resurfacing designs in Finland (20).

The cumulative 3-year revision rate of ReCap HRA was higher than that of ReCap THA in Australia (6.0%, 95% CI = 3.4–10.7 and 1.9%, 95% CI = 1.1–3.1, respectively). The cumulative 5-year revision rate of ReCap THA was 3.4% (95% CI = 2.1–5.5) (18). The cumulative 5-year revision rate of ReCap HRA was 6.4% (95% CI = 4.1–9.8) in England and Wales. Equivalent figures for ReCap THA were not available (19). There was no statistical significant difference in short-term revision rate between ReCap resurfacing and Bimetric/ReCap in our study. The total amount of Bimetric/ReCap combinations was high (5464). The short-term survival of Bimetric/ReCap with Magnum bearing surface has been promising also in previous studies (3, 21, 22). These data support the Australian finding of low short-term revision rate of ReCap THA.

No difference was found in the risk of dislocation revision between the implant pairs compared. Large head size seems to protect against dislocation, whether the prosthesis head is connected to femoral neck or to femoral component. No difference was found in the risk of revision for periprosthetic fracture between the implant pairs compared. At the early stage, the incidence of calcar fractures after cementless THA and femoral neck fractures after resurfacing seems to be similar. There was no difference in infection revision risk between the three LDH MoM THAs and analogous HRAs either. The supposed protecting effect of antibiotic cement of HRA designs was not supported by our data. LDH MoM THAs are probably performed by a higher numbers of surgeons than the resurfacings in Finland. Hip resurfacing has a reputation of being a relatively difficult procedure, and therefore, it has been centralized in the hands of the most experienced surgeons in many hospitals. However, the total amount of ASR THA and BHR THA in this study was low.

Different studies have shown that over 60° abduction angle might be a significant risk factor for increased metal-ion levels and ARMDs (11, 23). However, in a register-based study with a high number of patients, it is not possible to assess the radiographs of the patients.

In this study, elderly female patients had an increased risk of revision using ReCap HRA compared with ReCap THA. This is probably caused by the high number of femoral neck fractures. Elderly male patients had an increased risk of revision using ASR THA compared with ASR HRA. There was also a tendency for elderly female patients to have an increased risk of revision using ASR THA compared with ASR HRA. ASR THA may perform worse than ASR HRA due to wear of adapter sleeve.

In conclusion, there was no difference in risk for revision between BHR HRAs and THAs or between ReCap HRAs and THAs in short- to mid-term follow-up at a nationwide level. The ReCap LDH MoM adapter sleeve is made of titanium, not of chromium cobalt as in the other two models (10), which may have an effect on the development of ARMD. The revision risk of the ASR THAs was, however, significantly higher than that of ASR HRAs. The true prevalence of ARMD among patients with MoM hip replacements is not yet known, and these results need to be updated annually to see whether there are differences between the HRAs and THAs, as well as between designs from different manufacturers.

DECLARATION OF CONFLICTING INTERESTS

The authors declare that they have no conflicts of interest to disclose.

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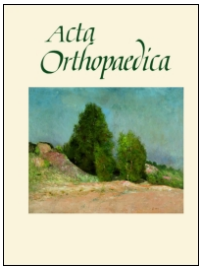

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Implant survival of the most common cemented total hip devices from the Nordic Arthroplasty Register Association database

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Implant survival of the most common cemented total hip devices from the Nordic Arthroplasty Register Association database

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Background and purpose — **According to previous Nordic Arthroplasty Register Association (NARA) data, the 10-year implant survival of cemented total hip arthroplasties (THAs) is 94% in patients aged 65–74 and 96% in patients aged 75 or more. Here we report a brand-level comparison of cemented THA based on the NARA database, which has not been done previously.**

Patients and methods — **We determined the rate of implant survival of the 9 most common cemented THAs in the NARA database. We used Kaplan-Meier analysis with 95% CI to study implant survival at 10 and 15 years, and Cox multiple regression to assess survival and hazard ratios (HRs), with revision for any reason as endpoint and with adjustment for age, sex, diagnosis, and femoral head material.**

Results — **Spectron EF THA (89.9% (CI: 89.3–90.5)) and Elite THA (89.8% (CI: 89.0–90.6)) had the lowest 10-year survivorship. Lubinus (95.7% survival, CI: 95.5–95.9), MS 30 (96.6%, CI: 95.8–97.4), and C-stem THA (95.8%, CI: 94.8–96.8) had a 10-year survivorship of at least 95%. Lubinus (revision risk (RR) = 0.77, CI: 0.73–0.81), Müller (RR = 0.83, CI: 0.70–0.99), MS-30 (RR = 0.73, CI: 0.63–0.86), C-stem (RR = 0.70, CI: 0.55–0.90), and Exeter Duration THA (RR = 0.84, CI: 0.77–0.90) had a lower risk of revision than Charnley THA, the reference implant.**

Interpretation — **The Spectron EF THA and the Elite THA had a lower implant survival than the Charnley, Exeter, and Lubinus THAs. Implant survival of the Müller, MS 30, CPT, and C-stem THAs was above the acceptable limit for 10-year survival.**

Cemented low-friction arthroplasty, pioneered by Sir John Charnley, is the basis of the modern total hip arthroplasty (THA). Charnley THA (DePuy; Johnson and Johnson, New Brunswick, NJ) is still considered to be the gold standard against which all other devices are compared (Warth et al. 2014). The Lubinus THA (Waldemar Link, Hamburg, Germany) and Exeter THA (Stryker Howmedica, Mahwah, New Jersey, US) are well-documented devices with tens of thousands of implantations worldwide (SHAR 2014, NJR 2015). There are, however, several other less common cemented devices with limited data available on implant survival.

The Nordic Arthroplasty Register Association (NARA) was established in 2007 in Sweden, Norway, and Denmark with the overall aim of improving the quality of joint replacement surgery by registry-based research collaboration. Finland became a member of NARA in 2010. The total population of the 4 countries is currently 26 million.

It has been stated, based on NARA data, that the survival of cemented implants for total hip replacement is higher than that of uncemented implants in patients aged 65 years or more (Mäkelä et al. 2014a). In younger patients, uncemented implants do not perform better regarding overall revision rate, but they have a lower long-term risk of revision due to aseptic loosening (Pedersen et al. 2014). In countrywise analyses, the differences in THA survival rates in different Nordic countries turned out to be considerable, with inferior overall results for cemented THAs in Finland. Implant survival of cemented THAs was higher in Sweden than in other Nordic countries (Mäkelä et al. 2014b).

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Table 1. Number and proportion of study implants, and demographic data

THA	n	Proportion %	Mean age	Female %	POA %	Mean follow-up years
Charnley	43,849	15	72	69	78	9.6
Lubinus	116,186	41	72	61	81	6.9
Exeter	75,880	26	72	64	84	7.0
Spectron EF	25,214	8.8	73	69	80	7.2
Müller	3,192	1.1	71	66	88	8.9
MS-30	8,674	3.0	71	64	89	4.3
CPT	6,222	2.2	73	66	85	8.8
Elite	5,647	2.0	70	66	74	10.1
C-stem	2,082	0.7	71	63	86	7.8
Total	286,946	100	72	64	82	7.4

POA: Primary osteoarthritis.

It is clear that brand-level implant survival data for cemented THA are required. We therefore determined the implant survival of the most common cemented THA brands in the Nordic countries based on the NARA database.

Patients and methods

Sources of data

The THA registries of Sweden, Denmark, Norway, and Finland participated. From 1995 through 2013, all 4 registries used individual-based registration of THAs and patients. A minimal NARA dataset was created, containing data that all the registries could deliver (Havelin et al. 2009). The degree of coverage and completeness in the Nordic registries is high (Pedersen et al. 2004, Arthursson et al. 2005, Espehaug et al. 2006, DHAR 2014, SHAR 2014, FAR 2015). Selection and transformation of the respective datasets and de-identification of the patients, including deletion of the national civil registration numbers, was performed within each national registry. Anonymous data were then merged into a common database.

Devices

360,584 primary all-cemented THAs were registered in the NARA database from 1995 through 2013. The 9 most common cemented THAs were assessed: Lubinus, Exeter, Charnley, Spectron (Smith and Nephew, Memphis, TN), MS-30 (Zimmer, Winterthur, Switzerland), CPT (Zimmer, Warsaw, IN), Elite (DePuy; Johnson and Johnson, New Brunswick, NJ), Müller THA (Zimmer, Winterthur, Switzerland), and C-stem THA (DePuy, Johnson and Johnson, New Brunswick, NJ) (Table 1).

We assessed survivorship of implant families consisting of all versions of the device (see Table 2, Supplementary data), as several versions of the study implants were introduced during the study period. The different versions of the study implants were not necessarily the same in the 4 countries. Furthermore, the study devices were not necessarily coded similarly in the 4 registries. Only those cup/stem combinations with at least 100 implantations in a country were included. The cup/stem combinations assessed are listed in Table 2 (Supplementary data). Elite, MS 30, C-stem, CPT, and Müller THAs were created by combining the study stem with a cemented acetabular component by the same manufacturer.

Due to similar coding of the cup component in all 4 national registries, we had sufficient numbers to perform separate analyses of the Exeter X3 Rimfit, Exeter Contemporary, Exeter All-poly, and Exeter Duration (Table 3).

Table 3. Number and proportion of Exeter-subgroup devices, and demographic data

Exeter THA	n	Proportion %	Mean age	Female %	Primary OA %	Mean follow-up years
X3 Rimfit	7,189	9.5	73	65	84	1.4
Contemporary	19,889	26	74	67	85	6.1
All-poly	25,032	33	72	65	81	9.3
Duration	23,770	31	71	61	86	7.0
Total	75,880	100	72	64	83	7.0

OA: osteoarthritis.

Statistics

We used Kaplan-Meier analysis with 95% confidence intervals (CIs) to assess implant survival at 10 and 15 years, until there were at least 100 THRs left at risk. Patients were censored at death or December 31, 2013, whichever came first. Outcome was revision for any reason, defined as removal or exchange of at least 1 of the components. Kaplan-Meier survivorship was also assessed separately for each device for 2 time periods, 1995–2004 and 2005–2013, using any reason for revision as endpoint. Furthermore, Kaplan-Meier survivorship for aseptic loosening of the cup, stem, or both components was assessed depending on the type of cement used (Palacos-type, Simplex-type, or other) (Espehaug et al. 2009). We used Cox multiple regression to determine survival rates and hazard ratios (HRs), with revision for any reason as endpoint, and with adjustment for age (< 60, 60–64, 65–69, 70–74, ≥ 75), sex, diagnosis (primary osteoarthritis, hip fracture, non-traumatic femoral head necrosis, inflammatory disease, childhood hip disease, or other/unknown), and femoral head material (metal, ceramics, or other/unknown). The assumption of proportional hazards was fulfilled, as evaluated by visual inspection of log-minus-log-plots.

Both Kaplan-Meier and Cox analysis are based on the assumption of non-informative censoring, an assumption that is not fulfilled when estimating revision risk and censoring for death. Thus, competing risk assessment was also performed using Stata 14 statistical software, and these data are available in Table 8 (see Supplementary data).

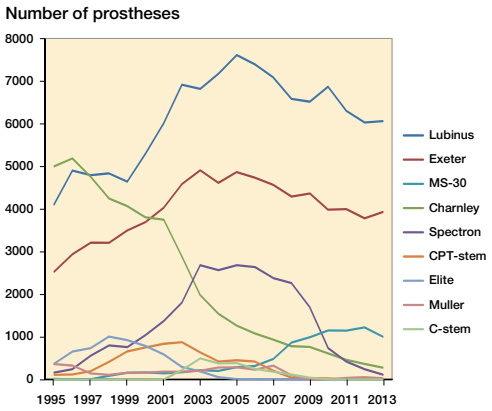

Figure 1. Time trends in using the study devices during the period 1995–2013.

Patients with bilateral procedures were included, as earlier research has shown that this does not bias the results (Lie et al. 2004, Ranstam and Robertsson 2010). We considered any p-values less than 0.05 to be statistically significant. For most statistical analyses, we used SPSS version 22.0.

Ethics

Ethical approval of the study was obtained through each national registry.

Results

The Lubinus THA was the most common study device, being used in 41% of all implantations. Mean age at the time of surgery was highest for the CPT THA (73 years). The proportion of female patients was highest for Charnley THA (69%) (Tables 1 and 3, and Figure 1).

Table 5. Implant survival at 7 years for the time periods 1995–2004 and 2005–2013, with any reason for revision as the endpoint

THA	At risk	7-year survival for 1995–2004 (95% CI), %	At risk	7-year survival for 2005–2013 (95% CI), %
Charnley	27,686	95.7 (95.5–95.9)	1,953	95.7 (95.1–96.3)
Lubinus	40,948	97.1 (96.9–97.3)	11,662	96.9 (96.7–97.1)
Exeter	27,748	95.8 (95.6–96.0)	7,411	96.1 (95.9–96.3)
Spectron	8,783	95.2 (94.8–95.6)	4,000	95.1 (94.7–95.5)
Müller	1,656	96.6 (95.8–97.4)	437	95.9 (94.5–97.3)
MS-30	1,005	97.3 (96.3–98.3)	493	97.5 (96.9–98.1)
CPT	3,609	96.6 (96.0–97.2)	719	95.1 (93.7–96.5)
Elite	3,959	92.7 (91.9–93.5)	13	-
C-stem	929	97.5 (96.5–98.5)	496	96.4 (95.0–97.8)

Several THAs had a 10-year survivorship of 95% or more, including Lubinus (95.7%, CI: 95.5–95.9), MS 30 (96.6%, CI: 95.8–97.4), and C-stem (95.8%, CI: 94.8–96.8). The lowest 10-year implant survival was observed in patients with Spectron EF THA (89.9%, CI: 89.3–90.5) and Elite THA (89.8%, CI: 89.0–90.6) (Tables 4 and 5, and Figures 2 and 3).

Implant survival of Charnley, Exeter, and Elite THAs with Palacos-type cement was higher than those of the same devices with other types of cement. Implant survival of Lubinus, Spectron, and Müller THAs with Palacos- and Simplex-type cement was higher than those of the same devices with other types of cement (Table 6).

Lubinus (revision risk (RR) = 0.77, CI: 0.73–0.81), Müller (RR = 0.83, CI: 0.70–0.99), MS 30 (RR = 0.73, CI: 0.63–0.86), and C-stem THAs (RR = 0.70, CI: 0.55–0.90) had a lower revision risk than Charnley THA. Spectron EF (RR= 1.73, CI: 1.62–1.84), Exeter (RR = 1.25, CI: 1.18–1.31), and Elite THAs (RR = 1.65, CI: 1.51–1.80) had a higher revision risk than Charnley THA after adjusting for age, sex, and diagnosis (Table 4).

In subgroup analysis of the Exeter devices, the Exeter X3 Rimfit THA had a similar revision risk to that of the reference

Table 4. Kaplan-Meier survivorship of the study devices at 10 and 15 years with revision for any reason as the endpoint, and adjusted revision rate (RR) (age, sex, diagnosis, femoral head material) for revision using Cox regression

THA	At risk at 10 years	10-year survival (95% CI), %	At risk at 15 years	15-year survival (95% CI), %	Adjusted RR (95% CI), %	p-value
Charnley	21,794	94.1 (93.9–94.3)	7,199	90.7 (90.3–91.1)	1.0	-
Lubinus	29,016	95.7 (95.5–95.9)	6,685	92.4 (92.0–92.8)	0.77 (0.73–0.81)	< 0.001
Exeter	19,606	93.5 (93.3–93.7)	4,066	86.0 (85.4–86.6)	1.25 (1.18–1.31)	< 0.001
Spectron EF	5,311	89.9 (89.3–90.5)	512	79.8 (78.2–81.4)	1.73 (1.62–1.84)	< 0.001
Müller	1,225	94.9 (93.9–95.9)	372	92.6 (91.2–94.0)	0.83 (0.70–0.99)	0.03
MS-30	834	96.6 (95.8–97.4)	-	-	0.73 (0.63–0.86)	< 0.001
CPT	2,756	94.9 (94.3–95.5)	391	91.6 (90.4–92.8)	0.94 (0.84–1.06)	0.3
Elite	3,201	89.8 (89.0–90.6)	986	83.9 (82.5–85.3)	1.65 (1.51–1.80)	< 0.001
C-stem	550	95.8 (94.8–96.8)	-	-	0.70 (0.55–0.90)	0.005

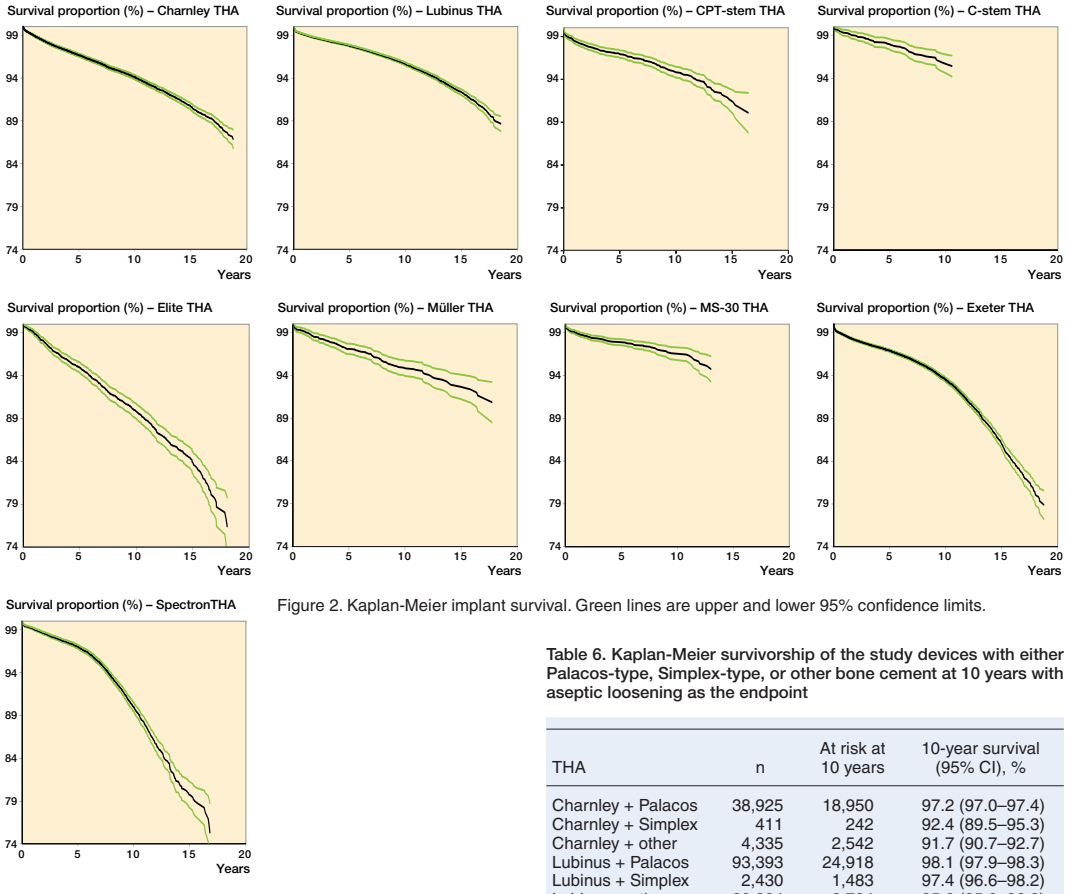

Figure 2. Kaplan-Meier implant survival. Green lines are upper and lower 95% confidence limits.

implant (Charnley) THA (RR = 1.13, CI: 0.91–1.39). The Exeter Duration THA had a lower revision risk than the reference implant (RR = 0.84, CI: 0.77–0.90) (Table 7).

Results of the competing risk assessments are given in Table 8 (see Supplementary data). The results varied slightly, but they did not change the ranking of the implants.

Table 6. Kaplan-Meier survivorship of the study devices with either Palacos-type, Simplex-type, or other bone cement at 10 years with aseptic loosening as the endpoint

THA	n	At risk at 10 years	10-year survival (95% CI), %
Charnley + Palacos	38,925	18,950	97.2 (97.0–97.4)
Charnley + Simplex	411	242	92.4 (89.5–95.3)
Charnley + other	4,335	2,542	91.7 (90.7–92.7)
Lubinus + Palacos	93,393	24,918	98.1 (97.9–98.3)
Lubinus + Simplex	2,430	1,483	97.4 (96.6–98.2)
Lubinus + other	20,224	2,724	95.6 (95.0–96.2)
Exeter + Palacos	51,729	12,200	97.2 (97.0–97.4)
Exeter + Simplex	13,366	4,148	96.2 (95.8–96.6)
Exeter + other	10,310	3,057	96.1 (95.5–96.7)
Spectron + Palacos	22,152	5,031	92.6 (92.0–93.2)
Spectron + Simplex	1,523	144	92.8 (90.1–95.5)
Spectron + other	1,497	141	85.0 (80.5–89.5)
Müller + Palacos	2,108	888	97.7 (96.9–98.5)
Müller + Simplex	234	140	97.9 (95.5–100)
Müller + other	850	233	92.9 (90.5–95.3)
MS-30 + Palacos	4,250	898	98.8 (98.2–99.4)
CPT + Palacos	5,630	2,610	98.7 (98.3–99.1)
CPT + other	469	116	97.3 (94.8–99.8)
Elite + Palacos	4,222	2,450	94.4 (93.6–95.2)
Elite + Simplex	166	98	87.8 (82.5–93.1)
Elite + other	1,254	668	88.2 (86.2–90.2)
C-stem + Palacos	1,599	683	99.0 (98.4–99.6)

Discussion

The Spectron EF and Elite THAs had a lower implant survival than the Charnley THA, the reference implant. Implant survival of Müller, MS 30, CPT, and C-stem THAs (94.9–96.6% at 10 years) was far above the acceptable limit for 10-year survival. However, the total amount of these devices was small compared to Charnley, Lubinus, and Exeter THAs, although all of them had been implanted in more than 2,000 hips. When an implant becomes more common and is used by an increasing number of surgeons, the results will be more representative since they can be assumed to reflect a wider range of differences in surgical technique.

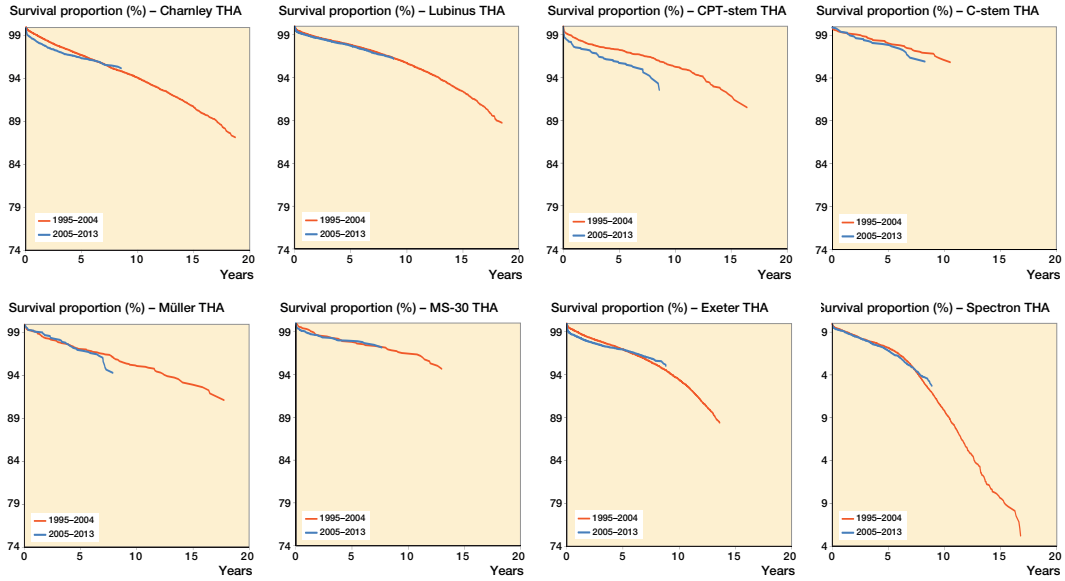

Figure 3. Implant survival of THAs for the time periods 1995–2004 and 2005–2013, with revision for any reason as the endpoint

Table 7. Adjusted revision risk (age, sex, diagnosis, femoral head material) for revision of the Exeter-subgroup devices

THA	Adjusted revision risk (95% CI)	p-value
Charnley	1.0	-
Exeter X3 Rimfit/Exeter	1.13 (0.91–1.39)	0.3
Exeter Contemporary/Exeter	1.41 (1.31–1.52)	< 0.001
Exeter All-poly/Exeter	1.47 (1.39–1.56)	< 0.001
Exeter Duration/Exeter	0.84 (0.77–0.90)	< 0.001

A major strength of the present study was the unique collaboration of the 4 national registries to create a multinational database with large numbers of patients and a long follow-up time. The main weakness of the study was that we were unable to assess every updated version of each device separately. The study devices were implant families, consisting of several versions of the device. Another weakness was that we were not able to assess cup and stem survival separately with revision for any reason as the endpoint. These data are were not available from the Finnish Arthroplasty Register, and they were therefore not included in the 4-country minimal dataset either. Furthermore, our data did not include information on parameters such as surgeon volume, hospital volume, ASA grade, or preoperative patient-reported outcome measures (PROMs).

Implant survival of Charnley THAs was high (94.1% at 10 years), but slightly lower than that reported by the NJR (10-year survival of 95.1% for Charnley Ogee/Charnley and 97.0% for Charnley/Charnley) (NJR 2015). In Australia, 10-year survival for Charnley Ogee/Charnley was 91.6%, whereas that for Charnley/Charnley was 93.0% (AOANJRR 2015). The total amount of Charnley THAs in Australia was low (1,300), which might explain the slightly inferior results compared to ours. The Charnley THAs studied consisted of several versions of the Charnley stem, such as Charnley flanged, Charnley flanged heavy, and Charnley flat and round-backed stems. It has been stated previously that the implant survival of the Charnley THA after 1995 has been good, and differences in implant survival between Charnley stems are minor (Espehaug et al. 2009). Similarly, the cup designs of the Charnley THA that were assessed varied. The use of Charnley THAs decreased drastically towards the end of the study period.

The Elite Plus THA was introduced in 1994 as the second modular evolution of the original Charnley THA. Several changes were made to the shape and the dimensions of the femoral component, to improve proximal load transfer and reduce contact stresses. The design also incorporated an undercutting of the neck flange (DePuy 1993). Overall survivorship of Elite THAs in our study was inferior to that of the reference implant. The Elite Plus stem has been withdrawn from the market due to divergent clinical results (Hauptfleisch et al. 2006, Kim et al. 2007, von Schewelov et al. 2010). Our results support these earlier findings. A weakness of our Charnley vs. Elite THA analysis was that Elite cups were sometimes—although rarely—used with Charnley stems, and vice versa, which may have biased our results.

Implant survival of the third DePuy device assessed, the C-stem THA (95.8% at 10 years), was higher than that of the Charnley THA, and comparable to previous reports (a 10-year survival of 94.6% for C-stem/Elite Plus in the AOANJRR, and a10-year survival of 98% for C-stem/Elite Plus Ogee in the NJR). The triple-tapered, polished cemented C-stem introduced in 1993 was based on the original Charnley concept of the flat-back polished stem (Purbach et al. 2013). However, the total number of C-stem THAs that have been implanted to date in the Nordic countries—and also worldwide—is low compared to the original Charnley THA.

Long-term survival of the Lubinus THA in our study was higher than that of the reference implant. Most of the study stems were SP II models (see Appendix) with a high degree of documentation (Annaratone et al. 2000, Wierer et al. 2013, Prins et al. 2014, SHAR 2014). However, most of the Lubinus THAs (79%) in our study were performed in Sweden, which has twice the population of each of the 3 other countries. In general, the implant survival of cemented THAs in Sweden is substantially higher than in the other 3 countries (Mäkelä et al. 2014). The Swedish Hip Arthroplasty Register has provided feedback to the profession and also continued training in cementing techniques for more than 30 years. So the excellent implant survival of Lubinus THA in the present study may have been biased by the "Swedish factor". The threshold for performing a revision operation is also culture-dependent, and may vary between the Nordic countries. X-linked Lubinus cups were coded separately in the NARA hip database only in Sweden, so we did not assess X-linked Lubinus THA separately. However, these devices will be able to be detected in the future using NARA data, when the catalog number-based register is ready.

We found that long-term survival of Exeter THAs was satisfactory, although inferior to that of the reference device. The overall implant survival of Exeter THAs in our study (93.5%) was slightly lower than that reported by the NJR (10-year survival of 97.1% for Exeter V40/Contemporary, and 96.3% for Exeter V40/Exeter Duration), but similar to that reported by the AOANJRR (10-year survival for Exeter V40/Contemporary of 94.1%). In the current study, the Exeter THA family consisted almost exclusively of Exeter Universal stems. The Exeter V40 stem was separately coded only in Denmark in the current NARA database, so the number of definite Exeter V40 THAs in the current study was low. However, we were able to do subgroup analyses for Exeter THAs according to the acetabular component (Table 6). The Exeter X3 Rimfit THA (X3-stabilized UHMWPE, the latest version of high crosslinking) was coded separately in each of the 4 registries. Implant survival of this device was comparable to that of the reference implant. The total number of Exeter X3 Rimfit THAs was, however, small compared to Exeter Contemporary THAs and Exeter All-poly THAs, and the follow-up time was shorter. Contemporary cups are made of Duration-stabilized UHMWPE, whereas all-polyethylene cups are not Duration-stabilized. Duration-stabilized UHMWPE was the first annealed (heated below melting temperature) moderately crosslinked polyethylene with 3 Mrad of irradiation. The long-term implant survival of Exeter Contemporary THAs and Exeter All-poly THAs was good, although not quite as good as that of the best performers. Based on previous Swedish data, the implant survival of Lubinus THAs and Exeter THAs is similar in Sweden (SHAR 2014). The "Sweden factor" appears to have a major impact on the survival of the Exeter THA also. The most common Swedish device was the Exeter Duration THA, with excellent survivorship. The Exeter Duration THA was named specifically in Sweden and Denmark only and we did not ask for subclassification in the other countries for this particular study. In England and Wales, implant survival of Exeter/Contemporary THA was slightly higher than that of Exeter/Exeter Duration THA, which was contrary to our findings. In Australia, Exeter/Duration THA is not assessed separately. However, 15-year survivorship of the Exeter THA in our study was inferior to that of the best performers. 15-year survival data for the Exeter THA are not yet available from the NJR or the AOANJRR.

It should be taken into account that the Exeter stem is very easy to revise, and the revision method of cementing a new smaller stem without removing the old bone cement is well established (te Stroet et al. 2014). The ease of the Exeter stem revision could have biased survivorship of the Exeter THA in our study. However, the revision risk of the Exeter stem regarding periprosthetic fracture is higher than for the Lubinus SP II stem (Thien et al. 2014).

Implant survival of Spectron EF THAs in our study (89.9% at 10 years, and 79.8% at 15 years) was inferior to that of other THAs, and also inferior compared to previous reports (with a 10-year survival of 92.1% for Spectron EF/Reflection in the AOANJRR and in Norway (Espehaug et al. 2009)). Spectron THA in our study consisted mostly of Spectron EF stems and Reflection cups. It has been shown in RSA studies that cups with ethylene oxide-sterilized polyethylene (such as the Reflection cup) have higher wear rates than those with gamma irradiation-sterilized polyethylene (Digas 2005, Kadar et al. 2011a, Jonsson et al. 2015). The modular Spectron EF stem was introduced in 1988, and in 1989 the roughness of the proximal part of the stem was increased. 5 years later, further modifications to the stem were introduced and the name was altered to Spectron EF Primary. The collar became polished and smaller sizes were introduced. This design performed worse than its predecessor, especially the smallest sizes (, Thien and Kärrholm 2010, SHAR 2014). It has been suggested that the addition of a rough surface to the Spectron stem has been detrimental to the long-term success of the prosthesis (Gonzalez Della Valle et al. 2006, Grose et al. 2006, Espehaug et al. 2009, Kadar et al. 2011b). Our results support these findings.

Implant survival of Müller THAs (94.9% at 10 years, and 92.6% at 15 years) was higher than that of the reference

implant, and comparable to that in previous reports (Mäkelä et al. 2008, Clauss et al. 2013, Nikolaou et al. 2013). The Müller THAs studied consisted mostly of Müller straight stems and of Müller all-polyethylene cups. Müller stems made of titanium alloy with a roughened surface finish were excluded due to previous reports of increased revision risk compared to polished cobalt-chrome Müller stems (Clauss et al. 2013, FAR 2015). Implant survival of another Zimmer device, the MS-30 THA (96.6% at 10 years) was also high, and comparable to those of previous reports (10-year survival of 97.5% for MS-30/Low Profile in the AOANJRR, and 10-year survival of 99% for MS-30/Low Profile in the NJR). However, stem survival as poor as 80% at 12 years has also been reported for the MS-30 (Witte et al. 2009). The original MS-30 (Morscher-Sportorno) stem was made of stainless steel, and was straight, three-dimensionally tapered, collarless, and matt-surfaced (Berli et al. 2005, Brigstocke et al. 2014). However, most MS-30 stems inserted in Sweden have been polished. The MS-30 stem was used in combination with Zimmer all-polyethylene cups such as the ZCA and highly crosslinked ZCA XLPE. A weakness of the Müller and MS-30 THA analysis was that all the Müller THAs studied were performed in Finland and in Sweden, and all the MS-30 THAs were performed in Sweden and Norway.

Implant survival of the third Zimmer device studied, the CPT THA (94.9% at 10 years, and 91.6% at 15 years), was comparable to that of the reference THA, and to those in previous reports (a 10-year survival of 95.4% for CPT/ZCA in the AOANJRR, and a 10-year survival of 96.4% for CPT/ZCA in the NJR). The CPT (collarless polished tapered) stem was originally developed as a collarless, highly polished, double-tapered prosthesis for distribution in the USA. Like the Exeter stem, from which the principles of its design were taken, the CPT also uses the taper slip concept. The CPT differs from the Exeter Universal stem in its broad lateral shoulder, more complete lateral taper, and more rectangular proximal geometry (Burston et al. 2012). CPT stems made of stainless steel and made of chromium cobalt were included in the current study, which may have caused bias. Although performed in all 4 countries, the total number of CPT THAs was small.

The long-term performance of cemented THAs depends on many factors in addition to the implant, such as the characteristics of the patient, surgical and cementing technique, and the properties of the bone cement used. Although all bone cements used today are based on methylmethacrylate, their performance may vary. Poor results have been found for some low-viscosity cements (Havelin et al. 1995, Furnes et al. 1997, Espehaug et al. 2002). We therefore also determined implant survival according to the type of cement used (Palacos-type, Simplex-type, or other) (Espehaug 2009). Implant survival of Charnley, Elite, and Exeter THAs was higher when used with high-viscosity, Palacos-type cement. Our results support previous findings (Havelin et al. 1995, Espehaug et al. 2002). Implant survival of the study devices was similar in the period 1995–2004 and the period 2005–2013. Cementing techniques appear to have become standardized in the Nordic countries over the last 2 decades.

In summary, several cemented THA brands perform well in the long term. However, there are substantial differences in implant survival between high and low performers.

Supplementary data

Tables 2 and 8 are available on the Acta Orthopaedica website att www.orthop.org, number 10004.

This paper is the result of close team work, all the authors participated in planning and design of the study and interpretion of the results. PP performed statistical analyses. MJ was responsible for writing the manuscript.

No competing interests declared.

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