Total Hip Arthroplasty in Young Patients

The Path to Restoration and Beyond

Ena Čolo

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CHAPTER 1

General introduction

GENERAL INTRODUCTION

Total hip arthroplasty (THA) is considered as one of the most successful and cost-effective surgeries in medicine and has been described as 'the operation of the century' by Learmonth et al[1]. THA can be performed in patients that suffer from symptomatic end-stage hip osteoarthritis. The goal of the procedure is to achieve relief of pain and restore mobility and function of the hip joint and therewith improve the patient's quality of life. It has been shown in many studies that THA effectively reduces the pain and improves the quality of life[2-4]. Given these predominantly excellent outcomes, Sloan et al. predicted that, by 2030, the demand for primary THA will grow by 70% up to 635,000 procedures annually in the United States alone based on 2000-to-2014 data[5]. In Germany, an increase of 23% for primary THAs between 2014 and 2040 is expected, despite an expected decline in population[6]. In The Netherlands, a historical increase in the number of primary THA of 50% was seen in the period of 1995-2005[7]. Based on trend projections, the number of THAs will increase with 149% by 2030[7]. The Dutch Arthroplasty Register (LROI) has already shown an increase of primary THAs from 23,331 in 2010 to 33,253 in 2019[8].

The results of THA in elderly patients (>65 years) are excellent in terms of quality of life, reduction in pain and prosthesis survival and can be considered exceptional[9-12]. Subsequently, the indications for THA have extended over the years. Nowadays, this procedure is increasingly offered to younger patients, including those who are 50 years or even younger. These younger patients can suffer from primary osteoarthritis, but end-stage secondary osteoarthritis is in fact the most common reason for THA in this patient group under 50 years with debilitating hip pain. Common causes of secondary osteoarthritis in these young patients are developmental dysplasia of the hip (DDH), avascular necrosis of the femoral head, rheumatoid arthritis or posttraumatic osteoarthritis[8].

Nevertheless, the increase in number of THA performed in younger patients is also a reason for concern. Although the short-term outcome for pain and function in general is very beneficial, literature shows that primary THA in young patients has inferior long-term results compared to the older population[9-11, 13-15]. The main concern is that the likelihood of implant failure in these younger patients is higher and the revision rate is increased. In addition, these patients are younger and will live longer with a THA implant in situ. Hence, they will inevitably face one or even more revision surgeries during their life and therefore this population remains to be a challenge for the orthopaedic surgeon[16].

This thesis describes the outcome of primary THA in young patients using a cemented THA with the use of impaction bone grafting in case of acetabular bone defects. In addition, this thesis also focuses on the outcome of the subsequent revision THA within this young, challenging patient group. The term Girdlestone-load is introduced, which describes a group of patients within a cohort that is not revisable and is left with a permanent disability due to a Girdlestone hip resection arthroplasty, most often due to a persistent infection.

A concise summary of the history of total hip arthroplasty

Hip osteoarthritis has been with the human population for a long time causing severe incapacitating suffering. Although prove of joint osteoarthritis has been evident from thousands of years ago, the surgical treatment for end-stage OA started at the end of the 18th century; especially excisions of the femoral head were common in those days. In 1891, a German surgeon from Berlin named Glück implanted an ivory ball and socket joint that he fixed to bone with nickel-plated screws. He also experimented with a mixture of plaster of Paris, to provide better fixation. This could be seen as a precursor to current use of cement. Subsequently, many other surgeons, among all Smith-Petersen, tried different options such as (soft tissue) interpositions like fat, gold foil and glass. Unfortunately, none of these techniques provided predictable satisfying results. In the period between 1920 and 1950 there were several surgeons in Europe and North-America who continued the search for improved THA techniques. Wiles (1938, London), introduced the first prosthetic THA. The Judet brothers (1948, Paris) started experimenting with acrylic pegged prostheses, while Moore (1952, Baltimore) implanted the first cobalt-chrome hemiarthroplasty with the feature for bone ingrowth on the femoral stem. However, he found variable fixation results and still obviously experienced acetabular erosion.

Despite the fact that all these surgeons experienced rather disappointing results, mostly because of inferior materials, poor designs, fixation failures, anaesthesiologic problems and unacceptable high infection rates, they did pave the way for Sir John Charnley, who is considered to be "The Man of the Hip". The surgical management of osteoarthritis remained a challenge and plagued the orthopaedic surgeon for many years, but Charnley revolutionized it in the early 1960s with his low friction arthroplasty, which was successfully implemented at the Centre for Hip Surgery in Wrightington in England. His concept existed of a forged, stainless steel monobloc femoral stem with a small, polished femoral head, rotating in a polyethylene (PE) cup. The low friction term refers to his aim to decrease the high torque forces on the implants, and thus to decrease complications such as loosening and wear. In addition, Charnley used polymethylmethacrylate bone cement to fixate both the cup and the femoral component to the bone, which is one of his other major contributions. Since then, many different concepts, designs and materials have been introduced in an attempt to further improve the survival of the THA. Improvements in both providing better durable fixation techniques as well as more resilient bearing materials have definitely led to better results of THA. Nowadays, cemented and uncemented implants are both used with impressive results, both in elderly as well as in younger patients. The metal-on-PE low friction articulation, as introduced by Charnley, is still used nowadays. Recently, with the introduction of ultra-high-molecular-weight PE (UHMWPE), the outcome of the metal-on-PE bearing has greatly improved as the wear of the cup made from this newer PE is now significantly less. In addition to the metal-on-PE bearing, other bearings such as ceramic-on-PE, ceramic-on-ceramic (C-o-C) and metal-on-metal (MoM) have been used as well. However, not all new bearings appear to be equally successful. Especially, MoM bearings have shown worrisome outcomes in the recent past.

The challenge of THA in young patients

As the number of THA in young patients has increased over the last decades, it is important to realise that this patient group is completely different and therefore not comparable to the elderly patient population with primary hip osteoarthritis in need of THA. Young patients with hip osteoarthritis often have underlying hip pathologies, in which frequently bone defects on the acetabular side are encountered. These acetabular defects are often seen in cases with secondary osteoarthritis after for example developmental dysplasia of the hip, which is known for an insufficient development of the acetabulum. This also holds true for Perthes' disease or previous hip trauma, in which bone defects on the acetabular side can cause a challenge for the treating surgeon. These acetabular bone defects hamper the fixation of acetabular components. Reconstruction of these defects, using bone grafts, can help to place the acetabular component in an adequate anatomical position to recreate native joint biomechanics as much as possible. Studies that describe the long-term survival data of THA in young patients, generally show satisfying long-term results of the femoral component. However, failure of the acetabular component is the most common reason for revision in young patients due to the aforementioned problems of acetabular bone stock loss, which is also shown in the studies in this thesis[17, 18]. In addition, young patients have higher activity levels and demands of their THA than the elderly THA population, which generates more stress on the hip implant and the implant-bone interface and can cause higher rates of wear resulting in an increased rate of loosening of the THA. Given these complications in combination with the young age at implantation, it is inevitable that the young THA patients will outlive their prosthesis and will, at some point, need one or more revision surgeries.

Kurtz et al. evaluated the projections for primary and revision THA in the young patient population (<65 years) in the United States and showed that in 2006 46% of all primary THA were in patients younger than 65 years at surgery[19]. By 2030, it is expected that 52% of primary THAs will be performed in patients younger than 65 years. In the age group of 45 to 54 years in need of a THA, an increased growth by a factor of 5.9 is expected (2006-2030). In the Dutch Arthroplasty Register (LROI) an increase of 32% of primary THAs in patients younger than 50 years was seen, from 1,047 in 2010 to 1,390 in 2019, resulting in a growth factor of 1.3[8].

Impaction bone grafting

Over the last decades, several methods have been introduced to address femoral and acetabular defects in primary and revision THA[20-25]. Bone loss on the acetabular side jeopardizes adequate implantation and fixation of the acetabular component as previously stated, both in cemented and uncemented cups. Therefore, an adequate reconstruction of bone stock is needed to facilitate the implantation and fixation of the acetabular component. Many methods try to 'fill up' this defect by using larger implants or augments, without actually restoring the bone stock by new bone. After all, metal will never convert to bone.
For patients with acetabular insufficiency due to developmental dysplasia of the hip, a surgical technique with the use bulk roof autograft is an option[22,23, 25-27]. However, varying results regarding this technique have been published. Clement et al. reported a good survival with bulk roof autograft in 62 patients (74 hips) with a survival of 83% (95% CI 76-90) after 20 years[27]. Another study showed less favorable results with a survival of the acetabular component of 80% at 14 years and 11% of unrevised acetabular components with radiolucent lines[26]. This study emphasizes that the long-term results of this technique are questionable.

Our philosophy is directed towards creating a long-term stable fixation and reconstruction that provides sufficient bone stock for future revisions. Impaction bone grafting (IBG) is a method to biologically restore acetabular deficiencies by using morselized bone grafts. Hastings and Parker were one of the first ones to describe the concept of using morselized bone grafts in combination with a cemented Vitallium cup in patients with protrusio acetabuli suffering from rheumatoid arthritis[28]. IBG as we know it nowadays, was developed by Slooff et al. at Radboudumc in 1979[25]. The essence of this technique is a vigorous impaction of these bone chips.

During primary THA surgery, following resection of the femoral head, preparation of the acetabulum with removal of all cartilage, sclerotic bone and cysts is performed and the acetabular defect can be assessed. In case of segmental bone defects, a metal wire mesh medially or superolateral can be used to create acetabular containment (Figure 1). These meshes can be trimmed and adjusted to the size of the defect with scissors and clamps. The mesh can be fixated with multiple screws. Next, drill holes are made in the remaining sclerotic area of the acetabulum. With pulse lavage all debris is removed and the socket is cleaned, which is an important step to create optimal incorporation of the graft and cement. Next, the bone chips can be impacted. These bone chips are either made of autograft using the patient's own femoral head or allograft chips of a femoral head from the bone bank, or a combination of both. In revision surgery, only allograft is used. Initially, these chips were made by hand using a large rongeur. The advisable size of the trabecular bone chips for the acetabulum is 0.7-1.0 cm in diameter[29]. As this is a tedious process, these bone chips can also be made using a special bone mill. However, not all bone mills will provide the correct

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size of the chips and in general chips produced by these mills are too small for acetabular reconstructions and can have a detrimental effect on the initial stability. Nowadays, both methods, either rongeurs or specialized bone mills, are still in use. After insertion of the bone chips in the acetabulum, impaction of the chips is performed by using specially designed impactors with increasing sizes and the bone reconstruction is built up layer by layer. Firm impaction using a hammer and metal impactors is mandatory in performing this technique and is the key in achieving adequate initial stability of the graft. The last used impactor corresponds with the size of the PE cup including its cement layer. Next, vacuum-mixed antibiotic-loaded cement is placed on top of the graft and pressurization of the bone and cement is performed. Finally, the polyethylene cup is placed on the cement layer. Earlier histological studies performed in our institution evaluated the incorporation of these bone grafts[30-33]. In a study from Buma et al, core biopsies from the acetabulum at revision surgery were taken in patients that previously underwent a THA with IBG. At 28 months, all specimens showed graft incorporation[31].

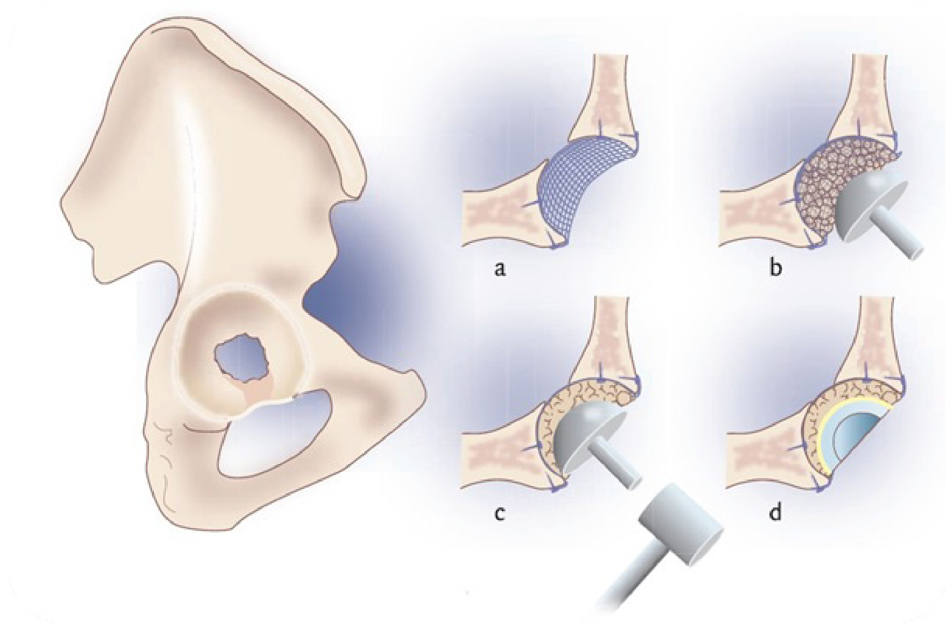

Figure 1. (**a**) A metal mesh is placed to create a contained acetabular defect, fixated with screws. (**b**) The bone chips are placed in the acetabulum on the mesh and impacted. (**c**) The bone chips are compressed layer by layer in the acetabulum with special impactors. (**d**) The bone cement is pressurized into the graft and the cup is then placed in an anatomical position.

1

Revision THA and the Girdlestone load

As mentioned before, patients that are young at primary THA placement, will outlive their prosthesis and face one or multiple revisions. Ong et al. showed that younger patients undergoing primary THA surgery had a higher risk of revision[34]. They also showed that patients undergoing a revision THA were approximately five times more likely to undergo a subsequent re-revision compared with patients undergoing primary THA surgery. The Dutch arthroplasty register (LROI, Annual report 2021) showed the highest cumulative 12-year revision percentage (8.0%, 95% CI 7.4-8.9) in patients below 50 years of age at primary THA, compared to the higher age groups (Figure 2)[8]. These problems in the young patient group are accompanied by a socioeconomic burden as well. Due to the complexity of revision surgeries, higher hospital costs, longer length of stay, longer operative time and more complications are encountered compared to primary procedures[35].

Therefore, the importance of the outcomes of revision surgeries, especially in younger patients, should be emphasized as well. Revision THA surgery is more complicated and challenging than primary THA surgery due to more extensive acetabular and/or femoral defects usually caused by osteolysis and loosening of the prosthesis. During primary THA placement in a young patient, one should already take into account that future revisions will follow and careful management of bone loss is mandatory. The future revisions are facilitated by choosing a biological reconstruction technique already at the primary THA, which can limit further bone loss and ideally even promote new bone formation. To evaluate the true value of techniques and implants that are used during THA surgery, both the primary and revision long-term outcomes should be described. It should be addressed that there is a paucity of studies in literature that describe both the primary and subsequent revision outcomes in this young patient group.

In some extreme revision cases and despite all efforts, unfortunately it is not possible to reimplant a prosthesis. An example is a persistent infection not responding to adequate antibiotic treatment or extreme bone loss. These patients will undergo a resection arthroplasty and a Girdlestone situation is created. This procedure is considered as a last resort and sometimes effective for pain relief. However, a Girdlestone procedure causes shortening of the affected leg, inability to walk unassisted and is associated with a serious decrease in mobility and functionality. This procedure has a great impact on the quality of a patients' life. The term Girdlestone-load is introduced in this thesis to describe the proportion of patients within a study group that did not receive a prosthesis at revision surgery and suffer from a permanent Girdlestone.

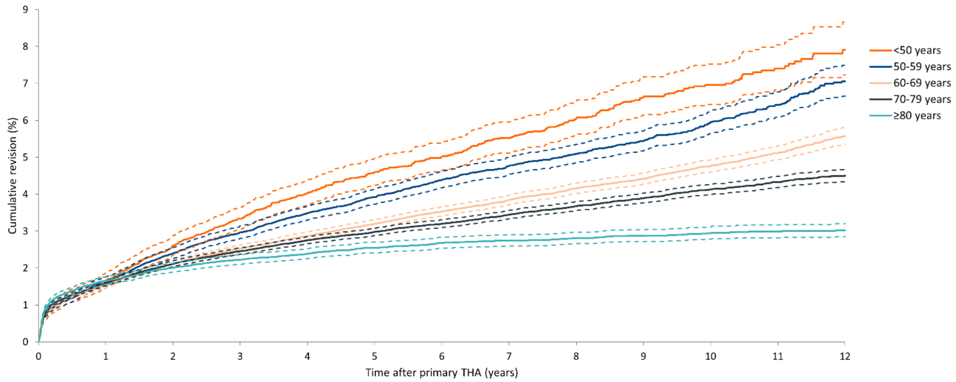

Figure 2. Cumulative revision percentage of total hip arthroplasties by age category in the Netherlands in 2007-2020 (n=351,937) (LROI Report 2-21, available from https://www.lroi-report.nl/app/uploads/2022/02/PDF-LROI-annual-report-2021.pdf)

OUTLINE OF THIS THESIS

At Radboudumc, all patients with end-stage hip osteoarthritis, always receive a cemented THA, also the younger patients. If there are any bone defects present, acetabular or femoral, these are reconstructed using impaction bone grafting and if needed, a metal mesh is used to reconstruct segmental defects.

The aim of this thesis is to evaluate the long-term results of cemented THA in young patients under 50 years, with or without IBG at Radboudumc. In addition, the second aim is to evaluate the outcomes of the revision THA surgeries within the original study cohort of THA in patients under 50 years and to report the Girdlestone-load in this young and challenging patient group.

Topics addressed is this thesis

Chapter 2 describes the history and evolution of cemented THA and impaction bone grafting. The specific surgical technique is described as well as our clinical experience and initial results of IBG. Several other forms of reconstruction are described and compared to the IBG technique.

In **Chapter 3**, the long-term results of primary THA in patients suffering from secondary osteoarthritis due to developmental dysplasia of the hip (DDH) are presented. DDH forms one of the main causes of secondary osteoarthritis in young patients and is a challenge for the orthopaedic surgeon because of the acetabular defects. We describe a cohort of patients that received a primary THA with a minimum follow-up of 15 years.

In literature, studies report inferior results in revision THA with the use of lateral rim meshes in combination with IBG in the presence of acetabular defects. In **Chapter 4** we studied patients that received a primary THA with IBG combined with a lateral rim mesh and compared them to patients that did not need a lateral rim mesh for segmental defect reconstruction. All patients were 50 years or younger at their primary THA.

In **Chapter 5**, we determined the outcomes of more than 1000 primary THA in patients under the age of 50 years in one of the larger series on this topic worldwide. There is little data available on the outcome of revision procedures in these young patients, especially from the same study cohort. In this chapter we emphasize the importance to describe the results of subsequent revision THA surgeries. In addition, we introduce the term the Girdlestone-load in this study to define the definitive failure of the treatment with a total hip.

In **Chapter 6**, we describe the results of a patient group younger than 30 years at primary THA. In this study, we focus on the outcomes of the (multiple) revision surgeries as well and report the Girdlestone-load in these extremely young patients.

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CHAPTER 2

The biological approach in acetabular revision surgery: impaction bone grafting and a cemented cup

E. Colo, W.H.C. Rijnen, B.W. Schreurs

Hip Int 2015;25(4):361-79

2

ABSTRACT

Acetabular impaction bone grafting (IBG) in combination with a cemented cup in revision total hip arthroplasty (THA) is a proven and well-recognized technique which has been used in clinical practice for more than 35 years. Nowadays, with cemented prostheses tending to lose a larger part of the THA market every year in primary and revision cases, and many young surgeons being only trained in implanting uncemented prostheses, this technique is considered by many as technically demanding and time consuming, making its use less appealing. Despite this image and many new innovative techniques using uncemented implants in acetabular revisions over the last 25 years, IBG with a cemented cup is still one of the few techniques that really can reconstitute bone and respects human biology. In this era of many biologically-based breakthroughs in medicine, it is hard to explain that the solution of most orthopaedic surgeons for the extensive bone defects as frequently seen during acetabular revision surgery, consists of implanting bigger and larger metal implants. This review aims to put the IBG method into a historical perspective, to describe the surgical technique and present the clinical results.

INTRODUCTION

IBG during THA on the acetabular side was initially performed in 1979 by Dr. Slooff in Nijmegen, the Netherlands. In that time, it became clear that re-cementation of failed cups, had inferior outcomes. Especially in cases with extensive defects, Dr. Slooff realized that the grip of the cement on the diminished acetabular bone stock was limited. He became inspired by the techniques used in acetabular protrusion[1,2]. In these techniques non-compressed chips or wafers of bone were used, and contact between the cement and bone grafts was limited. In contrast, Slooff decided to apply impaction of the bone grafts with a socket trial prosthesis. Initially, he used autograft bone chips obtained from the patient's iliac crest. In the early revision cases, patient's bone from the iliac crest was harvested first, which was afterwards stored in the refrigerator. After an in-hospital recovery of 2 weeks, the THA revision procedure was performed. Postoperative care included bed rest for 6 weeks, followed by mobilization with partial weight-bearing. After 3 months, patients were allowed to full weight-bearing. The first early outcomes of this clinical experience were reported in 1984[3].

Initially, a metal mesh was inserted on top of the bone graft to prevent extensive cement-graft contact, as it was thought that the cement could be harmful for the incorporation of the bone graft[4]. In case of a medial wall segmental bone defect, a medial wall mesh was used to cover the bone defect and the bone graft was impacted on this mesh and a second mesh was placed on top of the graft. In these cases the graft was contained as a sandwich between the two meshes. Impaction of the bone graft was done with acetabular trial prostheses and the final cup was chosen one size smaller than the last trial cup. The size of the bone chips were crouton-like. Thus from the beginning on, by serendipity, large chips made by hand with a rongeur were used. These early reconstructions were done with high viscous bone cement, that was pressurized into the acetabulum and subsequently a polyethylene cup was inserted.

In 1988, a shadow was casted on cemented THA after the publication of a critical paper of Hungerford et al[4]. Loosening of the prosthesis and osteolysis were contributed to the cement. However, in retrospect, the actual reason for these problems were most likely the polyethylene particles caused by wear due to the poor quality of the polyethylene during that time. The discrepancy between our clinical results and the suggested disadvantages of bone cement, especially in combination with bone grafts, caused the Nijmegen group to conduct mechanical and histological experiments, studying the behavior of these bone grafts in combination with cement[5]. Both mechanical tests were done in a goat model, as well as *in vivo* animal experiments. Cemented THAs were implanted in the goats with IBG on the acetabular side. These histological data showed that the bone grafts, despite the contact with the bone cement, did incorporate. In addition, we started to take biopsies at revision

THA surgery in patients who had a previous reconstruction using the IBG technique with a cemented cup. The revisions were done for various reasons, including aseptic loosening. The results of this study demonstrated that these grafts completely incorporate into a new trabecular structure[6]. Van der Donk et al demonstrated comparable outcomes in a larger group of patients[7]. The process of incorporation of these bone grafts was also studied by Heekin et al. Based on a human cadaveric study, they showed that the graft revascularized and gradually incorporated[8].

At that time we also conducted *in vitro* mechanical studies in human pelvic cadavers and in realistic acetabular models. One of the aspects we studied was the effect of impaction technique on the stability of the reconstructions[9]. From the beginning on we have always impacted these grafts vigorously, using a metal mallet and a metal hammer. Initially we used trial cups, later on special metal impactors, which later became available as the X-Change Revision impaction system (Stryker Howmedica, Newbury, UK). Some surgeons claimed to apply IBG by compressing the bone grafts with the reversed reaming technique. However, we felt that this was a completely different concept than the IBG technique we promoted, although this can be a sensible technique in some cases. In a relatively simple experiment we were able show that this technique leads to inferior cup stability relative to cups that had been reconstructed using our standard technique[9]. This difference was already obvious in a contained defect, so even larger differences can be expected in more extensive defects. We were also able to demonstrate that, as expected, more migration was observed in larger defects using an artificial model with a segmental superolateral defect that was reconstructed with a metal mesh.

A serious reason for concern was the fact that surgeons used all kinds of bone chip sizes. The question which sizes should be used for adequate cup stability was also investigated by other research groups[10,11]. The general findings were that larger bone chips (8-12 mm) produced a better cup stability in all cases, so smaller chips (2-4 mm) were not recommended for the acetabular revisions[9]. However, mixes of large and small chips also create an adequate stability, but small chips on its own are not recommended. This also might explain some of the less satisfying outcomes that have been published about this technique[12, 13]. It was also shown that it is essential to remove all the soft tissue debris and cartilage remnants from the head as these will hamper cup stability after IBG, as well as bone ingrowth[7, 14, 15].

We further investigated washing of the bone chips prior to IBG[10, 16, 17]. A theoretical advantage of washing is that it clears out cells, tissues and fat, possibly reducing the chance of infection and removing foreign protein structures that may activate the host immune system. Theoretical disadvantages of washing the grafts are that biologically active factors in the bone could get lost, which are needed for new bone formation and bone ingrowth. However, we have never been able to prove this hypothesis but based on mechanical tests, washed chips seem to improve stability[16, 18].

Urist et al introduced the use of bone morphogenetic proteins (BMPs) in the field of orthopaedic surgery and the application of BMPs has become more popular[19]. These proteins may be used in revision THA to improve incorporation of bone grafts and companies started to advocate these often very expensive products in combination with bone grafts in demanding revision procedures. Unfortunately, the effects were not as satisfactory as expected and 1 study even showed possible negative effects of BMP use in combination with femoral IBG[20]. The (human) cases treated with a combination of IBG and BMPs showed a tendency to more failures. On the other hand, in retrospect the BMPs might have been overdosed[20]. At our institution, we have performed an animal experiment in bone chambers on goats in realistic acetabular reconstructions. Initially some effect was seen, but at 12 weeks, there was no significant difference in incorporation[21, 22]. In our clinical practice we have never applied this product.

In addition, other biomaterials have been introduced to overcome the problems of the availability of human bone and risks of virus transfer with the use of allografts. Bolder et al concluded that especially in the reconstruction of large bone defects, tricalciumphosphate/hydroxyapatite particles seem an attractive bone graft extender[23]. Several other research groups have investigated the use of biomaterials in revision THA and some of them found successful results, even after a longer follow-up[24]. We also investigated if titanium particles could be used in combination with bone chips for impaction, or even as a complete bone graft substitute in combination with a cemented cup[25-27]. From a mechanical point of view these impacted titanium particles had a superior primary stability in synthetic acetabular models compared with bone particles[25]. Also, in a bone chamber model, incorporation of these impacted titanium chips was rapid, relatively complete and well predictable. Even in a realistic acetabular model and *in vivo* experiments in goats, the outcomes appeared promising[26, 27]. However, before clinical application, more clinical research has to be performed. A relatively new concept is the combination of metal (mostly titanium) augments with acetabular IBG and a cemented cup. There are indications that this method can provide a stable platform for IBG and enhance graft incorporation[28]. However, long-term clinical data are mandatory before introducing this technique on a larger scale.

Surgical technique

We use a posterolateral approach in all cases and after removal of the failed component, interface tissue is sent for cultures and, if indicated, frozen sections are sent to rule out infection. The acetabulum is reamed to create a bleeding bone bed. In case of superolateral segmental wall defects, metal meshes fixated with screws are used to reconstruct the wall of the acetabulum (Fig. 1). These meshes are fixed on the outer side of the acetabulum and the gluteal musculature can be lifted from the pelvic bone to create an optimal exposure. If needed, medial wall meshes are used as well.

Next, sclerotic areas are perforated by multiple 2 mm drill holes, to optimize vascularization and incorporation of the graft and cement. A fresh-frozen non-irradiated femoral head from the bone bank is obtained and morselized with a rongeur to create cancellous bone chips with a diameter of 0.7-1.0 cm. Then, extensive lavage of the acetabulum is performed and the grafts are impacted with metal impactors and a mallet (X-Change Revision impaction System; Stryker Howmedica, Newbury, UK). The original center of rotation is reconstructed at the level of the transverse ligament and the defect is reconstructed layer by layer until it is restored. Subsequently, vacuum-mixed antibiotic-loaded bone cement is pressurized into the acetabulum and on the impacted grafts with the use of a seal. The last impactor is at least 2 mm larger than the proposed acetabular prosthesis, to create a sufficient cement mantle.

Postoperatively, all patients receive thrombosis prophylaxis with low-molecular weight heparin during 6 weeks and non-steroidal anti-inflammatory drugs during 7 days to prevent heterotopic ossifications. Patients are mobilized under the supervision of a physical therapist and are allowed to toe-touch weight bear during the first 6 weeks, followed by another 6 weeks of 50% weight-bearing. At 3 months postoperatively, full weight-bearing is allowed. In smaller defects patients are allowed full weight-bearing after 6 weeks.

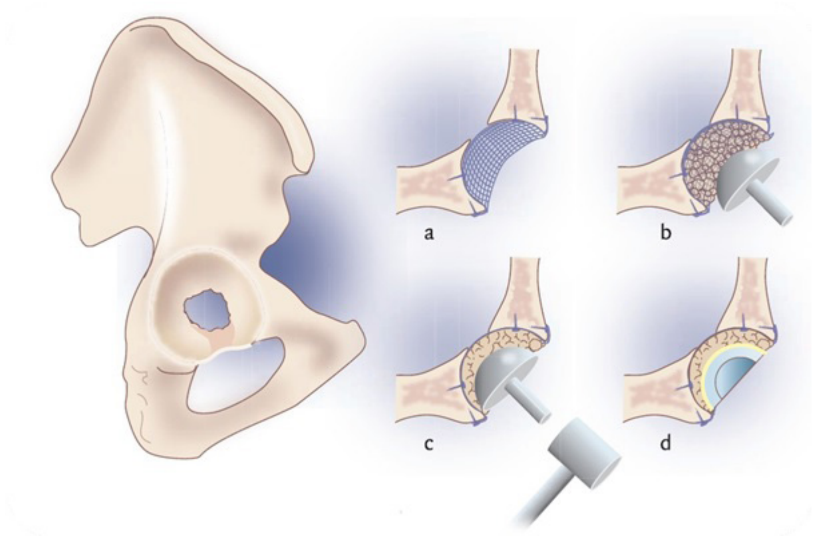

Figure 1. a) A metal mesh is placed to close the acetabular defect, fixated with screws. **b**) The allograft bone chips are placed over the mesh and impacted. **c**) The bone chips are compressed layer by layer in the acetabulum. **d**) The bone cement is pressurised into the graft and the cup is placed in an anatomical position

OUR CLINICAL EXPERIENCE

After the first results from our institution by Slooff et al in 1984, we have published several studies on the clinical outcomes of acetabular revisions with IBG[3]. These first results studied the use of a cemented cup with IBG in patients with protrusion of the acetabulum. This historical study group consisted of 43 hips (22 revisions) and showed union of the grafts in all cases and no further revisions at a mean follow-up of 2 years[3]. A later update of this study showed a survival of 95% at a mean of 5.7 years[29]. These initial results were very promising and longer-term outcomes soon followed. In a study with 10-15 years followup, we presented the results of 62 acetabular revisions that were performed between 1979 and 1986[30]. A 93% survival with rerevision for any reason as the endpoint at 10 years was found and when the septic loosenings were excluded, a 96% survival at 10 years was found. At this time, 5 acetabular re-revisions were performed. In all hips (n = 3) revised for aseptic loosening, the radiolucent lines were visible within the first 2 years postoperatively. In 2009, the 20-25 year data became available and 13 out of 62 cups were rerevised at follow-up[31]. Most hips showed a stable radiological appearance with uniform radiodensity of both graft and host bone. Radiological loosening was seen in four non-rerevised hips, of which 3 patients died during follow-up (at 7, 13 and 14 years after surgery), but had no rerevision as they only had mild symptoms. The surviving patient with a radiologically loose cup also had only minor symptoms and because of this, a rerevision was not performed. The survival rate with rerevision for any reason as the end point was 75% at 20 years and with rerevision for aseptic loosening it was 87% at 20 years. In another cohort from our institution, Van Egmond et al investigated the prosthesis survival and pain-free function in patients with extensive acetabular defects after acetabular revision with IBG and a cemented cup at a minimum follow-up of 4 years (mean 9.7 years)[32]. In total, 27 acetabular revisions were analyzed, of which 25 hips had an AAOS type III defect and 2 hips with a type IV defect. A total of 3 hips failed and underwent rerevision or removal of the implant (1 septic loosening, 1 aseptic loosening and 1 unstable cup). The cup survival at 10 years with endpoint rerevision for any reason was 88% and for aseptic loosening 95% at 10 years. The patient reported outcome measures (PROMs) were also collected and showed improved clinical scores in the surviving patients. This study showed that even in hips with extensive acetabular defects, IBG in combination with a cemented cup provides favorable midterm survival rates and clinical function. However, in these cases with an extensive acetabular defect, the postoperative weight-bearing protocol is of importance and the surgical skills using this technique are demanding and require experience. Acetabular revision with IBG and cemented cups also showed acceptable results in patients with rheumatoid arthritis at an average of 7.5 years (minimum 3 years) postoperatively[33]. These patients usually have a poor bone quality and in combination with loss of bone stock, the revision procedure can consequently be very challenging. In 35 revisions, 6 re-revisions were performed. In total 3 performed because of aseptic loosening at 2.6, 3.5 and 3.8 years after surgery. Survival rates of the acetabular component with endpoint rerevision for any reason were 85% at 8 years, and 90% with endpoint rerevision for aseptic loosening at 8 years. A follow-up report on this study showed 2 additional re-revisions, with an 80% survival at 12 years with endpoint rerevision for any reason and 85% with endpoint rerevision for aseptic loosening at 12 years[34]. The last challenging group in hip surgery, are the young patients that require THA. In our institution, we conducted multiple studies in both primary and revision THA in this specific patient group[35-37]. These studies showed that IBG in combination with a cemented cup provides good results and satisfying long-term outcomes in young patients. A study of Busch et al reviewed 37 patients that were less than 50 years at time of surgery and consisted of 19 (45%) revision procedures[35].

DISCUSSION

The number of THAs is still widely increasing and as a consequence, revision procedures will rise as well. Additionally, because of improvements in materials of prostheses, an increasing number of THAs are performed in young patients, which form a serious problem in orthopaedic surgery. Revisions in this younger patient group are inevitable due to the fact that these patients will outlive their prosthesis and have a higher activity level and higher demands. The acetabular defects that are present in these surgeries, need to be reconstructed. Nowadays, many surgeons tend to replace the bone defects by larger acetabular components or replacing the bone by metal, which can be detrimental in these cases. In this era, where medicine is focusing on biologically-based treatments, the answer to reconstruct these defects should not be to use simply more metal and certainly not in the younger patients. Suitable biological reconstruction techniques should create a stable situation with good long-term results (Fig. 2). In our opinion, it is therefore important to use a biological method to facilitate these further revisions as well, especially in the younger cases. When a graft is incorporated well and a cup fails for mechanical reasons, we know from our clinical experience, that due to the incorporation of the previous graft, the bone stock situation is improved and will facilitate the subsequent revision. Many of our studies, as well as others, have shown that a large part of the mechanical failures of acetabular revisions occur within the first years postoperatively[34,38,43]. Early migration of the cup might be a risk of applying IBG, as it takes time for the bone, cement and graft to interlock and form a stable construction. Therefore, we are convinced that partial weight-bearing postoperatively after large reconstructions with IBG is important. Only few studies have been conducted that report on the weight-bearing protocol after IBG. Ornstein et al (2003) found no significant differences in migration of the cup between immediate full weight-bearing and partial weight-bearing[49]. However, in this group only 1 patient had an extensive acetabular defect and all other acetabular defects were less extensive. Overall, it is not known what the most optimal postoperative protocol should be, although our histological studies show that during the first weeks and months postoperatively, the bone-graft-cement is remodeling and subject to many changes. Especially in the large reconstructions with meshes, one can image that immediate full weight-bearing might increase the chances of early failure. Of course, the use of IBG has some drawbacks. In contrast to cemented THA without IBG, patients are not allowed to immediate full weight-bearing and are instructed to partial weight-bearing during the first 3 months postoperatively, as it takes some time for the bone graft to become stable, probably by fibrous armoring and later on incorporation[50]. Additionally, there is a certain learning curve involved in applying the IBG technique. It is important that the impaction of the grafts is done vigorously, but carefully. Consequently, it might be unattractive for starting surgeons to start using this technique in larger defects. Moreover, access to a bone bank is necessary to obtain femoral head allografts, which also carries financial implications. Lastly, the operation time is increased by applying the technique. However, in our experience, once familiar with this method, the surgery will only be prolonged within acceptable limits. In our experience, complications in acetabular IBG are not very common. A possible intra-operative complication is an acetabular fracture, which usually does not compromise the success of the surgery, when recognized early and treated adequately. The acetabular defects at revision THA are usually severe, as the bone stock defect has worsened due to osteolysis and migration of the cup. The survival rates of acetabular revisions in the severe grades of defects are inferior compared to smaller defects[32,43]. A survival rate after 7.2 years of 72% with rerevision for aseptic loosening as the endpoint was found by van Haaren et al, using IBG with a cemented cup. However, it needs to be noted that most of these patients had large uncontained defects, even some with pelvic discontinuity. Also, most of their aseptic re-revisions were based on loosening of the acetabular component out of the cement mantle, which is very unusual. Several techniques have been developed to overcome the defects presented at revision THA surgery. As mentioned, von Roth et al found reasonable results with the use of uncemented jumbo cups at 20 years[44]. However, a large portion of the patients had already died at 20 years and no worst-case scenario analysis was performed. Unfortunately, von Roth et al do not report on the quality of the bone stock that was present during revision surgery of the jumbo cup. And even though reasonable results were found, using this technique the defect is just filled with a larger cup, without restoring the acetabular bone stock. Especially in young patients, this can cause serious problems in which there is no bone left for proper reconstruction of the acetabulum. A very recent publication of Te Stroet et al reported the long-term outcomes of 34 acetabular revisions with the use of IBG and cemented cups in patients less than 55 years of age[51]. In total 6 rerevisions were performed, of which 3 for aseptic loosening. The survival rates for rerevision of the acetabular component for any reason at 5, 10 and 15 years were 91%, 87% and 75%, respectively. Survival rates for rerevision for aseptic loosening at 5, 10 and 15 years were 97%, 97% and 84%, respectively. An aspect that has gained more importance and popularity in the past few years, are the patient reported outcome measures (PROMs). It is known that the clinical outcomes of

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revision THA are less satisfying than those in primary THA, however there still exists a discrepancy between the patient's expectations and the final functional outcome scores after revision THA[45,52]. Clinicians should be aware of this problem and prepare and educate patients about the impact and outcomes of this procedure.

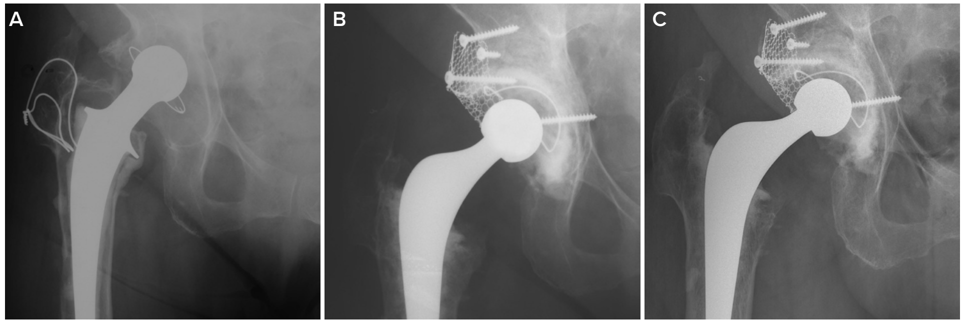

Figure 2. Radiographs of a patient that suffered from post-traumatic osteoarthritis and received a THA at another institution at the age of 45. **A**) 16 years postoperatively the cup had migrated cranially and appeared loose. **B**) An immediate postoperative radiograph shows the revision that was performed with IBG, a mesh and a cemented cup. Intraoperatively the cup was completely loose and there was a large segmental and cranial defect. **C**) A radiograph 20 years post-revision shows a good position of the acetabular component with good incorporation of the graft and without any signs of loosening.

CONCLUSION

The outcomes of acetabular reconstructions with the use of IBG and cemented acetabular components after revision surgery are satisfying and encourage us to continue the use of this technique. In our belief, the optimal way to reconstruct the defects, is to use the most biological way possible by trying to restore and improve the bone stock with the use of bone grafts which will also form a solid foundation for further revisions. This rationale has led us to applying IBG with a cemented cup in many patients, and certainly in those patients that are younger than 55 years at their revision surgery.

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CHAPTER 3

Satisfying results of primary hip arthroplasty in patients with hip dysplasia at a mean follow-up of 20 years

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ABSTRACT

Background

Developmental dysplasia of the hip (DDH) is a common cause of secondary osteoarthritis (OA) in younger patients, and when end-stage OA develops, a THA can provide a solution. Different options have been developed to reconstruct these defects, one of which is impaction bone grafting combined with a cemented cup. To determine the true value of a specific technique, it is important to evaluate patients at a long-term follow-up. As there are no long-term studies, to our knowledge, on THA in patients with DDH using impaction bone grafting with a cemented cup, we present the results of this technique at a mean of 15 years in patients with previous DDH.

Questions/purposes

We wished to determine (1) the long-term probability of cup revision at a minimum follow-up of 15 years for cemented acetabular impaction bone grafting in patients with DDH; (2) the radiographic appearance of the bone graft and radiographic signs of implant loosening; and (3) the complications and pre- and postoperative Harris hip scores with cemented THA combined with impaction bone grafting in patients with previous DDH.

Methods

Between January 1984 and December 1995 we performed 28 acetabular impaction bone grafting procedures for secondary OA believed to be caused by DDH in 22 patients; four patients died before 15 years, leaving 24 hips in 18 patients for retrospective analysis at a minimum of 15 years (mean, 20 years; range, 16–29 years). The diagnosis of DDH was made according to preoperative radiographs and intraoperative findings. All grades of dysplasia were included; five patients had Crowe Group I, eight had Group II, nine had Group III, and two had Group IV DDH. No patients were lost to follow-up. In all cases the acetabular defects were combined cavitary and segmental. Owing to the high number of deaths, we performed a competing-risk analysis to determine the probability of cup revision surgery.

Results

The competing-risk analysis showed cumulative incidences at 15 and 20 years, with endpoint revision for any reason of 7% (95% CI, 0%–17%), whereas this was 4% (95% CI, 0%–11%) with endpoint revision of the cup for aseptic loosening. Three revision surgeries were performed. Two cup revisions were performed for aseptic loosening at 12 and 26 years. Another cup revision was performed owing to sciatic nerve problems at 2 years. A stable radiographic appearance of the graft was seen in 19 of the 25 unrevised hips. Four hips showed acetabular radiolucent lines and two showed acetabular osteolysis. None of the unrevised cups showed migration or radiographic failure. Postoperative complications included a pulmonary embolus and a superficial wound infection. The Harris hip score improved from 37 (range, 9–72) preoperatively to 83 (range, 42–99) at latest follow-up.

Conclusions

Cemented primary THA with the use of impaction bone grafting shows satisfying long-term results in patients with previous DDH. For future research it is important to evaluate this technique in a larger cohort with a long-term follow-up. Other techniques also should be evaluated at long-term follow-up to be able to compare different techniques in this important and specific patient group.

Level of Evidence

Level IV, therapeutic study.

3

INTRODUCTION

Developmental dysplasia of the hip (DDH) is a common cause of secondary osteoarthritis (OA) in younger patients, and when end-stage OA develops, THA is a good surgical option[1]. However, THA in this patient group is a demanding procedure owing to the underlying acetabular bone stock defects, which hamper anatomic reconstruction. Therefore, these bone defects and the often-young age of these patients result in higher failure rates of their THAs relative to patients with primary OA[2,3]. One option to try to improve cup survivorship in this setting is impaction bone grafting combined with a cemented cup. This technique was developed by Slooff and was used primarily in hips with protrusio acetabuli and also for revision THA[4-7]. Slooff observed union of all grafts at an average follow-up of 2 years after primary THA in patients with protrusion[7]. With revision THA, using the same technique, Schreurs et al reported an 87% survival rate for the cup at 20 years with an endpoint of aseptic loosening[4]. We thought this technique might be an option in primary THA in patients with DDH to repair acetabular defects and possibly provide a durable solution in these difficult primary THAs. To the best of our knowledge, there are no studies that report the long-term outcomes of this technique in primary THA for patients with DDH. However, outcomes of other reconstruction methods have been reported at long-term follow-up for primary THA in this patient group[8-13]. Abdel et al reported 66% survival at 20 years in patients with DDH and uncemented cups, who underwent reconstruction with a bulk femoral head autograft[8]. Gill et al evaluated the use of reinforcement rings in 33 patients with DDH[9]. They reported nine (10%) revisions at a mean follow-up of 11 years, of which six were attributable to infection. Comparison of our technique with these other techniques is important to be able to provide the most optimal care for this patient group. Specifically, we sought to determine (1) the long-term probability of cup revision at a minimum follow-up of 15 years of cemented acetabular impaction bone grafting in patients with DDH; (2) the radiographic appearance of the bone graft and radiographic signs of implant loosening at long-term follow-up; and (3) the complications and pre- and postoperative Harris hip scores of cemented THA combined with impaction bone grafting in patients with previous DDH. In a previous report Somford et al presented the results of 28 THAs with a minimum follow-up of 10 years[14].

PATIENTS AND METHODS

We retrospectively studied all patients with secondary OA resulting from DDH, and who received a primary THA in one tertiary care institution between January 1984 and December 1995. We have always used cemented THAs, and in the case of acetabular defects, reconstruction with the use of impaction bone grafting and, if needed, a metal mesh. No other reconstruction techniques were used. All reconstructions were performed with impacted morselized bone grafts combined with a cemented THA. The original series consisted of 28 hips in 22 patients (Table 1); four patients died (four hips) before postoperative year 15; their data are included. Subsequently, we reviewed 24 hips in 18 patients with a minimum follow-up of 15 years (mean, 20 years; range, 16–29 years). Two patients (three hips) died at 16, 16, and 20 years postoperatively. In all cases, death was unrelated to the hip surgery and no reoperations had been performed at the time of death. No patients were lost to follow-up. The study group consisted of 17 females and one male with a mean age at surgery of 48 years (range, 26–74 years). Thirteen (54%) operations were performed in patients younger than 50 years and 22 (92%) were done in patients younger than 60 years. Six patients had bilateral THAs, and 12 procedures were right-sided. Two patients (four hips) were unable to visit the outpatient clinic and radiographs were not taken owing to the patients' age or poor health status, which was unrelated to the hip surgery. All the other patients who had not undergone revision surgery or had not died were seen in the outpatient clinic during the past 5 years. However, these patients were contacted and the questionnaires were completed by phone. The latest radiographic follow-ups of these patients were at 12, 13, 16, and 16 years postoperatively. In all cases the acetabular defects were combined cavitary and segmental (Type 3) according to the American Academy of Orthopaedic Surgeons classification[15]. The severity of dysplasia was graded according to the Crowe et al and Eftekhar classifications[16,17]. Five hips had Crowe Group I, eight had Group II, nine had Group III, and two had Group IV dysplasia. For the Eftekhar classification, seven hips were Type A, 12 were Type B, and five were Type C. A detailed description of the surgical technique was described previously[14]. In 23 hips an autograft from the femoral head was used and a combination of an auto- and allograft, obtained from the bone bank, was used in one. Nineteen Elite cups (DePuy, Leeds, UK) and nine Müller cups (Sulzer, Winterthur, Switzerland) were inserted. During that time, postoperative management consisted of systemic antibiotics for 5 days, indomethacin for 5 days for prevention of heterotopic ossifications, and anticoagulation for 3 months. Passive movement was started at 24 hours. Partial weightbearing was started at 3 weeks in five patients and at 6 weeks in 19 patients. Full weightbearing was allowed at 3 months postoperatively. For clinical evaluation, the pre- and postoperative Harris hip score was used[18]. Radiographic follow-up was done using AP and lateral views of the hip and was scored by two of the authors (EC, BWS) and classified on a consensus basis. The following parameters were scored: graft incorporation, height of the center of rotation, radiolucent lines (> 2 mm wide), or osteolysis in one of the three zones of DeLee and Charnley, and migration of the cup[19]. Radiographic failure was defined as the presence of radiolucent lines in the three zones of DeLee and Charnley or migration of 5 mm or more in any direction. Competing-risk analyses were performed to determine the probability of revision of the acetabular component in the presence of the competing event of death with endpoints of revision for any reason and aseptic loosening.

Table 1. Patient details

Variable	Number of hips (number of patients)	Results
Number of procedures and patients	28 (22)	No patients lost to followup
Deaths	7 (6)	Deaths at 3, 6, 10, 13, 16, 16 and 20 years without reoperation
Available with minimum follow-up of 15 years	24 (18)	4 cases died before postoperative year 15
Revisions	3 (3)	One cup revision due to sciatic nerve problems at 2 years One total hip revision due to aseptic loosening at 12 years One cup revision due to aseptic loosening at 26 years

RESULTS

The cumulative failure rate of the acetabular component, with use of the competing-risk analysis, was 7% (95% CI, 0%–17%) with the endpoint revision for any reason at 15 and 20 years, and 4% (95% CI, 0%–11%) at 15 and 20 years with the endpoint aseptic loosening (Table 2). One additional revision has been performed since the initial report by Somford et al[14]. Thus, in total, three revisions were performed during follow-up. The first patient to undergo revision surgery had Crowe Group III dysplasia and had sciatic nerve palsy develop postoperatively after reconstruction of a high hip center. A cup revision was performed to recreate a higher hip center to release the sciatic nerve. The second patient (with Crowe Group I dysplasia) showed progressive radiolucent lines in all three acetabular zones, which led to revision resulting from aseptic loosening. Both components were revised 12 years after the primary procedure. The last patient (with Crowe Group III dysplasia) showed progressive migration of the cup, and cup revision owing to aseptic loosening was performed 26 years after the primary procedure. A stable radiographic appearance of the graft and cup was seen in 19 of the 25 unrevised hips. Four hips showed radiolucent lines, three hips in acetabular Zone III (Fig. 1) of which two were progressive. The other hip had progressive radiolucency in Zones I and II. Two hips showed acetabular osteolysis; in one hip (follow-up, 18 years), this previously was scored as a radiolucent line but progressed to an osteolytic area. The other hip (follow-up, 29 years) showed osteolysis in Zone III, which remained stable during the past 5 years. None of the unrevised cups showed migration or radiographic failure. Additionally, none of the femoral components showed radiographic loosening. The mean height of the center of rotation was 31 mm (range, 19–50 mm), of which three hips had a center of rotation of 35 mm or greater.

Table 2. Cumulative failure rates

Endpoint	Followup (years)	Survival percentage (95% CI)
Revision for any reason	15	7% (0%-17%)
	20	7% (0%-17%)
Revision for aseptic loosening	15	4% (0%-11%)
	20	4% (0%-11%)

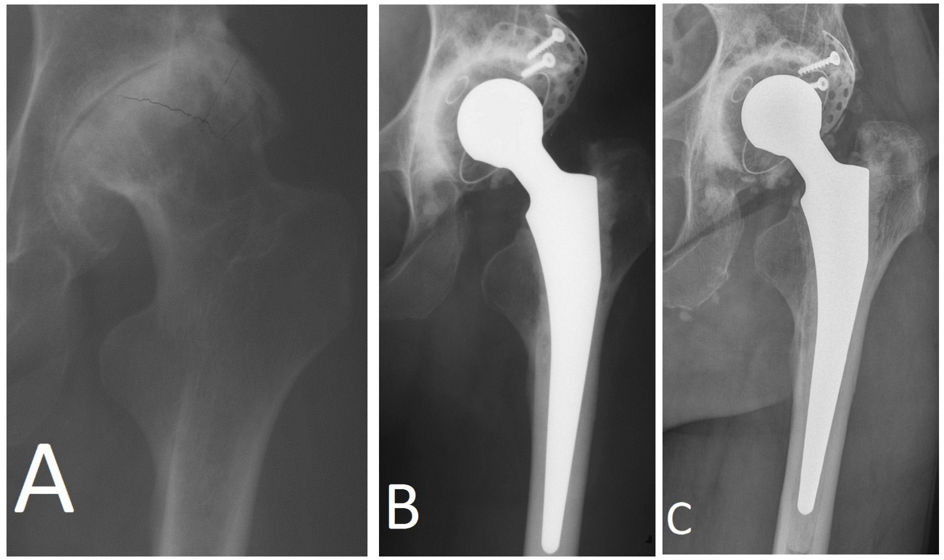

Figure 1A-C. (**A**) A preoperative radiograph, (**B**) immediate postoperative radiograph after a THA with a cemented cup, lateral metal mesh, and impaction bone grafting, and (**C**) after followup of 25 years are shown. The THA prosthesis is still in situ and the patient, a 49- year-old woman with Crowe Group II dysplasia on the left side, is without complaints and has good function. A radiolucency is visible in acetabular Zone 3, but has remained stable during the past 10 years.

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Table 3. Outcomes of different reconstruction methods in primary THA in patients with previous DDH.

Study	Number of hips (patients)	Classification of dysplasia	Mean follow-up, years (range)	Fixation method	Reconstruction method	Number and reasons of acetabular component revisions	Acetabular component survival	Radiographic appearance
Gill 1998 [13]	87 (70)	11 Crowe II, 65 Crowe III, 11 Crowe IV	9 (5-15)	Cemented	Reinforcement ring	8 cup revisions: 2 aseptic loosening, 6 septic revisions	n/a	5 cups: definitely loose/ 2 cups: probably loose / 13 cups: possibly loose/ 6 cups: migration / 15 cups: radiolucent lines
Rozkydal 2005 [27]	43 (43)	6 Crowe I, 31 Crowe II, 3 Crowe III, 3 Crowe IV	10 (9-11)	Uncemented	Structural femoral head autograft	No revisions	Any reason: 100% at 10 years, any reason with radiographic loosening: 88% at 10 years	No failures of bone graft. 1 cup: osteolysis / 1 cup: radiolucent line
Chougle 2006 [4]	292 (206)	161 Crowe I, 78 Crowe 2, 27 Crowe III, 26 Crowe IV	16 (2-31)	Cemented	Structural bone grafting in 48 hips	68 aseptic loosening, 4 septic revisions / 4 revisions in the bone grafting group	Aseptic loosening: 63% at 20 years, radiographic failure: 62% at 20 years	16 cups: complete demarcation / bone grafting group: 37 unions of the graft
Eskelinen 2006 [11]	68 (56)	68 high dislocations	12 (9-15)	Uncemented	Bulk femoral head autograft (unknown how many cases)	26 cup revisions: 12 aseptic loosening, 14 failed liners/ wear	Press-fit cup (n=59), any reason: 88% at 10 years, aseptic loosening: 95% at 10 years	1 cup: migration and radiolucent lines / 2 cups: periacetabular osteolysis.
Karachalios 2013 [20]	61 (44)	25 low dislocations, 36 high dislocations	24 (20-32)	Cemented	Cotyloplasty	29 cup revisions: 28 aseptic loosening, 1 dislocation	Aseptic loosening: 56% at 23 years	3 cups radiographic loosening
Abdel 2014 [2]	35 (29)	7 Crowe I, 5 Crowe II, 19 Crowe III, 4 Crowe IV	21 (13-26)	Uncemented	Bulk femoral head autograft	12 cup revisions: 9 shell/ liner revisions, one aseptic loosening, one fracture of liner, one instability	Aseptic loosening: 66% at 20 years	No identifiable resorption of the graft supporting the component

Table 3. Continued.

Study	Number of hips (patients)	Classification of dysplasia	Mean follow-up, years (range)	Fixation method	Reconstruction method	Number and reasons of acetabular component revisions	Acetabular component survival	Radiographic appearance
Iwase 2016 [18]	40 (38)	13 Crowe I, 15 Crowe II, 11 Crowe III, 1 Crowe IV	8 (3-10)	Cemented	Impaction bone grafting with a metal mesh	1 cup revision: septic revision	Any reason: 100% at 8 years, aseptic loosening: 100% at 8 years	No radiolucent lines or loosening
Current study	24 (18)	5 Crowe I, 8 Crowe II, 9 Crowe III, 2 Crowe IV	20 (16-29)	Cemented	Impaction bone grafting	3 cup revisions: 1 femoral nerve palsy, 2 aseptic loosening	Cumulative incidence: any reason: 7% at 20 years, aseptic loosening: 4% at 20 years	4 cups: radiolucent lines / 2 cups: osteolysis

DISCUSSION

Secondary OA of the hip attributable to DDH is a common indication for THA, especially in younger patients[1]. However, this specific patient group is challenging owing to the acetabular defects that usually come along with the dysplasia. Numerous studies have reported reconstruction methods for acetabular defects using various operative techniques[20-24]. Comparisons with other techniques and the presence of long-term follow-up reports are important to evaluate the durability of a technique or implant[18,23-26]. To the best of our knowledge, there are no other studies presenting 20-year results of this technique in patients with DDH. Our study showed a 7% probability of cup revision surgery with revision for any reason as the endpoint at 15 years and 20 years in patients with THA after previous DDH. A previous study showed a survival of 96% at 10 years with revision for any reason as the endpoint[14]. Limitations of the current study include the small number of patients and various grades of dysplasia were included, which could cause bias as the number of hips with high grades of dysplasia is low which makes it less reliable to draw conclusions for patients with severely dysplastic hips. Although the number of patients with severely affected hips is low, we decided to include all patients during this period. In addition, two patients (four hips) were not able to visit the outpatient clinic or have their radiographs taken. However, we contacted these patients and obtained information regarding their hip status. All other patients were seen in the outpatient clinic during the past 5 years. Finally, in some cases, the radiographic assessment can be hampered by the reconstruction material, cement, and prosthesis. We tried to minimalize this assessment bias by reviewing all subsequent radiographs of each patient and discussing the difficult radiographs until a consensus was reached. Several studies on THA in patients with previous DDH have been reported, using different reconstruction methods (Table 3)[8,9,11,25-28]. However, to our knowledge, there are no studies using cemented cups with impaction bone grafting reporting a minimum follow-up of 15 years. There are other study groups who have reported reasonable results for uncemented implants with the use of impaction bone grafting[29-32]. Lee and Nam reported a satisfying 12-year survival rate of 96% with uncemented cups and allograft impaction bone grafting in revision THA[29]. However, these studies did not stratify for the diagnosis of DDH. We have performed only one additional revision since the previous report by Somford et al, and that revision was 26 years after the primary THA and attributable to aseptic loosening[14]. The first revision occurred after 2 years in a patient with a sciatic nerve palsy. A cup revision with more-proximal placement of the cup was performed to release the sciatic nerve. It is a known problem that patients with THA with high grades of dysplasia are at risk for sciatic nerve problems owing to a change in the height of the center of rotation[31,33]. We now shorten the femur in these patients to avoid lengthening greater than 3 cm and subsequently reduce the risk of neurologic palsies[34,35]. A rationale behind the use of impaction bone grafting is that it possibly can improve the bone stock and therefore future revisions may be facilitated by the graft used at primary THA; however, future research will need to determine to what degree this might be true. In the current study, there were few revisions and no comparison group, therefore it is not possible to comment on this potentially important endpoint. Gill et al reported a high rate of cups that showed signs of radiographic loosening[9]. Iwase et al applied impaction bone grafting combined with cemented cups and a metal mesh and did not observe radiolucent lines or loosening of the cup in their patients (Table 3)[25]. In total in our patients, four hips showed radiolucent lines in one or two acetabular zones. However, none of these hips showed radiolucent lines in all three zones. Additionally, even after a follow-up of 15 years or more these hips showed no signs of migration or changes in cup position, which makes complications or loosening in the near future less likely[36]. Another two hips showed osteolysis around the cup and, although in one hip the osteolysis remained stable for the past 5 years, these patients need to be monitored closely for further progression of the osteolysis. Regarding clinical outcomes, the Harris hip score at latest follow-up improved compared with the preoperative score and is acceptable after such a long follow-up. Compared with the report by Somford et al, the Harris hip score remained consistent and satisfactory with time[14]. Abdel et al and Eskelinen et al reported comparable pre- and postoperative Harris hip outcome scores with the use of bulk femoral head autografts[8,28]. We found satisfactory long-term results of THA combined with impaction bone grafting and a cemented cup in patients with previous developmental dysplasia. Even after a mean follow-up of 20 years, the probability of revision surgery remains 7% and no radiographic failures were detected. Although in our study, this technique showed promising results, studies evaluating this technique in independent centers with larger cohorts are necessary to evaluate its true value in patients with DDH. In addition, other techniques used for these patients should be reported, with large cohorts and longer follow-up.

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CHAPTER 4

Lateral rim mesh in primary total hip arthroplasty: A suitable option to reconstruct segmental acetabular bone defects in young patients?

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ABSTRACT

Aims

The aim of this study was to analyze the effect of a lateral rim mesh on the survival of primary total hip arthroplasty (THA) in young patients, aged 50 years or younger.

Patients and Methods

We compared a study group of 235 patients (257 hips) who received a primary THA with the use of impaction bone grafting (IBG) with an additional lateral rim mesh with a group of 306 patients (343 hips) who received IBG in the absence of a lateral rim mesh during the same period from 1988 to 2015. In the mesh group, there were 74 male and 183 female patients, with a mean age of 35 years (13 to 50). In the no-mesh group, there were 173 male and 170 female patients, with a mean age of 38 years (12.6 to 50). Cox regression analyses were performed to study the effect of a lateral rim mesh on acetabular component survival. Kaplan–Meier analyses with 95% confidence intervals (CIs) were performed to estimate the survival of the acetabular implant.

Results

The hazard ratio for the use of lateral rim mesh, adjusted for potential confounders, for acetabular revision for any reason was 0.50 (95% CI 0.13 to 1.93; $p = 0.31$) and for acetabular revision for aseptic loosening was 0.29 (95% CI 0.020 to 4.04; $p = 0.35$). The Kaplan–Meier analysis showed a ten-year survival for aseptic loosening of the acetabular of 98% (95% CI 95 to 100, n = 65 at risk) in the mesh group and 94% (89 to 98, n = 76 at risk) in the no-mesh group. The 15-year survival for aseptic acetabular loosening was 90% (81 to 100, n = 35 at risk) in the mesh group and 85% (77 to 94, n = 45 at risk) in the no-mesh group ($p = 0.23$).

Conclusion

This study shows that the use of a lateral rim mesh in primary THA in young patients is not associated with a higher risk of revision of the acetabular component. Therefore, we consider a lateral rim mesh combined with IBG to be effective in reconstructing segmental acetabular defects in primary THA

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INTRODUCTION

Total hip arthroplasty (THA) in young patients (< 50 years) remains a matter of concern. Due to their young age, it is likely this patient group will face future (re-)revisions as they will probably outlive their prosthesis. Generally, these patients suffer from secondary osteoarthritis and, due to the underlying disorder, extensive acetabular defects are common. Where a large segmental defect of the lateral acetabular wall is present, the acetabular component can be implanted above the true acetabulum, creating a higher center of rotation. However, Pagnano et al showed that a higher center of rotation leads to an increased rate of failure for the acetabular component[1]. Therefore, an attempt should be made to position the acetabular component at or near the true acetabular origin. Various techniques have been described to reconstruct the acetabular defect and to enable insertion of the component near the true acetabulum in primary and revision THA[2-12]. In our clinical practice, acetabular defects in both primary and revision surgery are reconstructed with impaction bone grafting (IBG) and, if necessary, combined with a metal mesh (Fig. 1)[13-16]. Several reports have shown disappointing results of lateral rim meshes in revision THA[17-21]. GarcíaRey et al found that the most important factor that was associated with loosening of the acetabular component was use of a lateral mesh (hazard ratio (HR) 2.94, 95% confidence interval (CI) 1.33 to 6.52)[21]. However, no studies have been found to report the results of IBG combined with lateral rim meshes in primary THA. This has led us to investigate the long-term survival of primary THA in patients aged 50 years or younger with IBG and an acetabular lateral rim mesh. We compared this patient group with patients aged 50 years or younger with a primary THA with IBG, but where a lateral rim mesh was not used.

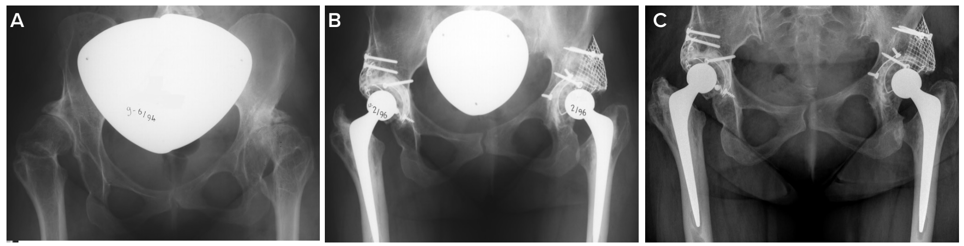

Figure 1. a) Preoperative radiograph of the pelvis of a 37-year-old female patient with severe bilateral secondary osteoarthritis due to developmental dysplasia of the hip. **b**) Bilateral total hip arthroplasty (THA) was performed with reconstruction using meshes and impaction bone grafting, with a slightly higher center of rotation on the right side. **c**) 23 years after bilateral THA placement with no signs of loosening, the patient is doing clinically well.

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PATIENTS AND METHODS

We performed a retrospective observational study on 530 consecutive patients (600 hips) who received a primary cemented THA with impaction bone grafting (IBG) at an age of 50 years or younger, between January 1988 and January 2016. A total of 235 patients (257 hips) had received IBG with a lateral rim mesh (mesh group), of which 41 hips (37 patients, 16%) had also an additional medial mesh. The other group consisted of 306 patients (343 hips) who received IBG without a lateral rim mesh (no-mesh group). In the no-mesh group, 46 hips (41 patients, 13%) had a medial wall mesh. Baseline characteristics for both groups are displayed in Table 1. In total, 15 patients (21 hips) died during the study period of causes unrelated to the surgery at a mean of nine years (0.5 to 19). The main indication for THA in the mesh group was developmental dysplasia of the hip (DDH, 153 hips in 129 patients, 60%), whereas avascular necrosis of the femoral head (AVN, 119 hips in 103 patients, 35%) was the main indication for the no-mesh group. All surgeries were performed by five experienced orthopaedic hip surgeons (including WHCR and BWS). All bone stock defects were classified according to the American Academy of Orthopedic Surgeons (AAOS) classification, with the American Society of Anesthesiologists classification (ASA) and Charnley score also provided (Table 1)[22,23,24]. All but two hips (two patients) in which a lateral mesh was used had segmental wall defects: in one hip with a small acetabulum, a lateral mesh was used to facilitate insertion of a larger diameter acetabular component; in the other hip, a lateral mesh was used to reinforce a weak posterior wall. Preoperatively, patients received a single dose of intravenous antibiotics on induction (Cefazolin). All operations were performed using a posterolateral approach. After reaming the acetabulum, drill holes were made in the sclerotic parts and, if needed, a medial mesh was inserted. In the mesh group, segmental bone defects were reconstructed with a lateral rim mesh, which was secured with screws. The excised femoral head was morselized into autograft bone chips of 0.7 cm to 1.0 cm in diameter. If the femoral head could not be used or the bone defect was too large, bone chips from the bone bank (0.7 cm to 1.0 cm in diameter) were used or combined with the autograft. In the mesh group, 166 autografts (65%), 26 allografts (10%), and 65 combined grafts (25%) were used. In the no-mesh group, 292 autografts (85%), 31 allografts (9%), and 20 combined grafts (6%) were used. The bone chips were impacted using metal impactors and a metal hammer. Next, cement loaded with antibiotics was pressurized into the acetabulum before the polyethylene acetabular component was implanted. Table 2 shows the types of acetabular components that were inserted. The postoperative protocol has changed over the years, from bed rest during the first weeks postoperatively, to partial weight bearing of 10% to 50% during the first six weeks, depending on the extent of the defect and reconstruction which had been performed. In the initial seven days postoperatively, all patients received antithrombotic prophylaxis and non-steroidal anti-inflammatory drugs were prescribed for the prevention of heterotopic ossification. Follow-up visits were scheduled at six weeks and 3, 6, and 12 months postoperatively, and then annually or biennially.

Table 1. Baseline characteristics for 600 hips in 530 consecutive patients

Characteristic	Mesh group	No-mesh group
Total, n (%)	257 (43)	343 (57)
Gender, n (%)		
Male	74 (30)	173 (70)
Female	183 (52)	170 (48)
Death, n (%)	4 (19)	17 (81)
Mean age, yrs (range)	35 (13.0-50.0)	38 (12.6-50.0)
Mean BMI, kg/m² (range)	26 (17.3-49.8)	25 (15.1-51.9)
Missing BMI, n (%)	0	1 (100)
Bilateral, n (%)	88 (37)	151 (63)
ASA, n (%)		
1	154 (50)	155 (50)
2	84 (38)	137 (62)
3	11 (24)	34 (76)
Missing	8 (32)	17 (68)
Indication, n (%)		
Primary osteoarthritis	3 (7)	43 (93)
Developmental dysplasia of the hip	153 (78)	42 (22)
Rheumatoid arthritis	5 (15)	28 (85)
Avascular necrosis	13 (10)	119 (90)
Post-traumatic	18 (38)	29 (62)
Other	65 (44)	82 (56)
Charnley score, n (%)		
A	132 (50)	131 (50)
B1	83 (38)	133 (62)
B2	37 (34)	72 (66)
C	5 (42)	7 (58)
AAOS defect, n (%)		
None	1 (0.5)	196 (99)
Type I	164 (90)	19 (10)
Type II	1 (0.9)	110 (99)
Type III	90 (84)	17 (16)
Type IV	0	0
Type V	1 (50)	1 (50)

ASA, the American Society of Anesthesiologists; AAOS, the American Academy of Orthopedic Surgeons

Table 2. Overview of the implanted acetabular components

Type of acetabular component	Mesh group (%)	No-mesh group (%)
Müller/Allopro cup (Zimmer, Sulzer, Wintherthur, Switzerland)	10 (36)	18 (64)
Charnley/Elite (DePuy Synthes, Leeds, UK)	24 (37)	41 (63)
Charnley/Ogee (DePuy Synthes)	1 (20)	4 (80)
Exeter Contemporary Flanged (Stryker/Howmedica, Newbury, UK)	156 (42)	216 (58)
Exeter Contemporary Hooded (Stryker)	28 (53)	25(47)
Exeter Rimfit (Stryker)	25 (49)	26 (51)
Exeter “other” (CDH, RSA, Full Profile) (Stryker)	12 (50)	12 (50)
Avantage (Biomet, Bridgend, UK)	1 (50)	1 (50)

Statistical analysis

Cox regression analyses were performed to study the specific effect of the lateral rim mesh on acetabular component survival. The variables studied were based on the approach described. The selection of which variables to include in our analyses in order to minimize bias was conducted based on the approach described by Shrier and Platt[25]. They describe a six-step approach by which one can identify the most important potential confounders in an analysis. This approach has been shown to reduce the degree of bias for the effect estimate in the chosen statistical method. We corrected for potential confounders: gender, age at time of surgery, bilateral THA, Charnley score, ASA, BMI, operation indication, and acetabular bone defect. Due to low numbers of ASA 2 and 3 patients, the ASA was dichotomized to ASA 1 versus ASA 2 to 3. Time to follow-up was defined as the time until the last clinical visit or radiograph available in our hospital or date of revision surgery. We used the Kaplan–Meier analysis to estimate the survival of the prosthesis with endpoint revision of the acetabular component for any reason and its revision for aseptic loosening at ten and 15 years. The log-rank test was used to evaluate significant differences between the Kaplan–Meier curves of the mesh group and no-mesh group. Statistical analyses were performed using R 3.2.4 program (R Foundation for Statistical Computing, Vienna, Austria). A p-value < 0.05 was considered to be statistically significant.

RESULTS

During the study period, 59 revisions (10%) of any component were performed. The mean follow-up of all the hips was 6.2 years (0.1 to 27.0). Mean time until revision of the acetabular component for aseptic loosening in the mesh group was 13.9 years (3.1 to 21.7) and in the no-mesh group was 13.2 years (3.6 to 24.3). In the mesh group, 18 acetabular components (7%) were revised, of which seven were for aseptic loosening and five for septic loosening. Other reasons for revision were wear (n = 1), recurrent dislocations (n = 3), neurological problems (n = 1), and traumatic loosening of the acetabular component (n = 1). Of all the acetabular revisions in the mesh group, 13 hips had an AAOS type I defect and five hips had AAOS type III bone defects. Most of the type I reconstructions that failed were in the group of the more extensive preoperative segmental bone defects. Of the type III defects requiring revision, only one had a rim mesh with an additional medial wall mesh. Of the aseptic revisions, six were isolated acetabular component revisions and one required revision of the femoral and acetabular components due to osteolysis around both components at another hospital. In one patient with revision for aseptic loosening, 21.7 years after primary THA, the original rim mesh was left in place during revision surgery as the mesh was still well incorporated and provided support for the new component. In the no-mesh group, 36 acetabular components (10%) were revised for any reason, of which 19 had a revision for aseptic loosening and eight for septic loosening. Other reasons for revision were wear (n = 1), recurrent dislocation (n = 6), stem fracture (n = 1), and traumatic loosening of the acetabular component (n = 1). The patient with the stem fracture also had the acetabular component revised because, intraoperatively, osteolysis was observed around the acetabular component. In total, there were 31 revisions of the femoral component for any reason, of which five only involved the stem. Of these, three were performed in the mesh group and two in the no-mesh group. The use of lateral rim mesh was not significantly associated with the risk of acetabular revision for any reason (unadjusted HR 0.64, 95% CI 0.34 to 1.20; p = 0.16). For acetabular component revision due to aseptic loosening, the unadjusted HR was 0.35 (95% CI 0.11 to 1.07; p = 0.07). Adjusted for potential confounders, the HR for acetabular component revision for any reason was 0.50 (95% CI 0.13 to 1.93; p = 0.31) and for aseptic loosening 0.29 (95% CI 0.02 to 4.04; p = 0.35) (Tables 3 and 4). The Kaplan–Meier survival rates are shown in Table 5 and corresponding Kaplan–Meier curves in Figures 2 and 3. The difference in component survival between both groups was not statistically significant (log-rank test; p = 0.30 for any reason, p = 0.23 for aseptic loosening).

Table 3. Hazard ratios (HR) with 95% confidence intervals (Cis) of the rim mesh versus no rim mesh with the endpoint of acetabular component revision for any reason

Variable	Univariable			Multivariable		
	HR	**95% CI**	**p-value***	**HR**	**95% CI**	**p-value***
Rim *vs.* no rim mesh	0.64	0.34 to 1.20	0.16	0.50	0.13 to 1.93	0.31
Gender, female *vs.* male	0.77	0.42 to 1.39	0.38	0.86	0.42 to 1.78	0.68
Age at time of the surgery, yrs	0.91	0.56 to 1.46	0.69	0.81	0.49 to 1.36	0.44
Charnley grade			0.78			0.91
B1 *vs.* A	0.97	0.51 to 1.86	0.93	1.10	0.50 to 2.39	0.82
B2 *vs.* A	0.63	0.25 to 1.60	0.33	0.86	0.31 to 2.44	0.78
C *vs.* A	1.08	0.25 to 4.71	0.91	1.55	0.25 to 9.58	0.64
ASA 2+3 *vs.* ASA 1	1.01	0.56 to 1.80	0.98	1.05	0.54 to 2.06	0.88
Body mass index	0.89	0.59 to 1.35	0.59	0.95	0.62 to 1.46	0.83
Indication			0.51			0.45
DDH *vs.* primary OA	0.79	0.18 to 3.52	0.75	1.26	0.24 to 6.64	0.79
RA *vs.* primary OA	0.71	0.13 to 3.78	0.69	0.62	0.09 to 4.08	0.62
AVN *vs.* primary OA	1.07	0.23 to 4.98	0.93	1.02	0.21 to 4.98	0.98
Post-traumatic *vs.* primary OA	1.44	0.29 to 7.22	0.66	1.36	0.24 to 7.69	0.72
Others *vs.* primary OA	0.54	0.11 to 2.53	0.43	0.54	0.11 to 2.75	0.46
Acetabular defect (AAOS)			0.07			0.06
Type I *vs.* none	0.81	0.33 to 1.98	0.64	1.54	0.36 to 6.63	0.56
Type II *vs.* none	0.60	0.23 to 1.54	0.29	0.67	0.25 to 1.83	0.44
Type III *vs.* none	0.21	0.06 to 0.72	0.01	0.34	0.06 to 1.90	0.22

*Wald test

ASA, the American Society of Anesthesiologists; DDH, developmental dysplasia of the hip; OA, osteoarthritis; RA, rheumatoid arthritis; AVN, avascular necrosis; AAOS, the American Academy of Orthopedic Surgeons

Table 4. Hazard ratios (HR) with 95% confidence intervals (Cis) of the rim mesh versus no rim mesh with the endpoint of acetabular component revision for aseptic loosening

Variable	Univariable			Multivariable		
	HR	95% CI	p-value *	HR	95% CI	p-value*
Rim *vs.* no rim mesh	0.35	0.11 to 1.07	0.07	0.29	0.020 to 4.04	0.35
Gender, female *vs.* male	1.18	0.43 to 3.25	0.75	1.40	0.36 to 5.39	0.62
Age at time of the surgery, yrs	0.80	0.37 to 1.71	0.57	0.74	0.32 to 1.68	0.47
Charnley grade			0.51			0.81
B1 *vs.* A	1.16	0.41 to 3.25	0.78	1.33	0.34 to 5.27	0.68
B2 *vs.* A	0.54	0.11 to 2.71	0.46	0.86	0.13 to 5.73	0.88
C *vs.* A	2.42	0.48 to 12.11	0.28	2.43	0.23 to 26.2	0.46
ASA 2+3 *vs.* ASA 1	0.85	0.35 to 2.09	0.73	0.57	0.16 to 2.02	0.39
Body mass index	0.71	0.34 to 1.50	0.37	0.91	0.44 to 1.89	0.80
Indication			0.73			0.67
DDH *vs.* primary OA	0.30	0.03 to 2.70	0.29	0.39	0.031 to 4.96	0.47
RA *vs.* primary OA	0.45	0.05 to 4.33	0.49	0.36	0.026 to 4.96	0.44
AVN *vs.* primary OA	0.47	0.05 to 4.73	0.53	0.34	0.030 to 3.92	0.39
Posttraumatic *vs.* primary OA	0.55	0.05 to 6.24	0.63	0.50	0.028 to 8.65	0.63
Others *vs.* primary OA	0.23	0.03 to 2.15	0.20	0.17	0.015 to 1.90	0.15
Acetabular defect			0.76			0.66
Type I *vs.* none	0.42	0.063 to 2.74	0.36	1.38	0.082 to 23.24	0.82
Type II *vs.* none	0.41	0.066 to 2.56	0.34	0.45	0.067 to 3.01	0.41
Type III *vs.* none	0.00	-∞ to ∞	0.62	0.00052	-∞ to ∞	0.67

*Wald test
ASA, the American Society of Anesthesiologists; DDH, developmental dysplasia of the hip; OA, osteoarthritis; RA, rheumatoid arthritis; AVN, avascular necrosis; AAOS, the American Academy of Orthopedic Surgeons

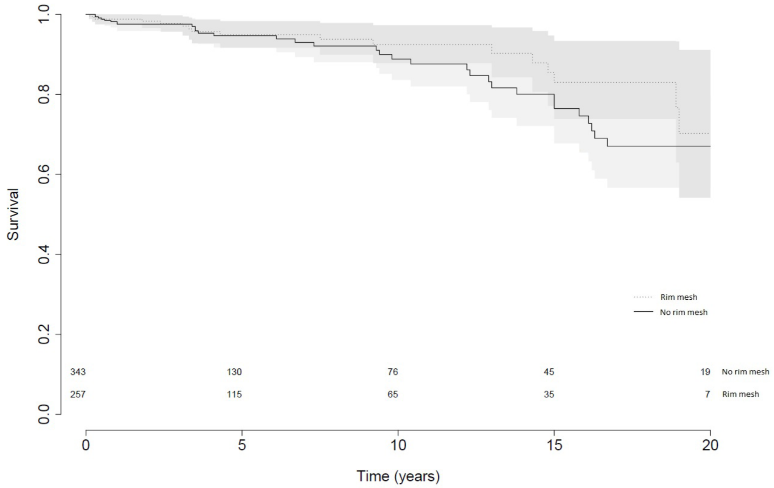

Figure 2. Kaplan-Meier survival curve with the endpoint revision of the acetabular component for any reason.

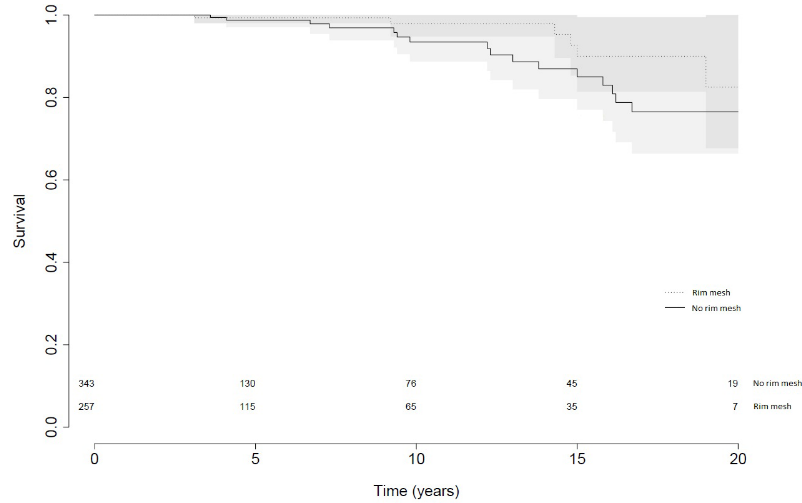

Figure 3. Kaplan-Meier survival curve with endpoint revision of the acetabular component for aseptic loosening

Table 5. Comparison of the Kaplan-Meier survival rates with 95% confidence intervals (Cis) for the two types of acetabular construction (log-rank test)

Endpoint	Survival (95% CI), mesh group	At risk, n	Survival (95% CI), no-mesh group	At risk, n	p-value
Revision for any reason, %					0.30
10-yr follow-up	92 (88 to 97)	65	89 (84 to 94)	76	
15-yr follow-up	83 (74 to 93)	35	77 (68 to 86)	45	
Revision for aseptic loosening, %					0.23
10-yr follow-up	98 (95-100)	65	94 (89 to 97)	76	
15-yr follow-up	90 (81-100)	35	85 (77 to 94)	45	

DISCUSSION

In the current study, the use of an acetabular lateral rim mesh was not associated with a higher failure rate of the acetabular component. As the reconstruction with an acetabular lateral mesh does not directly influence the implantation and survival of the stem, we specifically focused on the acetabulum. We could not identify any previous study reporting the influence of a lateral rim mesh on the survival of acetabular components in primary THA. In contrast, there are several reports on the influence of lateral rim meshes in revision THA surgery, mostly with large acetabular defects[17,20,21,26-29]. Their general message was that patients with the worst survival were those with the largest acetabular defects[18-21]. Rigby et al described their results on the survival of large rim meshes in 60 THAs with endpoint aseptic loosening as disappointing; of the 15 revisions for aseptic loosening, there were nine large rim mesh reconstructions (15%)[18]. To evaluate whether the acetabular component revisions that were performed were those with the largest defects, we retrospectively analyzed the extent of the acetabular bone defect of the acetabular revisions in the mesh group. Of the 18 acetabular revisions, the majority preoperatively had a large segmental defect. The AAOS classification for acetabular defects permits considerable variation in the assignment of type I defects. Not unexpectedly, the acetabular failures arose in the presence of the largest segmental acetabular defects. Nevertheless, the survival rates between the mesh and no-mesh group, remarkably, did not differ. Moreover, the mean time until acetabular revision was more than 13 years in both groups. Considering that the majority of the revisions due to aseptic loosening in the mesh group occurred in the presence of the largest acetabular defects, these findings are reassuring. We acknowledge the limitations in our study. We included a large study population of consecutive patients in one institute. We cannot discount that bias may have occurred, as the distribution of the diagnoses was not the same in each group. THA for DDH is a more complex procedure than THA for AVN. Despite this large variation in indication, even after correction in the Cox regression analyses, the ten- and 15-year survival for the mesh and no-mesh group were similar. We accept there are considerable baseline differences between the two groups studied, particularly regarding the classification of acetabular bone defect, suggesting that patients were selected for their intervention. Using multivariable Cox regression analyses, an attempt was made to correct for potential confounders. However, the possibility of residual confounding cannot be completely ruled out. Additionally, as we did not analyze the radiographs for our series, we have no information about the presence of radiolucent lines or component migration to determine the radiological survival of the prosthesis. However, the main goal of this study was to analyze the number of revisions that were performed and to be able to draw an overall conclusion about the value of lateral rim meshes. Various types of acetabular components were used throughout the years. However, all these components were cemented, and the same philosophy and technique was applied in all patients. Lastly, the study has a wide range of follow-up (0.1 to 27 years) with a mean of 6.2 years. This reflects our definition of follow-up: time until the last clinical visit or radiograph available or date of revision surgery. Over time, the number of patients aged under 50 years who have received a THA has increased, particularly in recent years, which has skewed the mean follow-up. García-Rey et al reported survival with the use of a lateral mesh of 80% at 15 years (95% CI 67 to 91)[21]. However, when combined with a medial wall mesh, the survival decreased drastically to 54% at 15 years (95% CI 31 to 76). Most studies reporting on the influence of a medial wall mesh on acetabular component survival applied a different type of mesh and generally smaller sizes of bone grafts[20,21,24]. In this study, only one (2.4%) of the 41 lateral rim meshes with an additional medial wall mesh required acetabular revision. In contrast to García-Rey et al, the survival in our study, between an isolated lateral rim mesh or combination with a medial wall mesh, did not influence the likelihood of for revision of the acetabular component for any reason (p = 0.169) or revision for acetabular aseptic loosening (p = 0.882)[21]. Busch et al used a structural graft for the reconstruction of a lateral acetabular defect in primary THA (74 hips in 62 patients) and also made a differentiation in patients below 50 years of age[5]. They described a ten-year survival for isolated acetabular component revision (without any stem revisions) for any cause of 93%. This resembles the survival of the acetabular component with revision for any reason found in our mesh group. Kim and Kadowaki evaluated bulk femoral head autograft for acetabular reconstruction in cementless primary THA (83 hips in 70 patients) for DDH and found a ten-year acetabular survival for any reason of 94% (95% CI 92 to 96)[30]. However, they did not stratify for young patients. Other options to reconstruct acetabular defects include reinforcement rings, shelf graft, and cages, with varying results[31-33]. The use of an acetabular bone graft, in combination with a lateral rim mesh, aims to restore the acetabular bone and can provide a solid base for future revision. THA in young patients with a cemented acetabular component and reconstruction with IBG in the presence of a lateral mesh offers comparable survival rates to reconstructions where a lateral mesh was not warranted. The lateral mesh provides a stable support for the graft and is considered a suitable method to reconstruct segmental acetabular defects in primary THA in young patients.

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CHAPTER 5

The outcome of subsequent revisions after primary total hip arthroplasty in 1,049 patients under 50 years; A single center cohort study with a follow-up of more than 30 years

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ABSTRACT

Aims

The aim of this study was to determine the outcome of all primary total hip arthroplasties (THAs) and their subsequent revision procedures in patients aged under 50 years performed at our institution.

Methods

All 1,049 primary THAs which were undertaken in 860 patients aged under 50 years between 1988 and 2018 in our tertiary care institution were included. We used cemented implants in both primary and revision surgery. Impaction bone grafting was used in patients with acetabular or femoral bone defects. Kaplan-Meier analyses were used to determine the survival of primary and revision THA with the endpoint of revision for any reason, and of revision for aseptic loosening.

Results

The mean age of the patients at the time of the initial THA was 36.7 years (SD 9.3). The mean follow-up of the THA was 8.7 years (2.0 to 31.5). The rate of survival for all primary THAs, acetabular components only, and femoral components only at 20 years' follow-up with the endpoint of revision for any reason, was 66.7% (95% confidence interval (CI) 60.5 to 72.2), 69.1% (95% CI 63.0 to 74.4), and 83.2% (95% CI 78.1 to 87.3), respectively. A total of 138 revisions were performed. The mean age at the time of revision was 48.2 years (23 to 72). Survival of all subsequent revision procedures, revised acetabular, and revised femoral components at 15 years' follow-up with the endpoint of revision for any reason was 70.3% (95% CI 56.1 to 80.7), 69.7% (95% CI 54.3 to 80.7), and 76.2% (95% CI 57.8 to 87.4), respectively. A Girdlestone excision arthroplasty was required in six of 860 patients (0.7%).

Conclusion

The long-term outcome of cemented primary and subsequent revision THA is promising in these young patients. We showed that our philosophy of using impaction bone grafting in patients with acetabular and femoral defects is a very suitable option when treating young patients. Surgeons should realize that knowledge of the outcome of subsequent revision surgery, which is inevitable in young patients, must be communicated to this group of patients prior to their initial THA

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INTRODUCTION

Total hip arthroplasty (THA) is one of the most successful operations, improving the life of millions of people, and increasingly being considered in young patients[1]. By the year 2030, 52% of primary THAs are expected to be undertaken in patients aged < 65 years, with the greatest increase in those aged between 45 and 55 years[2]. The short-term success after THA is attractive to young patients, as pain is usually dramatically reduced, function is restored, and quality of life is improved. However, for those aged < 55 years, the survival with the endpoint of revision of the implant for any reason has been shown to be inferior when compared with patients aged > 70 years, in many studies[3-5]. The main reasons for higher revision rates in younger patients include the fact that more are undertaken in those with acetabular and/or femoral defects, who have higher demands and activity levels, leading to early wear and loosening. Additionally, due to their young age at the time of the initial surgery, these patients will usually outlive their primary THA. Therefore, the real focus in studying outcomes of THA in young patients should be on the outcome of the subsequent revision surgery. Only successful revision will keep these patients mobile. In a study by Bayliss et al in which lifetime revision risk was used to describe the risk of revision following THA, the problems faced by younger patients were clearly outlined[6]. For those aged between 50 and 54 years, the lifetime risk of revision increased up to 29%, compared with 5% in patients aged > 70 years, with many revisions being performed within five years of the initial surgery. Revisions performed within five years after surgery also have a high risk of re-revision[5]. These numbers are worrying and show the importance of more long-term (re-)revision data, which are still lacking in young patients. To our knowledge, only two studies have reported the long-term outcome of revision THA in patients aged < 55 years at the time of revision[7,8]. One reported an alarming survival rate of 63% at ten years' follow-up and the other, using a biological reconstruction technique with impaction bone grafting, showed more promising results, with a ten-year survival rate of 87%[7,8]. The aim of this study was to analyze the outcome of subsequent revision procedures in >1,000 consecutive primary THAs undertaken in patients aged < 50 years, all performed at our institution using a routine procedure with cemented components. We analyzed the outcome of the primary THA and focused on the outcome of the subsequent revisions and re-revisions. We also wished to report the incidence of excision arthroplasty, a Girdlestone procedure, in these patients, as a measure of failure which seriously limits the mobility of the patient[9].

METHODS

This was a retrospective cohort study involving all patients, aged < 50 years, who underwent primary THA between 1 January 1988 and 31 December 2017 in our tertiary care institution (The Radboud University Medical Centre, Nijmegen, The Netherlands). Those patients in whom THA was undertaken for a primary or metastatic tumor were excluded. A total of

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1,049 primary THAs, performed in 860 patients, were included. Their mean age at the time of primary THA was 36.7 years (12 to 50), with 590 (56.2%) being female. During follow-up, 68 patients (92 THAs) died. These were included in the analyses, and censored at the time of death. A total of 114 patients (138 THAs) had not been reviewed in the outpatient department since 2015. Most of these were due to be updated in 2020, but due to the COVID-19 pandemic we had to postpone their review. However, follow-up data were included in the analyses and censored at the time of their most recent outpatient review. Approval for this study was obtained from our local medical ethical committee. No formal informed consent is needed from the patients for this kind of study in the Netherlands. All primary THAs were undertaken using the posterolateral approach, and cemented acetabular and femoral components. Acetabular defects are often encountered in these patients due to developmental dysplasia or trauma. Impaction bone grafting was used for the reconstruction of these defects. The femoral head was used as autograft in primary THA. In some primary cases with larger defects, the autograft was combined with a fresh frozen femoral head allograft. In patients in whom the femoral head was not available for autograft, only allograft was used. In those with a segmental or medial wall defect of the acetabulum, a lateral rim or medial wall titanium mesh was used, in combination with grafting. The graft was morsellized with a rongeur or a bone mill to provide chips with a diameter of 0.7 to 1.0 cm, which were introduced using a metal impactor. The aim was to reconstruct the original centre of rotation by using the transverse ligament as a landmark. Antibiotic-loaded cement was pressurized into the acetabulum before implantation of the component (Figure 1).

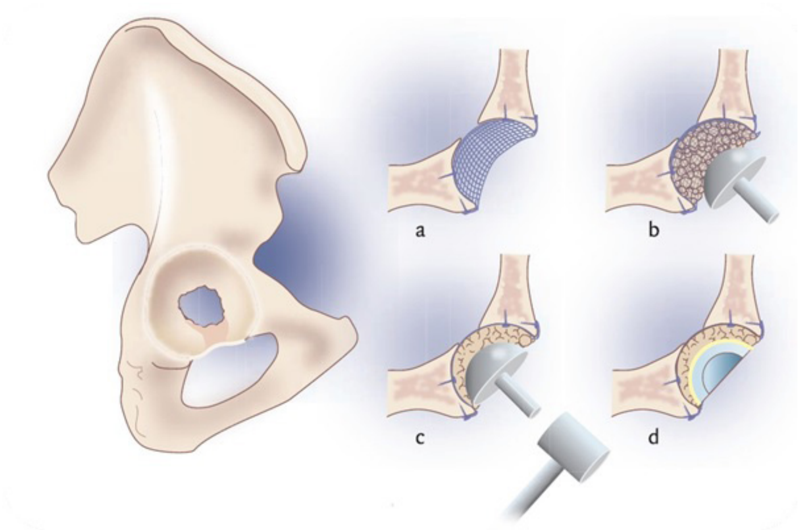

Figure 1. Acetabular impaction bone grafting **a**) A metal mesh is used to close the medial acetabular defect and a superolateral rim mesh is used to cover a superolateral bone defect. Meshes are fixated with screws. **b**) A femoral head is morselized to provide bone chips, which are impacted into the reconstructed acetabulum **c**) The chips are compressed layer by layer. **d**) cement is pressurized into the graft before the component is implanted.

The femoral component was implanted using third-generation cementing techniques. In subsequent revision procedures, after removal of the components, and taking microbiological cultures, bone defects were reconstructed using the same technique of acetabular impaction grafting and a cemented component. Impaction grafting was also used in patients with a femoral defect. In those undergoing revision for infection, a two-stage procedure was used. The techniques of impaction grafting have been extensively described[10-14]. This study was conducted and reported according to STROBE guidelines[15]. Statistical analysis. The survival of the primary THA was recorded as the time between the primary procedure and the date of revision, the death of the patient, or the date of the most recent outpatient review. In patients with an excision arthroplasty, follow-up ended at the time of removal of the components. Using Kaplan-Meier analyses, we estimated survival including 95% confidence interval (CI) of all primary THAs with revision for any reason, and revision for aseptic loosening as the endpoints. We also estimated the survival of the acetabular and femoral components separately with the endpoint of revision for any reason. Survival was stratified for sex, age group (< 30, 30 to 39, and 40 to 49 years), and different primary indications for THA. The rates of survival were reported, where possible, at ten-, 20-, and 25-years' follow-up. We determined the survival of the subsequent revision procedures, calculated as the time between the revision and re-revision procedures, the death of the patient, or the date of the most recent outpatient visit. Survival of the revision procedures was reported at ten- and 15-years' follow-up. The cumulative failure rates were also calculated. All analyses were performed using R v. 3.5.1 (R Foundation for Statistical Computing, Austria), and significance was set at $p < 0.05$.

RESULTS

The most common primary diagnoses were developmental dysplasia ((DDH) n = 299) and avascular necrosis ((AVN) n = 288). The mean follow-up for all primary THAs was 8.7 years (2.0 to 31.5). Other characteristics of the patients are shown in Table 1. The most used acetabular component was the Exeter Contemporary flanged component (Stryker, UK) (n = 582); the most used femoral component was the Exeter (n = 890). The components which were used are shown in Table 2. Acetabular impaction grafting was used in 751 THAs (71.6%); of these, an autograft was used in 581, a combination of both autograft and allograft in 97, and only allograft in 73 THAs. Of all primary acetabular components, a rim mesh was used in 240 THAs, a medial mesh in 52, and a combination of both in 44. A total of 138 revision procedures (13.2%) were performed involving any component for any reason. The mean age at time of the first revision was 48.2 years (23 to 72). In 127 THAs, the acetabular component was revised; in 61 this was done in combination with revision of the femoral component. In 74 THAs, the indication for acetabular revision was aseptic loosening, and in 27 the indication was septic loosening (Table 3). Only the femoral component was revised in ten THAs. The indication for femoral revision was aseptic loosening in four, dislocation in one, and other reasons in five. One revision involved only a change of the femoral head, due to recurrent dislocation (Table 3).

Table 1. Patient characteristics of 1,049 primary total hip arthroplasties.

Characteristic	Value
Mean age, yrs (SD)	38.6 (9.3)
Sex, n (%)	
Male	459 (43.8)
Female	590 (56.2)
ASA grade, n (%)	
ASA I	395 (37.7)
ASA II	329 (31.4)
ASA III to IV	82 (7.8)
Missing	243 (23.2)
Indication, n (%)	
Primary OA	88 (8.4)
DDH	299 (28.5)
RA	72 (6.9)
AVN	288 (27.5)
Post-Perthes'	69 (6.6)
Post-traumatic OA	74 (7.1)
Other	159 (15.2)

ASA, American Society of Anesthesiologists; AVN, avascular necrosis; DDH, developmental dysplasia of the hip; OA, osteoarthritis; RA, rheumatoid arthritis; SD, standard deviation

Table 2. Overview of the components which were used

Acetabular	n
Contemporary flanged	582
De Puy Elite Plus LPW Cup	141
Contemporary hooded	134
Exeter rimfit	61
Muller	57
Exeter	48
Charnley/Ogee	13
Avantage	10
Missing	3
Femoral	
Exeter	890
Charnley	123
Muller	33
Missing	3

Table 3. Characteristics of revisions and re-revision.

Characteristic	Revisions (n = 138)	Re-revisions (n = 22)
Mean age, yrs	48.2	51.1
Sex, n (%)		
Male	55 (39.9)	10
Female	83 (60.1)	12
Component, n		
Cup	127	20
Stem	71	10
Head	1	N/A
Indication for revision, n		
Aseptic	78	4
Septic	27	11
Dislocation	14	3
Wear	4	0
Other	12	4
Missing	3	0

N/A, not applicable; SD, standard deviation.

In four THAs (four patients), there was no reimplantation during the first revision due to infection, eventually resulting in a permanent Girdlestone arthroplasty. In all other patients with septic loosening, a second-stage reimplantation procedure was undertaken. Kaplan-Meier analysis showed a survival rate for all primary THAs with an endpoint of revision for any reason of 90.7% (95% CI 88.2 to 92.7) at ten years, 66.7% (95% CI 60.5 to 72.2) at 20 years, and 54.4% (95% CI 45.7 to 62.2) at 25 years' follow-up (Figure 2). The rates of survival for primary acetabular and femoral components separately, and survival rates with an endpoint of aseptic loosening, are shown in Table 4. Using competing risk analyses, we calculated the cumulative incidence of revision for any reason, with death considered as a competing risk. The cumulative failure was 29.9% (95% CI 24.9 to 35.1) at 20 years' follow-up for all primary THAs, and after a revision THA was 27.3% (95% CI 17.1 to 38.6) at 15 years' follow-up. A total of 253 cases (24.1%) were undertaken in patients aged < 30 years, 315 (30.0%) in those aged between 30 and 39 years, and 481 (45.9%) in those aged between 40 and 50 years. In patients aged < 30 years, survival for any reason was 90.3% (95% CI 84.4 to 94.1), 69.5% (95% CI 56.0 to 79.6), and 66.1% (95% CI 51.3 to 77.3) at ten-, 20-, and 25-years' follow-up, respectively. For those aged between 30 and 39 years, survival for any reason was 88.4% (95% CI 82.7 to 92.3), 68.6% (95% CI 57.4 to 77.4), and 56.4% (95% CI 39.8 to 70.0) at ten-, 20-, and 25-years' follow-up, respectively. For those aged between 40 and 49 years, survival was 92.4% (95% CI 88.9 to 94.9), 63.5% (95% CI 53.6 to 71.8), and 47.8% (95% CI 34.9 to 59.5) at ten-, 20-, and 25-years' follow-up, respectively (Table 5).

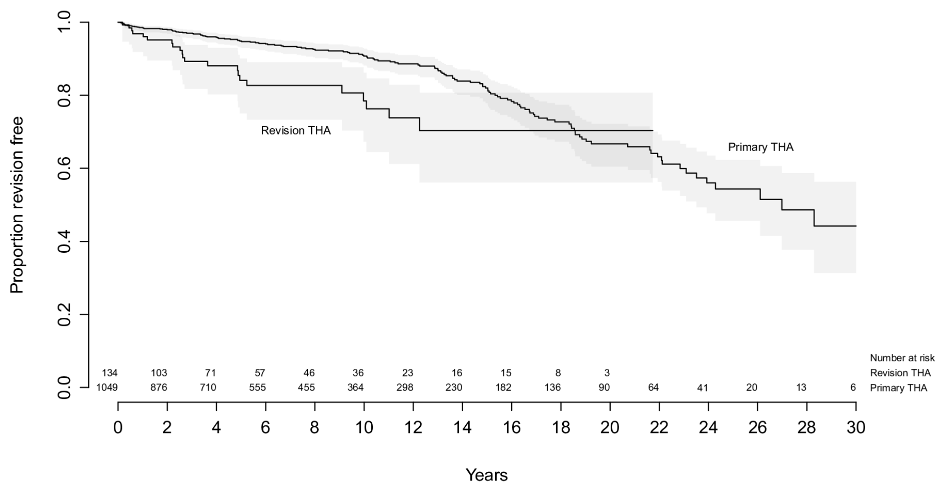

Figure 2. Survival of 1,049 primary total hip arthroplasties (THAs) and 138 revision procedures with an end-pointof (re-)revision for any reason

Table 4. Survival rates of all primary total hip arthroplasties with endpoints of revision for any reason and revision for aseptic loosening (95% confidence intervals).

Reason	10-yr follow-up	20-yr follow-up	25-yr follow-up
Overall, any reason	90.7 (88.2 to 92.7)	66.7 (60.5 to 72.2)	54.4 (45.7 to 62.2)
Acetabular component, any reason	91.7 (89.3 to 93.6)	69.1 (63.0 to 74.4)	56.6 (47.9 to 64.5)
Femoral component, any reason	94.3 (92.2 to 95.8)	83.2 (78.1 to 87.3)	76.9 (69.0 to 83.0)
All aseptic	95.8 (93.7 to 97.2)	76.5 (70.2 to 81.6)	62.3 (52.5 to 70.7)
Acetabular component, aseptic	96.3 (94.3 to 97.6)	77.5 (71.3 to 82.5)	63.6 (53.8 to 71.8)
Femoral component, aseptic	97.9 (96.2 to 98.8)	90.5 (85.6 to 93.8)	83.6 (75.1 to 89.4)

Table 5. Survival rates of all primary total hip arthroplastaies by age group with an endpoint of revision for any reason (95% confidence interval).

KM all primary THAs (1,049)	10-yr follow-up	20-yr follow-up	25-yr follow-up
<30 yrs (n = 253)	90.3 (84.4 to 94.1)	69.5 (56.0 to 79.6)	66.1 (51.3 to 77.3)
30 to 39 yrs (n = 315)	88.4 (82.7 to 92.3)	68.6 (57.4 to 77.4)	56.4 (39.8 to 70.0)
40 to 49 yrs (n = 481)	92.4 (88.9 to 94.9)	63.5 (53.6 to 71.8)	47.8 (34.9 to 59.5)

KM, Kaplan-Meier; THA, total hip arthroplasty.

The most common diagnosis at the time of the initial THA was DDH. Survival for patients with DDH was 89.9% (95% CI 84.5 to 93.5) and 83.7% (95% CI 75.6 to 89.3) at ten- and 15-years' follow-up, respectively. For those undergoing THA for AVN, survival was 90.3% (95% CI 84.6 to 94.0) and 81.2 (95% CI 72.1 to 87.6) at ten- and 15-years' follow-up, respectively. Survival rates of other indications for primary THA are shown in Table 6. Of the 138 revision THAs,

22 required a re-revision. The mean age of the patients at re-revision surgery was 51.7 years (33 to 71). The mean follow-up for the revisions was 6.5 years (0.1 to 21.7). In 20 re-revisions, an acetabular re-revision was undertaken, of which eight also involved a femoral re-revision. Aseptic acetabular loosening was the indication in four patients, and septic loosening in 11. All patients with septic loosening underwent a two-stage revision. Only a femoral re-revision was undertaken in two patients. The indication was dislocation in one and fracture of the femoral component in the other. Using Kaplan-Meier analysis, the survival of revision THA with the endpoint of re-revision for any reason was 78.5% (95% CI 67.3 to 86.2) at ten-year, and 70.3% (95% CI 56.1 to 80.7) at 15-year follow-up (Figure 2). For all revised acetabular components, survival was 78.7% (95% CI 66.8 to 86.8) and 69.7% (95% CI 54.3 to 80.7) at ten- and 15-years' follow-up, respectively. For all revised femoral components, survival was 85.0% (95% CI 72.1 to 92.3) and 76.2% (95% CI 57.8 to 87.4) at ten and 15 years, respectively (Table 7). Of the 22 re-revision procedures, seven required a second re-revision (Figure 3). The mean follow-up of all re-revision procedures was 3.5 years (0.2 to 11.7). Aseptic loosening was the indication in two, septic loosening in three, dislocation in one, and defined as 'other' in one. Both the acetabular and femoral components were changed in one second re-revision; in four, only the acetabular component was changed and it was not replaced in two, resulting in a permanent Girdlestone arthroplasty. A Girdlestone arthroplasty was undertaken in four of 138 revision procedures at 0.1, 0.3, 0.9, and 4.6 years, respectively, after the primary procedure; all for sepsis. Components were reimplanted in all 22 re-revision procedures, after which these patients remained mobile. A Girdlestone arthroplasty was undertaken in two of seven second re-revision procedures, at 8.9 and 6.7 years, respectively, after the primary procedure; both for sepsis. Thus, of the whole group of 1,049 primary THAs, in 860 patients, six (0.7%) had a Girdlestone arthroplasty, all for sepsis. No further surgery is planned in these patients. This incidence of Girdlestone arthroplasty, called the Girdlestone load, which includes the outcome of revisions and re-revisions, suggests that with our philosophy of treatment, the number of patients whose THA could not be revised during the study period was limited. Except for septic indications, all patients with a failed primary or revision procedure, underwent satisfactory reimplantation of components.

Table 6. Survival rates of all primary total hip arthroplasty by diagnosis with an endpoint of revision for any reason (95% confidence interval)

Diagnosis	10-yr follow-up	15-yr follow-up
Primary OA	92.8 (81.3 to 97.3)	86.6 (65.5 to 95.2)
DDH	89.9 (84.5 to 93.5)	83.7 (75.6 to 89.3)
RA	88.6 (77.5 to 94.5)	79.2 (65.0 to 88.2)
AVN	90.3 (84.6 to 94.0)	81.2 (72.1 to 87.6)
Other	93.0 (86.1 to 96.5)	80.7 (68.8 to 88.4)
Post-Perthes'	94.7 (79.1 to 98.7)	89.4 (68.2 to 96.8)
Post-traumatic OA	88.0 (75.5 to 94.4)	78.6 (59.1 to 89.5)

AVN, avascular necrosis; DDH, developmental dysplasia of the hip; OA, osteoarthritis; RA, rheumatoid arthritis

Table 7. Survival rates of all revision total hip arthroplasty by diagnosis with an endpoint of revision for any reason (95% confidence interval)

KM revisions (138)	5-yr follow-up	10-yr follow-up	15-yr follow-up
Overall	84.1 (75.0 to 90.1)	78.5 (67.3 to 86.2)	70.3 (56.1 to 80.7)
Acetabular component	85.1 (75.7 to 91.0)	78.7 (66.8 to 86.8)	69.7 (54.3 to 80.7)
Femoral component	85.0 (72.1 to 92.3)	85.0 (72.1 to 92.3)	76.2 (57.8 to 87.4)

KM, Kaplan-Meier.

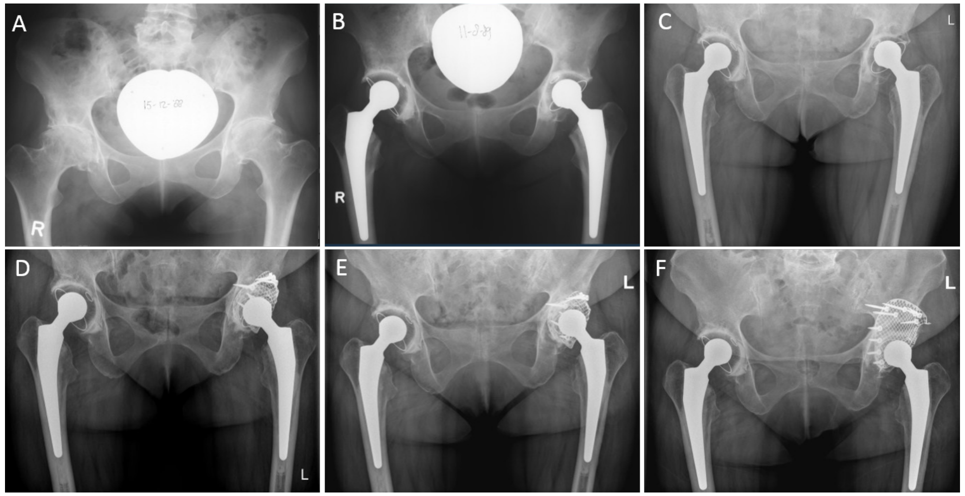

Figure 3. Anteroposterior (AP) radiographs **a**) after a primary total hip arthroplasty in a female patient with bilateral osteoarthritis secondary to epiphyseal dysplasia. **b**) She underwent bilateral cemented total hip arthroplasty when aged 36 years, in 1989. **c**) Preoperative radiograph from 2015 showing aseptic acetabular loosening on the left with no signs of loosening on the right (after 25 years). **d**) Postoperatively after left-sided acetabular revision. **e**) Preoperative radiograph from 2019, with septic acetabular loosening on the left. **f**) Postoperative radiograph after two-stage re-revision of the acetabular component. The initial right sided arthroplasty remains satisfactory, albeit with some evident acetabular wear after > 30 years. The left hip also remained satisfactory at the most recent review.

DISCUSSION

The aims of this study were to analyze the outcome and survival of both primary THAs and revision procedures, undertaken in a large cohort of patients aged < 50 years. We also determined the incidence of Girdlestone arthroplasty in these patients, as a measure of failure of THA. When performing THA in young patients, it is essential for the surgeon to have an idea of the outcome of the subsequent revision of the components, as revision procedures are inevitable in this group. The findings provide an important update to the literature on revision arthroplasty of the hip in young patients. To our knowledge, this is the largest long-term follow-up study of a single-center cohort of patients aged < 50 years, which includes the outcome of subsequent revisions. The importance of anticipating future revisions has to be emphasized. These patients are still young when they need a revision, with a mean age of 48 years at the time of revision surgery in our group. Even at the time of re-revision, they were still young, with a mean age of 52 years. In order to assess the true value of different techniques that are used worldwide for THA, it is not only important to report on the results of primary THA, but may be even more important to report the results of revisions and even re-revision procedures, as these outcomes will determine the long-term success of surgical treatment. Our method of using cemented THA combined with morselized bone grafts in young patients to reconstruct bone loss if needed, leads to very acceptable long-term outcomes of primary THA and subsequent revisions. At 20 years' follow-up, the survival of primary THA was 66.7% (95% CI 60.5 to 72.2) with the endpoint of revision for any reason, with 90 patients still at risk at that time. The acetabular component showed promising survival of 69.1% (95% CI 63.0 to 74.4) at 20 years' follow-up with the endpoint of revision for any reason, and a survival of 77.5% (95% CI 71.3 to 82.5) for the endpoint of aseptic loosening. Our results of primary THA in young patients are similar when compared with long-term follow-up data for patients aged > 60 years at the time of primary THA, which is remarkable. A large systematic review and meta-analysis by Evans et al showed a 25-year pooled survival of 57.9% (95% CI 57.1 to 58.7) in a group of patients with a mean age of 69 years, based on long-term follow-up data from the Australian and Finnish Registries[16]. Follow-up of the revision procedures in our study showed a survival of 70.3% (95% CI 56.1 to 80.7) at 15 years. The outcome of revision procedures in young patients has only been reported in a few studies and none also reported on the outcome of the primary THAs[7,17-21]. Strömberg and Herberts reported an overall survival of 76% after eight years' follow-up when using cemented revision THA[20]. Lee et al reported a survival after revision procedures of 63% at ten years' follow-up[7]. Girard et al reported 77 revision procedures in patients aged < 30 years, with survival at ten years' follow-up of 36%[18]. Raut et al reported a survival of 90% at six years' follow-up, for 87 cemented acetabular revision procedures in patients aged < 55 years[21]. Our results of revision arthroplasty therefore compare very favorably with the available literature. Importantly, we also determined the Girdlestone load in these patients, as the proportion of THAs which are no longer revisable. These patients generate high costs for society, in addition to the major impact of the permanent change to their lives, with limited mobility, a considerable leg length discrepancy, and often persistent pain[22]. Only six, of 1,049, THAs (0.7%) ended up as a Girdlestone arthroplasty. All these were required because of sepsis, further exposing the fact that an infected THA remains a devastating complication in young patients. The most common indication for revision was aseptic loosening (n = 78, 56.5%), followed by infection (n = 27, 19.5%). However, the indication for 11 of 22 re-revision was infection, and only four revision procedures were re-revised for aseptic loosening. A similar result was found in an analysis of revision procedures in the Dutch Arthroplasty Register[23]. In a study on 1,037 revision procedures after primary THA in patients aged < 55 years, the rate of infection was 16% in the all-revision procedures, which increased to 35% in all re-revision procedures. Thus, in the prevention of re-revision, the management of infection is of major importance[24]. Previous infection is not a contraindication to the use of impaction bone grafting in combination with a cemented implant. In our study, revisions for infection were all part of a two-stage procedure, when the reimplantation is undertaken in a controlled situation. Ammon and Stockley showed that the use of impacted bone grafts with a cemented acetabular component in revision THAs in patients with extensive bone loss is a valuable option, provided that it is combined with systemic antibiotics[25]. Cultures were taken at reimplantation in all patients, and in those with a positive culture appropriate systemic antibiotics were continued for 12 weeks. Rudelli et al showed that impaction grafting when used in a one-stage revision for infection is an option: in 32 patients with septic loosening, they only reported two re-infections[26]. We prefer a two-stage procedure for these revision cases. However, local antibiotics mixed with the bone grafts would be an option, also as part of a two-stage revision. A strength of this study is that we have been able to monitor almost all the patients throughout the period of the study. A total of 114 patients had not visited the outpatient clinic since 2015, and might therefore be considered to be lost to follow-up. However, this was partly because of the COVID-19 pandemic. Follow-up for these patients ended at the time of their most recent visit, and we therefore did not miss any failure of the prosthesis or death in our analysis. All revisions, except for one, were performed in our hospital. One acetabular revision was performed in a nearby hospital and we included the data of this patient until revision surgery. Although the use of uncemented THA is popular in young patients, there is little evidence that these implants are superior to cemented implants[27]. A recent study from the National Joint Registry in the UK, reported that the outcome of uncemented THA was not superior to that of cemented primary THA[28]. Data on the outcome of revision procedures in young patients using uncemented components are limited and disappointing[7,18]. In our study, the possible effect of competing risks had to be addressed[29,30]. Death might be a competing risk for our endpoint of interest: revision surgery. Using competing risk analyses, we assessed the cumulative incidence of revision for any reason, where death was considered a competing risk. We found a cumulative failure rate of 29.9% (95% CI 24.9 to 35.1) at 20 years' follow-up for all primary THAs, and the failure of revision THA was 27.3% (95% CI 17.1 to 38.6) at 15 years' follow-up. When comparing the cumulative failure rate with the Kaplan-Meier estimate of survival, the survival of both primary and revision THA in these patients might be underestimated when using Kaplan-Meier with an absolute difference of 3.4% and 2.4%, respectively. As well as the possible effect of competing risks, there are other limitations that should be identified. All patients in our center had a cemented THA, using the posterolateral approach. Although this provides homogeneity, the results might not be generalizable. However, the outcome of the subsequent revision undertaken using our technique can be used as a benchmark for other surgical approaches. Another critical consideration is the type of polyethylene which we used. Starting in 1988, all acetabular components which we used were made of traditional polyethylene. With the passage of time, we changed to a component made of a moderate crosslinked polyethylene (Duration; Stryker, UK), which we used until the end of the study. The results might have been better if highly crosslinked polyethylene had been used. We have recently started to use cemented acetabular components made of highly crosslinked polyethylene in young patients, which may reduce the number of future revisions for wear and aseptic loosening[31]. In conclusion, this study provides an important update on the outcome of revision THA in young patients, filling a gap in the literature. The findings can be used as a benchmark for other surgical approaches and arthroplasties used in young patients. Both the patient and surgeon must realize that revision procedures are inevitable in patients who undergo primary THA at a young age. Therefore, data on the outcome of revision procedures are essential for both patient and surgeon in the decision-making process prior to a THA

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CHAPTER 6

Total hip arthroplasty in patients under 30 years: A long-term report of 180 hips with a follow-up from 2 to 25 years

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ABSTRACT

Background

Total hip arthroplasty (THA) in extremely young patients under the age of 30 years is performed more frequently over the last decade. This patient group is more challenging due to anatomical difficulties and higher demands of the patients. Some studies have described outcomes of THA in this age group, however with a short-follow up, limited patient group or incomplete data. The aim of this study to describe the clinical and radiological outcomes of patients with a THA under the age of 30 years. The survival at 10 and 15 years of follow-up is reported. Additionally, the outcomes of the revisions within the same cohort are reported as well as the Girdlestone load.

Methods

All primary THAs performed in our institution between 1986-2014 in patients under 30 years were included (n=180). Only cemented implants were used. Acetabular impaction bone grafting was used in 127 (71%) of the cases to reconstruct acetabular bone defects. The Harris Hip Score, modified Oxford Hip Score and VAS scores for pain and satisfaction were collected. Assessment for radiological loosening of any component was performed. Kaplan-Meier survival analyses were used to determine the survival of primary THA with end-points revision for any reason, aseptic and septic loosening at 10 and 15 years. The results of the revision surgeries within this primary cohort are reported as well as the cases that ended in a permanent Girdlestone.

Results

Mean age at primary THA was 24 (13-30) years. Mean follow-up of primary THA was 8.7 (2-27.4) years. In total, 26 revisions of any component for any reason were performed during follow-up. Mean HHS of the surviving implants improved from 50 (range 20-77) preoperatively to 88 (28-100) postoperatively at last review. Mean postoperative VAS scores for pain in rest and activity were 8 (0-70) and 15 (0-90), respectively at the last follow-up. The mean postoperative VAS satisfaction score was 87 (10-100) and modified OHS was 41 (8-48). Radiographically, 3 non-revised acetabular components were loose, no femoral components showed radiographic loosening. Survival of the primary THA with endpoint revision of any component for any reason at 10 and 15 years was 87% (95% CI 79-92) and 77% (95% CI 65-86), respectively. Of the revised 26 hip arthroplasties, four re-revisions were performed within the follow-up period. One patient ended in a permanent Girdlestone, resulting in a Girdlestone load of 0.6 %.

Conclusions

The 10- and 15 year results of primary THA in patients younger than 30 years show acceptable results. This study shows that cemented THA is a valid option in these young patients, if needed in combination with impaction bone grafting for reconstruction of the bone defects. In this challenging patient group, it is important to report the outcomes of further revisions as well, to determine the true value of different techniques. By restoring bone stock during primary THA with impaction bone grafting, we believe re-revisions are facilitated.

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INTRODUCTION

Halley and Charnley were the first who reported the results of total hip arthroplasty (THA) in patients 30 years or younger in 1975[1]. However, even in those days, the authors already expressed their concerns about the long-term follow-up of THA in these extremely young patients, especially regarding the outcome of future revisions or even Girdlestone situations. Up to now, few other studies have reported the outcome of THA in patients under the age of 30 years[1-13]. In most of these studies the number of patients is limited, the follow-up is short or the study is focused on a very specific patient group such as rheumatoid arthritis patients. Overall, the outcomes of these series are not always promising. Data about revisions are lacking in nearly all studies. However, as reported by Bayliss et al., the life time revision risk of young patients operated between the age of 50 and 60 years was already very high, peaking up to 30 percent of patients in their early fifties[14]. More worrisome, about 50% of the revisions were performed within 5 years after the primary implantation. For patients under 30 years, the life time revision risk will be approaching 100 %. Unfortunately, it is known that revisions in young patients after a primary implant has a disappointing survival with more complications.

From our hospital hip database, we have selected 139 consecutive patients that received a THA (n = 180) below the age of 30 years and were treated between 1986 and 2014. During all these years we had a standard surgical treatment protocol. We determined the patient reported outcome measures (PROMs), radiological outcomes and revisions and survival data at 10 and 15 years of the THAs of this patient group. Perhaps even more important, we studied the outcomes of the subsequent revisions performed within the same cohort and report also the incidence of final excision arthroplasty performed, the Girdlestone load.

METHODS

This study was approved by our local ethics committee (study number 2008/031). From our hospital database we selected all consecutive patients who received a THA between 1986 and 2014 and were younger than 30 years at time of surgery. All patients had a minimum follow-up of 2 years. A total of 139 patients (180 hips) were included. Patients that received THA for oncological reasons were excluded. As a tertiary care center, all patients were treated in our hospital and no patients with complex osteoarthritis were referred to other centers. Patient characteristics are displayed in Table 1. The main indication for THA was avascular necrosis (AVN) of the femoral head (n=59, 33%) followed by developmental dysplasia of the hip (DDH) in 37 cases (20%). During follow-up 3 patients (3 hips) were lost to follow-up at 0.3, 1.0 and 3.0 years postoperatively. In total, 9 patients (12 hips, 6.7%) had died at time of review, these patients had a mean follow-up of 8.1 years (range 1.3-18.6 years). Their data were included until death, none of the deaths were related to the hip problem or surgery. The mean follow-up of the remaining unrevised patients was 8.7 (range 2.0-27.4) years.

Table 1. Baseline characteristics

		Total (n (%) or mean (range))
Total		180
Gender	Male	60 (33)
	Female	120 (67)
Death		12 (7)
Age in years		24 (13-30)
BMI		23 (15-52)
Indication	AVN	59 (33)
	DDH	37 (20)
	RA	27 (15)
	Perthes' disease	19 (11)
	Coxitis	7 (4)
	Multiple ephyphyseal dysplasia	6 (3)
	Bechterew	5 (3)
	Epiphysiolysis	5 (3)
	Other	15 (8)
Acetabular defect*	None	86 (48)
	Segmental	51 (28)
	Cavitary	26 (14)
	Combined	17 (9)

OA = osteoarthritis, DDH = developmental dysplasia of the hip, RA = rheumatoid arthritis, AVN = avascular necrosis
* according to the AAOS classification

Surgical procedure

During the years all patients were treated according to the same surgical protocol and the same philosophy. All procedures were performed through a posterolateral approach and a completely cemented prosthesis using metal-on-polyethylene bearing was implanted in all cases. An overview of the implanted acetabular components is displayed in Table 2. On the femoral side, 156 (87%) Exeter stems (Stryker) were implanted, 13 (7%) Charnley/Elite (DePuy Synthes) stems and 11 Muller straight stems (Zimmer). Cement in the cup was always pressurized using a seal, cement in the femur was injected in a retrograde manner after the insertion of a distal plug and pressurization was performed with a proximal seal. In case of acetabular bone defects we used acetabular impaction bone grafting (IBG, 127 cases, 71%), if needed in combination with a metal mesh, a technique that we have been using for decades and has been previously described in detail[15,16]. Bone stock defects were classified according to the AAOS classification (Table 1)[17]. In 82 cases (65%) the femoral head autograft was used as the source for the bone chips, in 26 cases (20%) this was combined with allograft bone chips from the bone bank. In 19 cases (15%) IBG was performed with allograft bone chips only. The postoperative rehabilitation protocol included full weight bearing for patients that did not receive acetabular reconstruction with IBG. Partial weight bearing was allowed for patients with IBG during 6-12 weeks, depending on the extent of the reconstruction. In our revision cases a strict protocol was used as well, with cemented implants and IBG in case of bone defects with allograft bone chips. Follow-up of the revision cases was similar as in the primary THA cases.

Table 2. Overview of the implanted acetabular components

Type of acetabular component	Total (%)
Müller/Allopro cup (Zimmer)	14 (8)
Charnley/ Elite (DePuy Synthes)	26 (14)
Exeter Contemporary Flanged (Stryker)	90 (50)
Exeter Contemporary Hooded (Stryker)	20 (11)
Exeter Rimfit (Stryker)	16 (9)
Exeter “other” (CDH, RSA, Full Profile) (Stryker)	14 (8)

Functional outcomes

Patients were seen on a regular basis in our outpatient clinic at 6 weeks, 3 and 6 months and 1 year. Thereafter, they were seen with intervals between 1 to 3 years, clinical and radiological follow-up was prospectively collected. During these visits, patient reported outcome measures (PROMs) were collected, which included the Harris Hip Score (HHS, 0-100), modified Oxford Hip Score (mOHS, 0-48), VAS scores for pain in rest and activity (0-100) and VAS score for satisfaction (0-100)[18,19]. Intra- and postoperative complications were collected.

Radiological evaluation

The radiographic assessment was performed by two of the authors (EC, BWS). Radiographs were reviewed for radiolucent lines, osteolysis and migration of the component. Radiographic failure of the cup was defined as radiolucent lines in all three zones and/or migration of 5 mm or more in any direction[20]. Femoral loosening was defined as radiolucent lines in all Gruen zones or 5 mm or more subsidence migration[21].

Statistical analysis

The survival was calculated using the Kaplan-Meier analysis with endpoints loosening for any reason, aseptic loosening and septic loosening. In addition, the results of the revision surgeries within this primary cohort are presented as well.

RESULTS

Revisions

During follow-up, 26 revisions of any component of the primary THA were performed between 0.3 and 23 years after primary surgery. The indication for revision was aseptic loosening in 15 cases, septic loosening in 5 cases, recurrent dislocations in 3 cases and 3 cases for other reasons (wear, femoral stem fracture and neurological deficit). In one case with septic loosening 0.3 years after primary THA, a permanent Girdlestone was created due to infection with tuberculosis. In 12 cases only the acetabular component was revised for aseptic loosening at a mean follow-up of 11 years (range 2-23 years). In 3 cases this was combined with a stem revision (at 7, 7 and 19 years). In the 3 cases revised for recurrent dislocations, 2 cups only were revised (at 0.4 and 1 years) and one stem only revision was performed (at 2 years). One cup was revised for the reason of wear at a follow-up of 19 years. One stem revision was performed 2 years after primary surgery due to a femoral nerve deficit in a patient with Perthes’ disease and a preoperatively high center of rotation. During revision surgery, a shortening osteotomy was performed combined with a femoral stem revision. After this revision surgery, the neurological deficit recovered. One stem revision was performed 17 years after primary surgery due to a stem breakage.

Survival

Survival of the primary THA with endpoint revision of any component for any reason at 10 and 15 years was 87% (95% CI 79-92) and 77% (95% CI 65-86), respectively. The survival rates for the separate components at 10 and 15 years of the primary THAs are displayed in Table 4. In Figure 1 and 2 the Kaplan-Meier curves are shown for revision with end-points aseptic loosening.

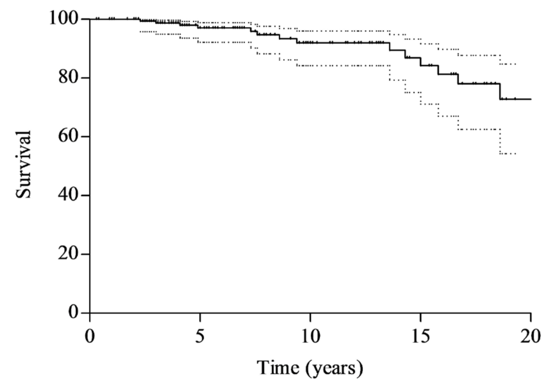

Figure 1. Kaplan-Meier survival curve with endpoint revision of any component for aseptic loosening.

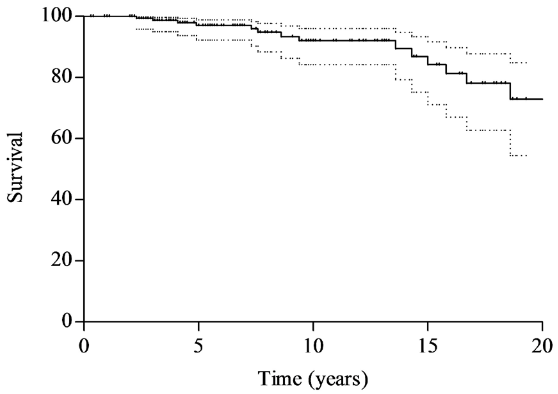

Figure 2. Kaplan-Meier survival curve with endpoint revision of the cup for aseptic loosening.

Clinical and radiographic outcomes of primary THA

The mean preoperative HHS was 50 (range 20-77, n=80), which improved to a mean of 88 (range 28-100, n=129) at final review. The majority of the patients had a high HHS, a score higher than 80 was achieved in 101 cases (78%). The mean postoperative VAS score for pain in rest was 8 (range 0-70, n=130) and for pain in activity the mean score was 15 (range 0-90, n=130). For postoperative satisfaction scores, the mean was 87 (range 10-100, n=129). The modified OHS showed a mean of 41 (range 8-48, n=129). Postoperative complications, excluding revisions, are displayed in Table 3.

Table 3. Postoperative complications

Complication	N
Early reoperation due to suspicion of deep infection	1
Dislocation	4
Neurological deficit	5
Periprosthetic fracture	1

A complete radiological follow-up was available in all cases. Of the unrevised acetabular components (n=157), 23 (15%) showed radiolucent lines. Fifteen cases showed radiolucent lines in 1 zone, 6 cases in 2 zones, and 2 cases in 3 zones. Acetabular osteolysis was observed in 11 cases (7%). One cup showed migration and tilting of 15 degrees. In total, 3 cups were radiographically loose according to our definitions (at 13, 17 and 18 years postoperatively). Regarding the unrevised femoral components (n=161), 17 stems showed radiolucent lines. Nine cases showed radiolucent lines in 1 Gruen zone, 3 cases in 2 Gruen zones and 5 cases in 3 Gruen zones. Femoral osteolysis was observed in 8 cases. None of the femoral components showed radiographic loosening.

Outcome of revisions and re-revisions

In 26 patients a revision was performed, in one case a permanent Girdlestone was created due to persistent infection. The 25 patients that underwent a revision with reimplantation, had a mean age of 32 years (range 21-42) at time of revision surgery. The majority of the patients that had revision THA surgery suffered primarily from AVN of the femoral head (11 cases, 42%) and rheumatoid arthritis (6 cases, 23%). The mean follow-up of the revision group after surgery was 6.8 years (mean 0-20 years). One patient died 4 weeks after revision surgery, the cause of death was unrelated to the surgery. The mean HHS score after revision was 82 (range 48-100, n=17), mean VAS at rest, activity and satisfaction was 14 (0-70, n=18), 21 (0-90, n=18), 80 (40-100, n=18) at last review respectively. The modified OHS after revision was 39 (22-48, n=18).

In total, 4 re-revisions were performed. In 3 cases re-revision was due to septic loosening (at 2.2, 2.7 and 11 years after first revision) and in one case due to aseptic loosening of the cup, 12.3 years after first revision that was performed due to septic loosening (Figure 3). Of the 3 cases that suffered from septic loosening, 2 underwent the first revision due to septic loosening as well. The Kaplan-Meier survival curve for the revisions is displayed in Figure 4.

Figure 3. An 18-year old woman that suffered from avascular necrosis of the femoral received a THA on the right side (**A**). Six years postoperatively there was septic loosening (**B**) and a two-staged revision was performed (**C**). Twelve years after revision there was aseptic loosening on the acetabular side (**D**) and a re-revision of the cup was performed. The patient is functioning well an no signs of loosening are visible 14 years after re-revision (**F**). Thirty-two years after primary THA this patient is still mobile with the used techniques and sufficient bone stock is available for future revisions.

Permanent Girdlestone

Of the original group of 180 THAs and including the subsequent revisions, in only one case a permanent Girdlestone was created due to septic loosening. The Girdlestone-load of this series was 0.6%.

Table 4. Survival rates of primary THA

Endpoint revision of	10-year survival (95% CI)	15-year survival (95% CI)
Any component for any reason	87% (79-92)	77% (65-86)
Any component for aseptic loosening	92% (84-96%)	84% (71-92)
Cup for aseptic loosening	92% (84-96%)	84% (71-92%)
Stem for aseptic loosening	100%	100%

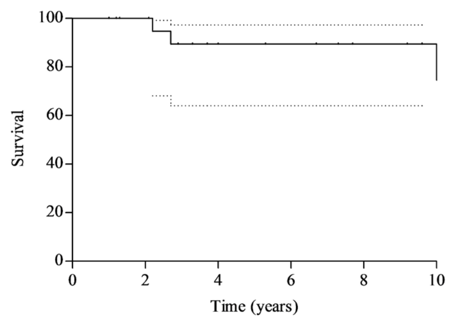

Figure 4. Kaplan-Meier survival curve with endpoint re-revision of any component for any reason

DISCUSSION

This study confirms that the outcome of THA in the very young patients is inferior to reports based on patients over 70 years of age, who have survival rates of 95% or more at 10 years after surgery[22]. However, given the fact that THA in younger patients is often technically more demanding and that these patients are more active, a survival of 87% at 10 years after implantation with endpoint revision of any component for any reason seems to be acceptable. This study shows only a slight deteriorating survival after 10 years, at 15 years more than 75% of the patients still have their original first implant. If we exclude revisions for infection and dislocation and only study those hips that have been re-operated for failure of the implant fixation, the survival is 84% (95%CI 71 - 92%) at 15 years. As in most studies, the acetabular side is the weakest link[11,12,23].

This study is one of the largest single-institute studies on the outcome of THA in patients under 30 years with a follow-up up to 25 years and also reporting revisions within the original cohort makes this study unique. Due to a consequent follow-up protocol, only few patients were lost to follow up. We also follow a very standardized treatment protocol, always using cemented implants and combining with acetabular impaction bone grafting in case of bone stock loss. This technique and the outcomes in several patient groups have been described in literature[15,24]. Although over the years, there is a worldwide tendency to use noncemented hips or resurfacing THA in young patients, this report shows that cemented THA with or without bone grafting can be an attractive option with favorable results up to 15 years as was also shown in other studies[25,26].

This study has some limitations. First, this is a single institute study, which decreases the generalizability of the study results. All surgeries were performed at our tertiary-care center and this population might have higher comorbidity rates and more complicated bone defects than the average arthroplasty center. In addition, 3 patients were lost to follow-up. Their data is included up to the latest visit. Secondly, there are missing PROMs, mainly preoperatively. Some cases were operated many years ago and in the ‘80s and early ‘90s, the PROMs were not part of the standard protocol, therefore these data are missing and cannot be collected retrospectively. In addition, several implants have been used over the years and the quality of polyethylene has drastically improved over the last decades from conventional to highly-crosslinked polyethylene, leading to less wear and osteolysis[27]. However, all implants were cemented on the acetabular and femoral side, a metal-on-polyethylene bearing was used and all surgeries were performed with the same technique and philosophy. All bone defects were reconstructed using the impaction bone grafting technique.

In the recent years, the amount of studies on THA in young patients has increased, giving more insight in the outcomes and problems this patient group is facing[11,12,23,28]. Unfortunately, most studies have small patient groups, use different techniques or prosthesis within the cohort, have a short- to medium term follow-up or do not report on the outcomes of the subsequent revisions within the same study group. We believe that reporting the outcomes of the subsequent revision is maybe even more important than the primary results in these extremely young patients. Our study shows that these patients are still extremely young at the time of revision with a mean age of 32 years. We are convinced that the outcome of the revision THA is influenced by the techniques used at primary THA. In addition, we consider that reporting the Girdlestone-load is as these patients often experience a great decrease in mobility, resulting in a permanent change of their lives, high costs for society and many other problems. In this study, only one out of 180 cases (0.6%) ended up as a Girdlestone arthroplasty.

Swarup et al. reported the outcomes of a large cohort of 548 primary THA in patients under 35 years and showed a survival of 87% at 10 years, with the majority of patients receiving noncemented implants[28]. In our study, we found comparable results with the use of only cemented implants. The Swedish Hip Arthroplasty Register showed a 10-year and 15-year survival of 90% and 78%, respectively in patients 30 years or younger with mostly noncemented fixation[12]. This study consisted of 504 hips with an average follow-up of 8 years and mostly noncemented fixation. Of course, radiological data and detailed clinical data are missing in a registry study.

Metcalfe et al. showed in a registry study in young THA patients under 20 years of age that the most common reason for revision was loosening (20%)[25]. They also showed there was no difference in survival between cemented and noncemented fixation. Most of the revisions that were performed in our study were due to aseptic loosening (58%). Kahlenberg et al. studied the causes of revision of THA in patients under 35 years, with mostly noncemented implants and found that causes of revision in this patient group differed from those in the general THA population, with 46% of revisions caused by aseptic loosening of any component[23]. Agrawal et al studied 101 primary THA in patients under 30 years with a mean follow-up of 12.6 years[11]. In total, 25 hips (25%) underwent revision, most commonly for aseptic loosening (72%), resulting in a survival of 71% at 10 years and 52% at 15 years of any component for any reason. Mostly noncemented components were used. They also showed that cemented and hybrid prosthesis out-performed uncemented prostheses.

Unfortunately, none of the studies mentioned above, except for Swarup et al., reported on the outcomes of the subsequent revisions[28]. The study of Kahlenberg et al. reports on the subsequent revisions of the primary cohort, however, many revisions from the cohort were performed elsewhere and therefore the follow-up of the primary cohort was not complete[23]. Still they reported 29% re-revisions at a mean of 5.3 years after first revision and 9 hips underwent a third revision[23]. In the current study, we found 4 re-revisions (16%) at a mean of 7 years after first revision. Three of these re-revisions were performed for septic loosening and two of these cases had a primary indication of rheumatoid arthritis.

Five out of 25 (20%) revisions were performed due to septic loosening. This may have a relation with the amount of patients with inflammatory arthritis in our study group (18%), which have higher rates of infection compared with the general population[29]. Mohaddes et al showed a revision rate for infection of 11% in patients of the same age group[12]. An analysis of 1103 revised THAs in patients under the age of 55 years in the Dutch Arthroplasty Register showed that the most common reason for re-revision was infection (35%). They described a poor survival of index revisions due to infection. At a follow-up of 5 years, almost half of the revision THAs due to infection resulted in a re-revision procedure[30].

This study showed acceptable results of a cemented THA in young patients under the age over 30 years at primary surgery and shows that THA in this patient group is a good option with satisfying results. However, it is very important to keep in mind that future revisions in these young patients will be inevitable. We think reporting the outcomes of subsequent revisions in studies on very young patients should be mandatory. In our study, of the 26 revisions that were performed within the original cohort, 4 re-revision were performed so far, most of the cases for septic loosening and only one for aseptic loosening at 12 years after first revision. By restoring bone stock during primary surgery with bone impaction grafting, we believe re-revisions are facilitated and less debilitating for patients.

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CHAPTER 7

General discussion and future perspectives

GENERAL DISCUSSION

Continuous developments and innovations have made that the total hip arthroplasty (THA) is one of the most successful major operations ever devised for the treatment of end-stage human disease[1]. Following the success of THA in the elderly patient group, there has been a logical increase in the number of THA in younger patients. However, when comparing the outcomes between these patient groups, literature clearly shows inferior results in younger patients compared to the elderly patient population. Several factors are responsible for this less favorable result.

Young patients often suffer from secondary osteoarthritis accompanied by bone defects, usually located in the acetabulum. These defects can compromise an adequate placement and fixation of the acetabular component, which makes these procedures technically more challenging and difficult. These problems are not only encountered at the primary THA, but also especially at revision surgery. These acetabular defects can be even more extensive than in primary cases as a consequence of progressive osteolysis and the loosening of the primary hip implant. In addition, young THA patients engage in higher activity levels than the elderly population and due to their longer life expectancy, it is very likely that they will wear out as well as outlive their primary prosthesis and hence face inevitable one or more revision THA surgeries. To obtain a better understanding of the true value of THA fixation and reconstruction techniques in this difficult young population, it is crucial to have access to long-term outcomes of THA. When studying THA in young patients, there is a tendency to mainly report the long-term results of only the initial THA, which obviously only reflects a single snapshot in the lifetime of a young patient with a THA. However, with the increasing number of inevitable revision procedures performed in these patients, the importance of reporting the long-term results of the revision surgeries becomes indispensable. For example, reporting on the outcome of the subsequent (re-)revisions from the original primary cohort should be a standard for research in this specific patient group. Using this way of outcome reporting, one will not only get a glimpse of a snapshot in the young patients' life with a primary THA, but one can follow the patient through a long course in his lifetime with a THA and the subsequent revision surgeries that are associated with it. This way of reporting results does not only provide a better understanding of the THA fixation and reconstruction techniques that are used, but the treating surgeon can set the patients' expectations in perspective based on these results. It is important for surgeons to realize that this patient group is still quite young even at revision THA, as shown in the studies described in this thesis.

The conducted studies in this thesis report on the outcomes of young patients that received a THA in the Radboudumc. This thesis shows that satisfying results can be achieved with THA in young patients below the age of 50 years by using a cemented prosthesis and if required, combined with impaction bone grafting (IBG). Even in the most challenging cases with extensive acetabular defects, such as in developmental dysplasia of the hip (DDH), this technique has shown satisfying long-term results (**Chapter 3**). Interestingly, the type of fixation of THA remains a matter for debate and although there is a worldwide trend towards more uncemented THA, cemented THA has shown to have an acceptable long-term survival, both in elderly and young patients[2-4]. In 2013, Troelsen et al. reported a shift towards uncemented THA fixation, despite registry data showing that cemented THA has lower revision rates in elderly patients, which they described as the 'uncemented paradox'[5]. In their follow-up study, published in 2020, this conclusion did not change. Nevertheless, the percentage of uncemented fixation in primary THA has even significantly increased since 2010, also in Scandinavian countries who were initially very orientated on cemented THA[6]. Although this study of Troelsen et al. does not focus on young THA patients and mainly comprises the older THA population, other studies, including register studies, have shown satisfying results of cemented THA in young patients[2, 7].

The studies presented in this thesis, included only patients that have received cemented THA both on the acetabular and femoral side, showing satisfying results of using this fixation technique that are at least comparable to uncemented fixation techniques. A cemented THA is not only a good option in primary THA cases, but also in revision procedures, even in the most demanding cases. Therefore, considering that the amount of uncemented THA is worldwide increasing, it would be regrettable if over the years residents and orthopaedic surgeons are not trained anymore in or are not able to maintain their technical skills of performing a well-cemented THA. A current example of losing the skills how to perform a cemented THA in the orthopaedic community is nowadays actual in the United States of America. After many years of promoting mainly uncemented THA in all patient categories, both by leading orthopaedic surgeons and the industry, there is a realization that cemented implants outperform uncemented implants in older patients. However, re-introducing the skills on how to perform a well-cemented THA on a large scale is not easy. As shown by the previously mentioned studies, there is a trend to perform uncemented implants in Europe as well. One factor driving this uncemented THA trend might be the shorter surgical time, allowing more THAs to be performed in one surgical day. Especially in high-volume time pressured centers, the uncemented THA can be favored above the cemented THA for this reason. However, there still is a substantial proportion of THAs in Europe that are being cemented and in general, the knowledge and skills for this fixation technique remain.

Next to the fixation technique, restoration of bone stock plays an important role in revisability of a THA. It is remarkable that in orthopaedic implants, there is a tendency to use more and larger metal implants to reconstruct bone defects. When bone stock deficiencies are encountered during surgery, we believe the IBG technique, and if needed in combination with a mesh, is a suitable option to replenish the bone stock with a strong focus on biology, especially in young patients. This technique has been developed in the Radboudumc and many studies have shown satisfying results in combination with a cemented THA[4, 8-12]. IBG is an attractive biological method to reconstruct the bone at primary THA. However, caution should be exercised when using this technique, as there are several technique-related factors that influence the incorporation and thereby the results of IBG in cemented THA[13]. It is important that the bone chips are trabecular and all cartilage and soft tissue is removed from the chips. The bone chips used for the acetabular side should have a size of 0.7-1.0 cm in diameter and it is advised to make the bone chips by hand using a bone nibbler. Bone mills often create bone chips that are too small, which can have a detrimental effect on the initial stability. Alternatively, there are some bone mills that produce larger chips (e.g., Novio Magus bone mill by Spierings Medical Technology, Nijmegen, the Netherlands). Another crucial factor in a well-performed IBG is the impaction technique. Impaction of the bone chips should be performed with specially designed impactors, with increasing sizes to build up the bone graft layer by layer. In this process, firm impaction using a metal hammer and a metal impactor is key. There is no indication for reversed reaming of the graft, as this will cause less optimal initial cup stability, shown in an in vitro model study[13]. In addition, in case of segmental defects, it is important to create a contained acetabulum with the use of segmental meshes, which can be fixed with screws. On top of this mesh, the bone graft can be impacted. **Chapter 4** in this thesis describes the use of these lateral rim meshes in patients with acetabular defects and shows that this is a safe option for the reconstruction of segmental acetabular defects. All these aforementioned technical factors are important and variations on this original technique can cause inferior results of IBG. Of course, the IBG technique has some disadvantages as well. Patients that have received IBG are not allowed to immediate full-weight bearing postoperatively. It is believed that immediate full-weight bearing might generate too much stress loading on the graft and might hamper full graft incorporation. However, during the years the postoperative protocol for patients that received IBG in THA has changed. In the initial years of THA with IBG, it was thought that 6 weeks of bedrest was necessary to prevent the graft from being put on excessive strain. After a few years, patients were allowed to 10% weight bearing postoperatively. Nowadays, patients that received IBG are allowed 50% weight bearing immediately postoperatively during 6 weeks and only patients with very extensive reconstruction with IBG are allowed 10% weight bearing during 6 weeks, followed by 50% weight bearing during 6 weeks. Most reports from other study groups also advice initial partial weight-bearing, but it has also been described that immediate full weight bearing after IBG was allowed[14]. As the originating center of this technique, we might be too conservative and perhaps full weight bearing for all patients might be a consideration for the future. Another disadvantage might be that the IBG technique is accompanied with a prolonged surgical time and certainly, the technique has a learning curve. However, it is not a difficult technique to perform, as long as it is taught in the right manner and a certain level of skills is maintained. A potential problem limiting the expansion of the IBG technique worldwide might be that IBG is often not considered in the first place in primary THA with acetabular bone deficiencies, as it is considered as a demanding and time-consuming technique. In our view, the focus should be on bone reconstruction from the beginning on in young patients. However, orthopaedic surgeons that are not optimally trained to do large reconstructions, apply IBG only in the most demanding revision THA cases in young patients. A better approach would be that surgeons start to perform IBG in simpler primary or revision cases and then gradually extend their experience with the technique. The IBG technique should be a part of every hip orthopaedic surgeon's armamentarium treating young patients. Another issue is that IBG is a technique that is unfortunately not specifically promoted by the orthopaedic industry, as there is not a great financial interest in the use of IBG, being a relatively cheap method for which not many materials and resources are necessary. This makes it more challenging to expose orthopaedic surgeons worldwide to this attractive biological reconstruction technique.

As shown in many studies, the problem in young patients receiving a THA is usually on the acetabular side, whereas the stem often has very satisfying long-term results. The excellent survival of cemented stems is also shown in the studies in this thesis. In one of the largest single-center studies (**Chapter 5)** of young patients with a THA, the survival of the cemented stems with endpoint aseptic loosening was 91% after 20 years. In addition, many other studies, have shown this satisfying survival of cemented stems in young THA patients, especially with the endpoint revision for aseptic loosening[15, 16].

In the past decades, many different implants and techniques have become available to overcome the acetabular bone defects, which can largely be divided in two categories: non-biological and biological reconstruction techniques. In non-biological strategies mostly large metal acetabular components, sometimes with additional augments or cages, are used and metal is used to address the bone loss. The disadvantage of these techniques is that they do not restore the bone stock itself and only act as a void filler. Once these metal implants loosen, the acetabular bone defect will even be more extensive hampering the next revision. In contrast, the aim of biological reconstructions such as IBG or a femoral head bulk graft, in addressing the bone deficient acetabulum, is to improve and restore the bone stock. Considering future (multiple) revisions, especially in the young THA patient, restoring bone stock already at the primary surgery is crucial. After all, the most important factor in successful long-term fixation is the availability of adequate bone stock. From our experience, it is frequently seen at revision procedures that graft incorporation of the previous procedure has occurred and is substituted by host bone, allowing a reimplantation of the THA with solid bone stock. In most revision surgeries that we encounter, reimplantation of a regular acetabular cup with IBG is possible, due to the fact that sufficient bone stock is created and available due to previously applied IBG. In these cases, there is no need to implant larger sized cups or apply other large reconstruction methods. In the Radboudumc, the IBG technique is used for all kinds of defects, both acetabular and femoral, in primary and revision THA surgery.

In this thesis we report the results of the largest single-center study of patients younger than 50 years that received a THA in the Radboudumc (**Chapter 5**). Additionally, the results of the revisions and re-revisions within the same cohort are presented as well. This local registry study showed a survival for all primary THA with end-point revision for any reason of 90.7 % (95% CI: 88.2-92.7) at 10 years and 66.7% (95% CI: 60.5-72.2) at 20 years. For the subsequent revision THA, a survival of 78.5 (95%CI: 67.3-86.2) at 10 years and 70.3 (95% CI: 56.1-80.7) at 15 years for endpoint re-revision for any reason. These data are acceptable, certainly in relation to data reported in the limited literature worldwide on this topic. However, it needs to be noted that in this cohort we included all primary THAs in patient younger than 50 years that were performed from 1988-2017 and in the early years the acetabular components were made from traditional polyethylene. It is known that these cups had higher wear rates and as a consequence higher rate of revision for aseptic loosening. Nowadays, we use highly-crosslinked polyethylene, resulting in a decrease in failure for aseptic loosening in the long-term. The hope and expectations are that the future long-term data of young patients with THA will even be more satisfying.

As previously mentioned, revision THA is inevitable in the young patient group and therefore this group needs to be treated with special attention. Revision THA can only be performed if there is sufficient bone stock available for reimplantation of a THA and if there are no signs of infection. If reimplantation of THA is not possible, a patient is left with a permanent resection arthroplasty, a Girdlestone situation. A permanent Girdlestone situation is considered as a last resort and can be extremely debilitating for a patient with serious limitations in daily life. A shortening of the affected leg, inability to walk unassisted, or even being wheelchair bound are consequences of a Girdlestone situation. Despite this decrease in mobility and functionality, a Girdlestone resection arthroplasty most often relieves the patient from the pain and further surgeries. As a Girdlestone is an important end-point in a patient with a THA with serious consequences, the term Girdlestone-load is introduced in this thesis. This term describes the number of patients within a study cohort that ends with a permanent resection arthroplasty. This variable gives an impression of which percentage of the study population is left with a permanent disability and definitive failure of THA. In **Chapter 5** the outcomes of THA in a group of 1049 cases were described and a Girdlestone-load of 0.7% (6 patients) was found in all THA surgeries performed from 1988-2018 in young patients. We strongly recommend that other research groups will also present this Girdlestone load in future studies.

An important topic that needs to be addressed are the patients that are confronted with a revision due to septic loosening, which is also disastrous in young patients. The Dutch Arthroplasty Register showed that the most common reason for re-revision was infection (35%) in patients under the age of 55 years[17]. In **Chapter 5 and 6** we describe the results of THA in young patients and the subsequent revisions within the cohorts. In Chapter 5, all permanent Girdlestone resection arthroplasties that were performed were due to persistent infection. Of all subsequent revision THA performed in that study, an important amount was due to septic loosening in patients that had a previous septic loosening of their THA. Remarkably, once a revision is performed for septic loosening, the chances are high that the subsequent revisions are often due to septic loosening as well. This indicates that somehow these patients are at risk for developing another infection, despite adequate treatment with a two-staged revision and antibiotics. It is recommended that the care for young patients with an infected THA is performed in highly specialized centers.

CONCLUSION AND RECOMMENDATIONS

In conclusion, this thesis shows satisfying results of cemented THA in young patients, if needed combined with impaction bone grafting for the reconstruction of acetabular defects. The use of additional acetabular meshes combined with IBG are a safe option to create a contained acetabulum.

This thesis emphasizes the importance to report results of THA in young patients in a new way, which includes combining outcomes of primary THA with the subsequent revisions within the same cohort to provide essential information and expectations of THA in young patients. Future research should focus on combining these results and try to identify factors that influence the results of revision surgery. Lastly, the term Girdlestone-load is introduced as a measure of permanent disability in a young THA cohort.

For the future, we propose the following recommendations:

- The use of alternative endpoints for studies on THA in young patients, such as the outcome of the subsequent revisions in the younger patients and to report the Girdlestone-load.
- Evaluation of alternative techniques for acetabular reconstruction in young patients with long-term outcomes. This can include an acetabular IBG, using the technique as described in this thesis with the correct bone chips size and firm impaction.
- Analysis of the possibility of postoperative full-weight bearing in patients that received a THA combined with IBG.
- Since the number of uncemented THA is predominating, long-term studies evaluating outcomes of primary and subsequent revision THA with the use of an uncemented prosthesis are needed.

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CHAPTER 8

Summary
Samenvatting

SUMMARY

The aim of this thesis is to evaluate the long-term results of primary and revision cemented total hip arthroplasty (THA) in young patients, with the use of impaction bone grafting (IBG). Young patients with end-stage hip osteoarthritis often suffer from secondary osteoarthritis, originating from conditions such as developmental dysplasia of the hip, in which acetabular defects are often encountered at primary THA placement. At the Radboudumc, patients with end-stage osteoarthritis, have always been, and are still, treated with the same philosophy: a cemented THA and, in the presence of acetabular or femoral defects, a biological reconstruction of these defects is performed using IBG. If needed, a metal mesh is used to make a segmental defect contained. All patients in the studies in this thesis were operated at the Radboudumc, a tertiary care center for orthopaedic surgery.

In this thesis the results of primary THA in this challenging patient group are described. In addition, the focus is on the results of revision THA surgeries within the original study cohort of young patients. By reporting the results of the subsequent revisions from the same primary cohort, one can get insight in the true value of the technique and fixation method that is used and follow the young THA patient during their lifetime. In this thesis, the term Girdlestone-load is introduced, which refers to the number of patients within a study cohort in which a reimplantation of a prosthesis could not be performed due to, for example, persisting infection or a very extensive bone defect. These patients are left with a permanent resection arthroplasty (Girdlestone) and end in an enormous decrease in mobility and permanent disability.

In **Chapter 2** the history and evolution of cemented THA and IBG is described. IBG in THA as known nowadays was first performed in 1979 by professor Slooff at the Radboudumc, inspired by the technique of morselized bone grafts used in patients with protrusio acetabuli suffering from rheumatoid arthritis. From 1979 on, IBG was used in primary THA with acetabular bone stock defects and in revisions with bone stock loss. At the Radboudumc, various mechanical and histological studies were performed regarding IBG and the incorporation of the graft. These studies showed that bone grafts incorporated well. Acetabular biopsies at revision THA surgery were taken from patients who had a previous reconstruction with IBG and these studies demonstrated complete incorporation of the graft into a new trabecular structure. The surgical technique of IBG is extensively described in this paper. A few important factors for successful execution of IBG are presented: bone chip size, preparation of the acetabulum for IBG and impaction technique. Ideal bone chip size should be between 7 and 10 millimetres in diameter and the use of only small chips is not recommended. This may also explain some of the less satisfying outcomes of IBG in other study groups. Several studies that report on the results of IBG from Radboudumc and other centres are described in this paper. Studies show that acetabular reconstructions with

IBG and a cemented component have satisfying results and are encouraging to continue using this biological method for reconstruction of bone defects in young THA patients.

Chapter 3 reports on the long-term results of primary THA in patients suffering from secondary osteoarthritis due to developmental dysplasia of the hip (DDH). DDH is one of the main causes of secondary osteoarthritis in young patients and is often accompanied with acetabular bone stock defects. This underdevelopment of the acetabulum in DDH hampers anatomic reconstruction. Compared to THA in primary osteoarthritis, THA in DDH is at risk of higher failure rates due to the often young age of these patients and the accompanied bone defect. In this study we describe the results of 24 primary THA procedures in patients with DDH with a minimum follow-up of 15 years (mean 20, range 16-29 years). The mean age of the study group was 48 years at surgery (range 26-74). The competing-risk analysis was used to determine the probability of revision of the acetabular component in the presence of the competing event of death with endpoint of revision for any reason and aseptic loosening. The cumulative failure rate of the acetabular component was 7% (95% CI 0%-17%) with endpoint revision for any reason at 15 and 20 years, and 4% (95% CI 0%-11%) at 15 and 20 years with endpoint aseptic loosening. In total, 3 revisions were performed at 2, 12 and 26 years of follow-up. The revisions at 12 and 26 years were due to aseptic loosening and the revision at 2 years was due to sciatic nerve problems. None of the unrevised cups showed radiographic failure at final follow-up and no dislocations or infections had occurred. The clinical Harris Hip Score improved from 37 (range 9-72) preoperatively to 83 (range 42-99) at latest follow-up.

This study showed satisfactory long-term outcomes of primary THA in patients suffering from DDH with the use of IBG to reconstruct acetabular defects. After 20 years of follow-up the probability of revision is rather low at 7%.

In literature, some studies report inferior results in revision THA with the use of lateral rim meshes in combination with IBG in revision cases in the presence of acetabular defects. **Chapter 4** describes the outcome of primary THA with IBG combined with a lateral rim mesh, compared to patients with primary THA that did not need a lateral rim mesh reconstruction. All patients were 50 years or younger at the primary THA. A group of 235 patients (257 THAs) who received primary THA with IBG and an additional lateral rim mesh was compared to a group of 306 patients (343 THAs) who received IBG without a lateral rim mesh in the period from 1988-2015. The mean age at surgery was 38 years (range 13-50 years) and the mean follow-up was 6 years (range 0.1-22 years). In the mesh group 18 acetabular components (7%) were revised, main reasons for revision were aseptic loosening (n=7) and septic loosening (n=5). In the no-mesh group 36 acetabular components (10%) were revised, main reasons for revision were aseptic loosening (n=19) and septic loosening (n=8).

The use of lateral rim mesh was not significantly associated with the risk of acetabular revision for any reason (unadjusted HR 0.64, 95% CI 0.3-1.2; p = 0.16). For revision of the acetabular component due to aseptic loosening, the unadjusted HR was 0.35 (95% CI 0.11-1.07; p = 0.07). Adjusted for potential confounders, the HR for revision of the acetabular component for any reason was 0.50 (95% CI 0.13 to 1.93; p = 0.31) and for aseptic loosening this was 0.29 (95% CI 0.02 to 4.04; p = 0.35).

Kaplan-Meier analyses were performed to determine the survival of the THA with end point revision of the acetabular component for any reason and for aseptic loosening at 10 and 15 years. The survival of the acetabular component for aseptic loosening was 98% (95% CI 95%-100%) at 10 years and 90% (95% CI 81%-100%) at 15 years in the mesh group. In the no-mesh group the survival for aseptic loosening was 94% (95% CI 89%-97%) at 10 years and 85% (95% CI 77%-94%) at 15 years. There was no statistical difference in component survival between the both groups. In conclusion, this study shows that the use of a lateral rim mesh in primary THA combined with IBG is not associated with higher risk of revision and is a safe option in reconstructing acetabular defects during primary THA.

In **Chapter 5**, the outcomes of 1049 primary THAs (860 patients) in patients under the age of 50 years in one of the largest single-centre series on this topic worldwide are reported. All procedures were performed at Radboudumc and all patients were treated with the same aforementioned philosophy; a cemented THA and reconstruction with IBG in case of bone defects. The mean age of the study group was 37 years (range 12-50 years) at primary THA placement and the mean follow-up of the primary THA was 9 years (range 2-32 years). The most common diagnoses were DDH (29%) and avascular necrosis of the femoral head (28%). In 751 THAs (72%) acetabular IBG was applied.

In total 138 (13%) revisions were performed, of which 127 acetabular component revisions. Main reasons for revision of the acetabular component were aseptic loosening (n=74) and septic loosening (n=27). The mean age at time of first revision was 48.2 years (range 23-73 years).

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The Kaplan-Meier analysis was used to determine the survival of the prosthesis. Survival for all primary THAs with an endpoint of revision for any reason was 91% (95% CI 88%-93%) at 10-years follow-up, 67% (95% CI 61%-72%) at 20-years, and 54% (95% CI 46%-62%) at 25-years follow-up. For the acetabular component only with endpoint revision for aseptic loosening, survival was 96% (95% CI 94%-98%) at 10-years follow up, 78% (95% CI 71%-83%) at 20 year and 64% (95% CI 54%-72%) at 25-years follow-up. The revision rates for different subgroups (age and diagnosis) were calculated as well and are presented in the paper.

In this chapter we emphasize the importance to describe the results of subsequent revision

THA surgeries. As there is little data available on outcomes of revision procedures in these young patients, especially from the same study cohort, we determined the survival of the subsequent outcomes within the cohort as well. Of the 138 revision THAs, 22 required a re-revision, of which 20 acetabular component re-revisions. In 11 cases infection was the reason for re-revision and in 8 cases there was aseptic loosening of the acetabular component. The mean age at re-revision was 52 years (range 33-71 years) with a mean follow-up of the revision of 6.5 years (range 0.1-22 years).

The survival of revision THA with endpoint of re-revision for any reason was 79% (95% CI 67%-86%) at 10-years and 70% (95% CI 56%-81%) at 15-years follow-up. For all revised acetabular components, survival was 79% (95% CI 67%-87%) and 70% (95% CI 54%-81) at 10- and 15-years follow-up, respectively. Of the 22 re-revision procedures, 7 cases required a second re-revision. The mean follow-up of the re-revisions was 3.5 years (range 0.2-12 years). Main reasons for second re-revision were aseptic loosening (n=2) and septic loosening (n=3).

This is the first study worldwide to report the Girdlestone-load to define the definitive failure of the treatment with a THA. In 4 cases, there was no reimplantation possible during first revision, due to infection. This eventually resulted in a permanent resection arthroplasty, a Girdlestone situation. In addition, a Girdlestone arthroplasty was undertaken in 2 out of 7 second re-revision procedures, due to infection. Thus, in the total study group 6 patients ended in a permanent resection arthroplasty, resulting in a Girdlestone-load of 0.7%, all due to infection. Except for these septic indications, all patients with a failed primary or revision procedure underwent satisfactory reimplantation of the components.

In this study promising long-term survival of primary- and revision THA were found. The used technique, a cemented THA in combination with IBG in case of bone defects, is a very suitable one and a proven long-term option that should be considered in these young patients.

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In **Chapter 6**, the results of THA in extremely young patients that were 30 years or younger at time of implantation are described. A total of 139 patients (180 hips) were included in this study with a minimum follow-up of 2 years and a mean age of 24 years (range 13-30 years) at surgery. The main indications for THA placement were avascular necrosis of the femoral head (59%) and DDH (20%). During follow-up, 26 revisions of any component were performed, mainly due to aseptic loosening (n=15) and septic loosening (n=5). IBG was used in 127 cases (71%) to reconstruct acetabular defects.

In this study, we were also able to evaluate the radiographic outcomes. In total, 3 acetabular components showed radiographic loosening and no femoral components appeared radiographically loose. We also collected the patient reported outcome measurements (PROMs), including the Harris Hip Score (HHS), modified Oxford Hip Score (mOHS) and VAS scores for pain in rest and activity and VAS score for satisfaction. The mean pre-operative HSS improved from a mean of 50 (range 20-77) to a mean of 88 (range 28-100) at final review. The mean postoperative VAS score for pain in rest was 8 (range 0-70) and for pain in activity the mean score was 15 (range 0-90). For postoperative satisfaction scores, the mean was 87 (range 10-100). The mOHS showed a mean of 41 (range 8-48) at final follow-up. In total, 26 revisions of any component of the primary THA were performed, mostly due to aseptic loosening (n=15) and septic loosening (n=5). Survival of the primary THA with endpoint revision for any component for any reason at 10 and 15 years was 87% (95% CI 79%-92%) and 77% (95% CI 65%-86%), respectively. The survival of the acetabular component with endpoint revision for aseptic loosening at 10 and 15 years was 92% (95% CI 84%-96%) and 84% (95% CI 71%-92%), respectively.

In one case, a permanent Girldestone was created during the first revision surgery, due to infection. A reimplantation was not performed due to persistent infection. Of the other 25 cases that underwent revision THA, 4 re-revisions were performed. In 3 cases due to infection and in one case due to aseptic loosening 12 years after first revision. The Girdlestone-load in this study was 1 out of 180 cases (0.6%).

This study showed acceptable results of THA with the use of a cemented THA with IBG in an extremely young patient group. However, one still needs to keep in mind that future revisions will follow and that these patients are still young at first and even at second revision surgery.

SAMENVATTING

Het doel van dit proefschrift is het evalueren van de langetermijnresultaten van gecementeerde primaire en revisie totale heupprothesen (THP) in jonge patiënten, zo nodig in combinatie met het gebruik van impaction bone grafting (IBG). Jonge patiënten met eindstadium artrose van de heup hebben vaak secundaire artrose, waar aandoeningen zoals bijvoorbeeld heupdysplasie aan ten grondslag liggen. Hierbij worden tijdens de plaatsing van een totale heupprothese, vaak acetabulaire defecten aangetroffen. In het Radboudumc zijn, en worden, deze patiënten altijd behandeld met dezelfde filosofie: een gecementeerde THP met het gebruik van een biologische reconstructie met IBG in het geval van acetabulaire of femorale defecten. Indien nodig, wordt er bij een segmentaal defect een metalen mesh toepast. Alle patiënten in de studies van dit proefschrift zijn geopereerd door de afdeling Orthopedie van het Radboudumc, een tertiair centrum voor orthopedische chirurgie.

In dit proefschrift worden de resultaten van primaire THP in deze uitdagende patiëntengroep beschreven. Tevens ligt de focus van dit proefschrift op de resultaten van de revisies die zijn verricht bij patiënten vanuit het originele studie cohort. Door het rapporteren van de uitkomsten van de daaropvolgende revisies van het primaire cohort, kan men inzicht krijgen in de daadwerkelijke waarde van de reconstructie- en fixatietechniek die gebruikt worden. Hiermee kan men de jonge THP-patiënten als het ware vervolgen gedurende het verdere leven. Daarbij wordt in dit proefschrift de term ‘Girdlestone-index’ geïntroduceerd, waarbij de proportie van patiënten wordt beschreven waarbij geen reïmplantatie kon worden verricht, bijvoorbeeld door persisterende infectie of zeer uitgebreide botdefecten. Deze patiënten behouden een permanente resectie van de heup (Girdlestone situatie) en blijven achter met een afname van mobiliteit en een permanente invaliditeit.

In **hoofdstuk 2** wordt de geschiedenis en de evolutie van de gecementeerde heup en IBG beschreven. IBG in de THP zoals we deze heden ten dage kennen, werd als eerste uitgevoerd in 1979 door professor Slooff in het Radboudumc, geïnspireerd door de techniek van het gebruik van botsnippers welke werd gebruikt in patiënten met reumatoïde artritis met protrusio acetabuli. Vanaf de beginjaren werd IBG gebruikt bij primaire heupprothesen met botdefecten aan de komzijde en revisies met acetabulaire defecten. In het Radboudumc werden verschillende mechanische en histologische studies uitgevoerd met betrekking tot IBG en de incorporatie van de graft. Deze studies toonden aan dat deze botsnippers goed geïncorporeerd werden. Acetabulaire biopsieën werden genomen bij revisie THP-chirurgie van patiënten die eerder een reconstructie met IBG hadden ondergaan en deze studies toonden een volledige incorporatie van de graft aan. De chirurgische techniek van IBG wordt uitgebreid beschreven in dit artikel. Enkele belangrijke factoren voor een succesvolle uitvoering van IBG worden beschreven: de grootte van botfragmenten, de voorbereiding van het acetabulum voor IBG en de impactie-techniek. De ideale grootte van botfragmenten is tussen 7 en 10 millimeter in diameter en het gebruik van alleen kleine fragmenten wordt niet aanbevolen. Dit zou ook enkele minder bevredigende resultaten van IBG van andere onderzoeksgroepen kunnen verklaren. Verschillende studies, van het Radboudumc en andere centra, welke over de resultaten van IBG rapporteren worden in dit manuscript besproken. Studies tonen aan dat acetabulaire reconstructies met IBG in combinatie met een gecementeerde THP bevredigende resultaten hebben en ondersteunen het gebruik van IBG als optie voor de reconstructie van botdefecten bij jonge THP patiënten.

Hoofdstuk 3 rapporteert over de lange termijn resultaten van primaire THP bij patiënten met secundaire coxartrose bij heupdysplasie. Heupdysplasie is een van de meest voorkomende oorzaken van secundaire coxartrose in jonge patiënten en gaat vaak gepaard met acetabulaire bot defecten. De onderontwikkeling van het acetabulum bij heupdysplasie bemoeilijkt een anatomische reconstructie. Vergeleken met primaire coxartrose, heeft een THP bij heupdysplasie een hoger risico op falen door de vaak jonge leeftijd van de patiënten en gepaard gaande botdefecten. In deze studie beschrijven we de resultaten van 24 primaire THP-procedures bij patiënten met heupdysplasie met een minimale follow-up van 15 jaar (gemiddeld 20, 16-29 jaar). De gemiddelde leeftijd van de onderzoeksgroep was 48 jaar bij de operatie (26-74 jaar). De competing-risk analyse werd gebruikt om de waarschijnlijkheid van revisie van de acetabulaire component te bepalen in aanwezigheid van het concurrerende evenement van overlijden met eindpunt van revisie om welke reden dan ook en aseptische loslating. Het cumulatieve risico voor falen van de acetabulaire component was 7% (95% betrouwbaarheidsinterval (BI) 0%-17%) met als eindpunt revisie voor welke reden dan ook na 15 en 20 jaar, en 4% (95% BI 0%-11%) bij 15 en 20 jaar met als eindpunt aseptische loslating. In totaal werden er 3 revisies uitgevoerd bij 2, 12 en 26 jaar follow-up. De revisies van 12 en 26 jaar werden verricht vanwege aseptische loslating en de revisie van 2 jaar vanwege nervus ischiadicus problemen. Van de niet-gereviseerde acetabulaire componenten waren er geen tekenen van radiologisch falen te zien aan het eind van de follow-up en geen dislocaties of infecties zijn opgetreden. De Harris Hip Score verbeterde van 37 (9-72) pre-operatief naar 83 (42-99) op het laatste moment van follow-up. Deze studie toonde bevredigende lange-termijn resultaten van primaire THP bij patiënten die lijden aan heupdysplasie met het gebruik van IBG om de bijkomende acetabulaire defecten te reconstrueren. Na 20 jaar follow-up is de kans op revisie vrij laag, namelijk 7%.

In de literatuur laten sommige studies inferieure resultaten zien bij revisie THP bij het gebruik van een laterale rim mesh, een metalen netje, in combinatie met IBG bij acetabulaire defecten.

Hoofdstuk 4 rapporteert de uitkomst van primaire THP met IBG in combinatie met een laterale rim mesh welke werden vergeleken met patiënten met primaire THP zonder

de noodzaak voor een laterale rim mesh reconstructie. Alle patiënten waren 50 jaar of jonger ten tijde van de primaire THP. Een groep van 235 patiënten (257 THP) welke een primaire THP met IBG en een additionele laterale rim mesh kregen werden vergeleken met een groep van 306 patiënten (343 THP) welke IBG ondergingen zonder laterale rim mesh in de periode van 1988-2015. De gemiddelde leeftijd ten tijde van operatie was 38 jaar (13-50) en de gemiddelde follow-up was 6 jaar (0.1-22). In de mesh groep werden 18 acetabulaire componenten (7%) gereviseerd. De belangrijkste reden voor revisie was aseptische loslating (n=7) en septische loslating (n=5). In de groep zonder mesh werden 36 acetabulaire componenten (10%) gereviseerd. De belangrijkste redenen voor revisie waren aseptische loslating (n=19) en septische loslating (n=8). Het gebruik van een laterale rim mesh was niet significant geassocieerd met een verhoogd risico op revisie voor welke reden dan ook (unadjusted Hazard Ratio (HR) 0.64, 95% BI 0.3-1.2; p = 0.16). Voor revisie van de acetabulaire component door aseptische loslating was de unadjusted HR 0.35 (95% BI 0.11-1.07; p = 0.07). Aangepast voor potentiële verstorende factoren, de Hazard Ratio voor revisie van de acetabulaire component voor welke reden dan ook was 0.50 (95% BI 0.13 - 1.93; p = 0.31) en voor aseptische loslating was dit 0.29 (95% BI 0.02 - 4.04; p= 0.35). Kaplan-Meier analyses zijn uitgevoerd om de overleving van de THP met als eindpunt revisie van de acetabulaire component voor elke reden en aseptische loslating bij 10 en 15 jaar, vast te stellen. De overleving van de acetabulaire component voor aseptische loslating was 98% (95% BI 95%-100%) bij 10 jaar en 90% (95% BI 81%-100%) bij 15 jaar in de mesh-groep. In de groep zonder mesh was de overleving voor aseptische loslating 94% (95% BI 89%-97%) bij 10 jaar en 85% (95% BI 77%-94%) bij 15 jaar. Er was geen significant verschil in component overleving voor beide groepen. Concluderend laat deze studie zien dat het gebruik van een laterale rim mesh bij een primaire THP in combinatie met IBG niet geassocieerd is met een hoger risico op revisie en dat het een veilige optie is voor het reconstrueren van acetabulaire defecten bij een primaire THP.

In **Hoofdstuk 5** worden de resultaten gerapporteerd van 1049 primaire THP (860 patiënten) bij patiënten jonger dan 50 jaar in een van de grootste series van een centrum over dit onderwerp wereldwijd. Alle procedures werden uitgevoerd in het Radboudumc en alle patiënten werden behandeld volgens dezelfde, eerdergenoemde filosofie; een gecementeerde THP en reconstructie met IBG in geval van botdefecten. De gemiddelde leeftijd van de onderzoeksgroep was 37 jaar (12-50 jaar) bij de plaatsing van de primaire THP en de gemiddelde follow-up van de primaire THP was 9 jaar (2-32 jaar). De meest voorkomende diagnoses waren heupdysplasie (29%) en avasculaire necrose van de femurkop (28%). Bij 751 THP (72%) werd acetabulaire IBG toegepast.

In totaal zijn er 138 (13%) revisies uitgevoerd, waarvan 127 acetabulaire component revisies. De belangrijkste redenen voor revisie van de acetabulaire component waren aseptische loslating (n=74) en septische loslating (n=27). De gemiddelde leeftijd ten tijde van de eerste revisie was 48.2 jaar (23-73). De Kaplan-Meier analyse werd gebruikt om de overleving van de prothese te bepalen. De overleving voor alle primaire THP met als eindpunt revisie om welke reden dan ook was 91% (95% BI 88%-93%) na 10 jaar follow-up, 67% (95% BI 61%-72%) na 20 jaar en 54% (95% BI 46%-62%) na 25 jaar follow-up. Voor de acetabulaire component alleen met als eindpunt revisie voor aseptische loslating was de overleving 96% (95% BI 94%-98%) na 10 jaar follow-up, 78% (95% BI 71%-83%) na 20 jaar en 64% (95% BI 54%-72%) na 25 jaar follow-up. De resultaten voor verschillende subgroepen (leeftijd en diagnose) werden ook berekend en worden gepresenteerd in het artikel. In dit hoofdstuk benadrukken we het belang om de resultaten van opeenvolgende revisie THP-operaties te beschrijven. Aangezien er weinig gegevens beschikbaar zijn over de resultaten van revisieprocedures bij deze jonge patiënten, vooral vanuit dezelfde t onderzoeksgroep, hebben we ook de overleving van de daaropvolgende resultaten binnen de groep bepaald. Van de 138 revisie THP hebben er 22 een re-revisie ondergaan, waarvan er 20 een re-revisie van de acetabulaire component. In 11 gevallen was infectie de reden voor re-revisie en in 8 gevallen was er aseptische loslating van de acetabulaire component. De gemiddelde leeftijd bij re-revisie was 52 jaar (33-71 jaar) met een gemiddelde follow-up van de revisie van 6,5 jaar (0,1-22 jaar). De overleving van revisie THP met als eindpunt re-revisie om welke reden dan ook was 79% (95% BI 67%-86%) na 10 jaar en 70% (95% BI 56%-81%) na 15 jaar follow-up. Voor alle gereviseerde acetabulaire componenten was de overleving respectievelijk 79% (95% BI 67%-87%) en 70% (95% BI 54%-81%) na 10 en 15 jaar follow-up. Van de 22 re-revisieprocedures hadden 7 gevallen een tweede re-revisie nodig. De gemiddelde follow-up van de re-revisies was 3,5 jaar (0,2-12 jaar). De belangrijkste redenen voor tweede re-revisie waren aseptische loslating (n=2) en septische loslating (n=3). Dit is het eerste onderzoek wereldwijd dat de Girdlestone-index rapporteert om het definitieve falen van de behandeling met THA te definiëren. In 4 gevallen was er bij de eerste revisie geen reïmplantatie mogelijk vanwege infectie. Dit resulteerde uiteindelijk in een permanente resectieartroplastiek, een Girdlestone-situatie. Daarnaast werd bij 2 van de 7 tweede re-revisieprocedures een Girdlestone-artroplastiek uitgevoerd, vanwege een infectie. In de totale onderzoeksgroep eindigden dus 6 patiënten met een permanente resectieartroplastiek, resulterend in een Girdlestone-index van 0,7%, allen vanwege infectie. Behalve deze septische indicaties ondergingen alle patiënten met een gefaalde primaire of revisieprocedure een bevredigende reïmplantatie van de THP. In deze studie werden veelbelovende langetermijnresultaten gevonden voor primaire en revisie THP. De gebruikte techniek, een gecementeerde THP in combinatie met IBG in geval van botdefecten, is zeer geschikte en een bewezen lange termijn optie die in overweging moet worden genomen bij deze jonge patiënten.

In **Hoofdstuk 6** worden de resultaten van THP bij extreem jonge patiënten beschreven, namelijk bij patiënten van 30 jaar of jonger op het moment van de implantatie. In totaal werden 139 patiënten (180 heupen) geïncludeerd in dit onderzoek, met een minimale follow-up van 2 jaar en een gemiddelde leeftijd van 24 jaar (13-30 jaar) tijdens de operatie. De belangrijkste indicaties voor THP waren avasculaire necrose van de femurkop (59%) en heupdysplasie (20%). Tijdens de follow-up werden 26 revisies van welke component dan ook uitgevoerd, voornamelijk vanwege aseptische loslating (n = 15) en septische loslating (n = 5). IBG werd gebruikt in 127 gevallen (71%) om acetabulaire defecten te reconstrueren. In dit onderzoek waren we ook in staat om de radiologische uitkomsten te evalueren. In totaal vertoonden 3 acetabulaire componenten radiologische loslating en waren er geen femorale radiologische loslatingen. Daarbij zijn er ook patiënt gerapporteerde uitkomstmetingen (PROM's) verzameld, inclusief de Harris Hip Score (HHS), de gemodificeerde Oxford Hip Score (mOHS) en VAS-scores voor pijn in rust en activiteit en VAS-score voor tevredenheid. De gemiddelde preoperatieve HHS verbeterde van een gemiddelde van 50 (20-77) naar een gemiddelde van 88 (28-100) bij de laatste beoordeling. De gemiddelde postoperatieve VAS-score voor pijn in rust was 8 (0-70) en voor pijn in activiteit was de gemiddelde score 15 (0-90). Voor postoperatieve tevredenheidsscores was het gemiddelde 87 (10-100). De mOHS toonde een gemiddelde van 41 (8-48) bij de laatste follow-up.

In totaal werden 26 revisies van welke component dan ook van de primaire THP uitgevoerd, voornamelijk vanwege aseptische loslating (n = 15) en septische loslating (n = 5). De overleving van de primaire THP met als eindpunt revisie voor welke component dan ook om welke reden dan ook op 10 en 15 jaar was respectievelijk 87% (95% BI 79% -92%) en 77% (95% BI 65% -86%). De overleving van acetabulaire componenten met als eindpunt revisie voor aseptische loslating op 10 en 15 jaar was respectievelijk 92% (95% BI 84%-96%) en 84% (95% BI 71%-92%). In één geval werd tijdens de eerste revisie-operatie een permanente Girdlestone gecreëerd als gevolg van infectie. Een reïmplantatie werd niet uitgevoerd vanwege aanhoudende infectie. Van de andere 25 gevallen die een revisie van THP ondergingen, werden 4 re-revisies uitgevoerd. In 3 gevallen vanwege infectie en in één geval vanwege aseptische loslating 12 jaar na de eerste revisie. De Girdlestone-index in deze studie was 1 op 180 gevallen (0,6%). Deze studie toonde acceptabele resultaten van THP met het gebruik van een gecementeerde THA met IBG in een uiterst jonge patiëntengroep. Men moet echter wel in gedachten houden dat toekomstige revisies zullen volgen en dat deze patiënten nog steeds jong zijn bij de eerste en zelfs bij de tweede revisie-operatie.

APPENDICES

Data management
Radboud Graduate School Portfolio
Dankwoord
About the author

DATA MANAGEMENT

Data used within this thesis was collected and stored according to the Findable, Accessible, Interoperable and Reusable (FAIR) principles. This thesis is based on data collected from electronic patients records from the Radboudumc. The use of medical records from patients for the studies in this thesis was approved by the medical and ethical review board Committee on Research Involving Human Subjects Region Arnhem-Nijmegen, Nijmegen, the Netherlands.

Data collected from electronic patients records from the Radboudumc were stored in a CastorEDC-database, which was created at the start of the project. No identifying variables are included in this Castor-database. Each record entered in the database received an unique record-ID. A separate key-file was created, and stored on the server of the department of Orthopaedics. The key for identification is only available for the research team. In order to ensure that data is generally accessible and interoperable, a manual was created in order to upload new data in the Castor-database, or to download data from the Castor-database for future analyses. Moreover, data cleaning and analyses programs performed in SPSS or R to produce the final results are saved together with the final datasets.
The data collected for this thesis will be available for further analyses for at least 15 years. The datasets generated and analysed are available from the corresponding author upon reasonable request.

PHD PORTFOLIO OF ENA ČOLO

Department: Orthopaedics
PhD period: 01/04/2015 – 01/06/2023
PhD Supervisor: Prof. B.W. Schreurs
PhD Co-supervisor: Dr W.H.C. Rijnen

Training activities	**Hours**
Courses	
- RIHS – Introduction course for PhD candidates (2015)	15.00
- Basiscursus Regelgeving en Organisatie voor Klinisch onderzoekers	42.00
(BROK) (2015)	50.00
- Radboudumc – Biometrics (2015)	84.00
- Radboud Universiteit – Academic Writing for PhD Candidates (2016)	20.00
- Radboudumc – Scientific integrity (2018)	450.00
Followed courses for orthopaedic training (2019-2023)	
FCCS, ATLS, AO basic principles of fracture management, AO Advanced, CASH-1, PACONU, Stralingshygiëne voor medisch specialisten, Heupprothesiologie cursus, Knieprothesiologie cursus, NVA arthroscopie cursus knie basis, Schouderfractuur cursus, DSATC, Osteotomiecursus, CCOC 1-2-3	
Conferences	
Oral presentation	
- European Federation of National Associations of Orthopaedics and Traumatology (EFORT) Congress, Praag, Tsjechië (2015)	10.00
- European Hip Society (EHS) Congress, München, Duitsland (2016)	10.00
- EFORT Congress, Genève, Zwitserland (2016)	10.00
- Nederlandse Orthopaedische Vereniging (NOV) Jaarcongres, 's Hertogenbosch, Nederland (2018)	10.00
- EFORT Congress Virtual meeting (2021)	10.00
- World Arthroplasty Congress (WAC) Virtual meeting (2021)	10.00
Poster presentation	
- EFORT Congress, Praag, Tsjechië (2015)	5.00
- American Academy of Orthopaedic Surgeons (AAOS) Annual Meeting, Las Vegas, Verenigde Staten	5.00
Teaching activities	
Supervision of internships	
- Supervision of research student Liz Leenders (2016)	28.00
- Supervision of research student Yara Eggen (2017)	28.00
Total	**787**

DANKWOORD

Eindelijk is het dan zover: het proefschrift is afgerond. Zonder de hulp en begeleiding van velen had ik dit niet kunnen voltooien. Het was een lange, maar mooie weg om te bewandelen. Een aantal personen wil ik graag in het bijzonder bedanken.

Prof. Dr. B.W. Schreurs (promotor), beste Wim, jij stond aan de wieg van mijn orthopedische carrière. Als jonge student heb je me op een enthousiaste en zeer laagdrempelige manier begeleid met mijn eerste stappen in het wetenschappelijk onderzoek. Jouw energie en enthousiasme zijn bewonderenswaardig. Ik kijk met plezier terug op onze overleggen waarin je me met humor, doortastendheid en doelmatigheid hebt geholpen met het verwezenlijken van dit proefschrift. Je bent een voorbeeld op wetenschappelijk, klinisch en persoonlijk vlak. Duizendmaal dank voor alles.

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Leden van de manuscript commissie, geachte prof. dr. ir. S.C.G. Leeuwenburgh, prof. dr. I.E. van der Vorst-Bruinsma en prof. dr. P.C. Jutte, dank voor uw bereidheid om dit manuscript nauwkeurig te beoordelen en goed te keuren.

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Martijn Kuijpers, samen hebben we ons succesvol door de Castor database heen geworsteld. Deze bureaucratische data-invoer was een stuk gezelliger om samen te doen. De vele overleggen onder het genot van 'goede' koffie waren altijd iets om naar uit te kijken. Uiteindelijk hebben we er beide een mooi proefschrift aan over gehouden.

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A

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Professor H. Malchau and C. Bragdon at the Harris Orthopaedic Laboratory in Boston. Thank you for supervising my research project during my internship and giving me this opportunity. Thank you for this wonderful experience.

Polimedewerkers en secretariaat orthopedie van het Radboudumc. Bedankt voor jullie inzet bij het verzamelen van data en het maken van alle afspraken. Zonder jullie was dit nooit gelukt.

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Stafleden orthopedie van het Radboudumc, bedankt voor alle ondersteuning die ik van jullie heb mogen ontvangen tijdens het uitvoeren van dit promotietraject.

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Collega AIOS-orthopedie, bedankt voor de prettige dagelijkse samenwerking, de collegialiteit en mooie dingen die we samen meemaken.

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A

Esther en Stijn, een vriendschap die begon tijdens onze studententijd en zich heeft ontwikkeld tot een leven dat op bijzondere wijze parallel loopt, met gedeelde ervaringen zoals opleiding, trouwen en promoveren. Bedankt voor jullie oneindige interesse, zelfs in dit proefschrift, en gezelligheid. Ik waardeer onze hechte vriendschap enorm en ben blij dat jij, Esther, mijn paranimf wil zijn.

My Bosnian family, thank you for all the wonderful family gatherings that we have every now and then. Although we all live in different countries and have busy lives, I am very grateful that we have each other and always find the time to be there for each other.

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ABOUT THE AUTHOR

Ena Čolo was born on the 7th of July 1990 in Foča in Bosnia and Herzegovina. In 1993 she came as a refugee to the Netherlands with her parents and brother. She was raised in Drunen in Noord-Brabant. After obtaining her Gymnasium diploma at the Dr. Mollercollege in Waalwijk in 2008, she started medical school at the Radboud University in Nijmegen.

During the first years of medical school, Ena became interested in Orthopaedic Surgery. While awaiting her clinical rotations in her Master program, Ena worked at the clinical scoring station in the Orthopaedic Department in the Radboudumc. During this time she started doing research under the supervision of prof. dr. Schreurs, which eventually resulted in this thesis.

In her senior year of medical school, Ena spent 6 months in Boston at the Massachusetts General Hospital/Harvard Medical School where she performed a research project under the supervision of prof. dr. Henrik Malchau and Charles Bragdon. Ena did her senior rotations of medical school at the Department of Orthopaedics in the Radboudumc and Sint Maartenskliniek in Nijmegen. She completed medical school in 2015.

After medical school, she dedicated one year to continuing her work on her thesis. After that, she started as a non-residential doctor at Rijnstate hospital in Arnhem. In 2019 Ena started as a resident at the department of surgery as part of the orthopaedic surgery training in the Canisius Wilhelmina Hospital (CWZ) under the supervision of dr. Polat. In July 2020 she continued residency in the Sint Maartenskliniek under the supervision of dr. Busch and drs. ten Ham. In 2022 Ena worked as a resident at the Radboudumc under the supervision of dr. Rijnen and dr. ir. van de Groes.

Currently, Ena is in her fifth year of residency at the Department of Orthopaedic Surgery in Rijnstate in Arnhem under the supervision of dr. van Susante and dr. Wagener. She lives with her husband, Dominique Lamers, in Nijmegen.

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