Clinical and experimental aspects of fixation, loosening, and revision of total hip replacement

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Clinical and Experimental Aspects of Fixation, Loosening, and Revision of Total Hip Replacement

Pieter T. de Jong
F. Harald R. de Man
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Academisch Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit van Amsterdam op gezag van de Rector Magnificus prof. dr. D.C. van den Boom ten overstaan van een door het college voor promoties ingestelde commissie, in het openbaar te verdedigen in de Aula der Universiteit op donderdag 12 februari 2009, te 10.00 uur door

Pieter Thomas de Jong
geboren te Shifnal, Engeland

en te 11.00 uur door

Frans Harald Roderick de Man
geboren te Amsterdam

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Faculteit der Geneeskunde

‘However beautiful the strategy, you should occasionally look at the results’
Sir Winston Churchill

‘Nothing shocks me, I’m a scientist.’
Indiana Jones
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Arthritic changes in hip and knee cause considerable disability and can lead to social isolation. The development of an operative treatment that both relieves pain and restores motion has therefore been of paramount importance to many patients suffering from osteoarthritis, rheumatoid arthritis, and arthritis secondary to other causes. The improvements in physical functioning are sustained in the long-term. The total hip replacement (THR) has therefore been referred to as “the operation of the century.”

History and development
After attempts at resurfacing the arthritic hip with fascia lata, skin and submucosa of pigs bladder, Smith Petersen covered the reshaped femoral head with vitallium. This is seen as the beginning of a new era of arthroplasty.

Wiles was the first to develop a total hip replacement in 1938, but total hip replacement was revolutionized by the invention of the low friction arthroplasty by Charnley (Fig. 1) in 1961. He introduced the concept of low frictional torque forces, fixation of the components using acrylic cement, and the use of high-density polyethylene as a bearing surface. These new elements finally guaranteed longevity in THR, leading to reported survival rates of 77% and 81% after follow-up of 25 years.
McKee (Fig.2) and Watson Farra8, realized that the Thompson and Austin-Moore metal femoral head replacements were only tackling half of the problem and introduced a ball and socket type of artificial joint with cobalt-chrome components in 1951. The first type was used as a cementless implant, but the implant was not stable and early loosening was the result. They followed Charnley and started using acrylic cement. The cup could now be sunk deep into the acetabulum, which facilitated the use of a larger, more anatomical head size. Although they realized the larger head could possibly cause more wear, they believed that only a small amount of movement occurred during weight bearing, with frictional forces at their greatest. Frictional forces were believed to be diminished by the distraction of gravity in the non-weight bearing phase. They also knew from experiments done at Stanmore, that cobalt-chrome alloy had a very low friction coefficient.

Müller developed another well-known THR, made of a chrome-cobalt-molybdenum alloy (Protasul®) to increase the strength of the stem, because breakage of the Charnley stem was one of the failure modes. He used polyethylene for the cup, just like Charnley, but preferred a somewhat larger head (32-mm) to the 23-mm Charnley head, because of the reduction in dislocation risk. An even larger head simply was not feasible, because the polyethylene had to have a sufficient thickness to be able to withstand the expected wear (1 mm per 5 years) over time.

Weber was another pioneer in the development of THR. He worked with Charnley and Müller, from whom he picked up many ideas. When he became director of the orthopaedic department in Sankt Gallen, Switzerland, in 1967, he put his ideas to the test and developed a stem made out of Protasul®, featuring a rotating trunnion to reduce friction in the ball and socket joint, thereby hoping to reduce wear and mechanical loosening of the acetabular component. Although he originally started with a large polyester head9, from 1971 onwards a metal 32-mm rotating head was used, articulating with a high-density polyethylene cup10. This became known as the Weber rotation prosthesis, which has been used as the standard prosthesis in the Binnengasthuis and later the Academic Medical Center in Amsterdam since 1974. Apart from the mechanical benefits of the trunnion mentioned above, another benefit was the ease with which a femoral head replacement, used in fracture surgery, could be changed into a total hip replacement. The large fracture head was easily removed and replaced by a smaller 32-mm head after implantation of the acetabular component. The stem could be left in situ. To further reduce wear, a ceramic head was added to the Weber rotation hip system in 1973.

Weber was again at the forefront of orthopaedic innovation when he realized that the metal-metal articulation of McKee and Watson-Farrar produced little wear and introduced Metasul11, starting a renewed interest in metal-metal articulations.

This introduction is not meant to be a complete summary of all the historic landmarks in the development of the total hip replacement, but these pioneers paved the way for a very successful procedure and inspired many others to perfect their invention.
Background concerning loosening of the implants

Loosening and implant-related factors: design and materials
By the end of the 1970’s, clinical studies reported on cemented prostheses showing signs of loosening at follow-up\textsuperscript{12-14}. Radiolucent changes around the components with or without subsidence of the implant were seen. This radiological phenomenon was related to osteolysis, which has now been more clearly defined as a process of: “progressive destruction of periprosthetic bony tissue characterized on serial radiographs by progressive radiolucent lines and/or cavitation at the implant-bone or cement-bone interface.” Radiolucency around femoral components can be classified as linear (equally distributed around the prosthesis) or focal (islands of bone loss or cavitations) in close relation to the implant.

These changes were initially believed to be the result of infection, but cultures did not reveal any growth of bacteria\textsuperscript{15}. In 1976, histological examination of tissue taken from these osteolytic areas showed the presence of cement-particles\textsuperscript{16}. In 1977, Willett described the loosening of components as a result of a granulomatous tissue reaction induced by cement wear-particles\textsuperscript{17}. This phenomenon was later called “cement disease”\textsuperscript{18} an aseptic process, hence leading to “aseptic loosening”. This led to the development and introduction of cementless THR-designs. Later, it turned out that not only cement particles, but polyethylene and metal particles also induced a foreign body-reaction, as became evident by osteolysis around uncemented designs. The term “cementless” disease was introduced.

Although improvements in surgical and cementing technique evolved, loosening remained a problem and various theories have been proposed since. Historically, the wear particle theory has been pre-dominant in efforts to comprehend this process of aseptic loosening\textsuperscript{19} and has become an orthopaedic paradigm. As a result, research has been focused on the causes of wear, its mechanisms and the identification and development of wear-resistant materials.

The causes of wear are multifactorial and influenced by patient- and surgical factors as well as by the properties of materials used. Patient factors include the duration of use, age\textsuperscript{20}, general health and activity of the patient\textsuperscript{21,22}, whereas the influence of gender and weight are less evident. Surgical factors are increased cup inclination with apical loading and decreased cup anteversion with impingement of the stem neck\textsuperscript{23,24}. Diminished wear rates can be realized by medializing the center of rotation\textsuperscript{25}, thereby increasing the stem offset and lever arm moment. By mechanisms of wear (Table 1), the change in morphology of materials that cause wear-damage is described. The conditions, under which the prosthesis was functioning when the wear occurred, are referred to as wear modes (Table 2).

<table>
<thead>
<tr>
<th>Modes of wear</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode 1</td>
<td>Intended motion of two primary bearing surfaces against each other, e.g. motion of a femoral head against a PE liner.</td>
</tr>
<tr>
<td>Mode 2</td>
<td>Unintended motion of a primary bearing surface against a secondary surface, e.g. motion of a femoral head, which has penetrated through the PE liner against the metal shell.</td>
</tr>
<tr>
<td>Mode 3</td>
<td>Two primary bearing surfaces move against each other, with the interposition of wear particles creating accelerated wear (also known as “third-body” wear).</td>
</tr>
<tr>
<td>Mode 4</td>
<td>Two secondary bearing surfaces move against each other, e.g. the femoral neck impinging on the rim of the cup.</td>
</tr>
</tbody>
</table>

Table 1 Modes of wear

<table>
<thead>
<tr>
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<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adhesion</td>
<td>This involves bonding of surfaces when they are pressed together under load. Sufficient relative motion results in material being pulled away from the surface, usually from the weaker material.</td>
</tr>
<tr>
<td>Abrasion</td>
<td>This refers to a mechanical process wherein asperities on the harder surface cut and plow through the softer surface, resulting in removal of material.</td>
</tr>
<tr>
<td>Fatigue</td>
<td>When local stresses exceed the fatigue strength of a material, that material then fails after a certain number of loading cycles, releasing material from the surface.</td>
</tr>
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Table 1 Mechanisms of wear
Research has focused on these issues, and tribology is the science that studies the properties of materials and interaction of surfaces in relative motion, including friction, lubrication, and wear. Over the years different materials, i.e. polyethylene, ceramics, and metal have been used for THR with the aim to decrease wear and loosening rates.

**Polyethylene bearings**

According to the Swedish Hip Arthroplasty Registry, the most frequently used THR is cemented with a polyethylene cup (PE), inspired by the success of the low-friction THR. PE is a polymer and it is the most common particle type found in periprosthetic tissue. High-density PE (HDPE) was the first type used PE in THR and has a historical wear rate of 0.1 mm per year. If wear simply were a linear process, it would take a century to erode through a standard size 10 mm thick cup. However, although linear wear may seem only a small problem, it has been estimated that billions of PE particles originate from the bearing surface per annum.

The resistance to wear of PE is influenced by many variables e.g. type of resin, manufacturing method, methods of sterilization (e.g. gamma radiation in air produces oxidative degradation and aging of PE and this method was abandoned as of 1998), shelf-time (oxidation) and the degree by which polymere strains are bonded (cross-linked).

In our cohort, we have used an all polyethylene cup (RCH 1000; Chirulen®, Hoechst, Germany). Schüller and Marti showed that after an average of 10 years, PE wear, using the metal rotating head of the Weber Rotation prosthesis averaged 0.96 mm with an average wear of 0.1 mm per year.

**Ceramic bearings**

Ceramics e.g. aluminumoxide (alumina), zirconiumoxide (zirconia) and silicon-nitride, are an attractive bearing material for use in THR because of its low coefficient of friction and high resistance to scratching. The disadvantage has been mainly increased brittleness and possible breakage.

Mittelmeier first used a double alumina bearing uncemented THR. Problems with this concept were early loosening, possibly due to a difference in elasticity between the extreme hard ceramic and bone (which is more than hundredfold), and component fractures. Later, comparison of cemented and uncemented alumina cups showed survival rates of 85% after 10 years and 64% after 1 year, respectively.

Although failure rates in these early series were relatively high, the ultra low wear properties of ceramic inspired surgeons to use ceramic heads in combination with polyethylene. Indeed, in our clinic, after 1978 ceramic/PE became our bearing of choice and wear in comparison to metal/PE was reduced to 0.26 mm at 10 years, with an average of 0.03 mm per annum. Others found similar results as well.

**Metal-on-metal bearings**

This first generation metal-on-metal articulation, using cobalt-chromium showed high loosening rates. The metal-on-metal concept was therefore abandoned in the late 1970’s and McKee himself stopped using his prosthesis in 1982. By then, the reasons of the high failure rates had become more apparent. They included technical production flaws, the use of an alloy with low carbon content, and the rim of the cup were in too close contact with the head leading to high frictional forces between the bearing surfaces and subsequently high torque forces between the components. These torque forces were higher than the bonding forces of cement.

However, in some designs where the point of contact in the bearing was between the apex of the head and the cup, the failure rates were lower. Moreover, measurement of wear of McKee-Farrar prostheses retrieved after 20 years of use, showed a combined femoral and acetabular linear wear of 4 microns per year, which is about 25 times less than was radiologically measured in metal/PE bearings in Charnley prostheses.
These findings induced a renewed interest in metal-metal bearing. For instance, B.G. Weber from Switzerland introduced the second-generation metal-on-metal articulation in the 1980’s, called Metasul (“Metalsulzer” from Sulzer Medica, renamed Centerpulse, now Zimmer, Warsaw, IN, USA). It is a wrought casted CoCrMo alloy, which is very strong, allowing thin cups to be used with large heads providing enhanced joint stability and range of motion\textsuperscript{11}. Clinical success with Metasul\textsuperscript{®} has been demonstrated in long term follow-up studies with a reported 0.2% incidence of mechanical loosening\textsuperscript{41}.

The small size of metal particles (less than 100 nanometer) is supposed to be advantageous, because they are below the critical size to induce macrophage reaction\textsuperscript{42}, which is considered a prerequisite for osteolysis. On the other hand, small particles can cross the blood-barrier leading to elevated serum and urine concentrations of both cobalt and chromium\textsuperscript{43,44}. At present, it is still unclear what the long-term effects of those higher concentrations might be, and therefore some do not recommend the use of metal-on-metal bearings in fertile women.

**Latest developments in tribological research**

In the quest for better and more wear-resisting materials there are two main directions of research: (i) improvement of the wear properties of PE by “cross-linking” and (ii) investigation of alternative bearing materials such as ceramic-on-polyethylene, ceramic-on-ceramic and metal-on-metal articulation. These types of bearing cause less wear and produce smaller size (submicron) particles than PE, and might decrease the chance of a host reaction.

This process of “cross-linking” is an important development, which seems to reduce aging of PE. This process means that by ionizing radiation polymeric chains can “cross-link” and become more resistant to degradation by oxidation then conventional UHMWPE\textsuperscript{45}. This highly “cross-linked” PE (HXLPE) has been on the market for clinical use from 1999 on. In vitro hip simulations\textsuperscript{46-49}, early and intermediate clinical studies\textsuperscript{50-53} and retrieval studies\textsuperscript{45}, have all demonstrated a reduction in wear of HXLPE as compared to conventional UHMWPE.

Already a second-generation HXLPE (X3-HXLPE) has emerged with seemingly even better survivorship in hip simulator studies\textsuperscript{54}.

Now that over the years, THR designs, cementing techniques and strength and quality of ceramics\textsuperscript{55,56} have improved, alumina-on-alumina articulation has regained new interest and clinical results have improved\textsuperscript{56,57}. It seems that alumina-on-alumina bearing has the lowest wear rate of all bearing combinations in clinical use\textsuperscript{56,58,59}. In addition, in retrieval studies of failed alumina-on-alumina THR, the least amount of particles are found\textsuperscript{59} and particles are not very biologically active\textsuperscript{61,62}. One animal experiment showed less bone resorption and inflammatory response of alumina particles as compared to titanium and polyethylene particles\textsuperscript{54}. The latest ceramics are “mixed” oxide ceramic (80% alumina and 20% zirconia)\textsuperscript{63} and silicon nitride\textsuperscript{65}, and they have been found to have better mechanical properties than conventional alumina, after retrieval and after mechanical testing, respectively.

Experimental research is being done using diamond coated metallic surfaces: after 15,000,000 test cycles corresponding to 15 years of clinical use, no measurable wear was found\textsuperscript{66,67}.

**Loosening and aseptic processes: current theories**

**Wear particle-induced osteolysis**

Although materials have become more wear-resistant, particles are still generated. In vivo studies suggested that the presence of wear particles lead to a cascade of events resulting in bone resorption. On a cellular level, particles are phagocyted by macrophages, which become activated\textsuperscript{68} and release cytokines causing bone resorption, either directly or through osteoclast activation and osteoclastogenesis. In particular, polyethylene particles\textsuperscript{69} and cement particles\textsuperscript{19} were observed to possibly induce particle-induced bone resorption. However, some studies contradict these findings\textsuperscript{70,71}. In vitro, particles have also been shown to inhibit osteoblast function leading to a decrease in bone formation\textsuperscript{72}.

On a biochemical level, soluble factors have been detected in the membrane surrounding loose prostheses that may cause bone resorption\textsuperscript{73,74}. In retrieved interface tissue of aseptically loosened THR’s from our cohort high cathepsin B activity was found\textsuperscript{75}. These findings will increase interest in studying pharmacological agents that may modify such responses.
Next to these biological aspects of the process of loosening, mechanical aspects may be involved.

**Insufficient initial fixation**

Early loosening has been proposed as (mechanical) reason for late clinical loosening. Fixation might have never occurred at the time of surgery, or might be lost shortly thereafter, due to improper implant sizing or flawed design, improper cementing technique, or inferior bone quality. Also, by preparation of the bone bed e.g. pressure-lavage or by thermal injury of cement, it is very likely that a superficial layer of bone dies. Remodeling of this dead bone can subsequently lead to mechanical instability and micromotion between bone and cement and/or implant is the result.

In animal models, such instability lead to the formation of a fibrous tissue interface between bone and a component. Motion with compression of such an interface was observed to lead to bone resorption.

**Stress shielding**

Stress shielding may be another reason for loosening with both mechanical and biological aspects. Insertion of a component in bone can lead to bone loss according to Wolff’s law which can be summarized as follows: bone will adapt to the load it is placed under. Thus, when loaded, bone will show remodeling over time to become stronger to resist the increased load. However, if the load decreases, the bone will become weaker during turnover as it is metabolically less costly to maintain and the stimulus to maintain bone mass through continued remodeling is absent. This phenomenon is known as stress shielding, because the load on the surrounding bone is partly taken over by the implant. Clearly, in stress shielding bone loss is not due to osteolysis. Stress shielding is associated with stiffer implants and is seen when press-fit metal backed cups and uncemented press-fitted stems are used. In comparison, stress shielding is a not a phenomenon frequently seen with cemented polyethylene cups or stems.

In our cohort, we consistently used a cemented PE cup for primary and, if necessary combined with a steel Eichler reinforcement ring in revisions. Both implant systems are thought to resemble the elasticity of bone (Young’s modulus) to a more optimal degree. This was especially observed in cases when superolateral autologous grafts were used because coverage of the cup was less than 90 %.

Partial remodeling without resorption of the grafts in the weight-bearing zone was found by Marti et al. which proves the absence of stress shielding of the grafts by the cemented PE implants.

**High fluid pressure**

Several reports suggest the physical influence of high fluid pressure on bone. Fluid pressures in pseudojoints after THR have reached 700 mmHg. Ultrasound has shown that capsular distension caused by high intracapsular pressures is common in loose THR, and uncommon in cases without clinical signs of loosening. High pressures (500 mm Hg) have been measured in pelvic osteolytic lesions at revision surgery.

These findings were reason to further investigate the influence of fluid pressure by our experimental research group. Van der Vis applied an exogenous high fluid pressure in rabbits and established bone resorption. An endogeneous applied pressure led to resorption as well. These findings very strongly suggest that high fluid pressure may be one of the key factors in the loosening process.

**Endotoxins**

When standard cultures of specimens obtained from periprosthetic tissue around a loose component do not show growth of microorganism, most orthopaedic surgeons have the tendency to label that component as “aseptically loosened”. However, sensitivity of standard cultures is reported to range between 65-94%, and polymerase chain reaction (PCR) has shown that DNA-remnants of bacteria are often found in these culture negative specimens. These remnants are cellular membranes that contain antigens or endotoxins that can remain even after bacteria have been eradicated by the immune system or by antibiotics. In animal experiments, endotoxins have been found on used particles and endotoxin-free particles produced less bone resorption. From these data, it seems that particles are merely a vehicle, and that adherent endotoxins might be, at least partially, responsible for bone resorption. The role of endotoxin contamination for prosthetic loosening is currently under investigation.
Theories of aseptic loosening: pros and contras

The findings of roentgen stereophotogrammetric analysis (RSA)\textsuperscript{102} make it difficult to accept that wear particles initiate the process of component loosening. These studies have shown a higher probability of late clinical loosening when components migrate within 6 months after implantation\textsuperscript{103,104}. This makes it more likely that loosening is initiated by mechanical causes, because generation of particles is a process that takes time and the amount of wear particles is unlikely to be high after such short period\textsuperscript{19}. Migration of a prosthetic component can only be possible, when a fibrous tissue membrane surrounds the component. Consequently, there must be a correlation between late clinical loosening, migration of a prosthetic component and the presence of a fibrous membrane\textsuperscript{76,105}. This fibrous membrane can act as an interstitial fluid compartment\textsuperscript{96,105} and at loading component micromotion can generate high fluid pressure (gradients). In an animal experiment, the fibrous tissue interface around a loose TKR exuded and imbibed fluid upon intermittent loading\textsuperscript{106}. In the clinical setting, micromotion may very well lead to increased production of wear debris at the interface, but the influence of debris on loosening may therefore be secondary to the effects of micromotion and subsequent implant loosening.

Furthermore, pressure differences may induce a fluid flow towards the “effective joint space”\textsuperscript{107}: the space around components, which is usually confined to the pseudocapsule. However, this effective joint space also includes the interface between prosthesis/cement, between prosthesis/bone, the membrane interpositioned, and small cement cracks in otherwise stable components\textsuperscript{108}, and bone cysts (such as in the retroacetabular bone adjacent to screw holes). This space is accessible to fluid with deleterious consequences due to influx of particles, cytokines and metalloproteinases as well as pressure effects\textsuperscript{100,109}. Via this route even distant periprosthetic bone can be influenced by cellular, biochemical and physical factors\textsuperscript{19,107}. This can explain the distant local osteolysis in well-fixed stems\textsuperscript{110}, where pressure gradients may damage osteocytes producing bone resorption by osteoclast-mediated resorption\textsuperscript{79}.

In contrast to results of in vitro studies, most animal studies failed to establish particle-induced bone resorption and rather a decrease in bone formation was seen\textsuperscript{70,71}. Other investigators did find particle-induced resorption\textsuperscript{112} but could not reproduce their initial results\textsuperscript{113}. In some studies, instability-induced resorption may have been misinterpreted as particle-induced resorption\textsuperscript{114}.

In clinical studies, some found a correlation between the amount of wear-particles and aseptic loosening of components\textsuperscript{115,116}. The difficulty of interpreting these results is that the question: “did wear induce loosening or did loosening induce wear?” remains\textsuperscript{76}.

Based upon these findings the wear particle-induced loosening theory comes under siege. The loss of bone around an implant may be primarily the result of bone resorption due to mechanical factors whereas the (later) presence of particles could add to the loosening process by inhibiting formation of bone.

Loosening and infection

In the early days of prosthetics, infections frequently ended with a Girdlestone hip. Since then, there have been many improvements in prevention and treatment of prosthetic joint infection (PJI). Nowadays, most infections can be cured, enabling the patient to retain their hip implant. Still, PJI remains, after aseptic loosening, the second most common cause of implant failure\textsuperscript{117} and is associated with high morbidity and high health care expenditures\textsuperscript{118}.

Prevention

Charnley’s early experience with THR, at the end of the 1950’s, yielded an infection rate of almost 9%\textsuperscript{119}. His efforts to lower this unacceptable high rate resulted in a reduction to 1.3% over the next few years\textsuperscript{119}. The decline of infection, in his view, was primarily related to the use of a laminar airflow system and a body-exhaust operative suit\textsuperscript{119,120}.

A prospective, randomized, multicentre study that was conducted by the end of the 1970’s, showed that the use of ultra clean air in the operating theatre was associated with a clear reduction in infection\textsuperscript{121}. Prophylactic antibiotics were not used in the initial studies of THR. After some early debate it became clear that prophylactic antibiotics were extremely effective in lowering the prevalence of infection\textsuperscript{122-124}. In a study by Lidwell et al, it was shown that when laminar airflow was used in combination with prophylactic antibiotics the prevalence of infection could be reduced even further\textsuperscript{125}. Cephalosporins remain the agents of first choice due to their broad-spectrum activity, low toxicity, and high tissue concentrations that are achieved. With this regimen a prevalence of deep infection after THR of 0.27% has been reported\textsuperscript{126}. 

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Charnley’s early experience with THR, at the end of the 1950’s, yielded an infection rate of almost 9%\textsuperscript{119}. His efforts to lower this unacceptable high rate resulted in a reduction to 1.3% over the next few years\textsuperscript{119}. The decline of infection, in his view, was primarily related to the use of a laminar airflow system and a body-exhaust operative suit\textsuperscript{119,120}.

A prospective, randomized, multicentre study that was conducted by the end of the 1970’s, showed that the use of ultra clean air in the operating theatre was associated with a clear reduction in infection\textsuperscript{121}. Prophylactic antibiotics were not used in the initial studies of THR. After some early debate it became clear that prophylactic antibiotics were extremely effective in lowering the prevalence of infection\textsuperscript{122-124}. In a study by Lidwell et al, it was shown that when laminar airflow was used in combination with prophylactic antibiotics the prevalence of infection could be reduced even further\textsuperscript{125}. Cephalosporins remain the agents of first choice due to their broad-spectrum activity, low toxicity, and high tissue concentrations that are achieved. With this regimen a prevalence of deep infection after THR of 0.27% has been reported\textsuperscript{126}. 

In clinical studies, some found a correlation between the amount of wear-particles and aseptic loosening of components\textsuperscript{115,116}. The difficulty of interpreting these results is that the question: “did wear induce loosening or did loosening induce wear?” remains\textsuperscript{76}.

Based upon these findings the wear particle-induced loosening theory comes under siege. The loss of bone around an implant may be primarily the result of bone resorption due to mechanical factors whereas the (later) presence of particles could add to the loosening process by inhibiting formation of bone.
Besides the use of a laminar airflow system and prophylactic antibiotics\textsuperscript{124,127}, the more careful selection of patients, the elimination of remote infections\textsuperscript{128}, and the limitation of “traffic” in the operating room have contributed to lowering of the rate of deep infection. The current rate is 1\% after primary\textsuperscript{129} and 3-5\% after revision surgery\textsuperscript{127,130,131} in centres that perform arthroplasty surgery on a large scale. Indeed, by using those means in our entire cohort of primary THR reported on, the prevalence of deep infection was kept at a low 1 percent (D. Haverkamp, unpublished data).

\textbf{Biofilm and antibiotics}

Infection that is associated with prosthetic joints is typically associated with bacteria that grow in biofilms. Bacteria can attach to the surface of foreign body and produce a highly hydrated matrix of polysaccharide and protein. This substance together with the embedded bacteria is collectively known as a biofilm\textsuperscript{132}. All bacteria are capable of producing such a biofilm and the less virulent microorganisms do this to a higher degree. Biofilm-associated bacteria are more protected against antibiotics and the host immune response than planktonic bacteria\textsuperscript{133}. Biofilms may act as a nidus for recurrence of infection when antimicrobial therapy is discontinued.

Antimicrobial agents effective against biofilm-producing bacteria have improved outcome in treatment of PJI. For staphylococci, rifampin (also known as rifampicin) has been proven to be effective in vitro and in animal models\textsuperscript{134,135}, and in clinical studies\textsuperscript{136,137}. Rifampin should not be used as a single agent because staphylococci rapidly develop antimicrobial resistance\textsuperscript{138}. For gram-negative bacilli, chinolones (e.g. ciprofloxacin) are useful agents\textsuperscript{136,137}.

For several microorganisms that cause PJI (MRSA, fungi, enterococcus species, small-colony-variant \textit{Staphylococcus aureus}, rifampin-resistant \textit{Staphylococcus aureus}, \textit{Pseudomonas}) there are no antimicrobial agents available that have good bioavailability, are effective against biofilm, and are well tolerated at the same time. In order to eradicate these pathogens, most likely the antimicrobial treatment should be administered in the absence of a foreign body e.g. prosthesis. For these reasons one can refer to these microorganisms in orthopaedics as “difficult-to-treat” microorganisms. They account for about 10\% of all causative pathogens of PJI.

\textbf{Clinical presentation and classification}

A widely accepted classification for PJI is that of Coventry\textsuperscript{139}. It uses the period of interval between the operation and the first manifestation of infection. PJI is classified as early (those that develop less than three months after surgery), delayed (3 months to 2 years after surgery), or late (more than 2 years after surgery). Early infections are typically manifested as an acute onset of fever, joint pain, effusion, erythema and warmth at the implant site, and are commonly caused by virulent microorganisms such as \textit{Staphylococcus aureus}, \beta-haemolytic streptococci or gram-negative bacilli. During the course of infection, cellulites or formation of a sinus with purulent discharge may occur.

In patients with delayed manifestation, the (low-grade) infection usually has been simmering for several months, giving rise to subtle signs and symptoms such as early implant loosening or persistent joint pain (also at rest). The involved pathogens, such as coagulase-negative staphylococci, \textit{Propionibacterium acnes} and \textit{Corynebacterium spp.}, are less virulent. Early and delayed infections are usually acquired during implantation of the prosthesis via the exogenous route. Early infections that are acquired via the hematogenous route are rare, and for example are caused by an acute urinary tract infection.

Late infections are predominantly acquired by hematogenous spread from a distant focus\textsuperscript{128}. A late infection can first manifest itself acutely in the form of sepsis, leading to an acute onset in the affected joint, or else can start gradually and lead to a deep-seated abscess.

\textbf{Diagnosis and definition of PJI}

The diagnosis of PJI is straightforward whenever there are specific signs of infection i.e. a sinus tract or frank purulence around a component at the time of surgery. More often though, the presentation of PJI is variable, and resembles that of aseptic loosening. PJI is suspected when there is a history of persistent wound drainage after surgery\textsuperscript{140}, pain at rest, elevated laboratory signs of infection or radiological signs of early component loosening sometimes with peristomal bone formation\textsuperscript{141}. In diagnosis of PJI, current microbiology laboratory methods depend on isolation of a pathogen by standard cultures. The reference standard for diagnosis of prosthesis joint infection is growth of microorganisms in culture, as well as the presence of granulocytes in tissue on histopathologic examination. These standards are used...
to define the validity of other tests. The use of swabs should be avoided because sensitivity is reportedly low (range 0 to 23%). Culturing of tissue specimen has yielded the highest sensitivity (range 65 to 94%). Nevertheless, sensitivity is not ideal. Hence, several investigators have come up with useful criteria for definite PJI, that include information on patient history, clinical signs and results of laboratory, microbiological, histopathological, radiological and nuclear examinations.

To further improve the diagnosis of PJI, culture-independent molecular methods have been developed. Broad-range polymerase chain reaction (PCR) is a molecular diagnostic method that allows for replication and amplification of genetic (DNA) material. This method was invented by Kary Mullis, for which he received the Nobel Price in chemistry in 1993. Since then, PCR has been applied to detect bacterial DNA in tissue and causative pathogens have successfully been identified in organ and native joint infections, even when conventional cultures remained negative. Although PCR has been advocated as a useful diagnostic tool for detection of PJI by some, this issue is still a matter of debate.

**Surgical treatment of PJI**

The goals of treatment of PJI are the eradication of infection and reconstitution of function of the affected limb. The mainstays of treatment are the operative debridement and antibiotic therapy regardless of how the infection is classified. Collaboration with an infectious disease specialist and/or a microbiologist with special interest in PJI’s is often required to define the appropriate antimicrobial therapy. Surgical treatments include a two-stage exchange, a one-stage exchange, debridement with retention of the prosthesis, resection arthroplasty and amputation. Debridement includes removal of hematoma, fibrous membranes, sinus tracts, and infected and devitalized tissue.

The classic treatment for deep infection has been a two-stage exchange with removal of all foreign body material, collection of tissue specimen for microbiologic and histopathologic examination, a debridement, a 6-8 week lasting Girdlestone situation often with traction-suspension, and total duration of administration of antibiotics of three months. The success rate with this regimen has been reported to range between 82 and 96%. Patients with deep infection in our cohort were treated with this approach with satisfying results. In the rare situation when infection could not be controlled or in case of a lack of bone stock or gross muscle damage, a definitive Girdlestone procedure was performed with a relatively satisfying result.

Although the control of infection after two-stage exchange is generally good, the disadvantages of this approach are the longer immobility and hospitalization, and the higher morbidity and costs. Hence, a one-stage exchange would be preferable for patient and economic reasons.

Series of one stage revisions, with direct exchange of the implant and debridement, have reported a rate of cure between 76% and 100%. Guidelines for selection of patients for a one-stage exchange have been proposed, that include (i) the presence of intact or mildly damaged soft tissues, and (ii) no involvement of difficult-to-treat pathogens. Such patient selection has lead to less recurrence of infection after 1-SE.

Successful results of debridement with retention of the implant also require careful patient selection. Good results can be achieved when (i) the episode is classified as an early or late hematogenous infection with duration of symptoms of less than 3 weeks, and (ii) the implant is stable, and (iii) no difficult-to-treat pathogen is involved, and (iv) the soft tissue is intact or slightly damaged.

Ideally, management of PJI should be standardized. Unfortunately, at present this is not the case because of the different clinical presentations and the lack of data from randomized, controlled trials. Over the last 25 years a treatment algorithm for PJI has been elaborated in the Kantonsspital Liestal, Switzerland, which is a tertiary care center for orthopaedic infections, in collaboration with the unit for infectious diseases, University of Basel, Switzerland. In this concept, the decision to perform a debridement with retention, a one-stage exchange or a two-stage exchange with or without spacer is based on several factors. Strict adherence to this algorithm has shown an overall success rate of 86% in curing the infection.
In reports of different treatment regimens for PJI, the infectiological outcome has been the topic of main interest. Patient satisfaction after hip surgery however, is highly influenced by the functional result\textsuperscript{168}. The functional outcome of the abovementioned algorithm was therefore the subject of a study conducted by the Kantonsspital Liestal, Switzerland in collaboration with the Academic Medical Center, University of Amsterdam. In a secondary study, we studied the effectiveness of broad-range PCR in diagnosis of PJI in current clinical practice.

Loosening and obesity

Obesity has a negative influence on health and mobility. It has been proven that osteoarthritis of the hip joint requiring THR is more frequent in obese patients\textsuperscript{169} and the outcome of this procedure in these patients remains an issue of debate. A negative influence of obesity on the result of THR was not shown in short term follow-up studies\textsuperscript{170-172}, whereas to our knowledge no long-term studies on this topic exist. Nevertheless, a recent large international survey performed in 12 European countries among orthopaedic surgeons, revealed that 90% believes that the long-term outcome of THR is impaired by overweight\textsuperscript{173}. In addition, the fear of complications is increased among surgeons. Over the years, we have regularly performed follow-up of patients who had received a THR. In this way, the long-term outcome of THR and its complications in obese patients could be compared to normal weight patients.

Cementing techniques

Although the use of acrylic cement, popularized by Charnley in the late 1950’s improved fixation of the prosthetic implants tremendously, mechanical loosening still was a problem, which became especially apparent when THR’s were used in younger patients. Apart from identifying flaws in the prosthetic designs, cementing techniques were also evaluated and changes were made to improve the adherence to bone.

Early or first generation cementing techniques involved little or no preparation of the bone bed, antegrade filling of the medullary canal and no pressurizing apart from fingerpacking\textsuperscript{3}. Charnley purely saw it as a filling\textsuperscript{174}, which functioned as part of the prosthesis, adapting it to the femur of the individual patient. This way, there was a large contact area, without the peak stresses of an uncemented prosthesis like the Thompson or Austin-Moore. Bonding to the bone by the acrylic cement was not considered a prerequisite for longevity. After reports of component loosening rates of 20% and more after 10 years in the late seventies, some surgeons abandoned cemented techniques. Others adapted their technique to improve fixation, especially on the femoral side. Although the literature suggests there are 3 generations of cementing techniques, it is hard to identify a standard second generation cementing technique. Several innovations were introduced during the 1980’s, but not all innovations were implemented by every surgeon and because different prosthetic implants were also used, comparison of outcome between patient groups because of these “improvements” need to be interpreted with caution. Even using an improved technique by the same surgeon, using the same implant is not without bias, because the surgeon will learn from experience.

However, the results of improved cementing techniques cannot be ignored. Mulroy and Harris\textsuperscript{175} for instance, reported a 3% femoral loosening rate in 105 hips after a minimum of ten years. Their improved cementing technique entailed using a cement gun, an intramedullary polymethylmethacrylate plug and stems of improved design. Pressurization was not used.

Kaplan-Meyer analysis of 169,000 hips from the Swedish hip registry between 1992-2006 showed a survival of 86.6% (± 0.9 %) after 15 years, using high-pressure techniques for the femoral side in comparison to 85.1% (± 1.0%) in the hips without the use of this technique. This difference in outcome was statistically significant (p<0.001 Log rank).

Third generation techniques further include pulsatile lavage, reduction of cement porosity (vacuum mixing), and precoating of the stem\textsuperscript{176}

Although many authors reported on modernizing cementing technique for the femoral component\textsuperscript{175,177-181}, papers on improved fixation of the acetabular component are scarce. Because of the persistent inferior results produced by cemented fixation of the acetabular component in comparison to the improved results of stems that were cemented according to improved techniques, several authors abandoned cemented fixation for the cups. The combination of a cementless cup and a cemented stem is known as a hybrid hip.
The difficulty in cemented fixation of the cup is the reproducible formation of good initial stability through an interlock between the cement and the bone, especially in the craniolateral part of the acetabulum. Radiographic studies have shown that the presence of a radiolucent line in zone 1 (deLee and Charnley\(^{182}\)) increases the chances of failure of that cup 40 fold\(^{183}\). A good bony interlock provides stability necessary to withstand the elastic deformation forces of the acetabulum. This changes from a high oval shape to a spherical shape during weight bearing\(^{184}\).

The bony interlock stiffens the periprosthetic bone, creating a stable interface between cement and bone to withstand these plastic deformation forces. Apparently in a well-cemented polyethylene cup, some plastic deformation should be possible, because cementing metal backed cups into the acetabulum produced worse results. If the implant is too stiff (large difference in elasticity moduli), stress shielding is usually the result in the dome of the acetabulum. This bone loss can eventually lead to weakening of the bone that is supporting the implant and eventually to loosening.

Bleeding from the bone bed and insufficient removal of fibrous tissue and necrotic bone fragments from the interface are the main reasons for failure of establishing a good bony interlock. These are the main features that need to be addressed in any attempt at improving cementing technique. Using adrenaline soaked gauzes and creating a hypotensive state in the patient\(^{185}\) can reduce bleeding. Pressurization of the cement is necessary to overcome the patient's blood pressure and reduce the amount of blood leaking into the interface. The shape of the acetabulum unfortunately does not allow for the kind of pressures that can be produced when the femur is distally plugged and proximally closed off by a pressurization device. The cementing technique of the acetabular component used in the Binnengasthuis and Academic Medical Center is described in chapter 5 and is combined in this chapter with the long-term results of cemented acetabular fixation.

These factors that compromise a good cement-bone interlock, are not an issue in cementless fixation of the cup. Good initial fixation in uncemented THR is usually reached by press fitting the cup, if necessary aided by screws or in case of screwcups like the Zweymüller\(^ 6\) (Zimmer, Warsaw, Indiana, USA), by screwing the cup into the bone. Fixation is later enhanced by ongrowth of bone, which may be enhanced by coatings like trabecular metal or hydroxyapatite\(^{186}\).

**Design changes in cemented THR**

Apart from changes in cementing techniques, implant designs were also changed to improve initial stability. Two types of stems evolved over the years, both successful, but very different in design. On the one hand, there are the stems that provide good initial stability within the cement mantle usually with a roughened finish and geometric shapes that control axial rotation (composite-beam or shape closed designs). On the other hand, there are smooth surfaced implants that allow for some controlled subsidence within the cement mantle (taper slip design).

The design of the cemented cup did not change much over the years, although a flange was added to some cups to improve pressurization of the cement. This was studied in cadavers and seemed to produce a more even distribution of the cement\(^{187}\), but a later study showed no significant difference in the average penetration of cement into the bone\(^{188}\).

**Straying from cemented fixation**

Due to disappointing results in the late 1970’s and the association of periprosthetic osteolysis with the use of cement ("cement disease"\(^ 17\)), cementless designs were developed, believing that by removal of the apparent cause of cement disease this would lead to a longer lasting fixation.

The hybrid hip\(^ {176}\) was developed because of disappointing results of the acetabular fixation with cement, whereas improved cementing techniques on the femoral side resulted in a better outcome. A cementless cup was therefore combined with a cemented stem.

Uncemented stem designs\(^ {189}\) can be divided into three categories: anatomic, tapered and cylindrical. Anatomically shaped stems showed a higher percentage of thigh pain\(^ {189,190}\), when compared to tapered or cylindrical designs. Cementless stems also led to proximal stress shielding. Proximal stress shielding and thigh pain were found to be related to a greater difference in elasticity modulus between the stem and the surrounding bone and to distal porous coating and increased diameter of the distal part of the stem\(^{191,192}\). Later designs therefore were made of titanium instead of cobalt-chrome, because of its lower elasticity modulus. They featured a porous coating on the proximal part of the implant only, and stiffening of the distal part, without increasing the diameter.
Uncemented cup designs are usually hemispheric in design or sometimes conical with a thread for screwing the cup into the acetabulum. The most used cups now are hemispheric press-fit cups. Screws, pegs or spikes can enhance its initial stability. Later stability is enhanced by ongrowth of bone onto the porous, hydroxyapatite or trabecular metal coating.

The first generation cups suffered from malfunctioning of the locking mechanism of the acetabular liner\textsuperscript{193-196}, accelerated polyethylene wear, and extensive periacetabular osteolysis\textsuperscript{197}. Screwholes were found to potentially increase the affective joint space, which could lead to retroacetabular osteolysis (“backside wear”). Therefore, screwless press-fit cups are preferred.

The difficult hip

From 1974, we have used the Weber rotating total hip replacement as the standard implant in primary THR. The wrought casted CoNiCrMo (Protasul\textsuperscript{10}®) curved stem was available in 4 different lengths. In 1980, a straight stem was added to the range of stems. Three different necklengths were available. A 32-mm head was always used, either metal (Protasul 10\textsuperscript{8}) or Al\textsubscript{2}O\textsubscript{3} ceramic (Biolox\textsuperscript{8}). Although larger heads were supposed to create more wear\textsuperscript{198}, it was felt that the larger head gave more range of motion, decreased the risk of impingement and also enhanced stability. The trunnion design, with its secondary articulation between the head and neck, allowed for some telescoping motion (Fig. 5). Perhaps this enhanced stability from the larger head and the trunnion is one of the reasons for a low dislocation rate. Indeed dislocation of a THR was a rare phenomenon in our entire patient cohort.

There was a choice of hemispherical and flat cups, the latter to facilitate implantation of a cup into a shallow acetabulum usually found in dysplasia. The all-polyethylene cup and the grit-blasted stem were cemented, using low-viscosity Sulfix\textsuperscript{8} cement. This system was not only used in primary THR, but it was also used for more difficult cases, like hips with insufficient bone stock (dysplasia, revisions).

An important factor in the survival of a total hip replacement is the surgical technique. This thesis presents several studies on the outcome of cemented THR in different situations, using the same implant (Weber rotation), and using the same surgical techniques and philosophy. The preservation of bone, the optimal usage of biological material (no waste), the creation of good coverage of the acetabular implant and the use of a standardized cementing technique are important items in this surgical philosophy. Other items like restoration of the centre of rotation and leaving the subchondral plate intact were also important items in the surgical technique.

Not only in acetabular dysplasia, but in all cases with an incomplete bony coverage of the acetabular implant, a roofplasty was added to the operative procedure. The addition of a superolateral bone graft decreased shear forces in a finite element study\textsuperscript{199}. This decrease in shear forces would supposedly lead to a decrease in the risk of loosening. Bone grafts were usually taken from the excised femoral head, so no biological material was wasted\textsuperscript{200}.
We used small corticocancellous grafts instead of large bulky grafts, that were known to produce good short-term results, but failed in the long term. Another technique, using compacted morselized allograft was popularized by Slooff from Nijmegen and Ling from Exeter. Although this technique has been shown to have its merits, Marti and his staff did not adopt it due to satisfactory results with the triflange corticocancellous small bone grafts in acetabular reconstruction.

In revision surgery, bone stock can also be insufficient to support the implant. Therefore, everything was done during primary total hip surgery or even prior to that in femoral osteotomies, to ensure sufficient bone stock in case of future revisions.

In large segmental defects, an augmentation ring (Eichler ring) was used. This steel implant was not as stiff as other designs like the Müller, Ganz, and Burch-Schneider. Because of its lower elasticity modulus, there supposedly is less stress shielding, which allows for load transfer to the acetabular bone, and therefore presumably results in a better incorporation of superolateral bone grafts especially.

In osteoarthritis secondary to preexistent anatomic deformities of the femur, surgery can also be more difficult than in the average hip. These smaller, i.e. hypoplastic femora, usually have a narrow canal requiring a smaller than usual component. Our cohort contained 86 hypoplastic hips, often with muscle contractions and shortening of the leg. In all these cases, the combination of the smallest size off-the-shelf Weber rotation prosthesis, often combined with a superolateral roofplasty, proved to be a good solution. There never was the need for a custom-made stem.

New developments

**Resurfacing and other bone preserving implants**

The success of the THR and the growing confidence in its longevity led to the expansion of indications for hip replacement surgery. Especially young patients obviously demand more from their implants. As traditional stiff uncemented implants resulted in stress shielding of the proximal femur, also quite often with thigh pain, focus was directed towards designing implants that could be well fixed proximally. One of these implants was the Mayo hip® (Zimmer®, Warsaw, Indiana, USA). This short-stemmed implant, which gets its stability from a three-point contact, might ultimately save femoral bone stock, especially in young patients for whom future revisions are to be expected.

Patient expectations have followed those of many surgeons, believing that full restoration of function should be possible, including sporting activity. To accommodate this, hip resurfacing was reintroduced. Earlier failures with resurfacing were ascribed to imperfect production of materials, leading to excessive wear and loosening. The idea behind resurfacing implants, like the Birmingham hip® (Smith&Nephew Inc, Memphis, Tennessee, USA) is that it restores normal anatomy and biomechanics of the hip joint and provides near normal proximal femoral anatomy and loading. Should future revision become necessary, most of the femoral bone stock is retained.

However, concerns have been raised about removing more bone on the acetabular side. Other authors have not confirmed this, stating that with the possibility of choosing a femoral head size in small increments, the acetabular component need not to be larger than in a conventional uncemented THR.

**Minimally invasive surgery**

Since 2000, new processes in THR have been emphasized. Changes in pain management and anaesthesia were made to facilitate rapid recovery protocols. To further enhance a rapid recovery, minimal invasive surgery was endorsed, fuelled by the industry seeing opportunities to explore a new market. Minimal invasive surgery should not just leave a small scar to reduce self-consciousness of the patient, but should ideally produce less muscle damage and aid in a faster recovery. In a psychological study by Dorr in 2007, patients were very pleased with a small scar after 6 weeks, but at 6-12 months, the length of the scar was less important. Many minimal exposures have been advocated, like the two incision technique by Berger, the mini posterolateral incision, the direct anterior, and the modified anterolateral exposure. The best exposure is subject of debate, but in the end, the experience of the surgeon with a certain exposure and technique will dictate the outcome. One of the risks of minimal invasive surgery is the malpositioning of implants and risk of intra-operative complications, like fractures, because of the impeded view. Specially designed instruments and computer navigation can aid in decreasing these risks.
References


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Contents of this thesis

This thesis includes many studies focused on the longevity of the cemented Weber rotation total hip replacement, used in primary and revision cases. It also includes one animal experiment and one retrieval study, both dealing with aseptic loosening, and two studies on prosthetic joint infection (PJI).

In Chapter 2, we describe the long-term outcome of primary cemented THR after a minimum of 5 and a maximum of 20 years.

In Chapter 3, the treatment of osteoarthritis secondary to hip dysplasia is addressed. In most cases, the acetabulum was augmented by a superolateral bone graft. We present long-term outcome and describe the technique of bone grafting superolateral defects.

In Chapter 4, the attention is focused on dysplasia of the femur. In femoral dysplasia, the diameter of the femur is smaller and most often does not allow for a standard implant. We present a series in which we used the smallest size, standard stem of the Weber Rotation THR.

Chapter 5 focuses on the cementing technique of the acetabular component.

In Chapter 6, we present an experimental study in rabbits, in which the effect of mechanical compression of a fibrous membrane interface, on prosthetic loosening, is investigated. In addition, we administered high-density polyethylene particles to see whether their presence influenced the effect.

In Chapter 7, retrieved interface tissues from aseptically loosened THRs were studied for the presence of activated matrixmetalloproteinases (MMP-2 and MMP-9) and their relationship to macrophage activity and wear particles.

In Chapter 8, we show the results of a study performed to follow-up on an earlier study of cemented revision THR. We now present the results after a maximum follow-up of 24 years.

In Chapter 9, we analyzed the results after revision THR with an acetabular augmentation ring, which is used in cases with large segmental defects.

In Chapter 10, we deal with the supposition that overweight might challenge the outcome of a THR.

Infection is one of the most dreaded complications in total hip surgery. In Chapter 11, the functional, radiological and infectiological outcome after treatment of prosthetic joint infection according to a strict algorithm is evaluated.

In Chapter 12, the diagnostic value of the polymerase chain reaction (PCR) technique to detect orthopaedic infection is discussed.
Chapter 2

Weber Rotation total hip replacement
A Prospective 5- to 20-Year follow-up study

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Abstract
Between 1974 and 1989, 315 primary total hip replacements (274 patients) were done using the cemented Weber Rotation prosthesis and a standardized operation technique, which was modified for the stem in 1978. After the first postoperative year, all patients had routine clinical and radiological examinations at 2-year intervals. Twenty-one patients (22 hips) were lost to follow-up. At the most recent follow-up, 30 of 293 hips (253 patients) had been revised: 24 hips for aseptic loosening, five hips for infection, and one hip for a femoral fracture. Survivorship analyses with revision for aseptic loosening as an end point for the 315 hips showed 93% and 78% survival after 10 and 15 years, respectively. Separate survival analyses for the socket showed 99% and 89% survival after 10 and 15 years, respectively. The stem had a survival of 94% and 81%, respectively during the same time. Survival at 15 years with radiological evidence of loosening as an end point was 85% for the socket and 72% for the stem. The cementing technique and the design of the acetabular component significantly influenced the rate of loosening. Survivorship analyses with revision for aseptic loosening of the socket, using a modified second generation cementing technique and a hemispheric socket, showed 100% survival after 10 years and 98% after 13 years.

Introduction
Since 1974, the modular Weber Rotation (Allopro, Baar, Switzerland) total hip prosthesis has been used by the senior author (RKM) as the standard for all primary total hip replacements. A special feature in this design was the head-to-neck junction, which consisted of a cylindrical rotating trunnion. This secondary joint was designed to diminish movement and wear in the primary head-to-socket joint and to reduce torque stresses on the femoral component. A similar trunnion bearing was used in the Christiansen total hip prosthesis in combination with a 37-mm, steel-capped, polyethylene head. However, this polyacetal-coated trunnion bearing frequently was observed to be jammed during revision surgery and was taken off the market because of a high wear rate and disappointing survival rates.

Certain aspects of the Weber Rotation total hip replacement such as wear of the polyethylene socket and of the rotating trunnion have been reported. These studies were based on patients included in the current study. Schüller and Marti showed that after an average of 10 years, polyethylene wear, using the metal rotating head of the Weber Rotation prosthesis averaged 0.96 mm with an average wear per annum of 0.1 mm. The use of a ceramic head on the rotation prosthesis reduced this wear to 0.26 mm at 10 years, with an average annual wear of 0.03 mm. Van der Vis et al looked at differences in wear between the Weber Rotation prosthesis and the Weber fixed prosthesis, both with a ceramic head. The average linear wear was 0.034 mm for the rotating bearing and 0.069 mm for the fixed head. In both studies, measurements were made radiographically according to the method of Scheier and Sandel as modified by Buchhorn et al. Van der Vis also did a retrieval study and calculated the mean wear of the trunnion bearing of 12 retrieved stems to be 2.4 µm per year (standard deviation, 1.4 µm). All the trunnion bearings functioned well after a mean follow-up of 11 years.

After reported experience with the Weber Rotation total hip replacement used in cemented revision hip surgery, the current authors reviewed the long-term clinical results of its use in primary total hip replacement.

Materials and methods
Features of the Weber Rotation total hip replacement System
The stem of the prosthesis was made from a wrought CoNiCrMo alloy (Protasul® 10, Sulzer AG, Winterthur, Switzerland), and the cylindrical neck (the trunnion) was made of a cast CoCrMo alloy (Protasul® 2) composite welded to the stem. With exception of the cone where the ball head is seated, the entire stem is grit-blasted with glass particles, resulting in a surface roughness of 1 µm to 2 µm. Two types of stems were used: four curved stems with increasing lengths and one straight stem, although only three curved stems were available until 1980. The cross-sectional geometry of the stem is trapezoidal with rounded corners. The 32-mm head was made from Protasul® 2 or Al2O3 ceramic (Biolox®, Feldmühle, Plochingen, Germany) and placed on a Protasul® 2 cylinder (Fig 1). This ceramic head is fixed on a taper cone on top of the rotation cylinder before placing the cylinder on the trunnion (Fig 2). Three different cylinder lengths are available: short (42 mm), medium (47 mm), and long (52 mm). The outer diameter of the all-polyethylene (RCH-1000 Chirulen®, Hoechst, Germany) socket ranged from 40 to 64 mm. The depth ranged from 24 to 37 mm. There was a choice of a standard hemispheric socket and a flat socket, which was designed for a shallow dysplastic
acetabulum (Fig 1). In the flat socket, the thickness of polyethylene was reduced. The difference in polyethylene thickness at the apex was 4 mm for the smallest size flat socket and 10 mm for the largest size. The stem and the all-polyethylene socket were cemented using low viscosity Sulfix® (Sulzer AG) cement.

Operative Technique and Postoperative Treatment

The operative procedure consisted of an anterolateral (Watson-Jones) approach with an osteotomy of the greater trochanter if necessary. Full bony coverage of the socket was considered imperative and in cases with acetabular roof deficiencies, either superolateral bone grafting was done using a hemispheric socket23, 24, 26, 33 or a flat socket was used.

Six to nine 8-mm drill holes were made in the subchondral layer of the acetabulum and the underlying cancellous bone was impacted before cementing the socket. The stem was positioned in valgus in all patients. A first generation cementing technique was used until 1978. The technique subsequently has been modified by using a polyethylene intramedullary cement restrictor and vacuum suction during introduction of the cement. This technique is referred to in this study as second-generation cementing technique.

Five days after surgery patients were mobilized non weightbearing. Full weight-bearing was permitted after 8 weeks. Routine clinical and radiological examinations were done at 8 weeks, 4 months, and 1 year postoperatively and biennially thereafter.

Patients

Between 1974 and 1989, 315 consecutive primary total hip replacements in 274 patients were done by the senior author (RKM), using the cemented Weber Rotation modular total hip prosthesis. Twenty-one patients (22 hips) were lost to follow-up, or had a follow-up less than 2 years. Forty patients had bilateral hip replacements. Of the 253 patients (293 hips) included in the study, 188 were women and 65 were men. The average age of the patients was 68.4 years (range, 23-86.6 years). The 224 patients (263 hips) who did not have revision surgery had a mean follow-up of 10.5 years (range, 3.8-20.3 years).

The numeric distribution for the different parts used was as follows: 127 Protasul and 166 ceramic heads, 27 straight and 266 curved stems, and 85 flat and 208 hemispheric sockets. Preoperative diagnoses included primary osteoarthritis (162 patients, 187 hips), dysplasia or congenital luxation or subluxation (56 patients, 68 hips), rheumatoid arthritis (seven patients, eight hips), posttraumatic (11 patients, 11 hips), avascular necrosis (10 patients, 12 hips), and other (seven
patients, seven hips). Sixty-two patients (70 hips) had surgery before the total hip replacement: intertrochanteric osteotomy (53 patients, 60 hips), acetabular reconstruction (three patients, four hips) and internal fixation (six patients, six hips). Functional activity was assessed according to the classification of DeLee and Charnley. Eighty-eight hips were Grade A, 105 hips were Grade B, and 100 hips were Grade C.

Methods
At follow-up, the Harris hip score was used to assess the clinical result. The standard system of terminology for reporting results as suggested by Johnston et al and the scoring system described by Dall et al were used to evaluate the radiographic results. In the system described by Dall et al, points are given for the acetabular and femoral components separately. The maximum score for the acetabulum is 10, and the maximum score for the femur is 15. Zero to 3 points are given for cement-bone radiolucencies, their width, and their localization. Migration and femoral subsidence also are considered. The lower the amount of points given, the better the result. Grading this radiographic result in a scale from 1 to 3 is done as shown in Table 1. In Grade 1, there are only mild changes, usually of minor significance; in Grade 2, there are moderate changes that need regular observation; and in Grade 3, there are severe changes indicating impending failure. Radiographic analysis was based on a lateral view and an anteroposterior radiograph of the pelvis taken with the patient standing, and with the ray centered on the hip. The first and third authors studied the first postoperative radiographs and all radiographs taken at 2-year intervals including radiographs obtained at the most recent follow-up. The two other authors then reviewed the radiographs with a radiologist who specialized in skeletal radiology. Interobserver variability was calculated by cross tabulation resulting in kappa values and a Spearman correlation value.

Survivorship analysis was done using the life table method with revision for aseptic loosening and radiographic evidence of loosening (Grade 3) as end points. Separate survivorship analysis for the cup and the stem were done.

The influence of the shape of the cup, the cementing technique used, and the material of the head was evaluated using log rank tests. Because the groups receiving a straight (27 patients, 27 hips) and a curved stem (187 patients, 266 hips) were not equal in duration of follow-up or in use of cementing technique, the influence of the shape of the stem on the results could not be evaluated. In most cases, the straight stems were used only when a curved stem did not provide an optimal fit. The relationship between radiographic signs of loosening (Grade 3) and a poor Harris hip score was evaluated using the chi square test.
<table>
<thead>
<tr>
<th>Socket</th>
<th>Score (points)</th>
<th>Stem</th>
<th>Score (points)</th>
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<td>Cement-bone radiolucency; number of zones</td>
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<td>radiolucency (DeLee and</td>
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<td></td>
</tr>
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<td>Subsidence of stem within cement</td>
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<td>5+ mm</td>
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<th>Stem</th>
<th>Score (points)</th>
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<td>Subsidence of stem with</td>
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<td>cement (cement mantle)</td>
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</table>

| Maximum total score          | 10             | Maximum total score stem                                             | 15             |
| socket                       |                |                                                                      |                |
| Total score socket           | Grade of       | Total score stem                                                     | Grade of       |
|                              | radiologic     |                                                                      | radiologic     |
|                              | loosening      |                                                                      | loosening      |
| 1-2                          | 1              | 1-4                                                                  | 1              |
| 3-5                          | 2              | 5-8                                                                  | 2              |
| 6-10                         | 3              | 9-15                                                                 | 3              |

Table 1. Scoring System of Dall et al.6 (with permission of DM Dall, and Springer Verlag GmbH & Co)

To make a comparison between two types of prostheses is difficult, because there are many factors influencing the outcome. The current authors searched the literature for similar studies of patients in the same age category who received a cemented total hip prosthesis, with the use of a first generation, second generation, or both generations cementing technique. The studies should include a survivorship analysis with revision as an end point. Eleven studies were found that met these criteria. To, 3, 10, 11, 16, 19, 27, 29, 31, 35, 36. Ten- and 15-year results were extracted from these studies and are shown in Table 2.
Results
At the latest follow-up, 30 revision surgeries had been done. Twenty-three patients (24 hips) had revision surgery for aseptic loosening, five patients had revision surgery for infection, and one patient had revision surgery because of a fracture. In addition, one patient had a second operation because of a nonunion after trochanteric osteotomy. In the group operated on after 1978, there were 20 revisions (15 for aseptic loosening). No fractures of the prostheses, including the ceramic heads, prosthetic disassemblies, or dislocations were seen during the follow-up. Of the 24 revisions attributable to aseptic loosening, three revisions were done for loosening of the socket, 14 revisions for loosening of the stem, and seven revisions for loosening of both components. The cumulative survival with aseptic loosening of components of the total hip replacement as an end point was estimated to be 93.3% at 10 years (126 hips at risk) and 78% at 15 years (31 hips at risk) and 20 years (two hips left at risk) (Fig 3, Table 3). Survival of the socket at 10 years was 98.7% and 89.2% at 15 years. For the stem, this was 93.8% at 10 years and 81.5% at 15 years (Fig 4).

Table 2. Overview of long-term follow-up studies of cemented total hip replacements

<table>
<thead>
<tr>
<th>Type of Prosthesis</th>
<th>Authors</th>
<th>Survival at 10 Years</th>
<th>Survival at 15 Years</th>
<th>Number of Hips</th>
<th>End Point definition</th>
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<td>Garellick et al10</td>
<td>94</td>
<td>85*</td>
<td>95</td>
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<tr>
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<td>70</td>
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<tr>
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<td>Kavanagh et al12</td>
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<td>89</td>
<td>333</td>
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<td>McCoy et al13</td>
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<td>Schulte et al15</td>
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*16 years
**Calculated from graph
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<th>Time in Years</th>
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<th>95% Confidence Interval</th>
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<td>78.52</td>
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Table 3. Life table for the Weber Rotation total hip replacement with revision for aseptic loosening as an end point.

Fig 3. The survival analysis with revision for aseptic loosening as an end point and 95% confidence intervals are shown.

Fig 4. The survival analysis with revision for aseptic loosening as an end point, compares survival of the socket with survival of the stem.
One hundred ninety-one patients (218 hips) who did not have revision surgery were seen for clinical examination. In this group of patients, an excellent clinical result (Harris hip score > 90 points at the latest follow-up), was seen in 110 hips (51.4%), a good result (Harris hip score 80-90 points) was seen in 50 hips (23.4%), a fair result (Harris hip score 70-80 points) was seen in 26 hips (12.1%), and a poor result (Harris hip score < 70 points) was seen in 28 hips (13.1%). Forty-two patients (45 hips) were not seen by the authors during the investigative period, and records did not allow the authors to calculate a Harris hip score. Forty of these patients died in the time between their latest clinical visit and the investigative period. The remaining two patients were unable to come to the hospital and therefore were questioned via telephone. Neither of these patients had any complaints of their total hip replacements.

Radiographs of 236 hips (201 patients) were available for analysis. Survivorship analysis with Grade 3 loosening as an end point showed 88.7% (95 hips at risk) survival of the Weber Rotation total hip replacement at 10 years and 67.8% (20 hips at risk) at 15 years (Fig 5). For the socket, the survival was 98.6% at 10 years and 85.5% at 15 years. For the stem, the survival was 89.5% at 10 years and 73.5% at 15 years (Fig 6).

Analysis of the interobserver variability between the two observer groups showed a kappa value of 0.77 for the cups (Spearman correlation 0.84), and a kappa value of 0.83 for the stems (Spearman correlation 0.9). There were no differences of opinion regarding the radiographs showing Grade 3 loosening between the two groups of observers.

Because the authors thought there were some factors that might have influenced the outcome, these factors were evaluated. In the authors’ experience the use of flat cups frequently was associated with loosening. Therefore, a log rank test was used to see whether there was a significant difference. There was a significantly higher rate of loosening ($p = 0.0018$) when the flat cups (85) were compared with the hemispheric cups (208).

Since 1978, a modified second-generation cementing technique was used. To study the influence of the cementing technique, the study group of 253 patients (293 hips) was divided into two groups. The first group consisted of 36 patients (39 hips) who were operated on before 1978 using a first generation cementing technique, and the second group included 223 patients (254 hips) who were operated on between 1978 and 1989 using a second-generation cementing technique. When the results were compared between the first group and the second group, there was a significant
difference (p = 0.0083), with better results in the second group. Because the shape of the cup as well as the cementing technique seemed to influence the outcome, survivorship was analyzed in the group where a second-generation cementing technique was used in combination with a hemispheric socket (196 hips); at 10 years, the estimated survival with revision for aseptic loosening of the hemispheric socket was 100% (67 hips at risk), and at 13 years this was 98% (27 hips at risk). At 15 years no socket had been revised for aseptic loosening, so survival remained 98%, but there only were eight hips at risk at 15 years. The use of a hemispheric acetabular component and a second-generation cementing technique, also improved survival with revision for aseptic loosening in the overall group (loosening of stem and/or cup). At 10 years survival was 96.7% (67 hips at risk) and 93.6% at 13 years (28 hips at risk). At 15 years, the survival was 86.4%, but there only were seven hips at risk. A log rank test was used to evaluate the influence of the choice of head on survival. It did not significantly change survival (p = 0.3048).

The clinical results of patients with Grade 3 radiographic loosening were excellent in six hips, good in four hips, fair in two hips, and poor in four hips. The chi square test showed that there was a very poor sensitivity when the Harris hip score was correlated to Grade 3 loosening. The chi square test could therefore not be applied. Fisher’s exact test gave a probability value of 0.051.

Discussion

The increasing turnover of different and innovative designs makes long-term follow-up studies scarce. Although the failure rates of several total hip designs are low after 10 years follow-up, these rates increase considerably thereafter. It therefore is essential to monitor the long-term survival of existing designs to be able to offer patients the best choice. To be able to compare the authors’ results with results from other long-term follow-up studies, revision for aseptic loosening was used as an end point in the survivorship analysis. There were 11 published studies on cemented total hip prostheses that used a first or second generation cementing technique and including a survivorship analysis (Table 2). Survivorship analysis with revision for aseptic loosening as an end point showed a good result with the use of the Weber Rotation total hip replacement in primary hip surgery after 10 years in comparison with other well-documented cemented total hip replacements such as the Charnley, Stanmore, and McKee-Farrar prostheses. After 15 years (20 hips at risk), the results seem less favorable in comparison.

The survival rate at 15 years in the current study clearly was influenced by the higher number of stem failures (19%) as compared with the socket failures (11%) (Fig 4). This difference was even more pronounced in the cumulative survival with radiographic evidence (Grade 3) of loosening as an end point (Fig 6). This may be explained partly by the use of first generation cementing techniques until 1978. Several authors have reported improved results using second- and third-generation cementing techniques. In the current material, nine of the 39 hips (23%) with a primary surgery before 1978 needed revision surgery for aseptic loosening. In contrast, 15 of the 254 hips (6%) operated on after 1978 with the use of a second generation cementing technique, needed revision for aseptic loosening. The results also are influenced by the use of the flat sockets in combination with the 32-mm head. These types of sockets have a relatively thin polyethylene layer centrally which could lead to more socket deformation by creep and subsequently to higher wear. Eight of the 10 socket revisions had a smaller sized flat socket (size 130/133).

When survivorship analysis with revision for aseptic loosening was done for the group in which second-generation cementing techniques were used in combination with hemispheric cups, the survival after 10 years was 96.7% (67 hips at risk) and 93.6% (28 hips at risk) at 13 years (Fig 7). This outcome is similar to the results that were published of well-established total hip replacements such as the Charnley and Stanmore prostheses (Table 2).
Fig 7. The survival analysis of the Weber Rotation total hip replacement with revision for aseptic loosening as an end point, using the second generation cementing technique and hemispheric sockets, is shown.

The choice of femoral components was limited in the early years of the Weber Rotation total hip replacement, sometimes requiring the surgeon to choose a suboptimal stem size (too large or too small) which may have influenced the quality of the cement mantle, and therefore the anchorage. The current authors think the outcome of the cemented curved stems depends on an optimal proximal anchorage with a substantial amount of cement supporting the prosthesis medially. To achieve this, the curved stem has to be placed in a valgus position. In the authors’ experience, the straight stems used seem to be more forgiving as far as malpositioning is concerned. However, the small number of straight stems used in the current study did not allow for comparison to be made between the two types of design.

The fact that a lower number of sockets needed revision as compared with the stems is in agreement with the results reported in the study of Dall et al7 and do not encourage the authors to change to a hybrid system (uncemented socket and cemented stem)12. The excellent result of the all-polyethylene cemented hemispheric socket may be attributed to several factors, such as the cementing technique with impaction of cancellous bone in the 8-mm drill holes and the optimal bony coverage of the socket. Full bone coverage of the socket always was achieved, if necessary, with use of a superolateral bone graft23, 24, 33, 26. Finite element analysis showed that load transmitting superolateral bone grafts may normalize the stress patterns at the lateral part of the acetabular roof35. Full coverage was not achieved by medialization of the socket, because then the subchondral bone, which is necessary for optimal socket fixation, is lost15, 20.

The use of a larger sized head (32-mm) may offer an explanation for the absence of early and late luxations in this study, although the anterolateral approach and the experience of the surgeon in this series are important additional factors. The use of a 32-mm head, however, is associated with a higher wear rate of the polyethylene socket21. This may be compensated by the design of the Weber Rotation total hip replacement because the rotating bearing was designed to reduce movement and wear in the joint between the head and the socket41.

Furthermore, it was established that the use of ceramic versus metal rotating heads leads to a significantly lower annual linear wear of the socket (0.03 and 0.1 mm, respectively)34.

However, in the current study, a significant difference was not found in survival between the two groups (ceramic versus metal). This might question the theory of wear particle-induced loosening and may underline the importance of an in vivo study that showed that polyethylene particles do not initiate aseptic loosening38. Mechanical factors such as micromotion and fluid pressure37 most likely play an important role in this process.

The results of the current study suggest that if a second generation cementing technique is used in combination with a hemispheric cup, the use of the Weber Rotation total hip replacement leads to a similar survival in comparison with some of the more established cemented total hip replacements like the Charnley or Stanmore prosthesis. Therefore, although the design did not lead to an improvement of the long-term survival expectancy, the design of the Weber Rotation total hip replacement does have the benefit of the use of a larger diameter head with reduction of the chance of dislocation.
Acknowledgement
The authors would like to thank the “Stichting tot Bevordering Wetenschappelijk Onderzoek Orthopaedie en Traumatologie Ziekenhuis Hilversum”, for supporting this research.

References


Total hip replacement with a superolateral bone graft for osteoarthritis secondary to dysplasia

A LONG-TERM FOLLOW-UP

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Abstract
We evaluated the long-term results of 116 total hip replacements with a superolateral shelfplasty in 102 patients with osteoarthritis secondary to developmental dysplasia of the hip. After a mean follow-up of 19.5 years (11.5 to 26.0), 14 acetabular components (12%) had been revised. The cumulative survival at 20 years was 78%, with revision for loosening of the acetabular component as the end-point. All grafts were well integrated and showed remodelling. In six grafts some resorption had occurred under the heads of the screws where the graft was not supporting the socket. Apart from these 14 revisions, seven acetabular components had possible radiological signs of loosening at a mean follow-up of 14.5 years, one had signs of probable loosening, and five had signs of definite loosening. These results indicate that this technique of bone grafting for acetabular reconstruction in hip dysplasia is a durable solution for cemented acetabular components.

Introduction
Dysplastic acetabula can provide a surgical challenge in total hip replacement. Schuller et al.1 showed that the lateral part of the acetabular roof is important for load transfer and a loaded bone graft in this location reduces stress on the cement-bone interface in a dysplastic hip. Since 1974 we have used multiple small femoral head autografts to reconstruct the superolaterally deficient acetabulum.2-4 Harris, Crothers and Oh5 described short-term success using bulk femoral head grafts combined with cemented sockets in patients with acetabular dysplasia. A follow-up report by Mulroy and Harris6 showed that 46% of these sockets had failed. Marti et al.4 reported the medium-term results for a group of 84 patients with a mean follow-up of 10.1 years and showed that all but one of the grafts had healed within three months. The ten-year survival was 92.6%, with failure defined as revision for loosening of either component. However, the series included 21 patients who did not have dysplastic hips.

We present here the long-term results for a series of primary cemented total hip replacements (THR) with superolateral bone grafting for osteoarthritis secondary to hip dysplasia at a mean follow-up of 19.5 years. Our technique of femoral head autografting is as described by Marti et al.4 in 1994, and differs from that described elsewhere5-8.

Patients and Methods
Between 1974 and 1993 the senior author (RKM) performed 116 primary THRs combined with a superolateral bone graft in 102 patients with osteoarthritis of the hip secondary to acetabular dysplasia. The mean age of the patients at operation was 64.4 years (35.5 to 84.3), and 76.9% were men.

The severity of dysplasia was estimated from the pre-operative radiographs by measuring the Sharp angle9 and the centre-edge (CE) angle of Wiberg10 in 63 patients (71 hips), but in the remainder the old radiographs had been destroyed. The mean Sharp angle was 45˚ (33˚ to 79˚) and the mean CE angle was 10.0˚ (-20˚ to +40˚). Two male patients had a CE angle of approximately 40˚ as a result of large superolateral osteophytes, although the osteophytes were too weak for weight-bearing and a shelfplasty was therefore performed.

The amount of subluxation of the femoral head was classified according to Crowe, Mani and Ranawat.11 A stage I subluxation was present in 85 hips, stage II in 16, stage III in two, and stage IV in 13. A total of 36 patients had undergone other procedures before their THR: 33 had a previous intertrochanteric osteotomy and three had a Tönnis triple osteotomy.

Technique.
All the operations were conducted in a laminar-flow operating theatre using the anterolateral Watson-Jones approach, with the addition of a trochanteric osteotomy in 33 hips. A cemented Weber Rotation total hip replacement (Allopro, Baar, Switzerland)12,13 with a 32-mm femoral head was used as the standard implant. All patients received prophylactic antibiotics and coumarin anticoagulation. Pre-operative planning identified hips which were likely to require an acetabular bone graft, the final decision being made at the time of operation. Although cover by bone of at least 70% of the acetabular component may be acceptable, the principle of supplementing the bone stock as an investment for the future contributed to the generous use of bone grafts.

After minimal reaming of the acetabulum to expose the subchondral bone, care being taken to preserve the subchondral plate superiorly, the acetabulum was assessed.
An attempt was made to use the standard hemispherical component with an outer diameter of 52 mm. If acetabular cover was inadequate superolaterally to support the trial implant, bone grafts were used.

The ilium, just proximal to the superolateral acetabular rim was lightly decorticated and femoral head autografts (usually three small grafts) were positioned against the iliac bone. The bone grafts were approximately triangular and measured about 1.5 x 2 x 3 cm. Cancellous bone was placed between the graft and the ilium. If the ilium was very sclerotic, the cortex was perforated by a few 2-mm drill holes. Usually, two corticocancellous bone grafts were secured by 4.5 mm AO cortical screws with a washer, the third graft being placed between the other two so that it was compressed into position (Fig. 1).

If the grafts covered more than a third of the acetabulum a buttress plate was added. The acetabulum was then reamed again to accommodate the 52 mm component with anchoring holes drilled in the cranial part of the acetabulum for cement engagement. All patients were instructed to bear partial weight for the first eight weeks using crutches, after which they were encouraged to relinquish their crutches and bear full weight.

Patient evaluation.
All patients were seen biennially after the first two post-operative years. The Harris hip score (HHS) was used for clinical analysis. Radiological evaluation was undertaken applying the terminology of Johnston et al to standardised AP pelvic and lateral hip radiographs. The radiographs were scrutinised for signs of loosening in the zones of DeLee and Charnley on the acetabular side and scored according to Hodgkinson, Shelley and Wroblewski. For the femoral side we used the criteria of Harris, McCarthy and O’Neill. Graft resorption was graded according to Gerber and Harris, and heterotopic ossification classified according to Brooker et al.

Statistical analysis was conducted using the statistical package, SPSS version 12.0 (SPSS Inc., Chicago, Illinois) with a p value less than 0.05 considered significant.

Results
Patients.
At the time of the review 42 patients had died, five of whom had undergone revision surgery. In one patient the acetabular component was revised after six years, in one patient both components were revised for a late infection after nine years, and in three hips in three patients the femoral component was revised, after three years in two cases and six years in the third.

After a mean of 8.1 years (1 to 15.8) 12 patients were lost to follow-up. All patients were included in the survival analysis for the follow-up time that was available. The remaining 40 patients (47 hips) were examined clinically and radiologically after a mean follow-up of 17.6 years (11.5 to 26.4).
Clinical evaluation.
The mean HHS for 54 patients with a mean follow-up of 16.5 years (6 to 26) was 90.5 (51 to 100). Thirty-four patients had an excellent score (90 to 100), 11 were good (80 to 90), six were fair (70 to 80) and three were poor (< 70). Five patients had a positive Trendelenburg sign at follow-up. To lessen the influence of comorbidity on the HHS, we divided the patients into Charnley categories A, B and C.16 Seven were Charnley category A with a mean HHS of 94.7 (87 to 100), 26 were category B with a mean score of 92.9 (71 to 100), and 21 were category C, with a mean score of 85.7 (51 to 100). The HHS was obtained at a mean age of 77.4 years (63.6 to 94.4).

Complications.
Four intra-operative complications occurred. In two patients the femur was cracked during preparation of the femoral canal. In the two other patients, the greater trochanter was fractured. These fractures healed, without additional treatment although the patients were kept nonweight-bearing for eight weeks. Two patients developed a post-operative infection requiring surgical debridement, but resulting in satisfactory healing. One osteotomy of the greater trochanter did not unite and required refixation, leading to union.

Survival analysis.
During a mean follow-up of 19.5 years (11.5 to 26.0), 20 hips were revised after a mean of 10.2 years (2.5 to 19.3). In six hips the femoral component was exchanged, in five the acetabular component, and in nine both components. With revision of the acetabular component as the end-point for the survival analysis, the ten-year survival was 95% (95% confidence interval (CI) 90 to 99), the 15-year survival was 85% (95% CI 77 to 93), and the 20-year survival was 78% (95% CI 67 to 90) (19 hips at risk) (Table 1). When the survival analysis was performed for all revisions (revision of the stem included), the ten-year survival was 90% (95% CI 84 to 96), the 15-year survival was 79% (95% CI 70 to 88), and the 20-year survival was 72% (95% CI 60 to 85) (16 hips at risk) (Table 1).
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<th>Withdrawals</th>
<th>At risk</th>
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**Revision of acetabular component**

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**All revisions**

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Table 1. Survival analysis (Life table method), with cup revision and revision for any reason as endpoints. 

CI* confidence interval.
Discussion

Since 1974, we have performed an acetabular roofplasty with autologous bone in THR whenever the containment of the standard 52-mm acetabular component was inadequate. In addition, restoration of the centre of rotation\(^{20-28}\), preservation of the subchondral plate, and ensuring sufficient thickness of the polyethylene cup as the femoral head was always 32 mm, have contributed to our frequent use of acetabular augmentation. In our earlier series of primary THRs\(^{13}\) 23% had an acetabular shelfplasty.

Pre-operative planning identified probable cases for acetabular augmentation but the final assessment was made intraoperatively after reaming down to the subchondral plate, which we aimed to retain and place the centre of rotation in the true acetabulum\(^{5,7,11,20-28}\). Jacob et al\(^{29}\) and Kobayashi and Terayama\(^{30}\) have shown the importance of leaving the subchondral plate intact to distribute the forces to the cortical shell and reduce excessive concentrations of stress on the cement-bone interface.

Radiological analysis.

The radiographs of all revision cases and of all patients for whom more than ten years of radiological follow-up was available (76 hips) were scored for radiological loosening of the cup after a mean follow-up of 14.5 years (5.6 to 26.3) (Table 2).

The femoral component was scored after a mean follow-up of 13.7 years (2 to 26.3) (Table 2). A survival analysis was performed using definite loosening of the acetabular component as the end-point, showing a ten-year survival rate of 94% (95% CI 89 to 99) (73 hips 91) (43 hips at risk).

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Table 2. Radiographic loosening

Heterotopic ossification was present in 13 hips (17%). Seven hips had Brooker grade I peri-acetabular calcification, three hips grade II and three hips grade III. All bone grafts showed integration and remodelling (Fig. 2). Six grafts showed partial non-progressive resorption under the screw heads. More extensive resorption in the weight-bearing part of the graft was not encountered.

Using Pearson’s correlation test no relationship was found between survival of the implant and the extent of subluxation as defined by the Crowe class (p = 0.299, r = 0.097), nor between survival of the implant and the severity of dysplasia as measured by the CE angle (p = 0.856, r = 0.22).

Using a log-rank test, we also compared rates of survival for the flat and hemispherical acetabular components and found that the difference was not significant (p = 0.0507).
Two types of acetabular component were available, flat and hemispherical, although the latter was mostly used because the flat polyethylene component was thinner at its apex. The flat component had a higher rate of failure in an earlier study from our unit on the long-term results of the Weber Rotation prosthesis in primary THR. In the current study, however, the difference in survival between the flat and the hemispherical sockets just failed to reach significance (p = 0.057), but the use of a hemispherical socket resulted in an increased need for an acetabular roofplasty.

Apart from these biomechanical considerations, the increase in bone stock for future surgery was an additional reason to use a femoral head as bone graft. This accounts for the relatively high number of patients with a Crowe I dysplasia (n = 85; 73%) in our study.

Many reports have shown that incomplete containment of the acetabular implant is associated with a poorer outcome. In a finite element study, Schuller et al showed the important role of the superolateral part of the acetabulum in load transfer. In a model, they showed that cement-bone interface stresses were considerably diminished by adding a superolateral graft to the acetabulum. As an alternative to bone grafting some authors have described the use of small acetabular components in an anatomical or superior position. Others have advocated proximal or medial placement of the acetabular component, sometimes even fracturing the medial wall. However, these methods compromise the biomechanics of the hip. The centre of rotation may be considerably displaced and/or the use of smaller components may give rise to a higher rate of wear.

Previous reports on the use of large bulky acetabular autografts generally described failure. This may have been because of the difficulty in revascularising and remodelling such large grafts, and the load they carried during this process. However, in series where smaller grafts were used, as in this study, results have been good. We accept that in this study group most patients (85 hips) had only minor dysplasia. Although the use of uncemented components might reduce the need for additional bone grafting, it remains a useful option, especially when a cemented acetabular component is used. The centre of rotation is retained, optimal cover is obtained and the subchondral bone layer is spared. It may also be used when an uncemented component needs excessive medialisation in order to obtain sufficient cover. The increase in bone stock is an added bonus, which may even have encouraged some authors to use bone grafts in uncemented procedures.

The 15-year survival for a primary THR with revision for aseptic loosening of the cup, using the Weber Rotation total hip replacement, as reported for a large consecutive series, was 85.5%, similar to the result in this study. This supports our belief that full bony cover of the acetabular implant by multiple small femoral head autografts leads to a long-lasting fixation of the acetabular component in total hip replacement.

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References


Small stem total hip arthroplasty in hypoplasia of the femur

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**Abstract**

Total hip arthroplasty in hypoplastic femurs is technically difficult and the incidence of complications and aseptic loosening is relatively high. Cemented, uncemented, off-the-shelf, and custom-made stems have all been advocated in these cases. From 1978 to 1997, we performed 86 total hip arthroplasties in 77 patients with a hypoplastic femur using a cemented, off-the-shelf, small, curved, cobalt-chromium stem. We hypothesized results equaled the results of the identical but larger-sized stems in normal-sized femurs which were used as comparisons. Clinical and radiographic evaluations were performed. Minimum follow-up was 4.2 years (mean, 12 years; range, 4.2-20.3 years); mean Harris hip score was 88, and mean hip flexion was 104°. Six stems were revised; four because of aseptic loosening, one after a femoral fracture, and one because of malpositioning. Complications included one perforation and one fracture of the femur, one fracture, one nonunion of the greater trochanter, and one deep infection. Implant survivorship for all hips at 15 years with aseptic revision of the stem as the end point was 90% (confidence interval, 82%-99%) which equaled results of the larger stems. The small off-the-shelf cemented Weber stem has a high long-term survival and a low complication rate. Survival compares favorably with other small-sized total hip systems.

**Introduction**

Since 1974 at our institution we have been using a cemented cobalt-chromium rotation THA, occasionally in combination with an acetabular roof augmentation, using two or three small, triangular shaped femoral head autologous grafts. In 2004, de Jong et al reported a long-term follow-up study of a single surgeon series of all primary THAs of all available stem sizes performed with this approach. Results at 15 years were good with a cumulative survival with aseptic loosening as an endpoint of 81.5% for the stem and 89.2% for the socket.

In THA for primary osteoarthritis (OA), standard-sized total hip components and a regular surgical technique are sufficient to obtain good long-term results with a low rate of complications. In OA secondary to preexistent anatomic deformities of the hip, e.g., developmental dysplasia of the hip (DDH), spondyloepiphyseal dysplasia, juvenile osteonecrosis (ON), and posttraumatic OA, surgery is more difficult. Clinical results are inferior compared with a patient group without these deformities. This may be the result of more frequent bone grafting, hypoplasia of the proximal femur with posterior migration of the greater trochanter requiring a smaller than usual femoral component, muscle contractures requiring muscular releases, or dislocation of the hip with difficulty in properly positioning components. The impact of inferior results in these patients is substantial because they typically are younger than the typical patient in whom THA is performed.

The numerous intermediate and long-term follow-up reports of THA in patients with DDH typically focus on the diminished acetabular coverage in relation to fixation of the cup, and survivorship analyses with aseptic loosening of the cup as an endpoint have been reported to range between 86% and 97.5% in intermediate-term studies and between 88% and 94% in long-term studies. However, the additional problems of the presence of a hypoplastic femur with a small intramedullary canal and the use of a smaller than usual femoral component seldom are discussed. There are even fewer reports of survivorship analysis of small-sized stems used in patients with DDH. In these reports survival at 15 years with aseptic loosening as an endpoint has ranged between 92.4% and 96%. The number of reports specifically addressing implantation of a stem component in a hypoplastic femur also is limited, and survival as reported in two studies only, was 100% at 9 years and 79% at 15 years. Several studies on small stems report relatively high rates of complications such as perioperative femoral fracture (10%), partial nerve paralysis (5%), recurrent dislocation (16%), and fracture of the component (5%). Clinical outcomes seem to deteriorate with decreasing patient height and diameter of the femur. Only five patients in the report by De Jong et al had a hypoplastic femur and subsequently received the smallest-sized Weber stem. We could not ascertain whether that subgroup had different results compared with patients with average-sized femora. Thus, there is still debate regarding the ideal choice of stem for femoral hypoplasia, whether cemented or uncemented, off-the-shelf, or customized, and some have the opinion that patients with femoral hypoplasia have less good results than patients without femoral hypoplasia.

We hypothesized long-term survival, revision rates, clinical scores, and complication rates of the small cemented stem we used in patients with femoral hypoplasia were similar to those with larger-sized stems used in patients with a normal-sized femur.
Materials and methods
Since 1978 we have been collecting data for all hip arthroplasties performed in our institution. From this database we identified two groups of patients: a study group of 77 selected patients (86 hips) with femoral hypoplasia who received the smallest available sized stem and a comparison group of 198 patients (231 hips) with normal femoral anatomy who received the identical curved type, but larger-sized stems. For both groups survivorship analyses, revision rates of the stems and cups, clinical scores, and incidence of surgical-related complications were assessed. We compared results between groups and also compared results of the small-stem study group with results of published reports of other small-stem hip systems. Preoperative diagnoses in the hypoplastic small-stem group included: (i) DDH in 71 hips (83%); classified according to Crowe et al.11 as Grade I in 52 hips, Grade II in 13 hips, Grade III in two hips (Fig.1) and Grade IV in four hips and with a mean CCD angle of 139°, (range 125°-170°); (ii) primary OA in five hips and posttraumatic OA in five hips (12% total); (iii) ON in four hips (5%), and (iv) rheumatoid arthritis in one hip (1%). Thirty-five hips (41%) had previous surgery, including 27 femoral osteotomies, three pelvic osteotomies, and five other hip-related procedures.

Fig. 1 This preoperative radiograph shows the left hip of a 49-year-old woman with bilateral femoral hypoplasia in the presence of developmental dysplasia of the hip and secondary OA.

In the normal anatomy group preoperative diagnoses included primary OA in 148 hips (25%), DDH in 58 hips (25%), posttraumatic OA in seven hips (3%), ON in two hips (1%) and rheumatoid arthritis in 58 hips (25%). Previous surgery was performed in 53 hips (23%) (Table 1).

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Hypoplastic group</th>
<th>Normal anatomy group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (hips)</td>
<td>77 (86)</td>
<td>198 (231)</td>
</tr>
<tr>
<td>Man : Woman</td>
<td>4 : 73</td>
<td>81 : 117</td>
</tr>
<tr>
<td>Median age, years (range)</td>
<td>65 (23-80)</td>
<td>69 (36-85)</td>
</tr>
<tr>
<td>Mean follow-up, years (range)</td>
<td>11.7 (4.2-20.3)</td>
<td>16.1 (4.7-23.1)</td>
</tr>
<tr>
<td>Median weight, kg (range)</td>
<td>64 (38-111)</td>
<td>68 (46-115)</td>
</tr>
<tr>
<td>Median height, cm (range)</td>
<td>160 (143-189)</td>
<td>168 (144-192)</td>
</tr>
<tr>
<td>Median body mass index, kg (range)</td>
<td>25.2 (16.9-41.1)</td>
<td>24.5 (18.4-37.2)</td>
</tr>
<tr>
<td>Preoperative diagnosis (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DDH</td>
<td>71/86 (83%)</td>
<td>58/231 (25%)</td>
</tr>
<tr>
<td>Primary OA</td>
<td>5/86 (6%)</td>
<td>148/231 (64%)</td>
</tr>
<tr>
<td>Posttraumatic OA</td>
<td>5/86 (6%)</td>
<td>7/231 (3%)</td>
</tr>
<tr>
<td>Osteonecrosis</td>
<td>4/86 (5%)</td>
<td>2/231 (1%)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>1/86 (1%)</td>
<td>58/231 (25%)</td>
</tr>
<tr>
<td>Other</td>
<td>0/86 (0%)</td>
<td>8/231 (3%)</td>
</tr>
<tr>
<td>Number of previous hip surgeries (%)</td>
<td>35/86 (41%)</td>
<td>53/231 (23%)</td>
</tr>
</tbody>
</table>

Table 1. Patient demographics. Statistical differences between the two groups:

1 Students t-test, p < 0.01
2 chi square, p < 0.01
3 Students t-test, p < 0.01
4 Students t-test, p < 0.01
5 Mann-Whitney U, p < 0.03
6 Students t-test, p < 0.01
7 chi square, p = 0.58
8 chi square, p < 0.01
9 chi square, p < 0.01
Twenty-one patients (21 hips) died after an average of 8.5 years postoperatively (range, 2.5-23.2 years), and one of these patients had a revision of both components after 7.8 years. Ten patients (12 hips or 14%) were lost by last follow-up in the hypoplastic group and 43 patients (52 hips or 22%) in the normal anatomy group; these patients were included in the survival analyses. Minimum follow-up in the hypoplastic group was 4.2 years (mean, 11.7 years; range, 4.2-20.3) and in the normal anatomy group 4.7 years (mean, 16.1 years; range, 4.7-23.7) (Table 1). Some demographic characteristics and surgical specifics were not equally divided between groups (Table 1,2). Three factors that were potentially confounding factors for outcome of aseptic component loosening were an increased (p < 0.01) percentage of women, a lower (p = 0.03) mean weight, and a lower (p < 0.01) mean height.

We used an anterolateral (Watson-Jones) approach in all patients. An osteotomy of the greater trochanter, in the oblique sagittal plane, was performed in 22 hips (26%) in the hypoplasia group and in 30 hips (13%) in the normal anatomy group (Table 2). Fixation was accomplished with two lag screws perpendicular to the osteotomy plane and/or cerclage wiring from around the trochanteric tip, in a figure-eight shape around the proximal femur. The psoas tendon was released in all patients. The stem of the off-the-shelf Weber Rotation Modular prosthesis (Allopro, Baar, Switzerland) we used is made of a wrought CoNiCrMo alloy (Protasul® 10; Sulzer AG, Winterthur, Switzerland) and has a cylindrical neck (the trunnion), which is made of a cast CoCrMo alloy (Protasul® 2) composite welded to the stem (Fig. 2). The cross section of the stem is trapezoidal with rounded corners. It is available in a curved shape in four different sizes and in a straight shape in one size.

<table>
<thead>
<tr>
<th>Data for surgery</th>
<th>Hypoplastic group</th>
<th>Normal anatomy group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of trochanter osteotomies</td>
<td>22/86 (26%)</td>
<td>30/231 (13%)</td>
</tr>
<tr>
<td>Number of acetabular roofplasties</td>
<td>22/86 (26%)</td>
<td>64/231 (28%)</td>
</tr>
<tr>
<td>Spherical cup : flat cup</td>
<td>69 : 15</td>
<td>NR</td>
</tr>
<tr>
<td>Ceramic : metal heads</td>
<td>42 : 42</td>
<td>143 : 83</td>
</tr>
<tr>
<td>Mean HHS (range)</td>
<td>88 (51-100)</td>
<td>89 (53-100)</td>
</tr>
<tr>
<td>Number of surgery-related complications (%)</td>
<td>4/86 (5%)</td>
<td>12/231 (5%)</td>
</tr>
<tr>
<td>Number of aseptic loosening stems (%)</td>
<td>6/86 (7%)</td>
<td>16/231 (7%)</td>
</tr>
<tr>
<td>Number of aseptic loosening cups (%)</td>
<td>4/86 (5%)</td>
<td>15/231 (6%)</td>
</tr>
</tbody>
</table>

Table 2. Specifics of surgery and results. NR = not reported; Statistical differences between groups:

1 chi square, p < 0.01  
2 chi square, p = 0.59  
3 chi square, p = 0.03  
4 Student’s t-test, p = 0.55
At surgery, all patients of the hypoplastic group had an intramedullary canal, which was either too small for the standard 103-sized rasp (length, 10.9 cm from medial collar to the tip; width at the middle level, 11 mm) to be used, or the shape of the proximal femur forced the 103 rasp into increased antetorsion and varus. We defined all such femurs as hypoplastic and used the smallest available 102 rasp (length, 9.6 cm from medial collar to the tip; width at the middle level, 9.5 mm) to prepare the canal for a 102 stem. Because of the typical narrow width of the femoral canal in these hypoplastic femurs, it was necessary to enlarge the canal with a special drill before rasping. This drill has sharp edges on the side that cut out the endosteal inner side of the shaft, and a blunt tip that prevents perforation of the cortex. Generally, the cortex was thickened proximally. In the normal anatomy group the larger-sized stems (length, 10.9 cm to 15.2 cm from medial collar to the tip; width at the middle level 11 to 16 mm) were used.

The all-polyethylene (RCH 1000; Chirulen®, Hoechst, Germany) sockets had either a hemispheric or a flat outer contour. The latter was designed for a shallow dysplastic acetabulum. In the hypoplastic group the spherical cups had a diameter of 44 mm in 14 cases, 47 mm in 42, 52 mm in 10, 54 mm in one, and 57 mm in two. The flat cups had a diameter of 47 mm in 12 cases and 52 mm in three. In two hips of patient lost to follow-up, the sizes and shapes of the cups could not be traced. Twenty-two hips (26%) in the hypoplastic group and 64 hips (13%) in the normal anatomy group had deficient support of the socket as suggested by templating on preoperative radiographs, a Sharp angle greater than 42°, and/or less than 90% coverage of the cup observed during surgery. We performed superolateral roofplasty in these 22 hips. We use three triflange corticocancellous bone grafts taken from the resected femoral head and fixed these to the roughened supraacetabular iliac bone with 4.5-cortical lag screws. The interfaces between the iliac bone and the grafts are impacted with cancellous bone.\textsuperscript{12, 43}

Thirty-two-millimeter metal (Protasul® 2) and ceramic (Biolox; Feldmühle, Plochingen, Germany) heads (Table 2) were used. The head was placed on a Protasul® 2 cylinder. The cylinder was placed on the trunnion of the stem, providing a secondary joint with the possibility for rotation and slight axial translation. Three different lengths of cylinders were available, ranging from 2.5 to 3.5 cm (Fig. 2). We used low-viscosity Sulfix® (Sulzer AG) cement with a second-generation cementing technique, ie, intramedullary restriction of cement and vacuum suction in all patients. The stem was aimed in slight valgus in all patients (Fig. 3).
Fig 3. The postoperative radiograph shows a 102-sized Weber stem on the left, and a larger 103 stem on the right after a trochanteric osteotomy with bilateral 52-mm cemented cups and roofplasties 17 and 18 years, respectively, after the index operation. No demarcation around the components is seen. The acetabular roofplasties are completely integrated and the trochanteric osteotomy is healed. Periacetabular ossifications (Grade II according to Brooker) were asymptomatic. The Harris hip score at the time of the last follow-up was 87 points for the left side and 100 points for the right side.

We (FHRdM, HMVdV, PPB, RKM) clinically examined patients at 6 weeks, 3 months, and 6 months postoperatively and annually thereafter. Patients completed a questionnaire to calculate the Harris hip score. In two patients (three hips), a reliable hip score could not be obtained as a result of severe dementia and recent brain infarction, respectively. Thus, clinical evaluation was possible in 37 patients (43 hips).

Standard anteroposterior and lateral radiographs of the pelvis of the surgically treated hip were obtained at each visit. We (FHRdM, HMVdV, PPB, RKM) analyzed radiographs for signs of osteolysis or loosening according to Harris et al. for the femoral component and Hodgkinson et al. and DeLee and Charnley for the acetabular implant.

Survivorship for the femoral and acetabular components was analyzed using the life-table method, with three endpoints: (i) revision for any reason, (ii) revision for aseptic loosening, and (iii) radiologic loosening (definite loosening of the stem and Grade III or IV loosening of the cup). We compared survivorship for all endpoints (log rank test) between the groups. We also compared the Harris hip scores (Student’s t-test) and surgery-related complication rates and rates of aseptic loosening of the cup and stem (chi square). Statistical differences in demographic and surgical characteristics between groups were detected (Student’s t-test and chi square for normal distribution and Mann-Whitney U test for nonuniform distribution). Characteristics that were different and potentially could lead to a confounding positive result of aseptic component loosening in the hypoplastic group were tested (Cox regression analysis).

Results
Survival rates for all endpoints were similar (0.26 < p < 0.81) in the two groups (Table 3). In the hypoplastic group 15-year survival of the small stem with aseptic loosening as an endpoint was 90% with a 95% confidence interval (CI) of 82% to 99%; with revision for any reason as an endpoint survival was 90% with a 95% CI of 82% to 99%; and with definitive radiographic loosening survival was 89% with a 95% CI of 79% to 99%. Survival of the cup in the hypoplastic group with revision for aseptic loosening or revision for any reason as an endpoint was 91% with a CI of 83% to 100%, and with Grade III or IV radiographic loosening as the endpoint, survival was 91% with a 95% CI of 82% to 100%. After correcting for differences
in percentage of women, lower mean weight, and lower mean height, we observed no difference in survival based on aseptic stem and cup loosening (p = 0.22 and p = 0.07, respectively).

<table>
<thead>
<tr>
<th>End point</th>
<th>Hypoplastic group (86 hips)</th>
<th>Normal anatomy group (231 hips)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Survival rate at 15-years (95% CI)</td>
<td>Survival rate at 15-years (95% CI)</td>
</tr>
<tr>
<td>Revision for any reason</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stem</td>
<td>90% (CI, 82-99)²</td>
<td>89% (CI, 84-94)</td>
</tr>
<tr>
<td>Cup</td>
<td>91% (CI, 83-100)</td>
<td>92% (CI, 87-96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Revision for aseptic loosening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stem</td>
<td>90% (CI, 82-99)</td>
<td>93% (CI, 89-97)</td>
</tr>
<tr>
<td>Cup</td>
<td>91% (CI, 83-100)</td>
<td>94% (CI, 90-98)</td>
</tr>
<tr>
<td>Radiologic loosening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stem</td>
<td>89% (CI, 79-99)</td>
<td>86% (CI, 80-92)</td>
</tr>
<tr>
<td>Cup</td>
<td>91% (CI, 82-100)</td>
<td>89% (CI, 83-95)</td>
</tr>
</tbody>
</table>

Table 3. Survival analysis according to the life-table method with different end points. CI = confidence interval; Hypoplastic vs. normal anatomy group (log rank test):

*p = 0.79  4 *p = 0.40
2 *p = 0.50  5 *p = 0.67
1 *p = 0.26  6 *p = 0.77

Cox regression analysis: outcome revision aseptic stem corrected for length and gender showed no significant difference, p = 0.22; outcome revision aseptic cup corrected for length and gender showed no significant difference, p = 0.07.

The revision rate for aseptic loosening of the stem was 7% in both groups. The revision rate for aseptic loosening of the cup was similar in the two groups (5% in the hypoplastic and 6% in the normal anatomy group) (Table 2). In the hypoplastic group two stems were revised for aseptic loosening. In two patients, both components were revised for aseptic loosening. One patient sustained a periprosthetic fracture and underwent revision of the stem and internal fixation. Three years later, the cup also was revised because of aseptic loosening. One hip had revision of the cup because of aseptic loosening and revision of the stem because of malrotation with subluxation of the joint. One 44-mm spherical cup was revised because of excessive wear (Table 4). At revision, all of the trunnions functioned well and no macroscopic damage to the rotating bearing was seen. There was no difference (p = 0.35) in incidence of aseptic loosening between the flat and the spherical cups.

<table>
<thead>
<tr>
<th>Acetabular component (years)</th>
<th>Femoral component (years)</th>
<th>Acetabular/Femoral</th>
</tr>
</thead>
<tbody>
<tr>
<td>—</td>
<td>6.2</td>
<td>Aseptic loosening</td>
</tr>
<tr>
<td>—</td>
<td>17</td>
<td>Aseptic loosening</td>
</tr>
<tr>
<td>5.7</td>
<td>5.7</td>
<td>Aseptic loosening</td>
</tr>
<tr>
<td>12.9</td>
<td>12.9</td>
<td>Aseptic loosening</td>
</tr>
<tr>
<td>10.5</td>
<td>7.5</td>
<td>Aseptic loosening/</td>
</tr>
<tr>
<td>7.8</td>
<td>7.8</td>
<td>shaft fracture</td>
</tr>
<tr>
<td>15.3</td>
<td>—</td>
<td>Wear</td>
</tr>
</tbody>
</table>

Table 4. Time between index operation and revision of components and reason for revision

The mean Harris hip score was similar (p = 0.55) in the two groups (mean, 88 and range, 51 to 100 in the hypoplastic group versus mean, 89 and range, 53 to 100 in the normal group). Average hip flexion was 104° (range, 70°-130°). A 1-cm leg-length discrepancy was present in five patients and a 4-cm discrepancy was present in one patient.
Surgery-related complications occurred in 5% of patients in both patient groups (Table 2). In the hypoplastic group one patient had a perforation of the femur treated by observation, one had a femoral fracture treated by cerclage wiring, one had a fracture of the greater trochanter after a previous intertrochanteric osteotomy treated with screw fixation, and one had surgical drainage of a hematoma. One patient had a deep calf venous thrombosis. All complications resolved completely after treatment. Late complications included a chronic infection in one patient who had few complaints and a hip score of 88. Therefore, the prosthesis was not revised. After an osteotomy of the greater trochanter, one patient had a nonunion that healed after screw fixation, tension band wiring, and cancellous autologous bone grafting. This patient had a hip score of 87, no Trendelenburg sign, and some residual pain not necessitating revision surgery.

Radiographic analysis revealed one stem was definitively loose and one stem probably was loose, but because both patients had few complaints and with hip scores of 88 and 84, respectively, the stems were not revised. Eight cups had Grade I loosening, but hip scores ranged from 89 to 100 and none was revised. All acetabular roofplasties showed remodeling and incorporation into pelvic bone with reformation of trabeculae.

Discussion

Total hip arthroplasty in patients with hypoplasia of the femur is technically difficult because of the associated anatomic abnormalities. Several studies report a higher incidence of complications11, 22, 40, 58 and less successful long-term results24, 58 regarding stem fixation in comparison to primary THA in osteoarthritic hips of patients without hypoplasia. We asked whether the results in patients with OA treated with the smallest-sized cemented stem because of femoral hypoplasia were different from results in patients treated with a larger-sized stem from our cohort. These results seem valid as the possible confounding factors of an increased percentage of woman who have a lower risk of needing revision than men19, and a lower height and weight in the study group were corrected for. Also, several unfavourable demographic and surgical factors were present in the study group: femoral anatomy was altered, median age was younger and subsequent activity level presumably higher, 38; 51 preoperative diagnosis of DDH, incidence of previous surgery, and use of trochanteric osteotomy and metal heads all were increased in comparison to the normal anatomy group. An explanation could be that an optimal cementing technique could be even more beneficial in the case of a small femur: the volume of cement is smaller and therefore the increase of cement pressure is greater leading to better results32, 37. Large series with long follow-ups of the cemented off-the-shelf Charnley stem (Thackray, Leeds, England) used in patients with femoral hypoplasia associated with DDH also show high survival rates (Table 5)35, 39, 41. Although in finite element53 and clinical studies30, 42 cemented curved designs have inferior results compared with cemented straight stems, the curved Weber stem seems to perform equally well. The explanation could be that not only the frontal, but also the cross-sectional shape matters in stem fixation; the oval-shaped cross section of the Weber stem leaves a thicker cement mantle, especially at the proximomedial femur, as compared with stems with a box-shaped cross-section,50 which is beneficial in long-term fixation2, 6, 19. Oh et al.17 reported an increased incidence of loosening when they used cement for the off-the-shelf anatomic medullary locking stem. This might be because stem stiffness does not match the stiffness of cement, which is illustrated in the fact that stem loosening was dramatically lower when this porous-coated stem was used without cement.

Reports specifically addressing patients with hypoplastic femurs16, 34, 47, 58 have advocated off-the-shelf 47, 58 and custom-made stems16, 34 (Table 5). Huo et al.34, and Di Fazio et al.19, used a custom-made varus-offset cemented straight femoral component in 19 small femora. The clinical score (Hospital for Special Surgery) was 35 of 40, no complications were recorded, and the revision rate after a mean
<table>
<thead>
<tr>
<th>Type of prosthesis/stem design</th>
<th>Authors</th>
<th>Percent survivorship analysis with an endpoint of aseptic stem loosening (95% CI)</th>
<th>Revision rate of aseptic or stem fracture (%)</th>
<th>Complication rate (%)</th>
<th>Number of hips</th>
<th>Median height (cm)</th>
<th>Mean follow-up (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identical stem design</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Off-the-shelf Weber, curved cemented all sizes</td>
<td>De Jong et al.¹³</td>
<td>82% (CI, NR) at 15 years</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Femoral hypoplasia with or without DDH |         |                                                                                 |                                             |                      |                |                 |                     |
| Off-the-shelf Charnley, cemented | Iida et al.³⁵ | 94% (88-100) at 15 years | 4 |                      |                |                 |                     |
| Off-the-shelf Charnley, cemented | MacKenzie et al.⁴¹, Klapach et al.³⁹ | 97% (CI, NR) at 15 years | 5 |                      |                |                 |                     |
| Off-the-shelf, AML, uncemented | Oh et al.⁴⁷ | 97% (CI, NR) at 12 years | 5 |                      |                |                 |                     |
| Off-the-shelf, AML, cemented |                | 77% (CI, NR) at 12 years | 25 |                      |                |                 |                     |
| Custom-made straight/offset cemented | Huo et al.³⁴, Di Fazio et al.¹⁶ | NR | 6 |                      |                |                 |                     |
| Customized CDH, straight cemented | Woolson and Harris⁵⁸ | NR | 5,5 |                      |                |                 |                     |

<table>
<thead>
<tr>
<th>Complication rate (%)</th>
<th>Number of hips</th>
<th>Median height (cm)</th>
<th>Mean follow-up (years)</th>
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</thead>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NR</td>
<td>315</td>
<td>NR</td>
<td>10,5</td>
</tr>
</tbody>
</table>

| Femoral hypoplasia with or without DDH |                |                   |                       |
| 20                                   | 133            | 150               | 12                    |
| NR                                   | 66             | NR                | 25                    |
| 0                                   | 40             | 157               | 7                     |
| 0                                   | 12             |                   |                       |
| 0                                   | 19             | 152               | 13                    |
| 19                                   | 69             | 156               | 5                     |

CI = confidence interval; DDH, developmental dysplasia of the hip; NR = not reported in the study.

Table 5. Results of studies with identical stem design or with diagnosis or femoral hypoplasia with or without dysplasia.
follow-up of 13 years was 6%. Woolson and Harris used a miniature cemented off-the-shelf straight femoral component. The revision rate for aseptic stem loosening after a mean follow-up of 5 years was 5.5%, the mean Harris hip score was 80, and surgery-related complications were relatively high at 19%. In both studies, the exact stem size was not stated. In a recent meta-analysis of studies comparing off-the-shelf cemented with uncemented THAs, cemented fixation had superior survival. However, when femoral anatomy is different, some advocate an uncemented custom-made stem. The concept is to completely fill the femur with a component, which would lead to less stress shielding of the proximomedial femur compared with a cemented implant. However, this is difficult to achieve because stress shielding will only decrease when stem fit is precise for the entire proximal femur and the necessary determination of femoral internal geometry is still inaccurate. Moreover, as a result of the smaller diameter at the femoral neck compared with the intertrochanteric area, it theoretically is impossible to insert a component from one side only and have a perfect anatomic fit. Furthermore, fabrication of a custom-made prosthesis is time-consuming and costly, regardless of cement use.

Surgery related complications were limited to 5%, which equaled the complication rate in the normal anatomy group, whereas these rates in patients with femoral hypoplasia have been reported to be as high as 19% and even 30% in extremely small femurs like in achondroplasia. We emphasize the need for a trochanteric osteotomy to obtain clear surgical exposure in these difficult cases. The incidence of nonunion after trochanteric osteotomy has been reported as high as 15%, but only 1% in our series. There were no dislocations, which might be explained by the use of 32-mm heads and the telescopic capacity of the rotating trunnion bearing, experience of the surgeon, and the use of an anterolateral approach.

In this series of relatively young patients after complex hip reconstructions resulting from a hypoplastic femur and OA, our data suggest the small cemented off-the-shelf Weber curved stem has high survival rates, is easy to use, is associated with few complications, and has outstanding long-term follow-up. Our results are in concordance with those of others for femoral hypoplasia and cemented off-the-shelf stems. We agree with Capello that if a cemented stem is used in small femora, the cured polymethylmethacrylate becomes part of the construct, which as a whole can be considered a customized implant. We believe that there is no need for costly custom-made implants with femoral hypoplasia.
References


Chapter 5

The long-term outcome of the cemented Weber acetabular component in total hip replacement using a second-generation cementing technique.

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Abstract
We report the long-term outcome of a modified second generation cementing technique for fixation of the acetabular component of total hip replacement. An earlier study has shown the superiority of this technique assessed by improved survival compared with first generation cementing.

The acetabular preparation involved reaming only to the subchondral plate, followed by impaction of bone into the anchorage holes.

Between 1978 and 1993, 287 total hip replacements were undertaken in 244 patients, with a mean age of 65.3 years (21-90) using a hemispheric Weber acetabular component with this modified technique for cementing and a cemented femoral component.

The survival with acetabular revision for septic loosening as the endpoint was 99.1% (95% confidence interval (CI) 97.9 to 100) after ten years, and 85.5% (95% CI 74.7 to 96.2) at twenty years.

Apart from contributing to a long lasting fixation of the component, this technique also preserved bone, facilitating revision surgery when necessary.

Introduction
The debate on cemented versus uncemented acetabular components in total hip replacement (THR) continues. Although some authors suggest abandoning the use of cemented implants, others show good survival rates of 90% after 25 years. Survival rates in these studies vary, but the common conclusion is that aseptic loosening is the main cause for revision in cemented acetabular components.

The Scandinavian arthroplasty registers show that in young patients, there is no significant difference in the overall survival rate with revision as endpoint, between uncemented and cemented cups. For all-polyethylene cups the 10-year survival was 87% (95%CI: 85%-90%) and for porous-coated uncemented cups 88% (95%CI: 85%-90%). Aseptic loosening was the main reason for revision when cemented cups were used. Uncemented components were also exchanged for other reasons, such as polyethylene wear and osteolysis.

Aseptic loosening is influenced by the cementing technique used, and it seems clear that this needs to be optimized. Several reports have been published on improvements in the technique of cementing the femoral component, but only a few papers have addressed the acetabular side.

Materials and Methods
Patients
Between 1978 and 1993, the senior author performed 287 total hip replacements (THR) in 244 patients, 65 of whom were men, using a hemispherical Weber socket (Allopro®, Baar Switzerland) implanted with a technique developed by him. In order to obtain a clear view of the outcome using this technique the number of variables were reduced by excluding operations performed by orthopaedic trainees and those where any other acetabular component was used. The mean age at the time of surgery was 65.3 years (21-90). The reason for the THR was idiopathic osteoarthritis in 140 hips, osteoarthritis secondary to dysplasia in 96, rheumatoid arthritis in eight, avascular necrosis of the femoral head in 23, posttraumatic osteoarthritis in 13, and other secondary osteoarthritis in seven. Previous surgery had been performed in 73 hips and included an intertrochanteric osteotomy in 56 patients, a pelvic osteotomy in two, a shelf plasty in two, and an internal fixation because of a proximal femoral or acetabular fracture in 13.

Operative technique and implants
All procedures were done with antibiotic prophylaxis, using an anterolateral approach with the patient in the supine position. The Weber Rotation (Allopro®, Baar, Switzerland) THR was used as a standard implant in all primary cases. The stem was manufactured from Protasul® alloy (Sulzer AG, Winterthur, Switzerland) with a cylindrical trunnion made of Protasul® (Sulzer AG) which permits rotation. To this trunnion 32 mm heads were attached, of which 100 were made of Protasul® and 187 of ceramic (Biolox®, Feldmühle, Plochingen, Germany). The head was placed on the rotating Protasul® cylinder, which was available in three lengths (42 mm, 47 mm and 52 mm). The Weber hemispherical acetabular component was used in every patient. This all-polyethylene component
(RCH-1000 Chirulen®, Hoechst, Germany) was available with an external diameter ranging between 40 to 64 mm, of which the depth varied between 24 to 37 mm. The rim of the acetabular component had a scalloped profile. The advantage of this profile was to allow partial or complete removal of the prominences giving a perfect fit of the component in the reamed acetabulum, creating intrinsic stability before cementing (Fig 1).

The interrupted shape also allowed compression of the cement between the prominences using a special impaction device during polymerisation of the cement. A 47 mm diameter component was used in 62 hips (21.6 %), the 52 mm in 179 hips (62.4 %), the 57 mm in 44 hips (15.3 %) and the 64 mm in two (0.7 %).

Cementing technique

Our technique for cementing the acetabular component involves reaming the acetabulum to the depth of the subchondral layer, making multiple (6-8) anchorage holes, which are conical in shape and have a diameter of 8 mm. Only the hard superficial bone of the subchondral plate is drilled. The cancellous bone beneath the anchorage holes is impacted instead of being removed, using a specially designed round-ended impactor with a diameter of 8 mm. Anchorage holes are produced to a depth of 0.5 cm to 1.5 cm, depending on the softness of the bone (Fig 2). This method lines the holes with a homogeneous layer of cancellous bone.

When the quality of the cancellous bone is poor and subchondral cysts are present, cancellous bone from the femoral head is impacted into the anchorage holes. In the presence of a very sclerotic acetabulum, a 6 mm drill is used to roughen the bony surface in between the holes.
For implantation of the acetabular component the anchorage holes are dried and filled with multiple gauze swabs. The swabs are removed, quickly followed by digital introduction of low viscosity Sulfix® cement (Sulzer AG, Wintherthur, Switzerland) into the holes, to avoid any bleeding between the cancellous bone and the cement, creating optimal compression of the cement-bone interface. The cement is not handled until initial polymerisation has commenced and it is losing its stickiness. This can be determined by the cement losing its shiny surface, which generally occurs after six to eight minutes. The cement must reach this phase to permit proper compression. The polyethylene acetabular component is then introduced and the cement is primarily compressed in the direction of the cranio-lateral anchorage holes. Shortly afterwards, anteversion and inclination are corrected, still under compression. By pressing the component in the cranio-lateral direction first, extrusion of cement on the medial side can usually be avoided and a high pressurization of the cement into the important anchorage holes is achieved. Approximately 40% of the full 40 g mix of cement is usually required to achieve good fixation.

A trochanteric osteotomy was performed in 48 hips. In 91 hips, bony coverage of the acetabular component was insufficient, which required the addition of an acetabular shelf plasty.19

Follow-up

The patients were seen at regular intervals, with an initial post-operative visit after six weeks, and then at three, six, and 12 months, two years and then biennially thereafter. The follow-up consisted of radiological and clinical evaluation. The Harris Hip Score20 was used to assess the clinical outcome. For the radiological analysis, weight-bearing anteroposterior (AP) pelvic and lateral X-rays were obtained and were scrutinized for radiological signs of loosening using the criteria described by Harris11 for the stem and the criteria described by Hodgkinson21 for the acetabular component.

A descriptive analysis was performed for the complications, clinical and radiological follow-ups. Survival analysis was calculated using the life-table method. The primary endpoints were revision for radiologically-proven aseptic loosening of the acetabular component and radiological evidence of loosening. Secondary endpoints included revision for any reason, revision for aseptic loosening of the femoral component, revision for loosening of either one of the components and definitive signs of radiological loosening of the femoral component. To evaluate the success of this technique in the younger and more active patient, we divided the group of 278 hips into patients under 55 years of age (n=39 hips) and those above that age (n=239 hips) and analysed them separately.

Results

Aseptic loosening necessitated isolated revision of the acetabular component in four patients. Eight patients had revision surgery for aseptic loosening, during which both components were exchanged. Two patients had septic loosening of their components, resulting in the removal of both components. At the latest follow-up, 107 patients (117 hips) of the 224 unrevised patients had died at an average of 9.6 years after surgery (range 0.01 to 25). Two patients died shortly after surgery as result of a myocardial infarction. In total 35 patients (44 hips) were considered lost to follow up, but were included in the survival analysis and radiological analysis until their last regular check at an average of 7.9 years (range 0.1 to 18.6) after surgery. A total of 21 hips in 20 patients were revised.
Apart from the cup revisions, five patients needed a revision of the stem. In these cases, the acetabular component was left in place. One patient had a revision of the stem after 9.1 years without revision of the acetabular component, which was revised 10 years later (19.1 years after the primary procedure). One stem was revised because of a peri-prosthetic femoral fracture (14.1 years after implantation). In two patients, septic loosening was the cause for revision of both components.

With revision for aseptic loosening of the acetabular component as endpoint, we found a 10-year survival rate of 99.1% (95% CI: 97.9-100), a 15-year survival rate of 95.7% (95% CI: 92.2-99.3) and a 20-year survival rate of 85.5% (95% CI: 74.7-96.2) (Table 1, Fig. 3).

The survival of the acetabular component in the patients less than 55 years of age with revision for aseptic loosening as the endpoint was 97.1% (91.4-100) at 10 years, dropping to 81.7% (64.6-98.7) at 16 years, when 14 hips were at risk. (Table 2)

### Table I. Life table analysing the survival data of the 287 hips, with revision for aseptic loosening of the acetabular component as endpoint.

<table>
<thead>
<tr>
<th>Interval (years)</th>
<th>Number entering interval</th>
<th>Number withdrawn</th>
<th>Deaths</th>
<th>Number at risk</th>
<th>Number with aseptic loosening</th>
<th>survival</th>
<th>SE</th>
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<td>255</td>
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<td>0</td>
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<td>2</td>
<td>244</td>
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<tr>
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<td>7</td>
<td>201</td>
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<td>9-10</td>
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<td>10</td>
<td>185</td>
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<td>5</td>
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Table I. Life table analysing the survival data of the 287 hips, with revision for aseptic loosening of the acetabular component as endpoint.
Table 2. Life table analyzing the survival data of 39 hips in patients under the age of 55, with revision for aseptic loosening of the cup as endpoint.

<table>
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<th>Interval (years)</th>
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<th>Deaths</th>
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<th>Number with aseptic loosening</th>
<th>survival</th>
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</tbody>
</table>

Figure 3a. Graphic presentation of survival.
Revision for aseptic loosening of the acetabular component.

Figure 3b. Graphic presentation of survival.
Revision for aseptic loosening or radiological signs of probable/definitive loosening of the acetabular component.
Radiological survival analysis revealed twelve acetabular components showing signs of possible loosening after an average of 15.4 years (range 8.4-22.9). No cups showed signs of definitive loosening (Fig 3).

Radiographs of the femoral components showed six cases with possible signs of loosening after a mean of 16 years (13.2 to 19.3), one with probable signs of loosening after 22.9 years, and five with definitive signs of loosening after a mean of 16.5 years (9.2 to 20.4). This survival for all the hips at various endpoints is presented in Table 3. In all, four patients needed a second operation without exchange of either prosthesis, one because of severe heterotopic ossification causing ankylosis and three because of non-union after osteotomy of the greater trochanter.

The Harris hip score (HHS) was obtained from 93 patients (112 hips) after an average of 14.9 years (range 10.0 to 23.7). The average score was 91.5 (range 24 to 100). HHS was under 70 in 4 hips, 71 to 80 in 10 hips, 81 to 90 in 27 hips, and 90 to 100 in 71 hips.

The total number of per- or peri-operative complications, was 22. Two femoral shafts were perforated during surgery. This was recognised but needed no additional action because the damage was only minor. In six THRs a crack occurred at the greater trochanter, in five of which there had been a previous intertrochanteric osteotomy. The problem was resolved by reattaching the greater trochanter with screws and cerclage wiring.

There were two sciatic nerve palsies, which both made a full recovery.

A haematoma developed in nine hips, five of which were treated with surgical debridement. Two wound infections healed with antibiotics and surgical debridement. One hip dislocated 14 year post-operatively, and remained stable after closed reduction.

### Table 3. Survival rates with different endpoints.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>10 year</th>
<th>15 year</th>
<th>20 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revision of either component for any reason</td>
<td>95.1% (92.3-98.0%)</td>
<td>89.2% (84.1-94.3%)</td>
<td>80.5% (70.5-90.5%)</td>
</tr>
<tr>
<td>Revision for aseptic loosening of the cup</td>
<td>99.1% (97.9-100%)</td>
<td>95.7% (92.2-99.3%)</td>
<td>85.5% (74.7-96.2%)</td>
</tr>
<tr>
<td>Revision for aseptic loosening of either component</td>
<td>97.2% (94.9-99.4%)</td>
<td>93.1% (88.8-97.3%)</td>
<td>83.8% (73.5-94.0%)</td>
</tr>
<tr>
<td>Cup revision for any reason</td>
<td>98.7% (97.3-100%)</td>
<td>94.6% (90.7-98.5%)</td>
<td>84.4% (73.7-95.2%)</td>
</tr>
<tr>
<td>Revision of the cup or radiological possible/definitive loosening</td>
<td>98.1% (96.3-99.9%)</td>
<td>91.8% (87.1-96.5%)</td>
<td>71.0% (58.4-83.6%)</td>
</tr>
</tbody>
</table>

### Discussion

Our study shows that excellent long-term results can be obtained with cemented acetabular components when using our cementing technique.

A recent meta-analysis of studies comparing cemented and uncemented fixation in THR has shown that cemented fixation still outperforms uncemented fixation in large subsets of the study populations. Although cementless fixation of acetabular components seems to reduce the rate of aseptic loosening, it has been reported that loosening of these devices frequently coincides with more extensive loss of acetabular bone. Polyethylene wear and osteolysis have caused concern in uncemented acetabular components.

Apart from wear debris as a causative factor in peri-acetabular osteolysis, it is proposed that stress shielding from a metal backed device may contribute to bone resorption around the acetabular implant. Earlier studies showed a more uniform distribution of stresses to the periprosthetic bone with metal-backed compo-
ments, but more recent work describes an apparent mismatch between the elastic modulus of the metal backing and the peri-prosthetic bone, as well as a difference in structural stiffness of the implant.

A 3-D finite element study by Manley, Ong and Kurz showed a more even distribution of stresses in the model using polyethylene rather than chrome-cobalt metal-backed implants. The model suggested that with the use of polyethylene as an implant, peripheral bone resorption would occur, but with the potential for bone formation at the dome.

Our reported survival rate for the cemented Weber cup using our cementing technique and the latest results of the Charnley acetabular component, indicate that there is still room for the use of a cemented acetabular component.

An important step in our cementing technique is the impaction of cancellous bone into the anchorage holes. This reduces bleeding from the bone and assists in the production of a dependable cement mantle.

We used finger-packing to insert the cement into the anchorage holes of the reamed acetabulum. Only one randomised prospective study using radiostereophotogrammetric analysis (RSA) compares finger-packing with a pressurisation technique. It showed that the pressurisation method was superior to finger-packing. However, the method of finger-packing analysed is not completely comparable to our method, in which low-viscosity cement is used at a relatively late stage, so that it performs like a high viscosity cement, allowing digital pressurisation into each keying hole. Flivik et al. pressurized each individual anchorage hole with a special device before pressurising the cement in the reamed acetabulum. In their finger-packing group, the anchorage holes were not separately filled with cement, but the whole acetabulum filled with a cement gun and then digitally compressed. The impacted bone in the anchorage holes and the preservation of the subchondral layer prevents cement from leaking into the peri-acetabular cancellous bone. We believe this preserves the elasticity modulus of the bone around the implant, and when acetabular component loosening prevails, limited destruction of bone stock occurs.

The role of the anchorage holes was investigated by Mootanah et al. using a finite element analysis. They showed that depth and size of the anchorage holes were of less importance than their inclination, and showed the optimal anchorage hole to be perpendicular to the acetabulum. This is the technique we employ.

We used both ceramic and metal heads, but have not analysed these separately. However, we do not believe this to have resulted in any difference in outcome. Although Schuller and Marti showed a difference in the amount of wear between these two heads, it was established in an earlier study that this did not lead to a significant difference in the rate of loosening.

Our study shows that excellent results can be obtained with hemispheric all-polyethylene cemented cups. Unfortunately, the described Weber component with an interrupted rim and the Weber Rotation stem are no longer available. We anticipate similar results from the Weber fix system, although it has been proved to produce more wear in comparison to the Rotation system. We believe that our cementing technique offers dependable acetabular fixation in cemented THR, with preservation of bone stock.

Fig. 5 a and b Radiographs of a 68-year old female patient.
Postoperative LAT radiograph (a) and LAT radiograph at 23-year follow-up (b). Note the apposition of bone in b.
References


Chapter 6

Effects of mechanical compression of a fibrous tissue interface on bone with or without high-density polyethylene particles in a rabbit model of prosthetic loosening

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Abstract
The mechanisms leading to aseptic loosening of a total hip replacement are not fully understood. A fibrous tissue interface can be present around the implant. Hypothetically, component micromovements can compress this interface and cause increased fluid pressure according to biphasic models. We tested the hypothesis that compression of a fibrous membrane with or without the presence of high-density polyethylene particles leads to bone degradation. A titanium implant was inserted in forty-five rabbit tibiae, and, after osseointegration was achieved, a fibrous tissue interface was generated. The animals were randomized to undergo a sham operation, treatment with compression of the fibrous membrane, treatment with high-density polyethylene particles, or treatment with both compression and particles. Morphometric analysis of the surrounding bone was performed on cryostat sections after Giemsa staining and staining of tartrate-resistant acid phosphatase activity. Forty specimens were available for analysis; five tibiae with an infection were excluded. After nine weeks, the controls showed vital bone, whereas the specimens treated with compression showed necrosis of bone and replacement of bone by cartilage in a discontinuous layer (p < 0.05 for both) but not fibrous tissue. Treatment with high-density polyethylene particles caused replacement of bone by fibrous tissue (p < 0.05) but not necrosis or cartilage formation. Compression combined with the presence of high-density polyethylene particles caused bone necrosis and loss of bone with replacement by cartilage and fibrous tissue (p < 0.05). In this in vivo study in rabbits, fibrous membrane compression led to bone necrosis and cartilage formation, possibly because of fluid pressure or fluid flow, whereas the presence of high-density polyethylene particles led to the loss of bone with replacement of bone by fibrous tissue. Cartilage formation may be a protective response to fluid pressure and/or fluid flow. Fibrous membrane compression may play an important role in the early stages of loosening of a total hip replacement. The findings of this study suggest that implantation techniques that prevent the formation of a fibrous tissue interface (which may act as source of fluid pressure and/or fluid flow) may be beneficial in reducing implant loosening.

Introduction
The most frequent, and often devastating, long-term complication after total hip replacement is aseptic loosening. Despite vigorous research, the precise mechanisms leading to aseptic loosening are not fully understood.

First, insufficient initial fixation or early loss of fixation have been suggested to lead to early loosening1. This may be caused by an implant of improper size or design, an improper cementing technique, or inferior bone quality2,3 inducing micromovements and subsequent detachment of the component at the interface.

Second, wear particles (in particular polyethylene) originating from components4 and/or cement have been considered to cause bone resorption1. This particle-induced bone resorption has been reproduced in in vitro studies5-7 but the results of in vivo studies have not been consistent. In some in vivo studies, particle-induced osteoclastic bone resorption has been observed8,9, whereas in other studies only a decrease in bone formation was seen10,11.

Third, high fluid pressure has been proposed to be, at least in part, responsible for the process of loosening12. Pressures as high as 0.1 MPa (780 mm Hg) have been measured in the pseudojoint cavity of total hip replacements during physiological activities13. High intracapsular pressures are often found in loose total hip replacements13,14, causing capsular distension as identified by ultrasound14. Capsular distension was less in hips that did not show clinical loosening, indicating that pressure was lower in those cases14. Peak pressures of 0.07 MPa (500 mm Hg) have been measured in the presence of pelvic osteolysis at revision surgery15. Pressure differences may induce a flow of joint fluid in the effective joint space, affecting periprosthetic bone3,16.

In experiments on rabbits, an exogenously derived (oscillating) fluid pressure was shown to cause bone resorption17,18. Furthermore, Van der Vis et al.19 were the first, as far as we know, to apply endogenous fluid pressure to a fibrous membrane in rabbits and they found bone resorption. Similar results have been obtained in rats20. In a study in which polymethylmethacrylate particles and endogenously derived fluid pressure were administered to rats, the fluid pressure appeared to cause distinct bone resorption, whereas polymethylmethacrylate led to minimal resorption only21.
Radiostereometric analysis showed that the probability of late clinical loosening is increased when prosthetic components migrate soon (within two years) after implantation. Migration of a prosthetic component should be possible only when the component is surrounded by a membrane of fibrous tissue. Consequently, there are correlations between the presence of a fibrous membrane, migration of a prosthetic component, and late clinical loosening. It has been speculated that the aforementioned fibrous membrane acts as an interstitial fluid compartment. It has been postulated that micromovements of the prosthesis cause repetitive compression of this membrane and thereby increase local fluid pressure that may affect the integrity of the surrounding bone. Resorption and subsequent loosening may be the result. Indeed, compression of a fibrous tissue membrane induced osteoclastic bone resorption in recent experiments on rabbits and rats.

In the present experimental study with rabbits, an endogenously derived fibrous tissue membrane interposed between the vital tibia and a titanium surface was compressed. Such a membrane can be thought of as a biphasic model consisting of a solid matrix and an interstitial fluid compartment with physiologic properties. In this study, it was hypothesized that compression would lead to a combination of stress in the solid matrix and elevation of fluid pressure in the fluid compartment. Furthermore, the effect of the presence of high-density polyethylene particles was also studied, especially as to whether their presence might lead to modulation of the response to interface compression.

Materials and Methods

Animals
Forty-five skeletally mature New Zealand White Rabbits (BMI, Helmond, The Netherlands) with a mean weight (and standard deviation) of 38.20 +/- 0.19 N, were used. The protocol for the animal experiments was approved by the animal ethical committee of the Faculty of Medicine, University of Amsterdam and all animal handling was performed according to Dutch laws for treatment of research animals.

The implant
The model used in this study is a modification of the model introduced by Van der Vis et al. (19). It consists of a cubical titanium implant that is inserted into the rabbit tibia. A fibrous tissue interface between the implant and vital bone is created, and the effect of compression of this fibrous membrane on bone is evaluated. Our modification allows the possibility of administering particles at the interface. The implant is a cube (7.2 mm³) with a cylindrical canal (diameter, 4.50 mm) and a groove (7.2 x 2 x 2 mm) on one end. It is made of commercially pure titanium with a surface roughness of 1.8 μm. A nonmoveable “static” cylinder with a diameter of 4.50 mm and a groove of 4.45 mm x 2 mm x 2 mm fits in the canal of the implant (Fig. 1, A).

When the device is implanted in bone (see section entitled Surgical Procedures), the roof of the groove faces the cortical bone surface and both sides of the groove are embedded into the bone. In this way, a bone bridge that is 7.2 mm long, 2 mm wide and 2 mm high is created, and it is surrounded by the titanium implant on all sides except for the endosteal surface toward the bone marrow cavity. In this study, the construct was allowed to integrate into bone for five weeks. Then, the “static” cylinder was exchanged for a “dynamic” cylinder (Fig. 1, B) which had a groove on one end of 4.45 x 2 x 2.2 mm; thus, its width was 200 μm in excess of the width of the groove of the “static” cylinder. The “dynamic” cylinder also had a biconcave handle on top that could be rotated to each side with a maximum amplitude of 100 μm. A stop screw prevented further rotation. Thus, a space of 100 μm, in which particles could be administered, was created between vital bone and the titanium surface at either side of the bone bridge (see section entitled Surgical Procedures).

During the following two weeks, a 100-μm-thick fibrous layer was allowed to form in this space at either side of the standardized bone bridge in the presence or absence of particles. After the two weeks of fibrous tissue growth, the biconcave handle of the “dynamic” cylinder was grasped through the intact skin and manually rotated alternately clockwise and counterclockwise, thus rotating the cylinder inside the implant, intermittently compressing the fibrous membrane on both sides of the bone bridge (see section entitled Test Phase). By means of this movement with controlled amplitude, only the fibrous membrane was compressed without direct mechanical contact with the underlying bone.
Fig. 1. Schematic drawings of a bone bridge and the implant with the “static” cylinder (A) and the “dynamic” cylinder (B). Implant dimensions are 7.2 mm³ with a cylindrical canal with a diameter of 4.50 mm. The groove on one end of the implant is 7.2 mm x 2 mm x 2 mm. The groove on one end of the static cylinder is 4.45 mm x 2 mm x 2 mm, and the groove of the dynamic cylinder 4.45 mm x 2 mm x 2.2 mm. Cross sections (inset) show the implant straddling the bone bridge in A, and with interposed fibrous tissue on both sides of the bone bridge (arrows) and bone formation towards the medullary cavity in B.
Particulate materials

The high-density polyethylene particles that we used were donated by Smith and Nephew Richards (Memphis, Tennessee, USA) and were produced by Shamrock Technologies (Newark, New Jersey, USA). They were small enough (mean diameter, 4.6 μm; range 0.4–8.0 μm) to be phagocytosed by macrophages. The particles were polymerized as high-density polyethylene and then were ground with a proprietary milling process into a smaller particle size. They were reported to be 100% high-density polyethylene particles and highly crystalline with a specific gravity of 0.95. The size of the particles was measured with use of a scanning electron microscope interfaced with a morphometric image analysis system (Beckham Coulter, Fullerton, California, USA). The particles were washed two times in alcohol followed by two additional washes in sterile water, and, after centrifugation, the supernatant was removed and the particles were air-dried in a sterile environment. The sterility of the particles was verified in anaerobic and aerobic cultures.

Surgical procedures

All animals had two operations under aseptic conditions. Anaesthesia was induced with 10 mg/kg xylazine (Bayer, Leverkusen, Germany) and 50 mg/kg ketamine (Aesculaap, Boxtel, The Netherlands) intramuscularly and was maintained with inhalation anaesthesia with a mixture of isoflurane, nitrous oxide, and oxygen. Antibiotic prophylaxis with use of 10 mg/kg of enrofloxacin (Bayer) administered subcutaneously was started one day before the operation and was continued until one day after the operation.

In each animal, the operations were performed on the right tibia. In the first operation, a medial parapatellar approach was used to expose the metaphyseal bone surface of the tibia. Onto this relatively flat area, a metal template with two longitudinal slots was fixed with two cortical screws (diameter, 1.45 mm; Mathys, Bettlach, Switzerland). The dimensions of the slots corresponded with the bars next to the groove of the implant. Cortical bone was removed with a water-cooled burr through the open slots. In that way, a bone bridge was created with the dimensions of the groove of the implant. Next, the template was removed and the implant was inserted over the bone bridge and was fixed with two reinserted cortical screws with use of the same holes as the ones used for the template. Then the “static” cylinder was inserted through the cylindrical canal and fixed to the implant with a screw. Finally, the skin was closed over the entire device with interrupted mattress sutures (Vicryl 3-0; Ethicon, Norderstedt, Germany). The animals received 0.05 mg/kg buprenorphine subcutaneously twice a day for two days as postoperative analgesia. As noted previously, the implants were allowed to integrate into bone for five weeks. During this period, the animals did not seem to be hampered by the implant. The animals were randomized into five groups of nine animals each. Group I consisted of the interface controls (to identify fibrous membrane formation); group II, the controls that received no treatment; group III, those treated with compression only; group IV, those that received particles only; and group V, those treated with compression and particles.

After five weeks, a second operation was performed on all animals. First, the screw was removed and then the “static” cylinder, with great care, was lifted in a vertical direction only, avoiding rotational movement that could damage the bone bridge. Then, the “dynamic” cylinder with the wider groove was inserted into the cylindrical canal of the implant thus creating the space of 100 μm on either side of the standardized vital bone bridge and allowing the formation of a 100-μm-thick fibrous membrane during the following two weeks. In animals in group IV (particles only) and group V (compression and particles), approximately 2.5 mg of high-density polyethylene particles (the equivalent of 0.5 × 108 particles) were administered subcutaneously on either side of the bone bridge. This load of particles was chosen to ensure that the bone tissue was exposed to an adequate number of particles, in light of the findings in a previous report that described the loads of particulate wear debris found in periprosthetic tissue retrieved from loosened total hip replacements. A stop screw secured the cylinder to the implant, restricting the cylinder from rotating.

Test phase

The application of membrane compression by movement in group III (compression only) and group V (compression and particles) was started at seven weeks after the first operation. The biconcave handle that protruded underneath the intact skin was grasped between thumb and index finger, and the rabbit leg was held in place with the other hand. The handle was rotated until firm resistance was encountered and the stop screw prevented further rotation; then the direction of rotation was reversed. Movement was applied twice a day, sixty times during two minutes, for fourteen days (Table I). During the application of movement, sedation of the animals was not necessary.
Table I. Time course for the five treatment groups.

<table>
<thead>
<tr>
<th>Time</th>
<th>Intervention</th>
<th>All Animals</th>
<th>I Interface Control</th>
<th>II Control</th>
<th>III Compression</th>
<th>IV Particles</th>
<th>V Compression and particles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>First operation: implant with &quot;static&quot; cylinder placed in right tibia</td>
<td>9 N = 9</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Day 1 up to week 5</td>
<td>Osseointegration of implant and randomization into groups</td>
<td>9 N = 9</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>End of week 5</td>
<td>Second operation: exchange of &quot;static&quot; for &quot;dynamic&quot; cylinder</td>
<td>9 N = 9</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>(Second operation: exchange of &quot;static&quot; for &quot;dynamic&quot; cylinder with administration of high-density polyethylene particles)</td>
<td>– N = 9</td>
<td>–</td>
<td>–</td>
<td>9</td>
<td>9</td>
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<tr>
<td>Week 6 to week 7</td>
<td>Allowing fibrous membrane formation</td>
<td>9 N = 9</td>
<td>9</td>
<td>9</td>
<td>–</td>
<td>–</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Allowing fibrous membrane formation and high-density polyethylene particles in situ</td>
<td>– N = 9</td>
<td>–</td>
<td>–</td>
<td>9</td>
<td>9</td>
<td></td>
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<tr>
<td>End of week 7</td>
<td>Killing of animals</td>
<td>9 N = 9</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>9</td>
</tr>
<tr>
<td>Week 8 up to week 9</td>
<td>Application of movement</td>
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<td>–</td>
<td>9</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High-density polyethylene particles in situ</td>
<td>– N = 9</td>
<td>–</td>
<td>–</td>
<td>9</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Application of movement with high-density polyethylene particles in situ</td>
<td>– N = 9</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>9</td>
<td></td>
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<td>End of week 9</td>
<td>Killing of animals</td>
<td>– N = 9</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

**Processing of specimens**

The animals in group I (the interface controls) were killed with an overdose of pentobarbital (60 mg/kg) at seven weeks after the first operation, and the animals in the other groups were killed in the same manner at nine weeks. The implants in the animals in group III (compression only) and group V (compression and particles), which had undergone movement, were checked to determine whether the cylinder had rotated properly. After removal of all soft tissues that covered the implant, the implant was cleaned of any bone overgrowth and the “dynamic” cylinder was removed. Next, the implant was carefully separated from the bone with the use of a chisel. Finally, the entire proximal metaphysis was removed with an oscillating saw.

The specimens were immediately imbedded in 8% gelatin white (Sigma, St. Louis MO, USA) and were slowly frozen in liquid nitrogen. Undecalcified cryostat sections (8 µm thick) were cut parallel to the surface of the bone bridges with the use of adhesive tape (Scotch tape 800; 3M, St. Paul, Minnesota, USA) to maintain the integrity of the sections. The sections were cut with the use of a tungsten-carbide-tipped knife (Spikker, Zevenaar, The Netherlands) and were stained with Giemsa (Merck, Darmstadt, Germany) for morphological orientation. Then, the pieces of tape to which the sections were adherent were cut out and mounted between two layers of glycerol jelly. For each bone bridge, three sections at different levels were selected for analysis: one was as close to the periosteal surface of the bone bridge as possible; another, as close to the endosteal surface as possible; and one, at approximately the middle of the cortex. Adjacent to the latter section, an additional section was used for localization of tartrate-resistant acid phosphatase (TRAP) activity to stain osteoclasts selectively and to establish the presence or absence of necrotic bone. Necrotic bone was characterized by the absence of cells containing TRAP activity in (bone) lacunae.

Spatially calibrated digital images were obtained by scanning an entire section using a 35-mm slide scanner (Coolscan 1000; Nikon, Tokyo, Japan). Interactively, tissue components, i.e., fibrous tissue, cartilage, and areas with absent TRAP activity, were delineated and segmented with use of the image processing program Object-Image.
Morphometric Analysis

All nine bone bridges from each of the five treatment groups were examined. TRAP activity was classified as present when cells stained brightly red and as absent when staining was hardly detectable or when cells did not stain at all. The regions of the bone bridges that contained cells without activity were qualitatively determined and labeled as necrotic. Thereafter, these areas were determined quantitatively with use of image analysis. Areas of cartilage and fibrous tissue were determined quantitatively with use of image analysis of the Giemsa-stained sections. Areas of necrosis, cartilage, and fibrous tissue were expressed as a percentage of the surface area of each bone bridge. The surface area was defined as the area of the bone bridge that had been subjected to the effect of membrane compression and/or particles, i.e., the area enclosed by both sides of the groove of the “dynamic” cylinder. Similar to the shape of the entire bone bridge, the shape of the surface area was rectangular. The median surface area for the bone bridges that were tested was 8.91 mm² (range, 8.85 to 9.04 mm²), corresponding with the length (4.45 mm) and the width (2 mm) of the groove of the “static” cylinder. The median values of the percentages of the tissue areas were calculated. The median values between groups were compared and analyzed. The nonparametric Mann-Whitney test (release 11.0; SPSS, Chicago, Illinois, USA) was used for statistical analysis; the level of significance was set at p < 0.05.

Results

Morphology

After five weeks, when the “static” cylinder was exchanged during the second operation, macroscopic inspection of the inner surface of the groove of the “static” cylinder never showed adhesion of (fibrous) tissue.

At the time that the animals were killed and the implants were removed, forty of the forty-five specimens showed macroscopic apposition of bone around the implant. After removal of this tissue, it appeared that the area between the outer surface of the implant and metaphyseal bone was tightly sealed and there were no signs of inflammation. Bone marrow cavities were sealed off from the bone bridge and interface area by the formation of new bone on the groove side of the implant, thereby providing a closed system in all cases (as in Fig. 1, B, inset). Sections of these bone bridges showed vital bone and bridge edges were sharp and regular.
All specimens in group I (the interface controls) showed a vital bone bridge as described above, with a thin fibrous membrane on both sides containing cells and extracellular matrix. Occasionally, cartilage was present. The thickness of the fibrous membranes was 100 µm, indicating that the space created by the broader groove at each side of the bone bridge had been completely filled with a membrane of fibrous tissue (Fig. 2, A).

Group II (controls) showed vital bone in the bone bridges as well, but, instead of an outer fibrous membrane, thin lamellae of new bone with osteocytes and areas of osteoid, with a thickness of 100 µm, were observed to have formed, (Fig. 2, B).

Only small amounts of fibrous tissue within the bone bridge were observed in group III, in which the fibrous membrane had been compressed. Conversely, larger areas of bone loss, with replacement by cartilage, were seen (Fig. 2, C). These changes were most obvious at all four corners of the rectangular surface areas where the amplitude of the movement of the “dynamic” cylinder was maximal and compression of the fibrous layer had been highest because of the design of the implant (Fig. 2, C).

Underneath the fibrous membrane, again especially at all four corners of the rectangular surface areas where membrane compression was highest, there were regions of bone tissue, including bone lacunae, that lacked cells with TRAP activity, indicating that these regions of bone tissue were not vital. In the areas of bone bridges where compression was lowest (in the middle of the rectangular surface areas), the numbers of cells showing TRAP activity in bone and lacunae were normal, indicating that bone was vital (Fig. 2, D). This pattern was consistent in all sections investigated. Areas of vital and nonvital bone were also sharply demarcated in all sections.

After membrane compression, sections of bone taken at the level of the endosteal surface demonstrated the formation of new lamellar bone. Morphometric analysis showed that bone bridges were qualitatively thicker in compressed specimens than in non-compressed specimens (approximately 1 mm compared with 0.5 mm) because of this new bone formation. However, the new bone formation occurred outside the area of analysis and therefore was not included in the study.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>I Interface Control</th>
<th>II Control</th>
<th>III Compression</th>
<th>IV Particles</th>
<th>V Compression and particles</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 8</td>
<td>0</td>
<td>0</td>
<td>2.82*</td>
<td>0</td>
<td>3.03*†</td>
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Table II. Morphometric findings for the five treatment groups. *The difference between the treatment and groups I and II with respect to cartilage, necrosis, or fibrous tissue was significant (Mann-Whitney test, p < 0.05). † The difference between group III and group V with respect to cartilage was not significant (Mann-Whitney test, p = 0.40). ‡ The difference between group III and group V with respect to necrosis was not significant (Mann-Whitney test, p = 0.76). § The difference between groups IV and group V with respect to fibrous tissue was not significant (p = 0.34).
Fig. 2 Photomicrographs of sections from bone bridges in group I, the interface controls (A); group II, the controls (B); Group III, which was treated with mechanical compression (C and D); group IV, which was treated with high-density polyethylene particles (E, F and G); and Group V, which was treated with a combination of mechanical compression and high-density polyethylene particles (H and I).

A: Photomicrograph of a specimen from a bone bridge in group I showing vital bone (V) with a fibrous layer (FL) on both sides of 100 µm. The rectangular surface area is the area enclosed by both sides of the groove of the “dynamic” cylinder; its four corners are indicated by (┌, ┐,└, ┘) (Giemsa staining, x11). B: Photomicrograph of a section from group II showing vital bone (V) with thin lamellae of new bone (NB) on both sides with osteocytes and areas of osteoid, which have replaced the fibrous layer (Giemsa staining, x11).

C: Higher-magnification photomicrograph of a bone bridge from group III, showing extensive loss of bone and replacement by cartilage (C), marked by the dashed line at the corner of the surface area (┌) (Giemsa staining, x160). Inset shows higher magnification of the area with bone loss and replacement by cartilage (C) (Giemsa staining, x150). D: Adjacent section to that shown in C after staining for TRAP activity. Dashed lines indicate borders between nonvital (NV) bone lacking cells positive for TRAP activity in bone and lacunae (∇), and vital (V) bone showing cells positive for TRAP activity in bone and lacunae (▲) and cartilage (C). Areas of necrosis and areas of cartilage are larger toward the corner (┌) of the surface area of the bone bridge (TRAP staining, x160). E: Photomicrograph of the middle of the rectangular surface area of a bone bridge in group IV (particles only), showing a fibrous tissue layer (FL). Toward the center of the bridge, there is bone loss with replacement by fibrous tissue (F). Particles (P) are surrounded by fibrous tissue. The remainder of bone is vital (V) (Giemsa staining, x155). F: Higher magnification of bone bridge in specimen from group IV (particles only) showing particles in clusters (V), as individual entities, or intracellularly (▲). Giant cells are not seen (Giemsa staining, x250). G: Photomicrograph of bone bridge in group IV specimen showing normal
TRAP activity in the bone bridge as well as in bone lacunae (BL), indicating vital bone (V). Inset shows a higher magnification of the area at P, with lacunae filled with particles and surrounded by TRAP-positive cells (V). (TRAP activity staining, x55; inset, x200). H: Photomicrograph of bone bridge in specimen from group V (combined compression and particles), with the corner (▼) of the surface area indicated. Areas of bone loss extend centrally into the bridge with replacement by fibrous tissue (F) and cartilage (C). Particles (P) are seen. The inset shows a higher magnification of this area, which demonstrates particles in clusters (▼), as individual entities, or intracellularly (▲) (Giemsa staining, x55; inset, x200). I: Photomicrograph of a specimen from group V (combined compression and particles), showing lacunae filled with clusters of particles (▼), surrounded by TRAP-positive activity (▲) (Giemsa staining, x250).

In group IV, in which high-density polyethylene particles had been introduced, fibrous tissue was not only present in the 100-µm-thick space on both sides of the bone bridges but it also replaced bone more centrally in the bone bridges. Fibrous tissue was more or less evenly distributed along the edges of the bone bridges, and it contained particles. Cartilage was sparsely present (Fig. 2, E). The presence of high-density polyethylene particles was confirmed by their typical birefringent appearance. Particles were present as individual entities, in clusters or intracellularly. Giant cells were not observed (Fig. 2, F). Qualitatively, the appearance of the bone tissue was normal, and TRAP activity and numbers of osteoclasts were present in amounts similar to that observed in the bone tissue in group I (the interface controls) and group II (controls). TRAP activity around lacunae filled with high-density polyethylene particles was not qualitatively increased compared with group I and group II. Necrotic areas of bone lacking TRAP activity were hardly present (Fig. 2, G).

After the combined administration of compression and high-density polyethylene particles in group V, both cartilage and fibrous tissue were observed to have formed in the bone bridge. High-density polyethylene particles were present in a similar way as in group IV (particles only). Giant cells again were not present (Fig. 2, H). Large areas of the bone bridges lacked TRAP activity, indicating necrosis. In these areas, we never observed particles. When lacunae were filled with particles, cells surrounding lacunae showed normal TRAP activity (Fig. 2, I).

Histomorphometry
As noted above, membrane compression in the absence of particles in group III (compression only) caused bone necrosis and loss of bone with replacement by cartilage. The areas of necrosis and cartilage were a median of 14% and 3%, respectively, of the surface area of the bone bridges (Table II, Fig. 3). The addition of high-density polyethylene particles without membrane compression in group IV (particles only) led to loss of bone with replacement by fibrous tissue. Fibrous tissue was found on a median of 6% of the surface area of the bone bridges. The combined application of compression and particles in group V induced necrosis, loss of bone with replacement by cartilage, and formation of fibrous tissue with median surface areas of 15%, 3%, and 4%, respectively. Compared with groups I and II (the controls), these changes were significant (p < 0.05). When we compared the effect of the combined treatment with the effect of membrane compression alone or high-density polyethylene particles alone on the formation of necrosis, cartilage, or fibrous tissue, the changes were not significant.
Fig. 3. Quantitative data on all individual animals with regard to the effect of mechanical compression of a fibrous tissue interface, introduction of high-density polyethylene particles, and a combination of the two on vital bone bridges in rabbits. The values are given as the percentages of the surface area of the bone bridges that were cartilage, necrosis, and fibrous tissue. *The difference between the treatment groups and groups I and II (the controls) with respect to cartilage, necrosis, and fibrous tissue was significant (p < 0.05). †The difference between group III (compression) and group V (compression and particles) with respect to cartilage was not significant (p = 0.40). ‡The difference between group III (compression) and group V (compression and particles) with respect to necrosis was not significant (p = 0.76). §The difference between group IV (particles) and group V (compression and particles) with respect to fibrous tissue was not significant (p = 0.34).
Discussion

Our model is intended to resemble the clinical situation of a prosthesis surrounded by a thin fibrous-tissue membrane producing micromovements upon weight-bearing, thereby compressing the fibrous tissue membrane. When components undergo early migration, the bone-prosthesis interface is unstable and interposition of fibrous tissue must be present. Successive component micromovements with compression of this fibrous tissue interface may generate a fluid pressure or fluid flow, leading to necrosis and subsequent loss of underlying bone. This may further impair bone fixation and may signify the onset of clinical loosening. This proposed pathological mechanism corresponds with radiostereometric analysis studies that have shown that early migrating prostheses have a higher prevalence of loosening.

Fluid pressure leading to loss of bone has been hypothesized by Landells as early as 1953. Indeed, recent animal experiments have shown that fluid pressure, either exogenously applied or through compression of a fibrous membrane, induces bone resorption and necrosis. On the basis of in vitro studies, high-density polyethylene particles and polymethylmethacrylate particles have been shown to induce osteoclastic bone resorption by mediating inflammatory reactions. However, some in vivo studies have described a decrease in bone formation due to the presence of particles, without an increase in resorption or even loss of bone. Therefore, it is still not clear whether and which particles cause loss of bone and, if so, whether this is through increased resorption by increased osteoclast activity or through decreased bone formation by inhibition of osteoblasts, or both.

In the present in vivo study in rabbits with a vital-bone prosthesis interface, we studied the effect of compression of a fibrous tissue interface, with or without high-density polyethylene particles, on bone and whether the combination of both stimuli has a synergistic effect on bone loss. High-density polyethylene particles were used because acetabular components of almost all total hip replacements, cemented and uncemented alike, are made of polyethylene and therefore seem to be the predominant particle type involved in the loosening process.

In all specimens of group I (the interface controls that had five weeks for healing after the first operation followed by two weeks without compression or particles), vital bone and a fibrous membrane of 100 µm on both sides of the bone bridge were present. In specimens in group II (the controls that had five weeks for healing followed by four weeks without compression or particles), the fibrous interfaces were replaced by thin lamellae of new bone containing osteocytes and osteoid, thereby proving the vitality of the bone bridges and the tendency for bone formation under stable circumstances.

Compression of the fibrous membrane interposed between the implant and vital bone, by movement of the “dynamic” cylinder, led to areas of necrotic bone in the bone bridges with lacunae, indicating early stages of necrosis. This fibrous membrane consisted of cells and proteins and interstitial body fluid with physiologic properties. If it is assumed that the behaviour of such a fibrous membrane is biphasic, compression led to a combination of stress in the solid matrix and high fluid pressure in the fluid compartment.

Necrotic areas were situated underneath the fibrous tissue membranes at all four corners of the rectangular surface areas of the bone bridges, whereas bone tissue in the middle of the bone bridges was not altered. Since the amplitude of the movement of the cylinder was at its maximum at the corners of the rectangular surface areas, membrane compression and the resulting fluid pressure or fluid flow was likely maximum in these areas. This may explain why the greatest changes to the underlying bone occurred at the corners.

Van der Vis et al., using a similar model, compressed a fibrous membrane interposed between the implant and vital rabbit bone with the same amount of pressure and for the same duration and found necrosis as well. They discussed the possibility that pressurization of interstitial fluid leads to lethal disruption of the canalicular processes of osteocytes. Moreover, induction of an interstitial fluid flow may affect the interstitial balance in the extracellular matrix of bone with subsequent osteocyte death.

In the present experiment, newly formed bone always sealed off the implant and fibrous interface area from the medullary space; thus, we assume that this was a closed system. Furthermore, the implant we used was similar to the implant used by Van der Vis et al., which has been shown to be watertight. Although our model can be considered as a closed system, reduction of the closed volume cannot be determined. We were thus unable to measure the pressure applied. We propose that by rotating the “dynamic” cylinder, the tissue fluid shifts lead to fluid flow as well as to a temporary local increase in fluid pressure. Therefore, the observed effects after membrane compression are likely to be due, at least in part, to the effects of fluid.
flow or fluid pressure, although the exact volume ratio between the solid matrix and fluid compartment in this membrane is not known. The advantage of the current model over the model of Van der Vis et al.17,18 is that the compression of the fibrous interface better resembles the clinical situation (compression of a periprosthetic membrane during weight-bearing).

Compression alone led to cartilage formation. This cartilage formation was observed mainly at the four corners of the surface areas. Mesenchymal cells can differentiate into cartilage or fibrocartilage cells when hydrostatic pressure or hypoxia are applied 35. In vitro, chondrocytes produce matrix when hydrostatic pressures of 3 MPa are applied 18. In an experiment with a rat bone chamber with application of hydrostatic stress of 2 MPa, chondrocytes were formed, usually in combination with necrosis 37. Interestingly, necrosis was absent when chondrocytes had formed a continuous layer in between the site where the pressure had originated and the underlying bone 37. Those authors hypothesized that cartilage formation was a protective response of bone to fluid flow and/or fluid pressure and prevented necrosis. According to this hypothesis, the finding of necrosis in the compressed specimens in our experiment was to be expected because in none of these specimens was cartilage generated as a continuous layer: thus, it could not act as a protective barrier.

The presence of high-density polyethylene particles led to bone loss and replacement by fibrous tissue with no necrosis or cartilage. In other in vivo studies, high-density polyethylene particles led to loss of bone because of both decreased formation and increased resorption of bone 38, or because of increased resorption of bone only 9, and bone resorption was associated with increased numbers of osteoclasts 9,38. In our experiment, bone loss in the presence of high-density polyethylene particles was not associated with an increase in numbers of osteoclasts. However, loss of bone can be the result of increased functional activity of osteoclasts without an increased number of cells 37. In addition, particles can suppress the function of osteoblasts 40 and inhibit proliferation and differentiation 41 of osteoblasts. Therefore, loss of bone could have been caused by increased osteoclastic activity or by decreased osteoblastic activity, or both. However, fibroblasts exposed to particles respond with proliferation, possibly explaining the abundance of fibroblasts and the subsequent formation of fibrous tissue after particles were added in our experiment.

Polymethylmethacrylate particles are more potent in causing bone resorption than high-density polyethylene, at least in vitro 42. However, Skoglund and Aspenberg 21 found formation of bone after applying polymethylmethacrylate particles to a rat bone surface. They hypothesized that particles had been inactivated by opsonization. Another explanation may be that the particle size in that study ranged between 5-10 µm, which is at the upper limit for macrophage resorption 26, whereas the particles that we used were smaller (mean size, 4.8 µm), causing a stronger cellular response 43.

The combination of membrane compression and high-density polyethylene particles did not lead to a significant increase in the amounts of cartilage, necrosis, and fibrous tissue compared with the effect of one stimulus only. This indicates that compression of the fibrous membrane leads to necrosis and cartilage but not fibrous tissue formation, and treatment with high-density polyethylene particles leads to the formation of fibrous tissue but not to necrosis or cartilage. In other words, the different stimuli induced different effects on bone, and therefore a synergistic effect between both compression and high-density polyethylene particles was not observed.

Skoglund and Aspenberg 21 found bone resorption after combined compression of a fibrous membrane with the administration of polymethylmethacrylate particles, but resorption was not greater than when pressure alone was applied. A synergism between pressure and particles on bone degradation could not be concluded. Particle release is a process that takes time 1. By adding a surplus of particles, we attempted to simulate a situation that is present only after a total hip replacement has been in situ for long period. Several retrieval studies have shown results that are similar to our findings: interface tissue retrieved from clinically stable but migrating prostheses showed extensive cartilage formation in the presence of a fibrous tissue interface membrane 44,45. Necrosis has been observed in large amounts in fibrous membranes from total hip replacements retrieved because of aseptic loosening 46-48, as well as in a series of retrieved interfaces that were being analyzed in our department at the time of writing (unpublished data).

The results of the present study suggest that compression of a periprosthetic fibrous interface, which induces fluid pressure and/or fluid flow, can be an important cause of early loosening of total hip replacements. Our results also suggest that polyethylene particles are involved in the loosening process as well, but probably only in later stages, when substantial amounts of these particles have been formed in the joint space 1. The formation of cartilage may be a protective response of bone to the necrotic effect of fluid pressure and/or fluid flow, but further studies are needed to clarify this observation.
Acknowledgements
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implants, and Leendert Blankevoort for his comments.

References


Wear particles do not elicit an aseptic inflammatory response in fibrous tissue interfaces of loosening total hip replacements

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Abstract

Long-term survival of total hip replacements (THRs) is still impaired by aseptic loosening. Although in vitro studies have suggested that wear particles are the main cause for osteolysis and loosening, in vivo studies have not always shown this particle-driven osteolysis. Elevated levels of matrix-metalloproteinases (MMP) -2 and -9 have been found around loosened THRs, suggesting that proteolysis plays a role in osteolysis. Activity of proteases is highly regulated at the posttranslational level. Therefore, we investigated tissues around loosened THRs for activity of these enzymes in situ, using in situ zymography in combination with immunohistochemistry. MMP-9 activity was restricted to macrophages and MMP-2 activity to endothelial cells. In contrast to the literature, we did not encounter particles in association with inflammatory response or accumulations of leukocytes. Our data indicate that aseptic loosening is not particle induced, but is rather caused by processes such as increased fluid pressure causing damage to bone and interface as has been shown in animal models.

Introduction

Hip replacement surgery is a successful and cost effective procedure. Although life expectancy of hip replacements has improved over the years, aseptic loosening still poses a clinical challenge, as it remains the most common reason for revision surgery.

Processes leading to aseptic loosening, the formation of an interface membrane, osteolysis, and eventually implant loosening have not been completely unraveled yet. Osteolysis has been suggested to be the result of wear of the implant, especially of the acetabular polyethylene component. Several reports have described the inverse relationship between wear rate and survival of the implant1-4.

Polyethylene particles have been shown to cause an inflammatory reaction leading to the activation of macrophages in vitro5 and6,7. In vivo studies have shown osteoclastic bone resorption2,8, induced by activated macrophages. However, studies in animal models have only shown decreased bone formation, suggesting that osteolysis cannot merely be induced by an inflammatory reaction to wear particles9,10.

Total hip athroplasties cause complex reactive responses in tissues and cells11-18. Proteolytic enzymes are considered to play a role in the process of loosening of total hip replacements. Takagi et al19 have shown that in periprosthetic granulomatous interface tissues, proteolytic enzymes such as MMP-1, -3 and -9 and membrane type 1 (MT-1) MMP play a role in osteolysis. It was also shown that MMP-2 and MMP-13 were present in pseudocapsular fluid in excess of their inhibitors (tissue inhibitors of MMP; TIMPs)20.

Other proteolytic enzymes have also been demonstrated in interface membranes, such as the cysteine proteinase, cathepsin B21, and serine proteinase cathepsine G22. Because proteolytic activity is highly regulated at the posttranslational level23,24, the mere presence of proteolytic enzymes or activity in tissue extracts is of limited value in understanding the role of proteolytic enzymes in loosening of THA in particular. In situ localization of activity of MMPs, especially those associated with the breakdown of the interstitial matrix and osteolysis, can give a better insight in their role in the process of loosening of artificial joints. Determination of the activity of key proteinases in this process could lead to the development of local targeted therapy using specific proteinase inhibitors. As our understanding of the microenvironment of hip replacements improves, modification of these processes comes into view25.
Goal of the study
To show the activity of MMP-2 and MMP-9 in situ in the interface of loosened THAs using in situ zymography in combination with the immunohistochemical localization of these gelatinases in relation with the presence of wear particles and macrophages, which are so often associated with osteolysis and loosening.

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Table 1. List of total hip revision patients

Material and Methods

Sampling
Synovium-like tissues were collected during revision surgery of 8 failed total hip replacements of 3 male and 5 female patients. Septic loosening was ruled out by several means, using the erythrocyte sedimentation rate, determination of the C-reactive protein (CRP) levels, macroscopic examination, tissue culturing and joint aspirates. The mean age of the patients was 71.9 years and the mean time between implantation and revision was 10.3 years. All patients were primarily operated for osteoarthritis of the hip (Table 1.). Tissue samples were frozen in liquid nitrogen and then taken to a storage freezer at -80 °C.

Histochemical analysis
Cryostat sections (thickness, 8 µm) were cut at -25°C for histochemical, immunohistochemical and in situ zymography staining. Sections were dried for 30 min at room temp and fixed either for 30 min at room temperature in 4% paraformaldehyde (Merck, Darmstadt, Germany) in phosphate-buffered saline (PBS) and rinsed in distilled water, or for 12 min in acetone at 4°C and dried for 10 min at room temp. For orientation in the fibrous tissue interfaces, sections were stained with a Giemsa solution (Merck) and subsequently rinsed in distilled water, ethanol, and xylene. Then, sections were mounted in Euparal (Chroma, Stuttgart, Germany). Serial sections were used for immunohistochemistry and in situ zymography.

Immunohistochemical staining was performed to analyze the cellular composition of the fibrous tissue interfaces. Fibroblasts were localized with the ASO2 primary antibody (dilution, 1:400; Dianova, Hamburg, Germany), monocytes with the anti-CD64 primary antibody (dilution, 1:400; Sanquin, Amsterdam, The Netherlands), macrophages with the anti-CD68 primary antibody (dilution, 1:100; Dako, Glostrup, Denmark), B cells with the anti-CD20 antibody (dilution, 1:10; Sanquin, Amsterdam, The Netherlands), and T cells with the anti-CD3 antibody (dilution, 1:100; BD, Mountain view, CA, USA). For negative controls, sections were incubated with mouse IgG (dilution, 1:1000; Dako) instead of the primary monoclonal antibody. Air-dried sections were rinsed three times in PBS containing 1% (w/v) fetal calf serum (FCS; Hyclone, Logan, UT, USA). Then, sections were incubated with primary antibody dissolved in PBS for 2 h at room temp and rinsed again three times in PBS containing 1% FCS and incubated with rabbit anti-mouse antibodies conjugated with horseradish peroxidase (dilution, 1:50; Dako) for 60 min at room temp. Sections were rinsed again three times in PBS containing 1% FCS and peroxidase activity was visualized by incubation for 10 min at room temp in a solution containing 1 mM 3-amino-9-ethylcarbazole (AEC; Sigma, St. Louis, MO, USA), 5% (v/v) dimethylformamide, 0.05% (v/v) hydrogen peroxide (Merck) and 50 mM acetate buffer (pH 4.9). AEC was dissolved first in dimethylformamide. Hydrogen peroxide was added to the solution immediately before incubation. After incubation, sections were rinsed in distilled water, and nuclei were counterstained with a haematoxylin solution for 3 sec. After rinsing in tap water and finally distilled water, sections were mounted in glycerin-gelatin.

MMP-2 and -9 were localized immunohistochemically²⁶. Primary monoclonal antibodies were anti-human MMP-2 and MMP-9 (each in dilution 1:400;
Neomarkers; Fremont, CA, USA). The immunohistochemical procedure was the same as described above for the detection of specific cell types.

Gelatinase activity was localized by in situ zymography as described by Mook et al.\textsuperscript{27} and Frederiks and Mook\textsuperscript{28}. Unfixed cryostat sections were dried for 30 min at room temperature. The substrate dye quenched (DQ)-gelatin (Molecular Probes, Leiden, The Netherlands) was dissolved in agarose solution and poured onto sections. After 60 min incubation at room temp, fluorescein isothiocyanide (FITC) fluorescence was present at sites of gelatinase activity. Control incubations were performed by adding 20 mM EDTA to the DQ-gelatin solution, which inhibits activity of MMPs\textsuperscript{27}.

Photomicrographs were made using standard light and fluorescence microscopy. Correlative light and electron microscopy was performed according to Vogels et al.\textsuperscript{29,30}

The tissue block that was used for cryostat sectioning, was brought directly from storage at -80°C into fixative (1% [vol/vol] glutaraldehyde [Merck] and 4% [wt/vol] paraformaldehyde) in 0.1 M phosphate buffer (pH 7.4) at 4°C. Fixation was performed for 48 to 72 hours at 4°C under continuous rotation of the vials. After rinsing overnight in the same buffer at room temperature, the tissue blocks were postfixed in 1% (vol/vol) osmium tetroxide (Merck) in 100 mM phosphate buffer (pH 7.4) for 1 hour in the dark at room temp. Dehydration and embedding in epoxy resin LX112 (Ladd Research Industries, Burlington, VT, USA) were performed according to routine procedures.

Semithin sections were obtained from the surface of the tissue block in which parallel cryostat sections had revealed structures that warranted further EM observations. These sections were stained with toluidine blue to select an area for ultrathin sectioning. Ultrathin sections were stained with uranyl acetate (Leica, Wetzlar, Germany) and lead citrate (Leica).

Results
The fibrous tissue interfaces of all patients investigated showed similar histology. All interface tissues contained cell-rich areas, areas mainly consisting of well-vascularized and poorly vascularized areas and areas containing accumulations of wear particles that never contained cells or extracellular matrix (Fig. 1).

\textbf{Fig. 1.} Photomicrographs of a fibrous tissue interface between bone and aseptically-loosened hip arthroplasty. Low (A) and higher power (B) overview of a Giemsa-stained cryostat section show cell-rich areas (cr), areas containing mainly extracellular matrix (e), well-vascularized areas containing capillaries (ca), larger vessels, and areas with accumulations of wear particles (p). Areas with accumulations of wear particles do not contain cells or extra-cellular matrix. Bar = 200 µm (A) and 60 µm (B), respectively. Low (C) and higher power (D, E) overviews of a cryostat section immunohistochemically-stained for MMP-2 protein. MMP-2 is present in endothelial cells of capillaries (cap) and is associated with thick collagen bundles. Areas of wear particles do not contain MMP-2 protein. Bar = 200 µm (C) and 60 µm (D, E), respectively. Higher power overview (F) of the localisation of MMP-9 protein. MMP-9 protein is present in a few cells only (arrows) that are not associated with accumulation of wear particles. Bar = 60 µm.
Its variation was not associated with either bone-facing side or arthroplasty-facing side. We did not find any area that showed signs of (aseptic) inflammation. All tissues investigated were quiescent as is shown in Fig. 2. Fibroblasts contained internalized wear particles, whereas loose extracellular particles were present as well. These particles never induced inflammatory responses. Cells consisted mainly of fibroblasts (Fig. 3A) and relatively few macrophages (Fig. 3C), hardly any monocytes (Fig. 3B) and almost no B and T cells (data not shown). Many areas of the interface tissues were well-vascularized (Fig. 1). Endothelial cells of these vessels were strongly positive for MMP-2 protein but not MMP-9 protein (Fig. 1 C-F). This endothelium-associated MMP-2 was active (Fig. 4). MMP-2 protein was also found in the acellular areas associated with collagen bundles. This MMP-2 was active as well (Fig. 1C-E and Fig. 4). MMP-9 was present in scattered cells (Fig. 1F) and was active (Fig. 3D). Based on comparisons of immunostained sections and in situ zymograms, we conclude that these MMP9 activity-containing cells were macrophages. However, we did not find specific areas with large amounts of inflammatory cells associated with gelatinolytic activity. Moreover, accumulations of wear particles were never associated with cells or gelatinolytic activity.
Discussion

A number of studies suggest an active role of proteases such as MMPs in degradation of periprosthetic bone. Takagi et al. detected gelatinolytic activity of MMP-2 and MMP-9 in extracts of interface tissue around total hip replacements that were revised for loosening. No differences were found between cemented and cementless implants. In the present study, we have confirmed the presence of MMP-2 and MMP-9 in interface tissues derived from loosened THAs and have also confirmed gelatinolytic activity using zymography in situ.

We have found active MMP-9 in the interface membrane surrounding hip implants, where it is considered to degrade the extra-cellular matrix in the osteoid, facilitating resorption by osteoclasts. However, active MMP-9 was found only in dispersed macrophage-like cells, which are known to be able to differentiate into osteoclastic bone resorbing cells, but the amount of cells containing MMP-9 was modest.

MMP-2 was found in endothelial cells lining capillaries and in acellular areas associated with collagen bundles. The exact roles of MMP-2 and MMP-9 in bone remodeling around prosthetic implants remain unclear. MMP-2 is associated with tissue degradation, and a recent report indicates its involvement in bone formation as well, because deficiency of MMP-2 was found to cause defective skeletal and facial development, decreased bone mineralization, joint erosion and defects in osteoblast and osteoclast differentiation. In MMP-9 null mice enchondral bone formation and formation of long bones is disturbed. There is an association between MMP-9 and the release of angiogenic factors from the extracellular matrix. We did not encounter MMP-2 and MMP-9 activity in association with accumulations of inflammatory cells and wear particles.

It indicates that wear particles in the interface tissue do not necessarily lead to activation of macrophages and induction of osteolysis. Wear particles were found to be present extracellularly and intracellularly in interface tissue without evidence for an inflammatory reaction. This is in contrast with current views, based on in vitro studies and the finding of increased levels of mediators of macrophage activation like TNF-alfa and IL-1. However, animal studies have shown that particles alone do not cause osteolysis, which is consistent with the findings in the present study.

Particle size has been shown to influence the macrophage response. The particles we found in the present study were within the range considered to initiate an inflammatory response. Osteolysis has been shown to be dependent on the concentration of wear particles. Although we did not measure the wear on the radiographs, the overall aspect of loosening was one of a radiolucent line completely surrounding the implant, without granulomas and a significant amount of wear. The present study shows the importance of examining the environment around prosthetic implants and investigating processes in situ, for the elucidation of molecular mechanisms involved in aseptic loosening of hip replacements. The absence of an inflammatory response in the presence of wear particles supports the view that considers fluid-pressure as a more likely cause for osteolysis and loosening.
Wear particles do not elicit an aseptic inflammatory response in fibrous tissue interfaces of loosening total hip replacements

References


Chapter 8

Revision cemented total hip replacement, using autologous bone grafts

A LONG-TERM FOLLOW-UP STUDY

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SUBMITTED
Abstract
We reviewed the results of eighty cemented revision total hip replacements (THR), up to 24 years after the index operation. The results of this patient group were previously reported on after 5 to 14 years, with a survival of 85% at 14 years. We now present the results extending the follow-up 10 years. We found a survival rate of 81% after 19 years when aseptic loosening of the acetabular components was taken as endpoint. Survival after 19 years, with revision for any cause as endpoint however was 57%. Twenty-three hips had a repeat revision, excluding two repeat revisions in which only the non-revised component was exchanged. There are only nine patients left alive, now aged between 86 and 100 years, without the need for a second revision and according to their radiographs without the need for a revision in the future.

Background
In 1990, Marti et al. reported on a consecutive series of seventy patients (eighty-one hips) who had a cemented revision total hip replacement between 1974 and 1983. After an average follow-up of 8.9 years, four hips had been revised for aseptic loosening, and two hips became infected. Another five femoral components were loose according to radiographic criteria. Three acetabular components showed migration radiographically, and were therefore considered loose. We now report on this group up to 24 years after the index operation (average 14 years for the patients that are still alive), in order to assess the efficacy of the operative technique.

Materials and Methods
Patients
We found 80 revision total hip replacements between 1974 and 1983, just like the group mentioned above. Unfortunately, we were not able to identify all the patients that were reported in the previous study, but at least 75 of the procedures were well documented, leaving 5 hips (5 patients) as a probable but uncertain match. We found 80 revision procedures in 73 patients. Seven patients had bilateral revision hip replacements. The average age at surgery was 68.6 years (26-86 years). Fifty-two patients (57 hips) had died at the time of follow-up. Nine patients (10 hips) had a repeat revision after an average of 8.05 years (0.5-16 years) before they died. One had an exchange of the component that was not revised during the index operation, after 16 years. Forty-two patients (46 hips) died without the need for a repeat revision after an average of 10 years (1-24 years). This left 22 patients (24 hips) for further evaluation. Fifteen patients (17 hips) were seen in the outpatient clinic and had a full physical and radiological examination. One patient was lost to follow-up 11 years after the index operation. Six patients were unable to make it to the hospital and were interviewed by telephone. All patients were entered in the survivorship analysis. Nine of these patients had no revision in the meantime.

Operation
In all patients, infection was ruled out by culture of a specimen of the preoperative aspirate as well as by culture of a specimen of deep tissue taken during the operation. A cemented Weber Rotation total hip replacement (Sulzer®, Baar Switzerland) was used routinely. This prosthesis has a rotating trunnion bearing with three different neck lengths, designed to reduce the wear of the polyethylene acetabular components.

The head is made of cobalt chrome alloy, but in 1978 a ceramic head also became available. Both heads were available with a choice of three neck lengths. In all cases, antibiotic loaded cement was used. There was no standard postoperative regimen as far as systemic antibiotics was concerned.

All operations were done by experienced orthopaedic surgeons using a standard technique, as was already described by Marti et al. in 1990. Substantial defects were treated with autologous bone graft from the iliac crest. Cranialateral segmental defects were treated by a cortico-cancellous graft. If the acetabular component was not sufficiently supported by these grafts, a reinforcement ring was used to support it. Medial wall defects were filled with bone chips or a cortico-cancellous graft if the defect was substantial.

Methods
We used the Harris hip score (HHS) for clinical evaluation. For radiological analysis we used the criteria of Harris for the stem and Hodgkinson for the acetabular component. The SPSS® 11.5 statistical package was used for statistical analysis. The life table method was used for survivorship analysis. Different endpoints were measured: revision for any reason, revision for aseptic loosening of any of the components, and revision for aseptic loosening of either the stem or the acetabular components.
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Table 1. Life table with revision for loosening (any cause) as endpoint.
The most remarkable finding was the survival of the acetabular component, when aseptic loosening was taken as endpoint. Survival after 10 years was 95%, after 15 years 87.3% and after 19 years still 81%.

Twenty-three total hip revision replacements were revised again after an average of 10.3 years (2-22 years). Two other patients had revision surgery because of loosening of the non-revised component after 8 and 11 years respectively. The revised component was left unchanged and they were both followed for another 8 years. The revised component therefore was left unchanged for 16 and 19 years respectively. Two hips were revised for infection after 4 and 6 years respectively.

One patient fractured her femur 13 years after surgery, and the subsequent open reduction and internal fixation resulted in an infection, which finally necessitated an amputation of her leg.

One hip was revised for trochanteric non-union after seven years. A surgeon outside our clinic believed the hip to be loose or infected and therefore saw an indication for a revision. At surgery, the hip was neither loose nor infected. The trochanteric non-union was treated surgically.

Eighteen hips were revised for aseptic loosening. Two for loosening of the acetabular component, 9 for loosening of the stem, and in 7 cases both components were loose. Clinical examination of the remaining nine patients, that were not revised a second time, revealed one HHS above 90 points, four above 80, 3 above 70 and 1 below 70. Radiological analysis showed no signs of loosening in the nine patients still alive and not revised again, so there seem to be no further imminent failures. These patients are now between 86 and 100 years old!

**Conclusions**

As far as we know, there is no study on cemented THR with such a long follow-up. Mulroy and Harris showed the benefits of their improved cementing techniques for the femur in revision THR at an average follow-up of 15 years. The study however, did not include a survivorship analysis. DellaValle showed excellent survival (97%) of the cementless Harris-Galante acetabular components after 15 years with aseptic loosening of the acetabular components as endpoint, but at fifteen years 30% of the acetabular components were associated with osteolysis. Stem survival, although different types of stems were used, was 58% at fifteen years.
Although we are aware of the fact that this cohort differs slightly from the cohort studied and reported earlier, we must emphasize that this patient group was operated under the same circumstances, by the same surgeons using the same technique as the cohort described by Marti in 1990. We therefore feel that it is justified to compare results between these two groups.

We did not include a survivorship analysis with radiographic loosening as endpoint, because the only patients left alive (n=9) and able to influence further survival outcome, had no radiographic signs to suggest any impending failure. The results at fifteen years seem inferior to the results reported earlier and at least suggest absence of selection bias in this study group.

Cementing techniques used in fixation of the stem were not much different from the techniques used in earlier studies on cemented revision THR, as already stated in our previous publication1. The most remarkable finding from this study however is the fact that in contrast to many studies on cemented total hip revisions8-11, survival with aseptic loosening of the acetabular components as endpoint in this study group is 81 % at 19 years. This is in concordance with our findings in primary hip replacement, where we also found a relatively superior outcome of cemented acetabular components (unpublished data). Restoration of bone stock has always been an important part of the operation because it creates a stable environment for the implant. Acetabular roofplasties were frequently used by the senior author (RKM) in primary THR, because of incomplete coverage of the acetabular implant in arthritic hips secondary to dysplasia3,12, but also in revision surgery with acetabular bone defects13. This study again shows the merits of carefully building up bone defects with small autologous bone grafts and the use of a good cementing technique3,12-15.

References


Cemented hip revision surgery in severe acetabular defects using a semirigid acetabular reinforcement ring

A 5 TO 25 YEAR FOLLOW-UP STUDY

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Abstract
Between 1978 and 1998, a total of 38 consecutive acetabular component revisions were performed in 38 patients. Average age was 67 years, and 87% of patients had severe uncontained segmental acetabular defects of more than 50%. We describe the operative technique of acetabular component revisions performed with bone grafting and a steel, semirigid acetabular reinforcement ring (Eichler), and long-term results are presented. After an average of 11.2 years follow up, one cup was revised after 0.8 years for mechanical loosening, but the ring remained stably fixed. Remodeling (partial) of autografts occurred in all cases. The average Harris hip score was 72.5. The Eichler reinforcement ring is a viable option for segmental acetabular defects in revision hip surgery, allows for restoration of pelvic bone, and makes future revisions feasible.

Introduction
The presence of large segmental acetabular defects caused by cup migration or migration of a hemi-prosthesis is a great challenge in hip revision surgery. During the loosening process of an acetabular component, bony defects can develop by (micro-) motion, by debris reaction and through bone resorption caused by fluid pressure waves induced by a loose prosthetic component. In small cavitary defects, when sufficient bony support is still present, a large(r) polyethylene cup can be placed in the anatomical position sometimes with additional bone grafting. When bone defects are larger and segmental, revision of the acetabular component is difficult: the structures required for the fixation of the cup are no longer intact, and it is impossible to place the cup in the anatomical position. This bone loss can be addressed with mega-implants or by creating bony support by means of bone grafting and/or reinforcement rings. The advantage of bone grafting and pelvic reconstruction is that future revisions are facilitated. Several types of reinforcement rings have been developed and have been reported on. They differ with respect to having no medial wall or a caudal hook. Because initial stability is imperative in preventing early loosening, rings are usually made of a more rigid material (eg, commercially pure [CP] titanium). Rigidity of components may cause stress shielding and is seen in press-fit metal-backed cups in primary total hip arthroplasty (THA). Since 1978, we have been using a reinforcement ring for revisions with large segmental acetabular defects, which is essentially different from other rings because it is made of steel and is semirigid. It has no medial wall and no peripheral but central flanges. This Eichler ring should give sufficient initial stability and theoretically should cause less stress shielding with less periprosthetic bone resorption allowing bone grafts to remodel under the existing pressure. This bone grafting can be used additionally to support the ring and fill defects to reconstruct the pelvic bone and make future revisions feasible. Our research question is whether the long-term and clinical results of acetabular revision surgery with the Eichler acetabular reinforcement ring is superior compared to the reported results of other (more rigid) reinforcement rings.

Material and Methods
Between 1978 and 1998, from a total of 240 hip revisions, 38 consecutive hip revisions (38 patients) were performed with the Eichler ring by the two senior orthopaedic surgeons (RKM, PPB). In 27 procedures, both acetabular and femoral components were exchanged, and in 11 procedures, only the acetabular component was revised. For 6 hips (16%), this was the second revision, and for 3 hips (8%), the third revision was on the acetabular side. Seven (16%) revisions were performed for septic loosening as a second-stage procedure. Patients were operated on at an average age of 67.3 years (range, 30.2-86.5 years). Twenty-nine patients (81%) were female. Indications for the primary THA were idiopathic osteoarthritis in 15 hips, developmental dysplasia in 11 hips, posttraumatic osteoarthritis in 11 hips, and rheumatoid arthritis in 1 hip.

The acetabular defects were scored according to the classification as described by Saleh et al. in having peripheral flanges or a caudal hook. Because initial stability is imperative in preventing early loosening, rings are usually made of a more rigid material (eg, commercially pure [CP] titanium). Rigidity of components may cause stress shielding and is seen in press-fit metal-backed cups in primary total hip arthroplasty (THA). Since 1978, we have been using a reinforcement ring for revisions with large segmental acetabular defects, which is essentially different from other rings because it is made of steel and is semirigid. It has no medial wall and no peripheral but central flanges. This Eichler ring should give sufficient initial stability and theoretically should cause less stress shielding with less periprosthetic bone resorption allowing bone grafts to remodel under the existing pressure. This bone grafting can be used additionally to support the ring and fill defects to reconstruct the pelvic bone and make future revisions feasible. Our research question is whether the long-term and clinical results of acetabular revision surgery with the Eichler acetabular reinforcement ring is superior compared to the reported results of other (more rigid) reinforcement rings.

All procedures were performed in a supine position, using an anterolateral approach combined with an osteotomy of the greater trochanter. The cup, cement mantle, granulation tissue, and non vital scar tissue are removed until the sclerotic bony surface is visible. After careful minimal reaming of the remaining acetabulum, the definitive classification of the defect is possible. At this point, it is decided whether a large(r) cup (with bone grafting) can be placed in the anatomical position or – usually in case of segmental defects - an Eichler ring is warranted (Fig. 1).
Cemented hip revision surgery in severe acetabular defects using a semirigid acetabular reinforcement ring  |  De Man

Fig. 1. The surgical algorithm for cemented hip revision surgery we have used since 1978.

Fig. 2. The smallest (diameter, 44 mm; 7 holes) Eichler acetabular reinforcement ring.

The Eichler ring (Fig. 2) is made of V2A steel (Sulzer, Protek, Baar, Switzerland) and comes in four sizes of 44, 50, 54, and 58 mm in diameter. The smallest size has 7 holes, and the largest size has 15 holes for screw fixation. At insertion, the central flanges can be (slightly) bent until intrinsic stability is reached. If the intrinsic stability is not optimal, screws are added to fix the ring (9 hips). Correct inclination and anteversion of the ring are not an absolute requirement because the position of the cup can be tilted approximately 20° in inclination and 15° in anteversion relatively to the position of the ring (Fig. 3). At this point, it is judged if and where additional bonegrafting is necessary. Cranialateral defects are grafted with autologous (bicortical) cortico-cancellous bone blocks from the contralateral iliac crest because the largest forces act in this part of the acetabulum. These grafts are fixated with screws and washers (Fig. 4). Defects of the medial wall are filled with autologous slices of the lamina interna of the iliac crest or donor grafts so that height and center of rotation of the hip are restored, and in addition, leakage of cement is prevented (Fig. 5).
Fig. 3. Correct inclination and anteversion of the Eichler ring are not an absolute requirement because the position of the cup is not related to that of the ring.

Fig. 4. A, Loosening with severe acetabular bone loss in a 30-year-old female patient. B, Postoperative radiograph after revision. The Eichler ring was inserted, restoring the height and center of rotation, but not in the correct amount of anteversion. Because initial intrinsic stability was judged as being insufficient, screws were added. Then, the remaining superolateral defects are filled with autogenous grafts from the contralateral iliac crest. The dotted line shows the border between the grafts and the supraacetabular bone. In this “new” acetabulum, the cup is cemented in the ideal amount of anteversion at the original height and center of rotation. C, Anteroposterior and lateral x-ray after 21.1 years of follow-up. There are no signs of component loosening. There is remodeling of the supraacetabular bone with complete restoration of bone stock.
Fig. 5. A. Loosening and migration of a THA in a 53-year-old woman. B. X-rays 2 years postoperatively; the autologous superolateral graft is completely restructured and incorporated. The slices of allograft used for the restoration of the central defect remain unchanged. C. X-rays 13.7 years postoperatively. No sign of loosening is visible. The central slices of allografts remained unchanged during follow-up.
Multiple anchorage holes with a diameter of 6 mm are made into the remaining acetabulum. If the stability of the Eichler ring and grafts is perfect, the Eichler ring and cup can be placed in a one-step cementing technique. However, we prefer a 2-step cementing technique to achieve an optimal fixation with a small amount of cement. The central flanges can be fixed with a small amount of cement inserted as a ball mass at high viscosity and then pressurized with the triacup-pusher to create a new acetabulum. A good visualisation of the defects and anchorage holes remains with using this 2-step technique, ensuring the optimal filling with cement by filling it digitally under compression. As the cement has hardened, the surface is roughened and new anchorage holes are made. A second (small) portion of cement at less high viscosity is then inserted to fix the cup in the right position. The cup is pressurized until the cement is hardened. The same prosthetic implant was used in all patients, a cemented Weber Rotation THA System (Allopro, Baar, Switzerland). Trochanter refixation was performed with 2 lag screws with additional tension-band cerclage wiring.

Survival analysis was performed using a life table method with revision for any reason of the acetabular component and/or ring as endpoint. All patients were invited to our outpatient clinic where a Harris hip score (HHS) was obtained. Because many patients had comorbidity that could influence the interpretation of the HHS, the patients were categorized according to Charnley. Class A means that only one hip is affected, in Class B the contralateral hip is also affected causing limited mobility, and comorbidity influencing mobility is present in Class C.

Weight-bearing anteroposterior pelvic and lateral hip x-rays were obtained at follow-up and compared with the available postoperative x-rays and radiographs made at annual or biannual follow-ups. Radiolucencies with a width of more than 1 mm were detected in the zones according to DeLee and Charnley and classified as lateral radiolucency (type I), as middle radiolucency (type II), and as medial radiolucency (type III). Horizontal and vertical component migration was measured by using the center of the prosthetic femoral head and the bottom of the teardrop as reference points as described by Nunn et al. Loosening of the cup and ring was classified according to the system by Gill et al. The cup was considered to be definitely loose (type III) if screws used for ring fixation were broken or if a complete, progressive radiolucent line medial or superior to the ring or around the screws was present or if there was evidence of migration of the cup or a fracture of cement was present. Probable loosening (type II) was considered if an incomplete progressive radiolucent line medial or superior to the ring was present. The acetabular component showed possible loosening (type I) if a nonprogressive radiolucency was present that did not involve the screws. Heterotopic ossification was graded according to Brooker et al. Remodeling of autografts was classified as no remodeling (class 0), incomplete remodeling (class 1), or complete remodeling (class 2). Resorption of the autografts was classified as no resorption (class 0), partial resorption (class 1), or complete resorption (class 2).

Results

Both 10-year and 15-year survival with revision for any reason as an endpoint was 97% (95% confidence interval, 92-100) (Table I); and with grade III definitive radiologic loosening as endpoint, this was 94% (95% confidence interval, 85-100). There was one revision of the acetabular component in one patient (2.6%) because of mechanical loosening, 0.8 years after the index operation. In this patient, 2 portions of cement had been used, and only the cup with the second portion of cement loosened and was revised, whereas the Eichler ring (and grafts) remained well fixed.

At the latest follow-up, 16 patients (42%) had died of causes unrelated to the procedure at an average age of 84 years (range, 64-93 years), reaching a mean follow-up of 8.1 years (range, 2.0-16.3 years). None of these patients had a revision of the acetabular component.

Clinical evaluation was possible in 14 patients (37%). Four patients (11%) were unable to visit our outpatient department because of logistic reasons, but a HHS could be obtained by phone interview. One patient (3%) was unable to visit our outpatient department and no reliable HHS could be obtained because of severe dementia, but the prosthetic implant was still functioning well. Two patients (5%) were lost to follow-up. Thus, hip scores could be calculated for 18 patients after an average follow-up of 11.2 years (range 5.8-21.1 years). The average HHS was 72.5 (range, 31-100). Three patients had poor hip scores of 31, 34 and 35, respectively: this was caused by recurrent dislocations of the prosthesis in one patient and by comorbidity in the other 2 patients (Charnley C category). Eight patients (44%) were classified as Charnley class A, 4 patients (22%) as class B and 6 patients (33%) as class C. The (average) HHS for each Charnley category is shown in Table 2. Five patients (28%) had a positive Trendelenburg sign.
Radiological evaluation including the one revised hip was possible for 20 hips after an average follow-up of 9.9 years (range 5.8-21.3) When the cups were scored for loosening, 7 hips (37%) were classified as no loosening, 6 hips (31%) as possible loosening (type I), and 4 hips (21%) as probable loosening (type II). The remaining 3 cups (10%) were scored as definitive loosening (type III), which occurred after 0.8, 6.2 and 17.8 years (Table 3). The case with early loosening was revised because of severe migration with complaints. The other 2 hips had very few complaints with hip scores of 78 and 90, respectively, and obviously a revision was not indicated. Remodeling of superolateral bone grafts was complete in 12 hips (including the one revised case) and partial in the remaining 8 hips. Areas of partial resorption of bone grafts were seen in 5 hips; in the remaining 15 hips, there was no resorption of grafts at all.

Surgery-related complications occurred in 4 patients (10%): one patient had recurrent dislocations of the hip, requiring additional surgery without component revisions; one hip dislocated once and responded well to conservative treatment; in one patient a sciatic nerve lesion occurred, which resolved partially; and in one patient, an intraoperative femoral fissure occurred requiring fixation with cerclage wiring only which lead to uneventful healing. No deep infections, trochanteric non-unions, or problems related to the harvest of iliac autologous bone grafting occurred. One patient had a period of hypotension during surgery; this occurred while the cement was inserted. Postoperatively, she presented with a hemiplegia due to an ischemic stroke.

<table>
<thead>
<tr>
<th>Post operative years</th>
<th>No. of hips at start</th>
<th>No. of withdrawals</th>
<th>No. of patients who died</th>
<th>No. at risk</th>
<th>No. of failures</th>
<th>Cumulative survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>38.0</td>
<td>0.0</td>
<td>0.0</td>
<td>38.0</td>
<td>1.0</td>
<td>0.97</td>
</tr>
<tr>
<td>1-2</td>
<td>37.0</td>
<td>1.0</td>
<td>0.0</td>
<td>36.5</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>2-3</td>
<td>36.0</td>
<td>3.0</td>
<td>2.0</td>
<td>34.5</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>3-4</td>
<td>33.0</td>
<td>1.0</td>
<td>1.0</td>
<td>32.5</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>4-5</td>
<td>32.0</td>
<td>1.0</td>
<td>1.0</td>
<td>31.5</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>5-6</td>
<td>31.0</td>
<td>4.0</td>
<td>2.0</td>
<td>29.0</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>6-7</td>
<td>27.0</td>
<td>5.0</td>
<td>0.0</td>
<td>24.5</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>7-8</td>
<td>22.0</td>
<td>2.0</td>
<td>0.0</td>
<td>21.0</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>8-9</td>
<td>20.0</td>
<td>1.0</td>
<td>1.0</td>
<td>19.5</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>9-10</td>
<td>19.0</td>
<td>4.0</td>
<td>2.0</td>
<td>17.0</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>10-11</td>
<td>15.0</td>
<td>1.0</td>
<td>0.0</td>
<td>14.5</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>11-12</td>
<td>14.0</td>
<td>1.0</td>
<td>0.0</td>
<td>13.5</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>12-13</td>
<td>13.0</td>
<td>1.0</td>
<td>0.0</td>
<td>12.5</td>
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<td>0.97</td>
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<td>13-14</td>
<td>12.0</td>
<td>3.0</td>
<td>1.0</td>
<td>10.5</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>14-15</td>
<td>9.0</td>
<td>3.0</td>
<td>3.0</td>
<td>7.5</td>
<td>0.0</td>
<td>0.97</td>
</tr>
<tr>
<td>15+</td>
<td>6.0</td>
<td>1.0</td>
<td>1.0</td>
<td>5.5</td>
<td>0.0</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Table 1. Survival rates with revision for any reason (life table method) as end point.

<table>
<thead>
<tr>
<th>Charnley category</th>
<th>No. of patients</th>
<th>Average HHS</th>
<th>Range</th>
<th>Average follow-up time</th>
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<tbody>
<tr>
<td>Charnley A</td>
<td>8</td>
<td>89.7</td>
<td>73-100</td>
<td>9.7</td>
</tr>
<tr>
<td>Charnley B</td>
<td>4</td>
<td>61.5</td>
<td>34-79</td>
<td>13.3</td>
</tr>
<tr>
<td>Charnley C</td>
<td>6</td>
<td>57.0</td>
<td>31-90</td>
<td>12.2</td>
</tr>
</tbody>
</table>

Table 2. Number of patients, HHS, and follow-up time for each Charnley category.
Radiolucenty was not measurable because of complete loosening of the acetabular component.

Remodeling of the autograft: class 0 = no remodeling, class 1 = incomplete remodeling, class 2 = complete remodeling. Resorption of the autograft: class 0 = no resorption, class 1 = partial resorption, class 2 = complete resorption.

Table 3. Radiological follow-up.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age at operation (y)</th>
<th>Follow-up</th>
<th>Zone with radiolucency¹/max. width</th>
<th>Loosening²</th>
<th>HO³</th>
<th>Remodeling/Resorption bone graft⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>♂</td>
<td>70.8</td>
<td>8.2</td>
<td>no radiolucence</td>
<td>I</td>
<td>0</td>
<td>2/1</td>
</tr>
<tr>
<td>♂</td>
<td>50.3</td>
<td>6.4</td>
<td>2+/3/2mm</td>
<td>I</td>
<td>0</td>
<td>2/1</td>
</tr>
<tr>
<td>♂</td>
<td>62.4</td>
<td>11.5</td>
<td>2+/3/2mm</td>
<td>I</td>
<td>0</td>
<td>2/1</td>
</tr>
<tr>
<td>♂</td>
<td>83.7</td>
<td>0.8</td>
<td>*</td>
<td>III</td>
<td>0</td>
<td>2/0</td>
</tr>
<tr>
<td>♀</td>
<td>56.1</td>
<td>9.4</td>
<td>no radiolucence</td>
<td>no loosening</td>
<td>0</td>
<td>1/0</td>
</tr>
<tr>
<td>♂</td>
<td>75.9</td>
<td>6.7</td>
<td>1+/3/1mm</td>
<td>I</td>
<td>0</td>
<td>1/0</td>
</tr>
<tr>
<td>♂</td>
<td>30.2</td>
<td>21.3</td>
<td>3/1mm</td>
<td>II</td>
<td>1</td>
<td>1/0</td>
</tr>
<tr>
<td>♂</td>
<td>60.7</td>
<td>9.8</td>
<td>3/2mm</td>
<td>II</td>
<td>2</td>
<td>1/0</td>
</tr>
<tr>
<td>♂</td>
<td>66.1</td>
<td>6.3</td>
<td>3/1mm</td>
<td>II</td>
<td>2</td>
<td>2/0</td>
</tr>
<tr>
<td>♀</td>
<td>55.4</td>
<td>19.8</td>
<td>no radiolucence</td>
<td>no loosening</td>
<td>1</td>
<td>1/1</td>
</tr>
<tr>
<td>♂</td>
<td>67.3</td>
<td>7.8</td>
<td>1/1mm</td>
<td>II</td>
<td>1</td>
<td>1/0</td>
</tr>
<tr>
<td>♀</td>
<td>52.3</td>
<td>11.7</td>
<td>no radiolucence</td>
<td>no loosening</td>
<td>0</td>
<td>2/1</td>
</tr>
<tr>
<td>♀</td>
<td>53.5</td>
<td>13.7</td>
<td>no radiolucence</td>
<td>no loosening</td>
<td>1</td>
<td>2/0</td>
</tr>
<tr>
<td>♂</td>
<td>69.6</td>
<td>6.7</td>
<td>no radiolucence</td>
<td>no loosening</td>
<td>1</td>
<td>1/0</td>
</tr>
<tr>
<td>♀</td>
<td>64.8</td>
<td>5.8</td>
<td>no radiolucence</td>
<td>no loosening</td>
<td>0</td>
<td>2/0</td>
</tr>
<tr>
<td>♂</td>
<td>70</td>
<td>6.7</td>
<td>no radiolucence</td>
<td>no loosening</td>
<td>0</td>
<td>2/0</td>
</tr>
<tr>
<td>♂</td>
<td>60.6</td>
<td>6.3</td>
<td>3/2mm</td>
<td>I</td>
<td>1</td>
<td>2/0</td>
</tr>
<tr>
<td>♂</td>
<td>67.2</td>
<td>17.8</td>
<td>1+/2+3/17mm</td>
<td>III</td>
<td>0</td>
<td>2/0</td>
</tr>
<tr>
<td>♀</td>
<td>42.0</td>
<td>6.2</td>
<td>no radiolucence</td>
<td>no loosening</td>
<td>1</td>
<td>1/0</td>
</tr>
<tr>
<td>♀</td>
<td>39.9</td>
<td>6.2</td>
<td>3/12mm</td>
<td>III</td>
<td>0</td>
<td>2/1</td>
</tr>
</tbody>
</table>

Table 3. Radiological follow-up.

1 Zones with radiolucency/max. width according to DeLee and Charnley: type I = lateral radiolucency, type II = middle radiolucency, type III = medial radiolucency
2 Loosening according to Gill et al.: type I = possible loosening, type II = probable loosening, type III = definite loosening.
3 HO = Heterotopic ossification according to Brooker et al.: class I = small islands of bone in the soft tissue; class IV = bone ankylosis of the hip.
4 Remodeling of the autograft: class 0 = no remodeling, class 1 = incomplete remodeling, class 2 = complete remodeling. Resorption of the autograft: class 0 = no resorption, class 1 = partial resorption, class 2 = complete resorption.

Discussion
In hip revision surgery, acetabular bone defects can be large (segmental), which makes sufficient restoration of defects by using a larger cup and solid bone grafting alone not possible. For such cases, various types of rigid rings⁸-¹⁴, ¹⁸, ³² providing the requested stability⁹ are in use. Eichler, in 1972, reported on the operative technique of a semirigid steel reinforcement ring, which was developed for protrusion coxarthrosis and used in the presence of a primary THA: the number of patients was small (17) and (clinical) results were not reported on reference³¹. Later, it was noted that in the case of revisions with pathological acetabula and bony deficiencies, the Eichler ring could be a valuable solution. In 1994, Weber and Brunnenmann reported their results of 38 hip revisions from a total of 304 hip revisions performed with the Eichler ring¹⁴. There were no re-revisions, but mean follow-up was 5 years and the number of patients who had died and/or were lost to follow-up was substantial. From these studies, a lack of information on surgical technique and (long-term) results of this specific augmentation ring remains. In this retrospective study, we asked whether the long term and clinical results of this “Eichler” reinforcement ring that we have been using since 1978 for revision hip surgery are superior compared to the reported results of other reinforcement rings with a different design and made of a more rigid material. In addition, we describe the surgical technique we used.

A possible limitation of this study is that a substantial number of patients (47%) had withdrawn. Because the studygroup contained several elderly patients, the main reason for this was that many had died during follow-up, whereas only two patients (5%) were actually lost to follow-up. For those patients who had died, we know from our records (standard annual or biannual follow-up) and from additional information from the general practitioner that they did not seek medical attention for a hip problem and no revisions occurred. Because the aim of revision surgery is to improve the quality of life and to prevent any further revision of the prosthetic implant, we do believe that the outcome for these patients can be considered successful. Also, when evaluating radiologic stability of components, it is important to have reliable methods of measurement of component migration³⁵. The precise measurement of migration is difficult because of overprojection of the ring on x-rays and the obscured anatomical landmarks in these multiple operated hips. This difficulty is also established by the great number of methods for measurement of migration described in the literature¹⁶, ¹⁰, ³⁶-³⁹. However, we believe that the method we used has proven to be simple and reliable.
In this study, we had only one (2.6%) re-revision, two cases (5.2%) of definitive radiological loosening, a 15-year survival of 97% for revision for any reason as endpoint and 94% for definitive radiologic loosening as endpoint, and a relatively low surgery-related complication rate of 10%. These results may be due to the mechanical properties of the ring. Although most other types of acetabular reinforcement rings are made of titanium, the Eichler ring is made of steel. The elasticity (Young elastic modulus) of steel is twice as high as titanium and therefore the Eichler ring can be denoted as semirigid. Furthermore, it has no medial wall, making it more elastic compared to rings that do have a medial wall. This allows for load transfer to the acetabular bone with subsequently remodeling and structural integration (according to Wolff Law) of the (superolateral) autogenous grafts as was also shown in a finite element study and in two previous clinical studies from our institution.

In this study, in the presence of a semirigid reinforcement ring, all superolateral autografts demonstrated partial or complete remodeling with no resorption of the grafts in the weight-bearing zone. This finding is in concordance with the occurrence of less retroacetabular stress shielding in primary THA when a cemented polyethylene cup is used compared to when a more stiffer press-fit uncemented cup is used. In our opinion, the fact that autografts incorporated was highly responsible for the low rate of failure of the ring and acetabular component and additionally can facilitate a future revision, should this be necessary. We did not use (bulk) allograft for superolateral bone reconstruction. As was seen in clinical studies and in a previous finite element study, the use of allografts is associated with early failure due to lack of bony ingrowth. Similarly, we did not see the same remodeling of the central allografts as compared to the superolateral autografts. Nevertheless, no protrusion of the rings and/or cups occurred and, obviously, the Eichler ring together with the first small portion of cement is able to withstand forces acting in a central direction. In a biomechanical study, Schatzker et al. compared the Eichler ring with wire mesh reinforcement of the medial wall alone and with the ring combined with wire mesh wall reinforcement: the latter situation showed the strongest resistance against a medially directed force. An important difference between Schatzker’s experiment and our approach is that he used morselized bone grafts, whereas we used solid slices of bone graft to support the medial wall. In our opinion, the combination of solid grafts with the Eichler ring makes it a strong construction.

The advantage of the Eichler ring combined with bone grafting seems to be that initial stability with pelvic reconstruction can be sufficiently achieved and long-term stability is not hampered by possible stress shielding. The central bone (allo-)grafting seems less important for long-term stability, but its volume is mainly needed to restore the center of rotation and to prevent leakage of cement into the pelvis.

In all hips, we used cement to fixate the Eichler ring and the cup; however, we did not use cement to fill bony defects. Filling of bone defects with cement has been associated with increased signs of (radiologic) cup loosening both in revision hip surgery with use of a Burch-Schneider (BS) augmentation ring after medium-term follow-up as well as in primary THA for dysplasia after long-term follow-up. Donor site morbidity is often mentioned when using autologous grafts. To lower this incidence, we always leave the outer layer of the iliac crest intact and we harvest from the contralateral iliac crest to avoid weakening of the ipsilateral crest. In our opinion, the possibility of donor site morbidity with our technique is outweighed by the advantages of autologous bone grafts, but in case of limited availability, the use of allograft can be considered. Bone defects can also be addressed with the use of mega-implants, but bone stock is not restored, which might compromise future revisions.

Other types of rings include the Muller acetabular reinforcement ring, which is made of titanium, has no medial wall and no peripheral flanges, and is recommended for smaller, contained, cavitary defects. In a meta-analysis performed by Starker et al. of a total of 535 hips, the acetabular reinforcement ring showed definitive radiologic loosening in 10.5%, whereas an additional 5.6% was revised for aseptic loosening after an average of 6 years. The titanium Ganz-ring has a medial wall and a distal hook that embraces the teardrop adding further stability and is recommended for intermediated-sized segmental defects. Midterm and longterm reports show a 9% to 10% rate of aseptic - including radiologic - loosening. The BS-ring has a medial wall and has two peripheral flanges and is indicated for larger segmental defects. The flanges are fixed to vital iliac crest bone, respectively, so that the underlying bone defects are bridged. Usually, homologous bone grafts instead of autologous grafts are used to fill these defects. The forces generated by loading of the hip are almost solely absorbed by the stiff titanium BS ring and remodeling of bone is theoretically decreased. In the same meta-analysis by Starker et al., 203 BS-rings showed radiologic loosening in 9.4% cases and an additional 6.9% revision rate for aseptic loosening after an average of 5.1 years follow-up.
Starker, in his own patient population (174 hips), found better results; after an average 5-year follow-up, 3.4% rings had radiologic loosening and 2.3% had had a revision. After an average 8.5 years follow-up of 63 BS rings, Gill et al.\textsuperscript{11} reported a 6% revision rate of aseptic loosening of the whole acetabular construct and an additional 2.5% rate of definitive radiologic loosening.

Based on our experience, the satisfactory long term result (especially in relation to results of other augmentation rings), and the low incidence of complications in these difficult acetabular cup revisions with large defects, it is our opinion that the Eichler ring should be considered for use in such cases, in combination with superolateral autografting and central allografting. It is possible that the semirigid properties of the Eichler ring enables the superolateral graft reconstruction to become incorporated. The eventual restoration of pelvic bone is beneficial in case of future revisions. In the authors’ opinion, this technique is preferable to those using mega-implants without osseous reconstruction of the acetabulum.

References


Is the long-term outcome of cemented THA jeopardized by patients being overweight?

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Abstract
Although the effect of being overweight on the long- and short-term outcome of THA remains unclear, the majority of orthopaedic surgeons believe being overweight negatively influences the longevity of a hip implant. We asked whether complications and long-term survival of cemented THA differed in overweight patients (body mass index [BMI] > 25 kg/m²) and obese patients (BMI > 30 kg/m²) compared with normal-weight patients (BMI < 25 kg/m²). We retrospectively analyzed 411 consecutive patients (489 THAs) treated with cemented THA between 1974 and 1993. Except for cardiovascular comorbidity, we observed no differences in demographics among these weight groups. We found no differences in the number of intraoperative or postoperative complications. The survival rates for the three BMI groups were similar. The 10-year survival for any revision was 94.9% (95% confidence interval, 91.6%–98.2%), 90.4% (95% confidence interval, 85.6%–95.2%), and 91% (95% confidence interval, 81.2%–100%) for normal-weight, overweight, and obese patients, respectively. Cox regression analysis showed BMI and weight had no major influence on survival rates. The differences in mean Harris hip score at final follow-up were 4.8 between normal-weight and overweight patients and 7.1 between normal-weight and obese patients. Being overweight and obesity had no influence on perioperative complication rates in this cohort and did not negatively influence the long-term survival of cemented THA.

Introduction
Whether being overweight influences the fate of a THA is still debated. One study suggests obese patients are more likely to undergo THA for osteoarthritis (OA) of the hip than control patients with lower body mass index (BMI). Therefore, it is important for the orthopaedic surgeon who is planning the joint arthroplasty to know the effect of obesity on the fate of THA. Although being overweight or obese have a negative influence on health and mobility, it is not certain whether they have a negative influence on the short- and long-term results after THA as well.

The assumption that being overweight or obese negatively influences the long-term survival of THA could preclude some obese patients from having joint arthroplasty. Recently, the Wall Street Journal mentioned more orthopaedic surgeons refuse to perform THA in obese patients because of the fear of complications. A large international survey of orthopaedic surgeons performed in 12 European countries revealed 80.9% believe the long-term outcome of THA is impaired by being overweight. Several short-term outcome studies, summarized in two reviews, however, failed to show a negative influence of obesity on the short-term results of THA.

We asked whether obesity influences the long-term survival, clinical outcomes scores, and perioperative complication rates. We also asked whether BMI and body weight were risk factors for revision.

Materials and Methods
We retrospectively reviewed the medical records of 411 consecutive patients (489 hips) who underwent primary THA between 1974 and 1993. We divided our patients into three groups based on body mass index (BMI) at the time of surgery: (i) patients with a normal body weight (BMI < 25 kg/m²); (ii) patients who were overweight (BMI > 25 kg/m²); and (iii) patients who were morbidly obese (BMI > 30 kg/m²). One hundred sixty-three patients (201 hips [35%]) had a normal body weight. One hundred forty-two patients (172 hips [35%]) had a BMI greater than 25 kg/m² and 35 (42 hips [9%]) of these patients had a BMI greater than 30 kg/m². For 106 patients (116 hips [24%]), no BMI (weight and/or height) was documented. One hundred sixty-three patients (201 hips [35%]) had a BMI greater than 25 kg/m² and 35 (42 hips [9%]) of these patients had a BMI greater than 30 kg/m². For 106 patients (116 hips [24%]), no BMI (weight and/or height) was documented preoperatively. To avoid selection bias, these patients were included in the overall (survival) analysis. During follow-up, 164 patients (184 hips) died after a minimum follow-up of 1 year (mean, 11.6 years; range, 1–29.3 years) and an additional 37 patients (50 hips) were lost to follow-up after a minimum follow-up of 0.1 year (mean, 6.8 years; range, 0.1–15.6 years). These patients are included in the survival analysis and radiographic analysis until their last outpatient clinic contact. Of these patients lost to follow-up, two had a BMI greater than 30 kg/m², eight had a BMI greater than 25 kg/m², and 12 had a normal BMI; for 16 patients, no BMI was documented.

Sample size power analysis was performed assuming a 10-year survival rate of 95% in normal-weight individuals. We assumed a difference of 10% survival rate in overweight patients was of clinical importance. When using a power of 0.8 and an alpha of 0.05, a sample size of 159 hips is needed per group. Our number of patients with a BMI greater or less than 25 kg/m² therefore seems sufficient.

For maximum follow-up, 210 patients (255 hips) were available. The minimum follow-up in these 210 patients was 10 years (mean, 14.9 years; range, 10–28.1 years). We then compared long-term survivorship, functional outcome, and
perioperative complication rate. The average age at the time of surgery was 67 years (range, 22–88 years). One hundred seventeen (24%) of these patients were male (Table 1). The indication for THA was idiopathic OA in 235 hips (48%), acetabular dysplasia in 165 hips (34%), rheumatoid arthritis in eight (2%), avascular necrosis in 30 (6%), posttraumatic in 23 (5%), and other causes in 28 (4%). Apart from cardiologic comorbidity, which occurred more often in overweight and obese patients (Fisher’s exact test, \(p = 0.028\) for BMI > 30 kg/m\(^2\) versus BMI < 30 kg/m\(^2\) and \(p = 0.044\) for BMI > 25 kg/m\(^2\) versus BMI < 25 kg/m\(^2\)), we observed no differences between the patients who were obese or overweight and the normal-weight patients (Table 1).

The average BMI of all patients was 25.3 kg/m\(^2\) (range, 17.9–41.1 kg/m\(^2\)). The same prosthetic implant and surgical procedure were used in all patients. All patients were placed in a supine position and all had an anterolateral approach and a cemented Weber Rotation THA System (Allopro, Baar, Switzerland) implanted. The stem and the nonhighly crosslinked polyethylene Weber socket were cemented using low-viscosity Sulfix (Sulzer AG) cement. Until the 1980s, we used two types of cups, a flat type and a hemispheric type. Because of the inferior results of the flat type, their use was discontinued. In this study, 112 flat type and 377 hemispheric type sockets were used. The percentages of flat cups used were not different among the weight groups.

We (DH, RKM, FHrDM) obtained Harris hip scores (HHS) for patients whose THA was not revised at final follow-up. We (DH, FHrDM) performed a radiographic analysis using the weightbearing pelvic and lateral radiographs taken at the latest follow-up. Loosening of the stem was ranked according to Harris et al.\(^\text{11}\) and loosening of the cup according to Hodgkinson et al.\(^\text{12}\) For both components, loosening was scored as definitive, probable, possible, or no loosening. Loosening was scored by comparing the radiographs at last follow-up with previous radiographs. Complications were retrieved from the clinical charts. We noted the presence of hematoma when patients underwent exploratory surgery for suspected hematoma. Early infection was defined as requiring antibiotic treatment and/or debridement within 3 months after the operation.

A survival analysis was performed using the Life Table Method using revision for aseptic loosening, revision for any reason, and radiographic loosening (definitive loosening) as end points. We performed survivorship analysis for the acetabular and femoral component separately and for both components combined. Because all patients were seen annually or biannually, all could be included in the survival analysis until their last follow-up. Equality of the survival curves for the normal-weight, overweight, and obese patients were compared using a log rank test. Differences in HHS among the three study groups were evaluated using analysis of variance. A difference greater than 4 points was considered clinically important.\(^\text{13}\)

<table>
<thead>
<tr>
<th>Demographics and comorbidity</th>
<th>BMI &lt; 25 kg/m(^2) (n = 201 hips)</th>
<th>BMI &gt; 25 kg/m(^2) (n = 172 hips)</th>
<th>p Value*</th>
<th>BMI &gt; 30 kg/m(^2) (n = 42 hips)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, (range)</td>
<td>65.0 (21-83)</td>
<td>65.7 (22-87)</td>
<td>0.50</td>
<td>64.0 (49-79)</td>
<td>0.56</td>
</tr>
<tr>
<td>Idiopathic OA, (percent)</td>
<td>90 (44.8%)</td>
<td>82 (42.7%)</td>
<td>0.46</td>
<td>23 (54.8%)</td>
<td>0.22</td>
</tr>
<tr>
<td>Female, (percent)</td>
<td>152 (75.6%)</td>
<td>134 (69.8%)</td>
<td>0.63</td>
<td>30 (71.4%)</td>
<td>0.84</td>
</tr>
<tr>
<td>Comorbidity Central nervous system</td>
<td>14 (7.0%)</td>
<td>17 (8.9%)</td>
<td>0.35</td>
<td>5 (11.9%)</td>
<td>0.33</td>
</tr>
<tr>
<td>Respiratory</td>
<td>11 (5.5%)</td>
<td>10 (5.2%)</td>
<td>1.0</td>
<td>5 (11.9%)</td>
<td>0.16</td>
</tr>
<tr>
<td>Cardiovascular §</td>
<td>43 (21.4%)</td>
<td>51 (26.6%)</td>
<td>0.07</td>
<td>16 (38.1%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8 (4.0%)</td>
<td>9 (4.7%)</td>
<td>0.62</td>
<td>4 (9.5%)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Table 1. Demographic data per BMI group shown in number and percentage. *p Values show comparison with the group with a BMI of less than 25 kg/m\(^2\). Age was compared using a Student’s t-test; § Cardiovascular comorbidity is higher (\(p < 0.05\)) in the group with a BMI of greater than 30 kg/m\(^2\); for all the other demographic data, no differences were found using a Fisher’s exact test; BMI = body mass index.
We also compared BMI as a continuous variable with the HHS at maximum follow-up by means of Pearson correlation analysis to explore the overall influence of BMI on outcome. Differences in loosening between the normal-weight, overweight, and obese patients were evaluated using Fisher’s exact test. Differences in perioperative and postoperative complications were compared using Fisher’s exact test. Cox regression analysis was performed for survival of the implant (any revision) with weight and BMI as risk factors.

Results
We observed no differences between the survival rates for normal-weight patients and overweight patients and morbidly obese and normal-weight patients for all end points using a log rank test (Table 2, Fig. 1). Fifty-four patients (64 hips) underwent revision surgery, of which five hips were revised for septic loosening, 54 for aseptic loosening of at least one of the components, and five for other reasons (periprosthetic fractures and heterotopic ossifications). The rate of infection causing septic loosening was similar in patients with a BMI of between 25 kg/m$^2$ and 30 kg/m$^2$ (n = 4) and with a normal body weight (n = 1) (p = 0.13).

Patients with a BMI greater than 30 kg/m$^2$ had lower (p = 0.02) HHS than patients with a BMI less than 25 kg/m$^2$ and patients with a BMI greater than 25 kg/m$^2$ had lower (p = 0.02) HHS than patients with a BMI less than 25 kg/m$^2$ (Table 3). The differences in average HHS between the three groups were greater than 4 points, indicating these differences were clinically relevant. Body mass index showed a poor correlation (rho = -0.17; p = 0.024) with HHS.

Several local and systemic complications occurred, which were similarly distributed among the normal-weight, overweight, and obese patients (Table 4). We observed no differences in the rates of radiographic loosening among the normal-weight versus overweight patients (p = 0.30) and normal-weight versus obese patients (p = 0.47) (Table 5). Body mass index and body weight were not risk factors for revision (Exp[B] = 1.00 [95% confidence interval, 0.93–1.08] and Exp[B] = 1.01 [95% confidence interval, 0.99–1.03], respectively).
<table>
<thead>
<tr>
<th>Number at risk and revisions</th>
<th>All</th>
<th>BMI &lt; 25 kg/m²</th>
<th>BMI &gt; 25 kg/m²</th>
<th>BMI &gt; 30 kg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number at risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At start</td>
<td>489</td>
<td>201</td>
<td>172</td>
<td>42</td>
</tr>
<tr>
<td>At 10 years</td>
<td>336</td>
<td>161</td>
<td>122</td>
<td>30</td>
</tr>
<tr>
<td>At 15 years</td>
<td>181</td>
<td>92</td>
<td>69</td>
<td>14</td>
</tr>
<tr>
<td>At 20 years</td>
<td>49</td>
<td>29</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>Any revision</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 10 years</td>
<td>92.4% (89.8-95.0)</td>
<td>94.9% (91.6-98.2)</td>
<td>90.4% (85.6-95.2)</td>
<td>91.0% (81.2-100)</td>
</tr>
<tr>
<td>At 15 years</td>
<td>83.7% (79.4-88.0)</td>
<td>85.9% (80.0-91.8)</td>
<td>83.1% (76.2-90.0)</td>
<td>79.5% (61.5-97.4)</td>
</tr>
<tr>
<td>At 20 years</td>
<td>72.6% (64.5-96.4)</td>
<td>75.6% (65.5-85.6)</td>
<td>68.3% (53.0-83.6)</td>
<td>79.5% (61.5-97.4)</td>
</tr>
<tr>
<td>Aseptic stem loosening</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 10 years</td>
<td>95.1% (92.9-97.2)</td>
<td>96.6% (93.9-99.3)</td>
<td>94.2% (90.3-98.1)</td>
<td>91.0% (81.2-100)</td>
</tr>
<tr>
<td>At 15 years</td>
<td>89.3% (85.7-92.9)</td>
<td>91.4% (86.6-96.2)</td>
<td>87.5% (81.1-93.9)</td>
<td>79.5% (61.5-97.4)</td>
</tr>
<tr>
<td>At 20 years</td>
<td>84.1% (78.1-90.0)</td>
<td>85.2% (76.4-94.0)</td>
<td>82.7% (73.8-91.6)</td>
<td>79.5% (61.5-97.4)</td>
</tr>
<tr>
<td>Aseptic cup loosening</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 10 years</td>
<td>96.9% (95.1-98.6)</td>
<td>97.7% (94.4-100)</td>
<td>97.2% (94.5-99.9)</td>
<td>97.1% (91.4-100)</td>
</tr>
<tr>
<td>At 15 years</td>
<td>90.0% (86.4-93.5)</td>
<td>89.6% (84.3-94.9)</td>
<td>91.5% (85.9-97.1)</td>
<td>84.9% (67.5-100)</td>
</tr>
<tr>
<td>At 20 years</td>
<td>79.9% (72.3-98.5)</td>
<td>79.4% (69.7-89.0)</td>
<td>80.0% (66.4-93.6)</td>
<td>84.9% (67.5-100)</td>
</tr>
<tr>
<td>Aseptic loosening, both components</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 10 years</td>
<td>94.0% (91.6-96.0)</td>
<td>96.0% (93.1-98.9)</td>
<td>92.8% (88.5-97.1)</td>
<td>91.0% (81.2-100)</td>
</tr>
<tr>
<td>At 15 years</td>
<td>85.9% (81.8-90.0)</td>
<td>86.7% (80.8-92.6)</td>
<td>86.1% (79.4-93.0)</td>
<td>79.5% (61.5-97.4)</td>
</tr>
<tr>
<td>At 20 years</td>
<td>74.5% (66.3-82.7)</td>
<td>85.2% (76.4-94.0)</td>
<td>70.8% (55.1-86.5)</td>
<td>79.5% (61.5-97.4)</td>
</tr>
</tbody>
</table>

Table 2. Survival rates. Values are expressed as percentages, with 95% confidence intervals in parentheses; BMI = body mass index
Is the long-term outcome of cemented THA jeopardized by patients being overweight?  

De Man

Fig 1A-C. Survival rates are shown for patients with (A) a BMI less than 25 kg/m², (B) a BMI greater than 25 kg/m², and (C) a BMI greater than 30 kg/m². The x-axis shows years and the y-axis shows survival rates. The solid line represents survival rate and the dotted lines represent the 95% confidence intervals.
BMI < 25 kg/m² | BMI > 25 kg/m² | BMI > 30 kg/m²
---|---|---
91.6 (89.3-93.9) | 86.8 (83.5-90.1)* | 83.7 (74.5-92.3)*

Table 3. Average Harris hip score per BMI group. Values are expressed as averages, with 95% confidence intervals in parentheses; * difference with group with a BMI of less than 25 kg/m² (p = 0.02); BMI = body mass index.

<table>
<thead>
<tr>
<th>Complication</th>
<th>All (n = 489 hips)</th>
<th>BMI &lt; 25 kg/m² (n = 201 hips)</th>
<th>BMI &gt; 25 kg/m² (n = 172 hips)</th>
<th>p Value*</th>
<th>BMI &gt; 30 kg/m² (n = 42 hips)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous thromboembolism</td>
<td>2 (0.4%)</td>
<td>1 (0.5%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cardiac</td>
<td>61.2%</td>
<td>1 (0.5%)</td>
<td>4 (2.3%)</td>
<td>1.0</td>
<td>2 (4.8%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Respiratory</td>
<td>30.6%</td>
<td>1 (0.5%)</td>
<td>1 (0.6%)</td>
<td>1.0</td>
<td>1 (2.4%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Abdominal</td>
<td>40.8%</td>
<td>2 (1%)</td>
<td>1 (0.6%)</td>
<td>1.0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other systemic (including urinary tract infection)</td>
<td>18 (3.7%)</td>
<td>8 (4.0%)</td>
<td>9 (5.2%)</td>
<td>0.62</td>
<td>1 (2.4%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Hematoma</td>
<td>10 (2.0%)</td>
<td>6 (3.0%)</td>
<td>2 (1.2%)</td>
<td>0.30</td>
<td>2 (4.8%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Early infection</td>
<td>5 (0.8%)</td>
<td>2 (1.0%)</td>
<td>3 (1.7%)</td>
<td>0.67</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Intraoperative complication</td>
<td>24 (4.9%)</td>
<td>11 (5.5%)</td>
<td>11 (6.4%)</td>
<td>0.67</td>
<td>2 (4.8%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Any complication</td>
<td>68 (13.9%)</td>
<td>30 (14.9%)</td>
<td>28 (16.3%)</td>
<td>0.78</td>
<td>6 (14.3%)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Table 4. Complications per BMI group. *p Values are given for the comparison with the group with a BMI of less than 25 kg/m² (Fisher exact test); BMI = body mass index.

<table>
<thead>
<tr>
<th>Component</th>
<th>Definitive loosening</th>
<th>Probable loosening</th>
<th>Possible loosening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetabular*</td>
<td>2</td>
<td>18.3 (18.2-18.3)</td>
<td>2</td>
</tr>
<tr>
<td>Femoral**</td>
<td>6</td>
<td>18.9 (15.9-22.6)</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 5. Radiographic analysis of the unrevised hips. Values are expressed as averages, with ranges in parenthesis; * according to the criteria of Hodgkinson et al.12; ** according to the criteria of Harris et al.11

Fig 2. A scatterplot shows HHS versus BMI. The ceiling effect of the HHS can be seen.
Is the long-term outcome of cemented THA jeopardized by patients being overweight? | De Man

Discussion
The influence of being overweight on the long- and short-term outcome of THA is controversial in the literature but the majority of orthopaedic surgeons believe being overweight negatively influences the longevity of a hip implant9. Because the issue is controversial, we asked whether obesity influences the long-term survival, clinical outcomes scores, and perioperative complication rates, and whether BMI and body weight were risk factors for revision.

We note several limitations of our study. First, we did not study wear. It could be hypothesized that more body weight causes more wear. Although it can be expected that excessive wear may influence the rate of revision, we did not see a difference in revision rates between the weight groups14. Second, we studied only patients with cemented THA. Our analysis may not be valid for uncemented THA. One study of 300 patients with the cementless PM prosthesis suggested obesity negatively influenced medium-term survival, showing a twofold increase in loosening/revision rate in obese patients3. Another recent study suggested no difference in the outcome of uncemented THA in obese versus normal-weight patients, although a high revision rate for the acetabular component was present15.

Our data suggest BMI and weight do not influence the long-term survival of cemented THA. We also found no differences in the incidence of THA-related complications for the overweight patients undergoing THA. Cardiovascular comorbidity was more common in the obese patients; however, we observed no differences in perioperative cardiac complications. The percentage of overweight and obese individuals in our study is lower than those reported in American studies. In a study including 1071 American patients undergoing THA, 36% of the patients had a BMI greater than 30 kg/m²16. In The Netherlands, the annual incidence of obesity (BMI > 30 kg/m²) gradually inclined from 5% in 1981 to 7% in 1993 and 10% in 200517. In our study, 9% had a BMI greater than 30 kg/m². For the overweight patients (BMI > 25 kg/m²), these percentages were 33% in 1981 and 37% in 1993 and 35% in our study. Because OA is more common in overweight patients, we believe these percentages indicate our patient group is comparable to the average Dutch population1. This also indicates absence of a selection bias. All patients were operated on in our hospital regardless of their weight. Another major difference between our Dutch population and the American population is that extreme obesity (BMI > 40 kg/m²) was low in our country before 1993. We had only two patients who had a BMI greater than 40 kg/m² (neither had revision and had HHS of 87 and 90).

This low number of patients with a BMI greater than 40 kg/m² means our study does not supply an answer for the long-term fate of THAs in these extremes.

Several publications report on the short-term results of THA in the obese in which the HHS after surgery are compared between obese and normal-weight patients. The literature contains controversial data suggesting either similar or worse outcomes for obese patients undergoing THA. Two large studies reported lower HHS in obese patients after short-term follow-up18, 19. Both showed lower HHS with an average difference of 5 points, but neither compared the preoperative HHS among the different groups. The clinical relevance of these small differences in the postoperative HHS without a comparison of the preoperative HHS is debatable, especially because other studies showed no differences in postoperative HHS between the several weight groups20. Another study suggested the level of activity is lower, which continues to be so after THA21. The same problem occurs in our study because no preoperative HHS was available for analysis. If patients who are more obese have initial lower HHS and similar improvement as normal-weight patients after the arthroplasty, the same difference remains. Although our data suggest differences between the average HHS in the weight groups, the differences between the mean HHS were small (4.8 and 7.1). However; the only study on the responsiveness and discriminative ability of the HHS showed a difference of 4 points is enough to be clinically relevant, indicating our measured differences are clinically relevant22. However, the correlation of HHS with BMI as a continuous variable was poor (rho = -0.17), but the content validity of the HHS is poor, e.g., a large ceiling effect is visible, which could influence the correlation coefficient measured (Fig. 2).

In a review of patient characteristics affecting the outcome of THA, a body weight greater than 70 kg was mentioned as a factor that negatively influences the outcome of THA22. They suggest weight alone is a much stronger predictor for the outcome than BMI because height has no influence on the prosthesis. In our series, neither body weight nor BMI influenced outcome. One study stated patients who underwent bariatric surgery before having THA had an excellent outcome, although the average postoperative BMI of 29 kg/m² still indicated overweight. The main question we would ask is whether the outcome would have been worse if no bariatric surgery was performed23.

4. Furthermore, a BMI > 40 kg/m² may not represent equal body weight, because other studies showed no differences in postoperative HHS between the several weight groups. Another study suggested the level of activity is lower, which continues to be so after THA21. The same problem occurs in our study because no preoperative HHS was available for analysis. If patients who are more obese have initial lower HHS and similar improvement as normal-weight patients after the arthroplasty, the same difference remains. Although our data suggest differences between the average HHS in the weight groups, the differences between the mean HHS were small (4.8 and 7.1). However; the only study on the responsiveness and discriminative ability of the HHS showed a difference of 4 points is enough to be clinically relevant, indicating our measured differences are clinically relevant22. However, the correlation of HHS with BMI as a continuous variable was poor (rho = -0.17), but the content validity of the HHS is poor, e.g., a large ceiling effect is visible, which could influence the correlation coefficient measured (Fig. 2).

In a review of patient characteristics affecting the outcome of THA, a body weight greater than 70 kg was mentioned as a factor that negatively influences the outcome of THA22. They suggest weight alone is a much stronger predictor for the outcome than BMI because height has no influence on the prosthesis. In our series, neither body weight nor BMI influenced outcome. One study stated patients who underwent bariatric surgery before having THA had an excellent outcome, although the average postoperative BMI of 29 kg/m² still indicated overweight. The main question we would ask is whether the outcome would have been worse if no bariatric surgery was performed23.
We do not intend to suggest being overweight has no risks. We believe it is important to motivate overweight patients to lose weight. Being overweight could increase the rate of OA and has an increased risk for several nonorthopaedic morbidities\(^7\). However, should a (cemented) THA be necessary in an overweight or obese patient, the arguments that survival is shorter in obese patients and that obese patients have a higher risk of perioperative complications do not seem valid.

Reference List


Chapter 11

Functional and radiological outcome after revision for prosthetic hip joint infection

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SUBMITTED
Abstract
Successful management of periprosthetic joint infection (PJII) includes both eradication of infection and maintaining functional mobility. At our institute, an algorithm for the different surgical treatment options of PJII has been established. In this cohort study, we analyzed the functional, radiological, and microbiological outcome of 70 patients (72 episodes) who had a hip-revision due to PJII, they underwent a one-stage exchange [1-SE] (n=22) or a two-stage exchange [2-SE] (n=50). All patients were treated strictly according to the algorithm. For 1-SE, we hypothesized that functional and radiological outcome would be similar to a matched group of patients who had been revised for aseptic loosening. After 1-SE, the mean Harris hip score was 84, incidence of limping 20%, and use of two crutches 10%. Two stems were revised for aseptic loosening. In general, the results were equal to those of the matched group. After 2-SE, results were 80, 30% and 28%, respectively. Two stems and three cups were revised for aseptic reasons. The functional outcome after 2-SE was slightly worse, but these patients had a more complex a priori situation. Regression analysis showed a poorer functional outcome in case of (i) a pre-existent deficient trochanter and (ii) a history of increased acetabular revisions with the need for a Burch-Schneider ring. One relapse of infection occurred in the 2-SE group. Adherence to our previously published algorithm leads to a successful outcome in both eradicating infection and maintaining functional mobility. However, results indicate that functional outcome might be improved if adequate surgical treatment were performed a priori.

Introduction
Infections associated with prosthetic joints cause significant morbidity and account for a substantial proportion of health care expenditures. The use of perioperative antimicrobial prophylaxis and laminar airflow surgical environment has reduced the risk of intraoperative infection to less than one percent after primary hip replacement. However, after revision arthroplasties, the risk is estimated to be between 4 and 6%. In our clinic over the past 25 years, in this concept, surgical therapies include debridement with retention, one-stage exchange (1-SE), or two-stage exchange (2-SE) with or without spacer, and excision without replacement. The decision for the particular surgical therapy is based on (i) duration of clinical signs and symptoms, (ii) stability of the implant, (iii) condition of the soft tissue, and (iv) antimicrobial susceptibility of the microorganism. Adherence to this treatment concept has shown a success rate of 86-100% in curing the infection, both at our institute and other hospitals. However, the functional outcome has not yet been evaluated. The importance of functional outcome is of major interest, in particular in studies for aseptic complications. Moreover, patient satisfaction after hip surgery is highly influenced by the functional result. Finally, a treatment concept for prosthetic joint-associated infection, irrespective of its success in curing infection, loses its significance if functional outcome is unknown or even poor.

We have previously observed that the functional outcome of surgical therapy for periprosthetic joint infection is good. Therefore, we hypothesized that the functional and radiological outcome after hip prosthesis exchange due to an implant-associated infection would be similar to that due to aseptic loosening. We compared various parameters in patients that were treated with a 1-SE due to a prosthetic hip joint-associated infection (PHJI) with those in patients that were treated with a 1-SE due to aseptic loosening.

A 2-SE requires a more complex surgical procedure than 1-SE, and hence, potentially could lead to poorer functional outcome. In order to evaluate this hypothesis, the same parameters were compared in patients treated with a 2-SE due to a PHJI with those in patients with 1-SE for septic loosening. For all patients, various variables were screened by multiple regression analysis for an association with functional impairment at follow-up. Finally, for the 1-SE and 2-SE group, we evaluated outcomes in terms of infection eradication.
Patients, Materials and Methods

Diagnosis of PHJI
In addition to clinical signs such as pain, effusion, erythema, induration, edema, and sinus tract at the implant site, the growth of the same microorganism in at least two cultures of synovia and/or periprosthetic tissue was required. Histopathological examinations of periprosthetic tissue as well as imaging studies (including arthrography) were used to establish diagnosis. In referred patients who were surgically or medically pretreated in another center, external charts were also reviewed for the above mentioned parameters.

Patients
Between 1985 and 2004, a total of 101 episodes (97 patients) from our cohort were treated with an exchange of the components of the hip arthroplasty due to an implant-associated infection. To evaluate the functional and radiological outcome of our previously published algorithm, we only included PHJI episodes that were treated strictly according to this protocol and could be clinically followed for at least 2 years.

Decision making on surgical procedure in PHJI
The following criteria were considered as an indication for joint replacement: (a) clinical symptoms that lasted more than three weeks, (b) unstable prosthesis, (c) moderately or severely compromised soft-tissue, and (d) presence of difficult-to-treat microorganism (e.g., methicillin-resistant Staphylococcus aureus, Pseudomonas spp., fungi, or any multidrug-resistant bacteria). A 1-SE was chosen when the condition of the soft-tissue was intact and a difficult-to-treat microorganism was absent. In case of compromised soft-tissue, a 2-SE with a spacer was performed. In infections with difficult-to-treat microorganisms, a 2-SE without a spacer was carried out, irrespective of the condition of the soft-tissue or duration of symptoms.

Surgical technique and index operation
Index operation was defined as the first operation due to infection in our center with removal or exchange of the implant. Hip reconstruction was done with the same implants as would have been used in case of an aseptic revision, independent of 1-SE or 2-SE. For reconstruction of the acetabulum, an uncemented cup (SL-Müller cup [Zimmer, Warsaw, IN]), a reinforcement ring (Müller, [Zimmer, Warsaw, IN]) or an antiprotrusio ring (Burch-Schneider [BS-ring], [Zimmer, Warsaw, IN]) was used with morcellized autograft for small defects and/or slices of allograft for larger defects. For reconstruction of the femur, an uncemented titanium stem (Wagner SL, [Zimmer, Warsaw, IN]) or a cemented (Gentamicin palacos) stem (Müller-straight stem, CDH, Virtec, [Zimmer, Warsaw, IN]) was used. Patients were operated upon in a supine position through a straight lateral approach often in combination with a transfemoral osteotomy according to Wagner and Wagner. After removal of the components, a thorough debridement was performed. In case of 2-SE without spacer, either a supracondylar extension or no device was used.

Control group
For comparison, we selected 22 patients (22 episodes) out of 474 consecutive revisions due to aseptic loosening who matched with patients treated with a 1-SE for PHJI. Patients were matched with decreasing order of importance for previous surgery (on trochanter, number of revisions of the cup, number of revisions of the stem), type of implant, use of transfemoral osteotomy, Charnley score, length of follow-up, age, and sex.

Antimicrobial treatment
In general, antimicrobial treatment was administered as previously described and according to the selected pathway of the algorithm. Because functional outcome is the main scope of this analysis, duration of antimicrobial treatment was not included as an outcome variable.

Follow-up
Patients were followed prospectively after 6 weeks, three months, six months, one year, two years and every five years thereafter. To establish the functional outcome, the Harris hip score was calculated and the presence of limping and the use of a support were recorded. These parameters were analyzed at the 2-year follow-up. To evaluate radiological outcome, the AP pelvis, whole femur and femur faux–profiles X-rays were scrutinized for signs of loosening. For the acetabular component the classification according to Gill et al. was used, in which components are considered to be (i) definitely loose if screws are broken, or if a complete, progressive radiolucent line medial or superior to the component or around the screws is present, or if there is evidence of migration of the component or a fracture of cement is present; (ii) probably loose if an incomplete progressive radiolucent line medial or superior to the component is present; and (iii) possibly loose if a nonprogressive radiolucency is present that does not involve the screws.
For the femoral component, the classification according to Harris17 was used. Migration of components, including subsidence of stems, was measured using bone reference points as described by Callaghan18. In case of osteotomy, images were screened for signs of pseudoarthrosis. Radiological parameters were analyzed on the latest available radiograph, irrespective of its relation to the clinical investigations. The infection was considered ‘cured’ when there were no clinical or radiological signs of infection present 2 years or longer after implantation. Relapse was defined as an infection with the same pathogen. Re-infection was defined as an infection with a different microorganism.

Study Outcomes

Primary endpoints included revision for (i) aseptic loosening, (ii) for any other reason, and (iii) for relapse. The endpoint for radiological outcome included definitive loosening of the stem, definitive loosening of the cup, or subsidence of the stem more than 3 mm.

Statistics

Comparison between groups for descriptive variables, surgical specifics, and clinical and radiological outcomes were conducted with chi square and the Student’s t-test. For non-parametric data the Mann-Whitney U test was used. Multiple regression analysis (ANOVA) was used to identify patient characteristics and surgical factors that would influence functional results. Calculations were made with the statistical software SPSS 15.0 (Microsoft) and statistical significance was set at p < 0.05

Results

Patient demographics and surgical procedure

In total, 29 out of 101 episodes were excluded. Reasons for exclusion are illustrated in Fig. 1. Therefore, 72 episodes of PHJI were included in this study, and consisted of 22 which were treated with a 1-SE, and 50 with a 2-SE (29 with spacer, 21 without spacer). In total, 71% of patients of the included episodes were referred cases. Our own cases qualified more often for a 1-SE than the referred cases (48% versus 23%; p = 0.04). Patient demographics, Charnley classification, surgical history, type of bone defects, prevalence of trochanter deficiencies, surgical specifics and mean time from index operation to follow-up were similar in the 1-SE and control group and are presented in Table 1,2 and 3.
Functional and radiological outcome after 1-SE due to infection is similar to that due to aseptic loosening.

At the 2-year of clinical follow-up, the incidence of limping, the use of a support, and the HHS (84 for 1-SE and 85 for the control group) were similar in both groups (Table 3). During the follow-up period, revision due to aseptic loosening was required in two episodes (one Wagner stem and one Virtuc stem) of the 1-SE group, and in one episode (Wagner stem) in the control group (after 0.8, 2.8 years and 4 years, respectively). No cups were revised in either group.

The mean radiological follow-up in the 1-SE group was 3.1 years (range 0.6-9.3) and in the control group 4.6 years (range 0.4-10). Apart from the three revised stems, no other stems showed signs of definitive loosening in either group. There was one possible stem loosening in the 1-SE group. For the acetabulum, in the 1-SE group, there was one probable loosening of a BS-ring. In the control group, two Müller reinforcement rings were definitely loose (however, the Harris hip scores were 100 and 95, respectively). All three cases did not require a revision.

There were no statistical differences between the 1-SE and the control group with regard to the number of cup or stem revisions, or the incidence of radiological cup or stem loosening (Table 3).

All transfemoral (12 episodes) and trochanteric (two episodes) osteotomies that were performed in both groups (Table 2) and all fissures of the proximal femur (4 episodes) that occurred during the index operation (Table 4), showed healing. One of the two trochanteric fractures developed a non-union.
<table>
<thead>
<tr>
<th></th>
<th>2-SE</th>
<th>1-SE</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of hips (patients)</td>
<td>50 (48)</td>
<td>22 (21)</td>
<td>22 (22)</td>
</tr>
<tr>
<td>Transglutal approach and no osteotomy</td>
<td>22</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Transglutal approach and transfemoral osteotomy</td>
<td>22</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Transglutal approach and greater trochanter osteotomy</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Transglutal approach and via pseudoarthrosis greater trochanter</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Spacer</td>
<td>29</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Acetabular component</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>SL-uncemented cup</td>
<td>24</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Müller reinforcement ring</td>
<td>23 †</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Burch-Schneider reinforcement ring</td>
<td>23 †</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Femoral component</td>
<td>27</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Uncemented</td>
<td>27</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Cemented</td>
<td>23</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Acetabular graft</td>
<td>27</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>No graft</td>
<td>9</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Autograft, morcellized</td>
<td>10</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Allograft, blocks &gt; 2 cm, slices</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Auto- and allograft</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 2. Surgical specifics. The 1-SE and control group were matched for all the listed items. † significant difference between the 2-SE and 1-SE group (p < 0.05, Mann–Whitney U test).
Functional and radiological outcome of 2-SE

At the two-year clinical follow-up, the mean HHS in the 2-SE group was 80, 30 patients had either no limp or only a slight limp, and 31 patients needed no support or only one crutch for walking. There were more disabled patients dependent on crutches and one patient was unable to walk than in the 1-SE group. Outcomes were lower than in the 1-SE group, but not significantly different (p = 0.26 for HHS; p = 0.09 for limping; p = 0.36 for use of support). A spacer did not influence HHSs (Table 3).

After the index operation, revision due to aseptic loosening was required in a total of 5 episodes in the 2-SE group: One Wagner and one Virtec stem showed definitive loosening after 4 months and one year, respectively, and were revised accordingly. One Müller reinforcement ring was revised after three years. In two cases with BS-rings, there was a capsular laxity with recurrent dislocation of the head. The cups were exchanged after three months c.q. one year, but the BS-rings were stable and remained in situ.

In addition to the two stems that were revised, there were two further episodes with definitive radiologic loosening: a loose Virtec stem caused minor complaints, and surgery was not possible due to the patient’s preconditions; a second patient died shortly after loosening of a Wagner stem was recognized. One stem showed possible loosening. For the acetabulum, besides the three revised cases, two BS rings showed definitive loosening: one patient additionally had severe symptoms resulting from a spinal stenosis, the other had only minor complaints and no revision surgery was indicated. There were subtle type I changes around 4 other components.

In comparison with the 1-SE group, there was no statistical difference with regard to the number of stem or cup revisions, nor to the incidence of radiological cup or stem loosening.

Two out of the 5 preexistent non-unions of the greater trochanter, one of the 22 transfemoral osteotomies, and one osteotomy of the greater trochanter that we performed did not heal (Table 2). All 5 fractures of the greater trochanter/proximal femur that occurred at the index operation (Table 4) healed.

Patients requiring a 2-SE had more surgical interventions prior to the index operation

Thirty-nine hips out of 50 (78 %) in the 2-SE group versus three hips out of 22 (14 %) in the 1-SE group had had previous surgery: they had more cup revisions for any reason (p < 0.01), more stem revisions for any reason (p = 0.01), more debridements for an (infected) hematoma (p < 0.01), and more trochanteric deficiencies (p < 0.05) (Table 1).

Risk factors for functional outcome

For the multiple regression analysis, all patients were considered together as one group. Increased limping was associated with a deficient greater trochanter (p = 0.01) and the use of a BS-ring (p = 0.03). There was a trend towards increased use of walking support when a trochanteric osteotomy (p = 0.052) had been performed, when there was a deficient trochanter (p=0.054), or when there was a history of increased number of cup revisions (p=0.06). A 2-SE, undergoing a transfemoral osteotomy, the use of a Wagner stem, the use of a spacer, and a history of increased stem revisions did not influence functional scores.

Complications

In the 2-SE group, two patients died shortly after the second operation as a result of an acute coronary heart disease and of pneumonia, respectively. In the 2-SE group there were more complications (p = 0.03), and a higher number of reoperations (p < 0.01) than in the 1-SE group (Table 4).

Microbiological outcome

Causative microorganisms are listed in Table 5. None of the episodes in the 1-SE group and only one episode in the 2-SE group experienced a treatment failure. The relapse with the same bacteria required again a 2-SE of both components without a spacer, 8 months after index operation.
### Table 4. Complications. † significant difference between the 2-SE group and the 1-SE/control group (p < 0.05, Mann-Whitney U test).

<table>
<thead>
<tr>
<th></th>
<th>2-SE</th>
<th>1-SE</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of hips (patients)</td>
<td>50 (48)</td>
<td>22 (21)</td>
<td>22 (22)</td>
</tr>
<tr>
<td>Number of perioperative complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fracture greater trochanter</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>fracture/fissura proximal femur</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>early death</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Number of postsurgery complications, necessitating reoperation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hematoma</td>
<td>17</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>superficial wound infection</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>pintract infection</td>
<td>1</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>dislocation of spacer</td>
<td>1</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>dislocation of hip</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>total number of reoperations</td>
<td>26 †</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Hospitalization related</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>trombo-embolic</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>miscellaneous</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

### Table 5. Causative microorganisms

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>2-SE</th>
<th>1-SE</th>
<th>Both groups (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>17</td>
<td>5</td>
<td>22 (28)</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci (CoNS)</td>
<td>8</td>
<td>10</td>
<td>18 (23)</td>
</tr>
<tr>
<td>Viridans group streptococci</td>
<td>3</td>
<td>3</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Beta-hemolytic streptococci</td>
<td>4</td>
<td>1</td>
<td>5 (6)</td>
</tr>
<tr>
<td>Gram-negative rods</td>
<td>5</td>
<td>3</td>
<td>8 (10)</td>
</tr>
<tr>
<td>Propionibacterium acnes</td>
<td>3</td>
<td>0</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Difficult-to-treat pathogens</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>7</td>
<td>/</td>
<td>7 (9)</td>
</tr>
<tr>
<td>Rifampin-resistant CoNS</td>
<td>1</td>
<td>/</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>4</td>
<td>/</td>
<td>4 (5)</td>
</tr>
<tr>
<td>MRSA</td>
<td>1</td>
<td>/</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Staphylococcus aureus small-colony-variants</td>
<td>2</td>
<td>/</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Abiotrophia adiacens</td>
<td>1</td>
<td>/</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Total number of pathogen cultured</td>
<td>56</td>
<td>22</td>
<td>78 (100)</td>
</tr>
</tbody>
</table>

| Number of episodes with negative cultures     | 2    | 1    | 3 (4)           |
| Number of polymicrobial episodes              | 8    | 2    | 10 (14)         |
Discussion

The main goals in the treatment of PHJI are to eradicate infection and to restore the functional integrity of the limb. Patient satisfaction after hip surgery is highly influenced by the functional result\(^9\), but in surgical treatment strategies reported for infection, functional results are rarely investigated\(^{19-22}\). Here, we have extensively analyzed the functional and radiological outcome of three pathways of an established algorithm for PJI, namely 1-SE, 2-SE with spacer and 2-SE without a spacer.

One limitation of the present study is that preoperative scores were not available. However, since many patients have had previous surgery and complaints due to an infection, such an assessment would most likely be unreliable. Another possible drawback is the use of various implants which might have influenced the functional results. However, in revision surgery, the variability in the local situation is significant, requiring an individual choice of the implant. In our surgical strategy, the choice of implant and technique is entirely dictated by the bony situation and by the surgeon’s preference rather than by the presence of infection.

An important feature of the technique we use is the safe removal of components, which can be achieved by a transfemoral osteotomy, e.g., as described by Wagner and Wagner\(^{13}\). In this series, such osteotomy was performed in 34 episodes (36%) out of the total of 94 revisions. In the 72 episodes of PHJI, it was used in 27 episodes (38%) and particularly for an infected patient, the possibility to perform a thorough debridement is an additional advantage. This technique, did not lead to a significant number of relapses, periprosthetic fractures, or non-unions. In combination with this osteotomy, we mainly used the uncemented Wagner SL stem. Frequent subsidence of this stem, as previously reported\(^{12,23,24}\), was not a problem in our series and accounted for 2 revisions. Acetabular defects were treated with reinforcement or antiprotrusio rings\(^{16,25}\). In our study, the incidence of loosening of acetabular and femoral components was low and similar to that of identical implants used in aseptic revision surgery with equal durations of follow-up\(^{26-28}\). However, it is important to acknowledge that these follow-ups have to be considered as medium term.

The traditional treatment concept for PHJI is a 2-SE (with or without spacer) with an up to 6 month interval\(^{21,29-36}\). Only recently has 1-SE have been advocated\(^{7,22,37-41}\). The advantages of 1-SE include lower perioperative morbidity, a shorter hospital stay, lower costs\(^1\), and earlier rehabilitation\(^42\). Yet, a higher recurrence rate has been suspected\(^{38,39}\).

Because our surgical technique was not influenced by the presence of infection, case-matching for 1-SE could be readily performed. In patients who were selected for 1-SE according to our algorithm, we found no differences in functional or radiological outcome, or in the number of revisions as compared to revisions without infection. In a report of 31 1-SE due to PHJI, the mean HHS was 75 after 3.5 years\(^43\). In a recent meta-analysis of 24 studies of aseptic revisions, a mean HHS of 81.5 after a mean follow-up of 4 years was found\(^8\). Our results are more favourable and may be explained by the design of the algorithm that selects the less complex cases that usually have no compromised soft tissues or bone stock. Our criteria for ‘surgical decision making’ select a less complex subpopulation of infected cases, suitable for 1-SE, in which not only infection is eradicated, but also functional and radiological outcome is similar to revision due to aseptic loosening.

On the other hand, our treatment protocol selects the more complex cases for a 2-SE. The HHS (80 in 2-SE versus 84 in 1-SE) and other functional scores were still at a high level and not significantly different compared to a 1-SE. However, a HHS with a difference of 4 points may be enough to be clinically important\(^{44}\), which is conceivable in our study due to complexity of the 2-SE cases. Still, our results are comparable to those of the literature, since HHS after 2-SE have been reported to range between 78 and 91\(^{19,21}\). However, in these studies, all PJI were treated with a 2-SE approach, including less complex cases which are considered suitable for 1-SE according to our algorithm. In contrast, our 2-SE episodes consisted of only cases with moderately or severely damaged soft-tissue, or with the involvement of a difficult-to-treat microorganism, and the higher number of previous surgery reflects the more complex preoperative condition. Yet, a comparison between studies would be difficult due to the variability in patient co-morbidity, number of previous (revision) surgeries, different length of follow-up and rate of re-infection\(^{15,42,45,46}\).
Difficult-to-treat microorganisms are even more difficult to eradicate in the presence of an implant. The main problem is the lack of an antimicrobial agent with activity on a surface adhering micro-organism and with good oral bioavailability. Therefore, the recommendation is the vigorous removal of all foreign material. We consequently avoided the use of a spacer in the presence of difficult-to-treat bacteria in order to prevent bacterial adherence to the newly inserted foreign device. It is commonly accepted that a spacer maintains functional mobility and makes re-implantation easier\textsuperscript{20,47}, moreover, the risk of hematoma in the dead space is diminished. Therefore, we preferred the use of a spacer in absence of a difficult-to-treat microorganism.

Patients who needed a 2-SE were mostly referred, and they had had more previous surgeries with the accompanying potential of damage the abductor system. Indeed, a higher incidence of greater trochanter deficiency was found in the 2-SE group. The increased use of BS-rings in the 2-SE group reflected the higher number of previous cup revisions and the more extensive bone defects.

Multiple regression analysis showed that trochanter deficiency and the use of a BS ring had an increased risk for limping. Whereas the presence of a deficient trochanter by impairment of the abductor apparatus can explain this finding, this is less clear for the presence of a BS-ring. It could be hypothesized\textsuperscript{49} that the exposure of the ileum might have damaged the anterior part of gluteus medius muscle or even the superior gluteal nerve\textsuperscript{49,50}. But patients with the BS-ring also had a more complex situation, and in 6 of the 14 patients with a deficiency of the greater trochanter a BS-ring has been implanted. Therefore, whether limping can be attributed solely to this type of ring remains questionable.

Not surprisingly, the more complex patients treated with a 2-SE experienced more complications than those who underwent a 1-SE. This can be partially explained by the high rate of previous surgery, the condition of the soft tissue prior to the index operation, and the more extended surgery.

To summarize, 1-SE was more frequently possible in our own than in the referred cases. Most of the episodes requiring a 2-SE had had previous surgery on the hip, hence presented with already compromised soft-tissue. We hypothesize that some of these cases could have been treated with a 1-SE a priori, instead of multiple unsuccessful trials of implant retention, ultimately resulting in 2-SE. In this series it has been shown that if the correct patient population is selected, 1-SE has a high cure-rate for infection, as was shown in previous reports\textsuperscript{6,7,22}. Moreover in 1-SE, we used the same surgical technique as in case of aseptic loosening and found almost identical functional and radiological outcomes. The use of a transfemoral osteotomy, as well as a 2-SE were not per se risk factors for a worse functional result. In contrast, a history of frequent acetabular revision with the subsequent need for large(r) acetabular rings, and the presence of a deficient greater trochanter at presentation, were both associated with a compromised functional outcome.

In conclusion, correct surgical strategy for PHJI should be defined early in order to avoid treatment failures and potential impairment of the functional outcome. In this study, strict adherence to the treatment algorithm provided a high rate of cure for PHJI while maintaining good functional mobility.
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Chapter 12

Broad-range PCR
in selected episodes of
prosthetic joint infection

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Abstract
Prosthetic joint infection (PJI) is associated with high morbidity and costs. For the diagnosis of PJI, the results of microbiological cultures are frequently used as the reference standard, but culture-independent molecular methods have been developed to improve the detection of the causative pathogen. Polymerase chain reaction (PCR) has yielded good results in detecting soft tissue infections. This study reviewed patient characteristics and the diagnostic value of PCR in 26 patients with 29 episodes of suspected PJI and their complex history: infection and/or multiple interventions for the same arthroplasty and/or antimicrobial treatment prior to presentation were evident in the majority of patients’ histories. The specificity and sensitivity for the bacterial culture were 71% and 58%; for PCR, 94% and 50%, respectively. The cumulative sensitivity of the combination of both methods was 67%. In this study, PCR showed a limited diagnostic value but helped to identify false-positive culture results in few episodes. The high expense and the limited diagnostic value of broad-range PCR in PJI argue against its routine use in addition to bacterial culture.

Introduction
Prosthetic joint infection (PJI) is, after aseptic loosening, the second most common cause of implant failure. PJI is associated with high morbidity and high health care expenditures. Successful outcome requires detection and identification of the causative pathogen(s) in order to select the appropriate antibiotic regimen. Current microbiology laboratory methods to diagnosis PJI depend on the detection of a pathogen by culture. However, the sensitivity of these methods is not ideal due to e.g., prior antimicrobial exposure, an inappropriate culture medium, or a low bacterial load. Furthermore, the specimen could be contaminated, decreasing specificity of tests. Therefore, culture-independent molecular methods have been used to improve the diagnosis of prosthetic joint infection. Polymerase chain reaction (PCR) is a molecular diagnostic method that enables replication and amplification of genetic (DNA) material. For the diagnosis of infection in the clinical setting, the target is usually the 16S ribosomal RNA gene, present in all bacteria. PCR has been used successfully to detect pathogens that cause organ and native joint infections. As an extension of these practices, several investigators have reported the use of PCR to diagnose PJI. However, a diagnostic advantage over the bacterial culture has as yet not been clearly established.

Materials and Methods
The study population consisted of patients with a joint prosthesis who were seen at our clinic between 2001 and 2005, and from whom specimens both for bacterial culture and PCR had been obtained, either when there was suspicion of PJI based on (i) clinical signs (joint pain, effusion, erythema and warmth at the implant site), elevated laboratory signs of inflammation, signs of implant loosening or (ii) the presence of a sinus tract or a reported purulence surrounding the component during a previous intervention. Patient history prior to the diagnostic intervention was assessed for (i) antimicrobial treatment, (ii) number of interventions performed on the affected arthroplasty, (iii) a confirmed and treated infection involving the affected joint within the previous 24 months, and (iv) implant loosening ≤ 12 months after implantation without other clinical signs of infection. Specimens (synovial fluid and/or biopsies from periprosthetic tissue) were obtained either during aspiration prior to surgery or during arthroscopy or open surgery. Bacterial culture and histopathologic diagnostics were performed as previously described. The decision whether or not to use PCR was made by the physicians in charge after reviewing patient history and prior to the intervention. However, they were not involved in either analyzing or interpreting the data. Specimens were sent to a reference laboratory for analysis. The broad-range PCR technique consisted of amplification of bacterial 16S ribosomal RNA. As a reference with which to compare test results, we used well-defined criteria for the diagnosis of definitive...
PJI. Infection was considered to be definite in case of the presence of one of the following: (i) clinical signs of infection in combination with laboratory or radiological signs of infection, (ii) a sinus tract communicating with the prosthesis, (iii) purulence surrounding the prosthesis at surgery, or (iv) acute or chronic inflammation consistent with infection on histopathologic examination19,22. Infection was excluded when none of the above-mentioned criteria had been fulfilled, no antimicrobial treatment had been administered after the episode, and no relapse had occurred for at least one year19.

Results
In 29 episodes (26 patients) with a suspicion of PJI, specimens for both PCR and bacterial culture had been obtained. This number accounted for 7.6% (23 episodes) of all revision arthroplasties (n = 301) and 6.8% (6 episodes) of all joint punctures (n = 88) during the study period. Patient characteristics are presented in table 1. Most episodes (48%) included a history of ≥ 3 surgical interventions (median 4, range 3-5) on the affected arthroplasty within a median time of 3.25 years (range 0.9-10.5) prior to the diagnostic intervention. The median number of specimens obtained per patient for bacterial culture was 5 (range 3-7) and for PCR 1 (range 1-2).

In 17 (59%) of the 29 episodes, no infection was present, although duration of follow-up was ≤ 12 months in 2 cases (4, 11 months) due to non-episode-related death and loss to followup. In all 17 cases with clinically excluded infection, PCR was negative. In contrast, there was bacterial growth in 5 episodes, but interpreted as contamination. In the infection episodes, one inaccurate PCR result was considered as false-positive. Based on these findings, the specificity for bacterial culture was 71% and that for PCR, 94%.

In 12 (41%) of the 29 episodes, criteria for PJI were fulfilled; these 12 episodes accounted for 8.5% of 142 confirmed PJI episodes (including 62% referred cases) during the study period. The results of bacterial culture and PCR are presented in table 2. In 5 episodes, both diagnostic methods identified the same microorganism. However, in 2 of these, PCR revealed only one pathogen, while two distinct microorganisms grew in culture. In 2 further episodes, the pathogen was identified either only by bacterial culture or only by PCR. Hence, the sensitivity for bacterial culture was 58% and that for PCR, 50%.
Discussion

Standard microbiological cultures are frequently used as the reference standard for diagnosing PJI. However, prior antibiotic treatment, low numbers of the organism, or fastidious pathogens may be responsible for false-negative results. The method of broad-range PCR is capable of detecting bacterial DNA, even when cultures are negative, and this technique has proven useful in the diagnosis of native joint infection. As a result, several investigators have addressed the usefulness of PCR in diagnosing PJI. Using this approach, while a high specificity (95% to 100%) has been reported, the sensitivity was often poor (≤ 50%), and the conclusion was that PCR provided no advantage over the standard cultures in diagnosing PJI.

From these studies, however, little information is available to select episodes in clinical practice for which PCR could be superior or complementary to bacterial culture to diagnose PJI. The previous history of the patients included in this study (table 1) highlights the importance of distinguishing PJI from other causes of joint failure. Therefore, it was reasonable to expand diagnostic means by an additional tool in these selected episodes.

Specificity was excellent in our selected episodes, in accordance to earlier studies. In all episodes with a previous history of multiple revisions or previously treated PJI, PCR remained negative when no infection was present. Also, in only 1 out of 6 episodes with early implant loosening (≤ 12 months after implantation) an infection was present without other clinical signs of PJI, and the PCR results matched accordingly. Importantly, in 5 episodes PCR was useful in identifying bacterial culture false-positives. The sensitivity of PCR in our study was poor (50%). The overall sensitivity in diagnosing PJI increased to 67% when both PCR and bacterial culture were considered together (i.e. one or other or both were positive).

Mariani et al. performed PCR on synovial fluid of 50 symptomatic TKAs and detected bacterial DNA in 60%, whereas standard tissue cultures revealed pathogen growth in only 30% of the cases. These results suggested that PCR is more sensitive in diagnosing PJI than standard cultures. However, the presence of PJI was not defined by well-formulated standard criteria, as was in our study; therefore it is possible that some PCR results were false-positive.

Table 2: Results of bacterial culture and broad-range PCR in 12 episodes of confirmed PJI.

<table>
<thead>
<tr>
<th>Episode</th>
<th>Sample origin</th>
<th>Bacterial culture number of positive/total number of specimens</th>
<th>Broad-range PCR number of positive/total number of specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Synovial fluid</td>
<td>2/2 Streptococcus pyogenes</td>
<td>1/1 Streptococcus pyogenes</td>
</tr>
<tr>
<td>2*</td>
<td>Periprosthetic tissue</td>
<td>2/13 Propionibacterium spp.</td>
<td>1/8 Streptococcus infantis</td>
</tr>
<tr>
<td>3</td>
<td>Synovial fluid</td>
<td>1/1 Staphylococcus aureus</td>
<td>Negative</td>
</tr>
<tr>
<td>4</td>
<td>Periprosthetic tissue</td>
<td>1 no growth</td>
<td>Negative</td>
</tr>
<tr>
<td>5</td>
<td>Periprosthetic tissue</td>
<td>1 no growth</td>
<td>Negative</td>
</tr>
<tr>
<td>6</td>
<td>Synovial fluid</td>
<td>1 no growth</td>
<td>1/1 Streptococcus bovis</td>
</tr>
<tr>
<td>7</td>
<td>Periprosthetic tissue</td>
<td>5/11 Staphylococcus aureus</td>
<td>1/1 Staphylococcus aureus</td>
</tr>
<tr>
<td>8</td>
<td>Periprosthetic tissue</td>
<td>6 no growth</td>
<td>2 negative</td>
</tr>
<tr>
<td>9</td>
<td>Periprosthetic tissue</td>
<td>6/9 Staphylococcus epidermidis</td>
<td>1/1 Staphylococcus epidermidis</td>
</tr>
<tr>
<td>10</td>
<td>Periprosthetic tissue</td>
<td>5/6 Pseudomonas aeruginosa</td>
<td>2/2 Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>11</td>
<td>Periprosthetic tissue</td>
<td>1/5+ Staphylococcus epidermidis</td>
<td>1/1 Staphylococcus epidermidis</td>
</tr>
<tr>
<td>12</td>
<td>Periprosthetic tissue</td>
<td>5 no growth</td>
<td>1 negative</td>
</tr>
</tbody>
</table>

* Identification of the pathogen in this episode was inconclusive, since in both diagnostic methods the ratio of number of positive : total number of specimens was low. However, based on the previous history (duration of symptoms 19 months) and the small fragment for amplification isolated from the biopsy, Propionibacterium spp. was interpreted as possible pathogen, and Streptococcus infantis as contamination.

+ Results from diagnostic arthroscopy. Four weeks later, a one-stage revision of the TKA was performed and Staphylococcus epidermidis grew in 8 out of 16 obtained biopsies.
To our knowledge, there are two studies\textsuperscript{15,18} that used well-formulated criteria to diagnose the infection and which found a higher sensitivity of PCR in diagnosing PJI as compared to standard cultures\textsuperscript{23}. Panousis et al\textsuperscript{15} performed PCR on synovial fluid in 92 episodes of failed arthroplasties (both TKA and THA) and reported a sensitivity of 92%, but specificity was a low 74% which was possibly the result of contamination, and therefore the regular use of PCR was not recommended. Mooijen et al\textsuperscript{18,} performed PCR on tissue samples. The sensitivity was 97%, but 5 out of 40 PCR positive results did not have an infection, leading to a specificity of 88%, which was lower than the specificity of the standard culturing. Moreover, the characteristics of the included episodes were heterogeneous: 17 episodes out of a total of 76 were not associated with an arthroplasty. Hence, these results might not be completely applicable to a group of patients with possible PJI. Since our study was performed retrospectively, and patients selected for PCR were not recruited according to strictly predefined criteria, the study could be influenced by a selection bias. Therefore, no immediate recommendations about the use of PCR in PJI can be made.

However, in our opinion and that of others\textsuperscript{10,11,14,15}, the expense and diagnostic value of PCR in comparison to bacterial culture warrants only selective use of this molecular method; it is not suited for routine use in addition to a bacterial culture. In our center, PCR was performed in less than 10% of all revision arthroplasties (i.e., in patients with a complex history of joint disease); the limited diagnostic value was shown. PCR was helpful in recognizing false-positive culture results in less than 20% of the episodes. For clinical practice, more studies are required in order to identify both a patient population and a diagnostic strategy in which the use of this molecular method would be beneficial in diagnosing or excluding the possibility of PJI.
Reference


23. Trampuz A, Steckelberg JM, Osmon DR, Cockerill III FR, Hanssen AD, Patel R. Advances in the laboratory diagnosis of prosthetic joint infection. Reviews in Medical Microbiology 2003; 14:1-14
Summary and conclusions

P.T. de Jong and F.H.R. de Man
Chapter 2. Between 1974 and 1989, 315 hip replacements (274 patients) were treated with a cemented Weber rotation total hip replacement (THR). Survivorship analysis with aseptic loosening as endpoint showed a survival of 93% at ten years and 78% at 15 years. Twenty-four hips were revised for aseptic loosening, five for infection and one because of a femoral fracture. From a log rank test, we could establish the influence of the change in cementing technique and the use of either hemispheric or flat cups. Survivorship with aseptic loosening of the hemispheric cup and a second generation cementing technique showed survival of 99% at ten years and 89% at 15 years.

In Chapter 3, the outcome of the cemented THR in the dysplastic osteoarthritic acetabulum is investigated. To improve the coverage of the acetabular component, 116 hips (102 patients) with a mean Sharp angle of 45° (33°-79°) and a mean CE-angle of 10° (-20° to +40°) received a superolateral bone graft. Survivorship analysis, with loosening of the acetabular component as endpoint, after a mean follow-up of 19.5 years (11.5-26 years), showed a survival of 78% after 20 years. Fourteen acetabular components were revised during the follow-up period. All grafts were well integrated and showed remodelling. In six grafts some resorption had occurred where the bone did not support the acetabular component, under the screw heads. The results from this study indicate that the described technique of bone grafting poses a durable solution for cases with a superolateral defect due to developmental dysplasia of the hip (DDH).

In Chapter 4, the long-term results of the smallest sized (medial collar-to-tip length of 9.6 cm) stem of the Weber Rotation THR system are presented. In developmental dysplasia of the hip, attention is usually focused on the acetabulum. However, the altered anatomy associated with hypoplasia of the femur can also be a surgical challenge. While some advocate an (uncemented) custom made stem for these cases, in 77 patients (87 hips) with femoral hypoplasia that were treated between 1978 and 1997, we were always able to use this “off-the-shelf” type Weber stem. Patient’s data were later analyzed and after a mean follow-up of 12 years, we found a mean Harris hip score (HHS) of 88, a total of 6 revisions of the stem, and a surgical complication rate of 5%. Survival analyses for this stem with revision for any reason and radiologically definitive loosening as endpoints, showed 90% and 89% survival, respectively, after 15 years. These outcomes did not differ from those in our cohort for the identical type stem in larger-sizes. We concluded that the cemented, smallest size Weber stem provides a good solution for these difficult cases.

In 1978, changes in the cementing technique were introduced to improve fixation. Although many authors have claimed successful changes in their femoral cementing technique, attempts at improving cemented fixation of the acetabular component seems a more difficult task.

In Chapter 5, the improved cementing technique of the cup is described in detail and the outcome of this technique in a cohort of 287 hips (244 patients) is presented. Survivorship analysis with aseptic loosening of the cup as endpoint, showed a survival rate of 85% after 20 years. A separate analysis in this study shows that with careful cementing technique long-lasting acetabular component fixation can be reached, even in younger patients.

In Chapter 6 an experimental animal study is presented that simulated a THR that compressed an interface through micromovements. In forty-five rabbit tibiae, a titanium implant was inserted, and after osseous integration was achieved, a fibrous tissue interface was generated. In contrast to a previous model we had used, in this model particles could be applied at the interface. Hence, we could study the influence of (i) compression forces, (ii) of HDPE particles, and (iii) the combination of compression and particles on interface and adjacent bone. After morphometric analysis of sections of forty vital bone bridges we found that (i) compression led to bone necrosis and cartilage formation and (ii) particles led to loss of bone and replacement by fibrous tissue. Compression of a fibrous tissue membrane may possibly lead to a high fluid pressure or fluid flow, yielding bone degradation. Cartilage formation could be the protective response. These processes could play an important role in the early stages of THR loosening. If so, implantation techniques that prevent the formation of a fibrous tissue interface (which may act as source of fluid pressure and/or fluid flow) may be beneficial in reducing implant loosening.

Chapter 7. In this study, we verified the presence of matrix metalloproteases (MMP) -2 and -9 in the interface tissues of loosened THRs. These proteases are assumed to play a role in osteolysis and therefore may play a part in aseptic loosening of THRs. Because we were interested in the proteolytic activity in situ and its localization in relation to wear particles, we used immunohistochemistry in combination with in situ zymography. MMP-9 activity was restricted to macrophages and MMP-2 to endothelial cells. However, we found neither an inflammatory response nor accumulations of leukocytes in association with the presence of wear particles. This strengthens our view, that contrary to what is found in the literature, aseptic loosening of THRs is not particle induced.
Chapter 8 In 1990 Marti et al published a report on a group of 80 revision total hip replacements. In this study, we present a longer-term follow-up of up to 24 years. The 81% survival rate of the acetabular component (aseptic loosening of the cup) is a strikingly good outcome in comparison to other studies concerning the outcome of cemented THR revisions. Since the overall survival rate with aseptic loosening of either cup or stem, is 57% at 19 years, there seems to be room for improvement of the fixation of the femoral component.

In Chapter 9 we describe the operative technique of acetabular component revisions performed with a semi-rigid acetabular reinforcement ring (Eichler) and bone grafting. In addition, we present the long-term results of 38 patients (38 hips), treated with the Eichler ring, between 1978 and 1998. In 87% of these cases, the acetabulae were severely damaged, with uncontained and segmental defects. After a mean follow-up of 11 years, the average HHS was 73, one cup had been revised for mechanical loosening, whereas the Eichler ring was stable and was preserved. Remodeling (partial) of autografts had occurred in all cases. We conclude that the Eichler reinforcement ring is a viable option for segmental acetabular defects in revision hip surgery. It allows for restoration of bone, makes future revisions feasible and is a more biological solution than the option of using “mega-implants”.

Chapter 10 deals with the common assumption among orthopedic surgeons that outcome of THR in overweight or obese patients, is impaired. In this study, a consecutive patient population of 412 patients (489 hips), treated with the Weber Rotation THR between 1974 and 1993 was analyzed. Three study groups were created, (i) patients with a body mass index (BMI) < 25 kg/m2, (ii) patients with a BMI ≥ 25 kg/m2, and (iii) patients with a BMI ≥ 30 kg/m2. Comparison of long-term survivorship and peri-operative complication rates showed no differences among the groups. Furthermore, a Cox regression analysis showed that neither a high BMI, nor a high body weight were risk factors for revision surgery. HHSs were lower in the highest BMI group, but these may have already been low preoperatively, and could be influenced by the overweight of the patients. From this study we could not confirm the common assumption that a patient with a higher BMI or higher body weight is more at risk for revision surgery or at risk to have peri-operative complications.

In Chapter 11 the focus is on functional outcome after revision for prosthetic hip joint infection (PHJI). Between 1985 and 2004, in 70 patients (72 episodes) of PHJI, a revision of the prosthesis was performed. Patients were selected for a 1-stage exchange (1-SE; 22 episodes) or a two–stage exchange (2-SE; 50 episodes) according to a strict algorithm which has proven successful for treatment of infection. It was possible to match the 1-SE group with 22 patients (controls) who had had an aseptic revision because the choice of implant and technique was irrespective of the presence of infection. After comparison, functional outcome (Harris hip scores of 84 and 85, resp.), radiological outcome, and revision rate were similar. The 2-SE patients had a more complex a priori situation, and all outcomes were slightly worse. Infection relapse only occurred in one hip, in the 2-SE group. Regression analysis showed a poorer functional outcome in case of (i) a pre-existent deficient trochanter or (ii) a history of increased acetabular revisions with the subsequent need for a Burch-Schneider ring. It can be concluded that the algorithm used provides for good functional and infectiological outcome. It was speculated that early correct treatment of infection prevents a later 2-SE, with possible less good functional result.

In Chapter 12 we analyzed the diagnostic value of broad-range polymerase chain reaction (PCR) technique to identify PJI. The study group consisted of 26 patients with 29 episodes of suspected PJI. In these selected patients, diagnostic difficulties were anticipated due to at least one of the following: (i) multiple previous interventions, (ii) confirmed or treated infection of the same arthroplasty, (iii) prior antimicrobial treatment. Standard cultures and PCR were performed on joint fluid or peri-prosthetic tissue specimens. The specificity and sensitivity for cultures were 71% and 58%, respectively, and for PCR, 94% and 50%, respectively. The sensitivity for both methods being used together was 67%. In conclusion, PCR showed a limited diagnostic value but helped to identify false-positive culture results in few episodes. In our opinion, the expense and diagnostic value of broad-range PCR in PJI argue against its routine use in addition to bacterial culture.
Samenvatting en conclusies
P.T. de Jong en F.H.R. de Man
Hoofdstuk 1 geeft u een overzicht van de ontwikkeling van de totale heup prothese, de diverse aspecten van het loslatingproces en nieuwe ontwikkelingen. Deze inleiding plaatst de verrichte onderzoeken in de juiste context.

In Hoofdstuk 2 worden de lange termijnresultaten van een groep van 274 patiënten (315 heupen) beschreven die behandeld werden met een gecementeerde Weber rotatie prothese. Survival analyse laat zien dat, wanneer het eindpunt revisie voor aseptische loslating is, er een overleving is van 93% na 10 jaar en 78% na 15 jaar. 24 heupen werden gereviseerd wegens aseptische loslating, 5 vanwege een infectie en 1 als gevolg van een femurfractuur. De invloed van de verandering in cementeertechniek en de invloed van de vorm van de cup werd geanalyseerd middels een log-rank test. De beste overleving werd gevonden bij een THP met een hemisferische cup en een 2e generatie cementeertechniek. Deze bedroeg 99% bij 10 jaar en 89% bij 15 jaar.

In Hoofdstuk 3 behandlesen de lange termijnresultaten na een gecementeerde totale heupprothese (THP) met pandakplastiek wegens arthrose ten gevolge van de ontwikkelingsdysplasie van de heup. Honderd en zestien THP's (102 patienten), met een gemiddelde Sharp hoek van 45° (33° tot 79°) en een gemiddelde CE-hoek van 10° (-20 tot +40°), kregen een pandakplastiek om de overdekking van de acetabulaire component te verbeteren. Na 20 jaar bleek de overleving 78% te zijn, als revisie voor loslating van de cup als eindpunt werd genomen. Van de 116 cups werden uiteindelijk 14 gereviseerd gedurende de gemiddelde periode van 19,5 jaar (11,5-26) waarin de patiënten gevolgd werden. Een geringe resorptie van de botplastiek werd gevonden in 6 gevallen onder de schroefkopjes, maar nimmer in het dragende deel van de graft. De resultaten in deze studie laten zien dat er duurzame resultaten te behalen zijn met de beschreven techniek, in gevallen met een craniolateraal defect door een ontwikkelingsdysplasie van de heup.

In Hoofdstuk 4, presenteren we de lange termijnresultaten van de kleinste maat steel van de Weber Rotation THP (lengte 9.6 cm van mediale collar tot tip). Bij de chirurgische behandelings van arthrose ten gevolge van ontwikkelings dysplasie van de heup, gaat de meeste aandacht naar het acetabulum, de juiste keuze van type cup, de wijze van fixatie van de cup en de survival op lange termijn. Echter, heup dysplasie is ook vaak geassocieerd met een hypoplasie van het femur, hetgeen eveneens een chirurgische uitdaging betekent. Voor deze gevallen, wordt door sommigen het gebruik van een (ongecementeerde) custom-made steel geadviseerd. In de 77 patiënten (87 heupen) met femorale hypoplasie die behandelde zijn over de jaren, kon echter in alle gevallen de “off-the-shelf” Weber steel gebruikt worden. Deze groep patiënten werd retrospectief geanalyseerd. Na een gemiddelde follow-up duur van 12 jaar, had deze groep een gemiddelde Harris hip score (HHS) van 88, waren 6 stelen gereviseerd, en was het percentage chirurgische complicaties 5%. Overlevings analyse van deze kleinste maat steel met als eindpunten revisie voor elke reden en radiologische loslating, toonde een respectievelijke overleving van 90% en 89% na 15 jaar. Alle uitkomsten verschilde niet van die van het cohort van de grotere maat stelen, die dienden als controlegroep. Wij concludeerden dat de gecementeerde kleinste maat Weber steel een goede oplossing biedt voor deze moeilijke gevallen van femorale hypoplasie.

In 1978 werden wijzigingen doorgevoerd in de cementeertechniek die moesten leiden tot een duurzamere fixatie. Meerdere auteurs hebben verbeterde resultaten beschreven als gevolg van het gebruik van modernere cementeertechnieken bij implantatie van de femurcomponent, maar literatuur betreffende verbetering van de gecementeerde fixatie van de acetabulaire component is schaars.

In Hoofdstuk 5 beschrijven we de verbeterde cementeertechniek van de cup en de resultaten in een cohort van 287 heupen (244 patiënten). Na 20 jaar is er een overleving van 85%, als revisie wegens aseptische loslating van de cup als eindpunt wordt genomen. De huidige studie laat zien dat er zorgvuldige uitvoering van deze cementeertechniek kan leiden tot goede lange termijn resultaten, ook bij patiënten jonger dan 50 jaar, die als aparte groep werden geanalyseerd, aangezien in deze groep over het algemeen slechte resultaten met gecementeerde cups werden gerapporteerd.
In **Hoofdstuk 6** worden de resultaten van een dierexperimentele studie gepresenteerd. Het gebruikte model simuleert een THP die microbeweging vertoont en daardoor een interface comprimeert. Een titanium implantaat werd geïmplanteerd in de tibiae van 45 konijnen. Nadat het implantaat was ingegroeid, werd een fibbreuze weefsellaag als interface gegenereerd. In tegenstelling met een eerder door ons gebruik model konden nu partikels toegevoegd worden ter plaatse van de interface. Op deze wijze kon de invloed van (i) compressie, (ii) high-density polyethylene (HDPE) partikels, en (iii) de combinatie van compressie en HDPE partikels op de interface en het aanliggende bot worden bestudeerd. Na morfometrische analyse van secties van 40 vitale botbalkjes bleek dat (i) compressie van de interface leidde tot necrose van aanliggend bot en de formatie van kraakbeen en (ii) de aanwezigheid van partikels leidde tot botverlies met vervanging door fibreus weefsel. Compressie van een fibreuze weefsellaag of interface genereert mogelijk een hoge vloeistofdruk of vloeistofstroom, waardoor botafbraak optreedt. De formatie van kraakbeen, die daarbij optreedt zou een beschermende respons kunnen zijn. Deze processen spelen mogelijk een belangrijke rol gedurende de eerste fase(n) van loslating van een THP. Het voorkomen van de vorming van een fibreuze interface laag rondom een THP (die fungeert als potentiële bron van hoge vloeistofdruk of vloeistofstroom) door (verbeterde) implantatie, methoden zou een vermindering van het aantal late loslatingen van componenten kunnen betekenen.

**Hoofdstuk 7.** In deze studie werd de aanwezigheid van matrix metalloproteinases (MMP)-2 en -9 bevestigd in de weefsels direct rondom losse heupprothesen. Van deze proteasen wordt aangenomen dat ze een rol spelen in osteolyse rond de heup en dus in het proces van aseptische loslating. Omdat met name de activiteit van deze protheses in situ iets zegt over hun mogelijke rol en we geïnteresseerd waren in de relatie tussen deze activiteit en de aanwezigheid van slijtagedeeltjes, maakten we gebruik van immunohistochemie in combinatie met in situ zymografie. MMP-9 activiteit beperkt tot de macrofagen en die van MMP-2 tot endotheel cellen. Opvallend was dat de aanwezigheid van slijtage deeltjes niet kon worden geassocieerd met een ontstekingsreactie en de opstapeling van leukocyten. Deze bevinding maakt het waarschijnlijker dat, in tegenstelling tot de huidige opvattingen, aseptische loslating geen proces is dat geïnduceerd wordt door slijtage partikels.

**Hoofdstuk 8.** In 1990 werd door Marti et al. de resultaten van een groep van 80 revisie THP’s beschreven. De huidige studie is een verlenging van deze studie, waarbij de controle wordt verlengd tot 24 jaar. Opvallend in vergelijking met andere studies, is de goede overlevingsduur in deze studie van 81% van de acetabulaire component na 19 jaar, als revisie wegens aseptische loslating van de cup als eindpunt wordt genomen. Na 19 jaar is de overleving echter 57%, als het eindpunt revisie van cup en/of steel wordt genomen.

In **Hoofdstuk 9** wordt een acetabulaire revisie methode beschreven waarbij een semi-rigide reinforcement (Eichler) ring samen met botgrafting wordt gebruikt. Tevens worden de lange termijnresultaten gepresenteerd van 38 patiënten (38 heupen), die in de periode van 1978 tot 1998 met een dergelijke Eichler ring zijn behandeld. In 87% van deze gevallen was het acetabulum ernstig beschadigd en was er sprake van segmentale “uncontained” defecten. Na een gemiddelde follow-up duur van 11 jaar, was de HHS 73 en was er één cup gereviseerd vanwege aseptische loslating waarbij de Eichler ring stabiel was en in situ bleef. Volledige of gedeeltelijke remodelering van superolaterale autografts vond in alle gevallen plaats. We concluderen dat in revisie heupchirurgie, het gebruik van de Eichler reinforcement ring een goede oplossing biedt voor de reconstructie van gecompliceerde segmentale “uncontained” defecten van het acetabulum. Het gebruik van dit implantaat biedt de mogelijkheid tot herstel van bone stock door de combinatie met botplastieken. De Eichler ring maakt derhalve eventuele toekomstige revisies mogelijk; het biedt een meer biologische oplossing dan een zogenaamd “mega-implantaat”.
Het thema in Hoofdstuk 10 is de heersende opvatting onder orthopaedisch chirurgen, dat de uitkomst na een THP bij patiënten met overgewicht of obesitas slechter zou zijn dan bij de patiënt met een gemiddeld gewicht. In een retrospectieve studie werd een opeenvolgende patiëntenpopulatie van 412 patiënten (489 heupen) geanalyseerd, die behandeld waren met de Weber Rotation THP in de periode van 1974 tot 1993. Drie studiegroepen werden geïdentificeerd, (i) patiënten met een body mass index (BMI) < 25 kg/m², (ii) patiënten met een BMI > 25 kg/m² en (iii) patiënten met een BMI > 30 kg/m². Vergelijking van de lange termijn overleving en peri-operatieve complicaties toonde geen verschil tussen de groepen. Ook een Cox regressie analyse toonde dat, noch een hoge BMI, noch een hoog lichaamsgewicht een risicofactor was voor revisiechirurgie. De HHS was lager in de groep patiënten met de hogere BMI, maar deze waren mogelijk al lager pre-operatief en beïnvloed door het hogere lichaamsgewicht. De resultaten van deze studie konden de heersende opvatting dat een patiënt met een hogere BMI of lichaamsgewicht een grotere kans heeft op revisie heupchirurgie, dan wel peri-operatieve complicaties, niet bevestigen.

In Hoofdstuk 11, wordt het functionele herstel na revisie van een THP vanwege infectie behandeld. In de periode van 1985 tot 2004, werd er bij 70 patiënten (72 episodes) met een diepe infectie van de THP, een revisie van de prothese verricht. Patiënten werden geselecteerd, ofwel voor een one-stage (22 episodes) of voor een two-stage (50 episodes) revisie, volgens een strikt algoritme dat voor de behandeling van heupprothese infecties eerder succesvol is gebleken. De one-stage groep kon gematched worden met 22 patiënten (controle groep) die een revisie hadden ondergaan voor een aseptische loslating, omdat de keuze van implantaat en de techniek van implantatie onafhankelijk was van het al dan niet aanwezig zijn van een diepe infectie. Vergelijk tussen deze twee groepen, leverde geen verschil op in functie scores (HHS 84 en 85, resp.), radiologische scores of het aantal revisies. De two-stage patiënten, met de meer complexe a priori situatie, scorreerde op alle uitkomsten minder goed in vergelijking met de one-stage revisiegroep. Er was 1 recidief diepe infectie, in de two-stage groep. Regre"ssie analyse toonde een minder goede functie score wanneer er (i) een preëxistente trochanterdeficiëntie was, of (ii) er een voorgeschiedenis bestond van acetabulaire revisies, waardoor gebruik van een Burch-Schneider ring noodzakelijk was. We konden concluderen dat het gebruikte algoritme in combinatie met de chirurgische techniek leidt tot een zowel functioneel als microbiologisch goed resultaat. Ofschoon speculatief, stelden wij dat vroege correcte behandeling van een (heup) prothese infectie de noodzaak van een two-stage revisie, met een mogelijk minder goed functioneel herstel, kan verhinderen.

Hoofdstuk 12, is een studie naar de diagnostische waarde van de broad-range polymerase chain reaction (PCR) techniek bij een diepe prothese infectie. De studiegroep bestond uit 26 patiënten (29 episodes) met verdenking op een diepe prothese infectie. In deze geselecteerde gevallen werd er geanticipeerd dat het stellen van de diagnose infectie door standaard microbiologische kweken alleen, moeilijk zou zijn vanwege (i) een voorgeschiedenis van multiple interventies, (ii) een bevestigde of inmiddels behandelde infectie van het zelfde implantaat, of (iii) recent antibiotica gebruik. Standaard microbiologische kweek en PCR analyse werd verricht van gewrichtsvloeistof of peri-prosthetisch weefsel. De specificiteit en sensitiviteit van microbiologische kweek was respectievelijk 71% en 58%, en die van PCR 94% en 50%. De cumulatieve sensitiviteit van de combinatie van beide was 67%. In deze studie was de diagnostische waarde van PCR beperkt, maar leidde in enkele gevallen tot de identificatie van fout-positieve kweek uitslagen. Naar onze mening zijn zowel de hoge kosten als de beperkte diagnostische waarde van PCR, redenen om deze test niet routinematig naast de standaard microbiologische kweek te verrichten.
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Pieter Thomas de Jong was born in Shifnal, England, on February 22, 1963. He attended primary school at the Mariaschool in Ulvenhout and vwo at the Mencia de Mendoza lyceum in Breda until graduation in 1981. He started his medical training in Antwerp (RUCA) in 1981, but switched to the Erasmus University in Rotterdam in 1982. After graduation in 1990, he joined the Navy to fulfil his military service, as a medical officer. From February 1992 until August 1992 he was senior house officer (orthopaedics) in Alton, Hampshire, England, where he started his career in orthopaedics. After returning to the Netherlands, he became an AGNIO in general surgery at the Twenteborgh Ziekenhuis in Almelo until he was granted a post as AGNIO at the department of orthopaedic surgery at the Academic Medical Center (AMC) in Amsterdam (head of department: professor R.K. Marti). In 1996, he was able to start his orthopaedic surgery training, starting with general surgery at the Rijnland Ziekenhuis Leiderdorp, (head of department: dr. J.F.W.B. Rijksen), followed by orthopaedic surgery at the AMC and the Tergooiziekenhuizen, Hilversum (head of department: dr. G.H.R. Albers). After a year as chef de clinique in the Spaarne ziekenhuis in Haarlem, he returned to the AMC, as a member of the staff in 2003. He started his present position as orthopaedic surgeon at the Sint Jansdal Ziekenhuis in Harderwijk in October 2005. He now lives in Putten (Gelderland) with his wife Emma and their three children, Mari Carmen, Thomas and Benjamin.

Frans Harald Roderick de Man was born in Amsterdam, the Netherlands on November 19, 1967. He graduated from the Amsterdams Lyceum in 1986 and began his medical studies at the University of Amsterdam in 1987. However, he devoted a major portion of his time to alpine skiing for the Dutch National Ski team and developed a special interest in traumatology and orthopedics. In 1991, he returned to full time study. His special internship orthopaedics, in Sankt Moritz, Switzerland (supervisor Professor R.K. Marti) confirmed his desire to become an orthopedic surgeon. Upon graduation from Medical School in 1997 he worked in the Academic Medical Center, first as an orthopaedic resident (head of the department Professor R.K. Marti) and later as experimental research assistant in the department of experimental surgery (under Professor Th. Van Gulik), during which the first steps for this thesis were made. After his surgical training at the Rode Kruis Ziekenhuis, Beverwijk (head Dr. R. Brederveeld) he commenced his orthopaedic training at the Academic Medical Center (Professor R.K. Marti and later Professor C.N. van Dijk) and afterwards at the Tergooiziekenhuizen, Hilversum (head Dr. G.H.R. Albers). He worked at the Kantonsspital Liestal, Switzerland (head Professor P.E. Ochsner) following the completion of his orthopaedic training, where his special interest in the treatment of orthopaedic infections emerged. Much of the work for this thesis was initiated or completed during that period. In 2006 he returned to the Netherlands as an orthopedic staff member at the Sint Maartenskliniek, Nijmegen. He remains a passionate practitioner of alpine activities. He is married to Margot de Jong and they have three children, Julia, Jens, and Rutger.