Pitfalls in Traditional and Innovative Hip Replacement Surgery

Bart H. Bosker

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Bart Hans Bosker

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CHAPTER 1

General introduction and aims

GENERAL INTRODUCTION

Osteoarthritis of the hip is a well-known disease with numerous historical reports about its different treatment methods. It has evolved from a salvage procedure with poor long-term outcomes, only reserved for the most infirm patients, to one of the most successful and most frequently performed elective procedures.[1]
Before 1800, amputation of the affected limb was the treatment of choice. In an attempt to find less radical alternatives, Henry Park described total extirpation of the articulation, in an effort to cure the disease by the means of callus formation.[2,3] In 1821, excision arthroplasty was introduced by Anthony White. He removed the head, neck and trochanters of the femur.[4,3] After these still very invasive alternatives to amputation, a less invasive treatment by using osteotomies followed in 1826.[5] The first experiments with interpositional materials were performed by the Czech surgeon Vitezlav Chlumsky in the late 19th century. He experimented with a wide variety of materials. Among these, muscle, celluloid, silver plates, rubber struts, magnesium, zinc, glass, pyres, decalcified bones, wax and celluloid were used.[3,6] The idea of interposition was followed by Sir Robert Jones in 1912. He resurfaced the shape of the bone and applied a gold layer to make it run smoothly. Good clinical results were reported after a period of 20 years, at that point the longest follow-up in the history of arthroplasty.[7]

It was only as recent as in 1930 that Wiles described the first Total Hip Arthroplasty (THA), in which both femur and acetabulum were replaced by metal components.[8] The concept was further developed by McKee and Watson-Farrar in the 1950s. They introduced their metal-on-metal total hip, switching from stainless steel to a cobalt-chrome-molybdenum alloy.[9] In 1953, Sir John Charnley populated the use of bone cement and advocated the use of polyethylene instead of using a metal-on-metal bearing. Thereby introducing the now "*traditional*" metal-on-polyethylene bearing. In the 1970s metal-on-metal implants had virtually disappeared due to the success of Charnley's high-density polyethylene low friction arthroplasty using acrylic bone cement.[10] It was in the early 1990s that the metal-on-metal bearing revived using a new design. The resurfacing prosthesis was introduced. It had certain benefits over the "*traditional*" arthroplasty being more bone preserving on the femoral side and providing increased range of motion and stability, subsequently making it suitable for the young and more active patient group.

The technique of total hip arthroplasty is only 80 years "old", but in this short period of time it has evolved to one of the most successful and most performed procedures in the history of medicine.[11,12] Successful does not imply that there are no shortcomings of the procedure. Complications do occur and can significantly influence implant survival and patient morbidity. Well known complications associated with hip arthroplasty are: infection, dislocation, fracture, thrombosis, leg length discrepancy and wear of the bearing surfaces.

Malpositioning of components is probably one of the most important surgeon-related causes of complications. It is associated with instability, leg length discrepancy, reduced range of motion and increased wear. In conventional bearings, wear can result in early failure due to particle disease and loosening of the implant. Better training of surgical skills and understanding of human anatomy can lead to more precise positioning of components contributing to a more stable prosthesis with subsequently lower associated complication rates.
Besides surgical skills and peri-operative measures, new technologies have been developed in an effort to minimize malpositioning. Computer Assisted Surgery (CAS) was introduced for more accurate component placement. Also new "*innovative*" implant designs were developed and brought on the market. Metal-on-Metal articulations were re-introduced, because of their purported advantages over "*traditional*" bearings. Although good clinical follow-up of these bearings was initially reported, more recent studies report serious complications associated with the metal-on-metal articulation. The complications mentioned are thought to be related to metal debris, leading to adverse local tissue reactions (pseudotumors/ ARMD) and systemic effects from prolonged exposure to metal ions (cobalt and chromium).[13] Reported failure rates of metal-on-metal arthroplasties differ for yet still unknown reasons. Implant design, gender and orientation of components are thought to play an important role in the failure mechanism.[14,15] Because of the serious complications and unknown causes, the Dutch Orthopaedic Association decided to halt the implantation of these implants in the Netherlands. Another important decision they made was to stress the importance of the national orthopaedic implant registration, which enables tracking implants and patients. It enhances easy follow-up of implants in large patient groups. An implant or institution with poor results will consequently be detected more easily and appropriate actions can be taken sooner.

AIMS OF THE THESIS

This thesis focusses on pitfalls in treatment of osteoarthritis of the hip, by total hip arthroplasty. It is divided in two parts: *traditional* and *innovative* hip replacement surgery.

Traditional

In the first part, the inaccuracy of freehand cup implantation is investigated. We further analyse factors that could contribute to, and explain why this method is inaccurate. In the last chapter of the first part, we discuss a less invasive procedure to treat recurrent dislocation, by using an augmentation ring.

Innovative

The second part of the thesis focusses on the innovative metal-on-metal articulation. It was introduced because of its advantages over the metal-on-polyethylene articulation. We will discuss the new pitfalls that this type of bearing presents. The first two chapters investigate the incidence of pseudotumors, their risk factors and association with metal ions. In the last chapter of the second part we discuss the possible relation between pseudotumors and the unique design of the prosthesis, as used in our clinic.

Based on this introduction, we formulated the following questions:

- Is freehand cup positioning an accurate technique and what is the rate of cup malposition?
- Is the sequence of applying anteversion or inclination first important in positioning the cup in THA, when a freehand technique is used?
- Is acetabular augmentation arthroplasty a good alternative in recurrent dislocation of a THA?
- What is the incidence of pseudotumors and revisions in patients, treated with a large head metal-on-metal stemmed total hip arthroplasty?
- What is the importance of deploying an extensive screening protocol in determining the incidence of pseudotumors, in patients treated with metal-on-metal THAs?
- What is the most important risk factor for developing a pseudotumor in large head metal-on-metal stemmed total hip arthroplasties?
- Is wear of the modular titanium taper interface related to wear at the bearing articulation in large head metal-on-metal stemmed total hip arthroplasties?

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CHAPTER 2

Poor accuracy of freehand cup positioning during total hip arthroplasty

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ABSTRACT

Several studies have demonstrated a correlation between the acetabular cup position and the risk of dislocation, wear and range of motion after total hip arthroplasty. The present study was designed to evaluate the accuracy of the surgeon's estimated position of the cup after freehand placement in total hip replacement.

Peroperative estimated abduction and anteversion of 200 acetabular components (placed by three orthopaedic surgeons and nine residents) were compared with measured outcomes (according to Pradhan) on postoperative radiographs.

Cups were placed in 49,7 (SD 6,7) degrees of abduction and 16,0 (SD 8,1) degrees of anteversion. Estimation of placement was 46,3 (SD 4,3) degrees of abduction and 14,6 (SD 5,9) degrees of anteversion. Of more interest is the fact that for the orthopaedic surgeons the mean inaccuracy of estimation was 4,1 (SD 3,9) degrees for abduction and 5,2 (SD 4,5) degrees for anteversion and for their residents this was respectively 6,3 (SD 4,6) and 5,7 (SD 5,0) degrees. Significant differences were found between orthopaedic surgeons and residents for inaccuracy of estimation for abduction, not for anteversion. Body mass index, sex, (un) cemented fixation, surgical approach were not significant factors.

Based upon the inaccuracy of estimation, the group's chance on future cup placement within Lewinnek's safe zone (5-25° anteversion and 30-50° abduction) is 82,7% and 85,2% for anteversion and Abduction separately. When both parameters are combined, the chance of accurate placement is only 70,5%. The chance of placement of the acetabular component within 5° of an intended position, for both Abduction and anteversion is 21,5%, this percentage decreases to just 2,9% when the tolerated error is 1°.

There is a tendency to underestimate both abduction and anteversion. Orthopaedic surgeons are superior to their residents in estimating abduction of the acetabular component. The results of this study indicate that freehand placement of the acetabular component is not a reliable method.

INTRODUCTION

Acetabular cup position after total hip arthroplasty is correlated with the risk of dislocation, wear and range of motion. [1-6] Lewinnek et al described a safe range (5-25° anteversion and 30-50° abduction) to position the cup. Within this range the dislocation rate was 1.5% and outside this range 6.1%.[7] Although the position of the cup is important for the prognosis and function of the hip, most surgeons place the cup without any specific guidance devices. During surgery the surgeon estimates the position of the acetabular component and decides if it meets the desired orientation before securing it.

In this study the accuracy of the surgeons peroperative estimation of the position of the cup is evaluated.

MATERIAL AND METHODS

All patients undergoing primary total hip arthroplasty were enrolled in the study. Patient characteristics as name, sex, age, operated side and the body mass index were recorded. All cooperating surgeons (three orthopaedic surgeons and nine residents) received a list on which the following data concerning the operation were recorded: fixation (cemented or uncemented), cup model, surgical approach, complications and the peroperative estimated anteversion and abduction of the acetabular component.

Two days after the operation two standardised X-rays were made. One anteroposterior X-ray was taken with the beam centered over the hip, the second was a plain AP radiograph centred on the symphisis, showing both hips. Radiographic cup anteversion was measured on the first radiograph, according to Pradhan[8], and cup abduction was assessed on the second by measuring the angle between the teardrop line and the line bisecting the opening of the acetabular cup. The combination of both radiographs was used to determine if a cup was in the ante- or retroverted position , as described by Flabeck et al.[9]

For both anteversion and abduction the inaccuracy of estimation was determined by calculating the difference between peroperative estimation and postoperative X-ray measurements. Mean values and standard deviations were calculated for measured cup position, estimated cup position and inaccuracy of estimation. A comparison of these values was assessed between orthopaedic surgeons and residents, using student's t test ($P<0.05$ assumed as significant) and a multivariate linear regression analysis was applied on the data in order to investigate which factors influenced the inaccuracy of estimation.

RESULTS

Two hundred cups in 194 patients, placed between June 2003 and May 2005, were included in the study. There were 55 males and 139 females. At time of operation the mean age of the patients was 72,4 years (34-92) with a mean body mass index of 27,5 (16,6 – 38,1). The cups were placed by 12 different surgeons. Eighty-five cups (42,5%) were placed by three orthopaedic surgeons and 115 (57,5%) by nine of their residents, always under supervision

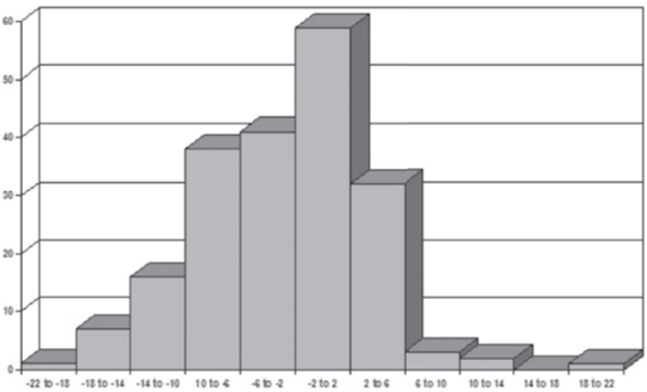
of one of the surgeons.
One hundred fifty-seven (78,5%) cups had a cemented and 43 (21,5%) an uncemented fixation; 89 (44,5%) cups were placed in the patients right hip and 111 (55,5%) in the left. Two surgical approaches were used. The anterolateral approach according to Mallory was used in 57 cups (28,5%), supervised by one orthopaedic surgeon and the posterolateral approach by the other two surgeons in 143 cups (71,5%). The residents used the approach of their supervising surgeon. Using the anterolateral approach according to Mallory, mean placement of the cup was in 11,8° anteversion and 47,1° abduction. Positioning of the cup differed significantly when approached posterolateral, namely in 17,7° anteversion and 50,7° abduction (both p<0,001). Comparing the anterolateral with the posterolateral approach, no significant differences were found for inaccuracy of estimation for either anteversion (4,9° versus 5,5° respectively) or abduction (5,3° versus 6,1°).
Table 1 shows relevant data of estimations and the measurements of the acetabular component by both orthopaedic surgeons and residents. None of the cups was placed in retroversion.

	Cups N	Anteversion (degrees) Estimated	Measured	Difference	Mean inaccuracy of estimation
Ia					
Orthopedic surgeon	85	14.5	14.7	-0.2	5.2 (SD 4,5)
Residents	115	14.7	16.9	-2.2	5.7 (SD 5,0)
Total	200	14.6 (SD 5,9)	16.0 (SD 8,1)	-1.4	5.5
Significance		-	-	-	-
	Cups N	**Abduction (degrees) Estimated**	**Measured**	**Difference**	**Mean inaccuracy of estimation**
Ib					
Orthopedic surgeon	85	47.2	48.6	-1.4	4.09 (SD 3,9)
Residents	115	45.6	50.5	-4.9	6.28 (SD 4,6)
Total	200	46.3 (SD 4,3)	49.7 (SD 6,7)	-3.4	5.4
Significance		0.001	0.043	0.000	0.001

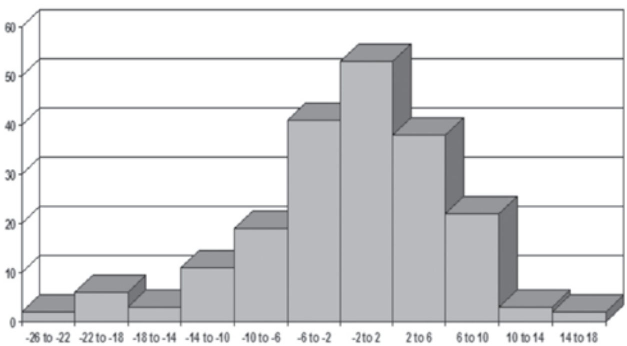
Table 1. Mean estimated and measured anteversion and abduction.

From the data from which Figure 1 was constructed, it was derived that 129 cups (64,5%) were placed within 5 degrees of the estimated abduction, for anteversion this was the case in 122 cups (61%). There is a tendency to underestimate both abduction and anteversion.

Figure 1. Results of the distribution of the difference between the estimated and measured values (degrees) for abduction (a) and anteversion (b) of the acetabular components



1a. Results of the distribution of the difference between the estimated and measured values (degrees) for abduction.



1b. Results of the distribution of the difference between the estimated and measured values (degrees) for anteversion.

Table 2 demonstrates the results of the chance for cup placement according to Lewinnek (5-25° anteversion and 30-50° abduction), based upon inaccuracy of estimation for the orthopaedic surgeons, their residents and the group in total. Virtual intended cup placement was set at 15° anteversion and 40° abduction. Only 70,5 % of the cups were placed in this safe zone according to their measured abduction and anteversion.

	Anteversion (%)	Abduction (%)	Placement according to Lewinnek (%)
Orthopedic Surgeons	85.7	93.7	80.3
Residents	80.5	78.9	63.5
Group	82.7	85.2	70.5

Table 2. Results of the chance for cup placement within the limits according to Lewinnek (5-25° anteversion and 30-50° abduction) for the orthopedic surgeons, their residents and the entire group. Intended cup placement was virtually set on 15° anteversion and 40° abduction.

Table 3 shows the percentage for the group and orthopaedic surgeons and residents separately, for cup placement within different ranges (20,10,5,2.5 and 1°) of an intended cup position X.

	X +/- 20 (%)	X +/- 10 (%)	X +/- 5 (%)	X +/- 2.5 (%)	X +/- 1 (%)
(a) Group					
Abduction	100	85,2	46,8	26	16,4
Anteversion	99.9	82,7	46	26,7	17,5
Combined	99,9	70,5	21,5	6,9	2,9
(b) Surgeon					
Abduction	100%	93,7%	59,3%	34%	21,2%
Anteversion	99,9%	85,7%	48,3%	27,5%	17,6%
Combined	99,9%	80,3%	28,6 %	9,4%	3,7%
(c) Residents					
Abduction	99,8%	78,9%	39%	20,7%	12,7%
Anteversion	99,8%	80,5%	44,5%	26,2%	17,4%
Combined	99,6%	63,5%	17,4%	5,4%	2,2%

Table 3. Deviation in % of cup placement in between 20°, 10°, 5°, 2.5° and 1° of position X for the entire group (orthopaedic surgeons and residents): (a), the orthopaedic surgeons: (b) and the residents:(c).

A multivariate regression analysis was applied in order to identify any factors that might be responsible for the inaccuracy of the estimation. A significant result was found for abduction and anteversion, concerning age of the patient and if the patient was operated by an orthopaedic surgeon or resident. Other factors like Body Mass Index, sex, operated side, (un)cemented fixation of the acetabular component, model of the cup and the surgical approach did not reveal any significant differences.

DISCUSSION

Malposition of the acetabular cup is probably the most important factor for dislocation of a total hip prosthesis. Therefore it is essential that the surgeon has maximum control over the position of the socket during the operation. Free hand positioning with the patient in a standardized position and a cup positioner with the patient and floor as reference is the routine method. Specific mechanical alignment guides were designed to add precision as do navigation systems in the concept of CT guided computer assisted surgery. Surprisingly there are very limited data on the precision rate of free hand positioning of the acetabular shell. The aim of our prospective study was to determine the accuracy of the free hand technique. Only then the presently introduced systems can be tested against this standard. The term free hand is not used uniformly in the literature. Either is referred to pure manual positioning or with the aid of the acetabular cup impactor-positioner provided with the implant. In the present study the latter definition was applied.

One comparable study is that of Saxler et al[10] who showed, in a retrospective CT-controlled design, that 27 out of their 105 cups (25.7%) were placed within the safe zone of Lewinnek. A second study by DiGioa et al[11] with a specific mechanical acetabular alignment guide (with A-frame) where the results were controlled peroperatively with a hip navigation system in 74 hips aimed at 45° of abduction and 20° of flexion. With their specific guide only 22 % of the cups were placed within Lewinneks safe zone. Compared with these two studies our prospective data demonstrate an accuracy within the safe zone of 70.5%.

There is an elegant in vitro study by Jolles et al[12] comparing free hand (without the help of any guide), mechanical alignment guide and computer assisted cup placement. One hundred-fifty acetabular implants were placed in 10 identical models of the pelvis (covered with artificial soft tissue of soft cast and foam) by 10 surgeons. The mean accuracy for anteversion was 8 ° (5.0-10.5) for free hand with cup positioner and 4° (3.0-5.5) for abduction; with computer navigation this was 1.5° (1.0-2.0) and 2.5° (2.0-3.5) respectively. In the present in vivo study the data were 5.5° for anteversion and 5.4° for abduction with 200 acetabular shells. Jolles et al. state that their in vitro conditions of ideal approach and anatomic relations and perfect placement of the patient would favour the free hand positioning as computer assisted surgery devices are only slightly sensitive to modifications of these parameters and inaccuracy of the freehand will be enhanced greatly in vivo. Our study proves this statement not to be the case as results are quite comparable.

Without doubt it is essential to actually place what is aimed for. Our present study shows that the 70.5% positioned within the safe zone is remarkably good for free hand placement compared with literature. But when the target is reset from the wide safe zone of Lewinnek to for instance within five or even one degree of error from the judged position for both abduction and anteversion only 21.5 and 2.9% of our sockets are placed within this narrow definition of safe zone. CT-guided navigation systems have demonstrated that they can apply better to this narrowed safe zone.

We believe that the power of our study comes from the distinctive set up where the recorded data are a reflection of the surgeon's perception of cup placement. To our opinion this is superior then to allow for a wide range or set a predefined target. At the actual point of cup placement a surgeon is also committed to or governed by the patient's anatomy which will influence the actual position. For instance when less anteversion is accepted in the socket; the stem will be given some additional anteversion.

Another important item as stipulated by DiGioia et al[11] is the actual position of the patient in the lateral decubitus position. They demonstrated that the mean difference of pelvic orientation on the operating table with the desired position during acetabular alignment was 18 degrees in version and 3 degrees in abduction. This effect is not completely eliminated with the use of computer navigation as these systems are influenced by pelvic tilt. [13]
Considering the estimation of abduction, significant results were found in favour to the orthopaedic surgeons compared to their residents. A learning curve as a result of experience is probably responsible for this difference. As to surgical approach, cups placed posterolateral were measured to have a significantly higher degree of anteversion and abduction. One explanation for the difference in anteversion could be that the cups placed according to Mallory deliberately were given less anteversion to decrease the change on luxation associated with this approach. Although both approaches take a different route to the acetabulum, this doesn't seem to have influence on the accuracy of cup placement in our series. Important factors like vision on, and presentation of the acetabulum don't seem to be hindered by the approach used.
The minority of the cups were placed according to Mallory. The reason for this is that only one surgeon in our clinic uses this approach with the consequence that the numbers are too small for statistical significance. Further research of surgical approach and accuracy of cup placement needs to be done before a relationship can be detected.

An important potential flaw of this investigation is the use of planar radiographs for the evaluation of true abduction and especially anteversion. Variations in pelvic flexion-extension during imaging are responsible of variations in anteversion up to -26° to +10° [14] This study concludes that radiographic measurements are not a reliable method to evaluate cup orientation, especially flexion or anteversion alignment. [14] Pradhan however stated that his method, as used in our study, proved to be reliable in an in vitro model in which the calculated anteversion on the X-ray was compared with the true (known) cup anteversion. In our study special attention was given for optimal positioning of the patients pelvis to minimize rotation and tilt before the x-ray was taken. From a practical point of view it is preferable to determine the actual cup position with planar radiographs rather than with CT as in most clinics the availability and the costs of a CT scan combined with the high radiation dose for the patient are reasons not to use this instrument as a routine method.
From this prospective study it is concluded that an accuracy of 70.5% for placement of the socket with an acetabular shell impactor-positioner within Lewinnek's safe zone and of only 21.5% within an error of 5° for both abduction and anteversion is unacceptable. Therefore this method is invalid and according to literature the position of the acetabular component is best controlled by computer navigation systems.

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CHAPTER 3

Is there still a place for freehand cup positioning? The inaccuracy of freehand cup positioning explained by a theoretical model

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Submitted

ABSTRACT

Freehand cup implantation, according to literature, often leads to malpositioning and therefore shortened survival of the prosthesis. In this study we analyze freehand cup implantation and the reasons for its inaccuracy.

A 3D modeling program was used to predict true cup position after first applying inclination and subsequently anteversion and *vice versa*. The influence of pelvic motion on cup position during placement was calculated.

We demonstrate the difference between true- and planar anatomical dimensions of the cup and how this leads to misinterpretation of cup orientation. We show how pelvic movement influences judgment of cup positioning.

Cup positioning is more accurate when anteversion is applied before inclination. Inclination followed by anteversion leads to overestimation of true anteversion, ranging from 1.5 to 18 degrees. Slight pelvic movement (5-15° in any direction) leads to misinterpretation of cup position with ranges of 1.1-15° anteversion and 0.6-15° inclination.

Many factors lead to inaccurate cup placement in freehand cup positioning. If freehand cup positioning is used, placement is more accurate by first applying anteversion, followed by inclination. Pelvic movement considerably influences cup positioning. Guidance tools should be considered in order to achieve a more reliable cup placement.

INTRODUCTION

With annually more than one million worldwide, total hip arthroplasty (THA) is considered one of the most successful procedures in modern orthopedic surgery. [1] Correct orientation of components is mandatory for adequate survival, range of motion, wear and stability of the prosthesis. [2-4] The most cited safe zone for the acetabular component is 40±10° inclination and 15±10° anteversion[5], although this is supposedly subject to individual variations. Correct cup placement remains a challenge in freehand positioning as shown in previous studies where approximately 50% of the free hand positioned cups are not within the stated safe zone. [6,7] Many factors contribute to this inaccuracy. They might be patient related (obesity, hip dysplasia, distorted anatomy after fracture, etc), surgeon related (surgical technique, experience, patient positioning, etc) or both.[8] Many surgeons use reference points for orientation when inserting the cup in the bony acetabulum. These points can be the operating table or floor, the pelvis, pre-bend inserters or the transfers acetabular ligament. In this study we analyze freehand cup implantation by a theoretical model.

Definitions

Knowledge of anatomical definitions is important in understanding how freehand cup placement leads to misinterpretation of the cups true orientation in the acetabulum.
The definitions describe the difference between the "true-" and "planar-" orientation of inclination and anteversion.
As demonstrated in figure 1a-c: the true inclination is the angle of the cup opening with a longitudinal axis measured and in line with the coronal plane.
Planar inclination: is the angle of the cup opening with a longitudinal axis measured in a plane perpendicular to the cup opening, but not in line with the coronal plane.
True anteversion: is the angle of the cup opening with a sagittal axis, measured in a transverse plane.
Figure 1b shows planar anteversion: the angle of the cup opening with a sagittal axis measured in a plane perpendicular to the cup opening. The rotation does not take place in the pelvic transverse plane, but in a plane perpendicular to the cup opening.
Figure 1c shows by over projecting the two dimensions that true and planar (anteversion) represent different angles.

Figures 1a-c. Figure 1a shows the cup in 45° true inclination and 0° anteversion. From this position anteversion is applied. Rotation from this position does not take place in the pelvic transverse plane, but in the plane perpendicular to the opening of the cup (fig 1b). The acetabular component is thus positioned in planar instead of true anteversion. Figure 1c combines the definitions of true and planar in inclination and anteversion.

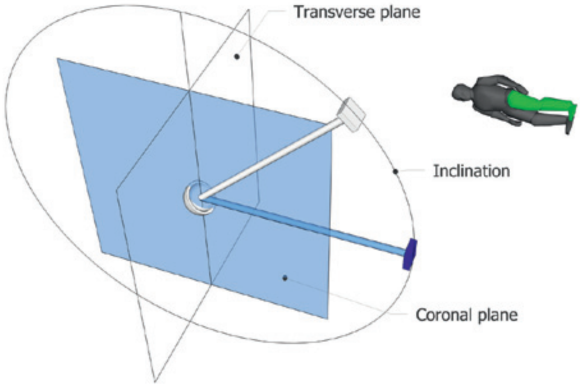

Figure 1a. The cup in 45° true inclination and 0° anteversion

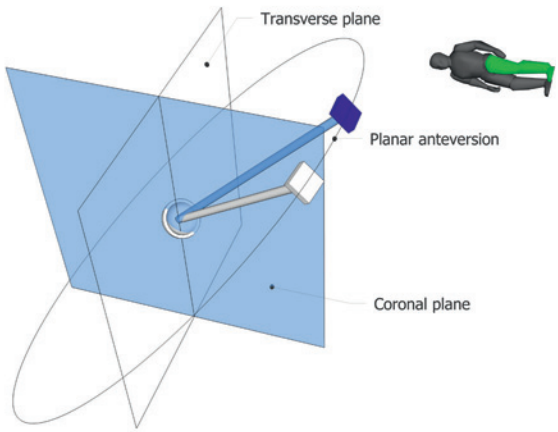

Figure 1b. Rotation does not take place in the pelvic transverse plane, but in the plane perpendicular to the opening of the cup.

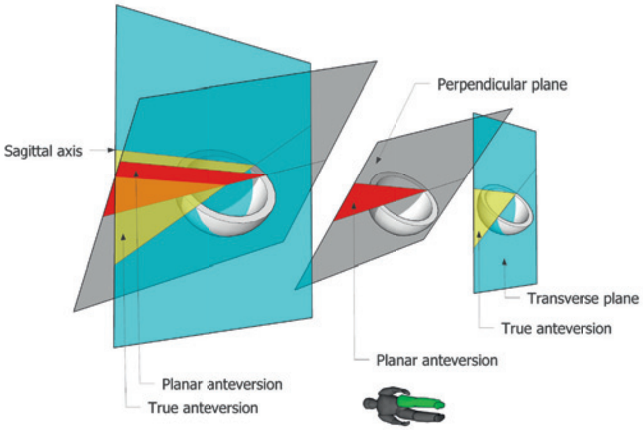

Figure 1c. Combines the definitions of true and planar in inclination and anteversion.

The anatomical orientation of the acetabulum is invariably measured as "true" anteversion and "true" inclination. The difference between planar and true is important because they represent different angles. If a cup is first positioned in the desired amount of (true) inclination and from this position rotated in the desired degree of (true) anteversion, the rotation takes place in the planar dimension and therefore the desired degree of true anteversion is misinterpreted. This mismatch also takes place when the cup is brought into (true) anteversion first, followed by (planar) inclination. We called this phenomena sequencing and it leads to misinterpretation of the angle in which the second orientation is set.
As derived from the definitions, the orientation that was set first (inclination or anteversion) is always in its "true" dimension. The second (inclination or anteversion) always into planar.

The significance of this misinterpretation of the second orientation was analysed for several different cup orientations within Lewinnek's safe zone.

METHODS

A 3D model program[9] was used. The program uses a 3D coordinate system to calculate cup orientation. Three planes were drawn (perpendicularly connected) to represent the anatomical planes (and axes) of the human pelvis. A half sphere model represented the acetabular cup. Manipulating the half sphere with a rotation tool, all possible cup rotations can be simulated. With use of a protractor tool different rotations (inclination and anteversion) were accurately determined with respect to the planes representing the anatomical planes of the pelvis. This sequence is illustrated in Figures 2a-c. The program was used to assess the influence of sequencing on true cup position for various aimed positions within Lewinnek's safe zone.

Figures 2 a-c. Example of measuring true anteversion and inclination for a cup ultimately positioned in 45° inclination and 18.5° anteversion.

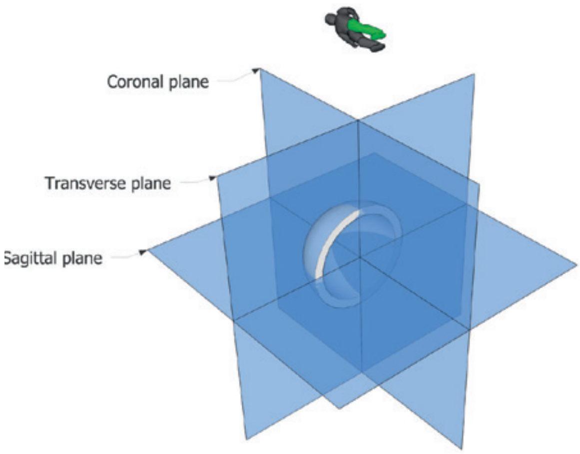

Figure 2a. Cup in neutral position in the anatomical planes of the pelvis.

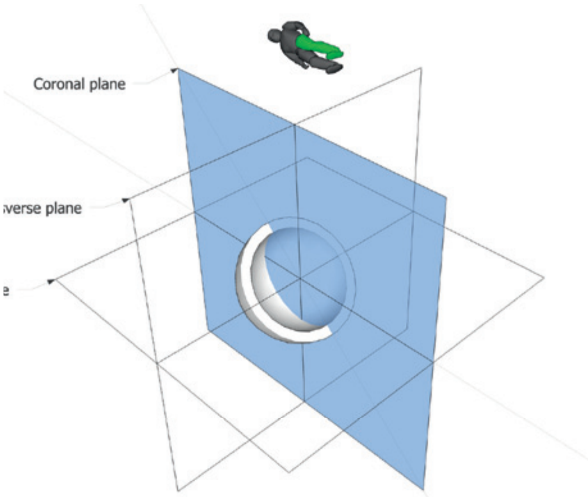

Figure 2b. Cup rotated 45° in the coronal plane measuring inclination 45°.

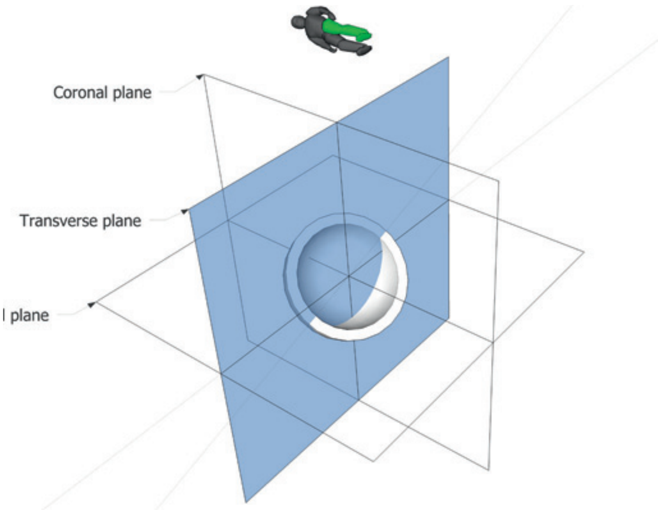

Figure 2c. The cup is rotated into anteversion aimed at 15° anteversion, measuring the true anteversion angle in the transverse plane of 18.5°.

The effect of changes in pelvic orientation was studied by rotating the three perpendicularly connected planes with respect to the half sphere and simulating posterior tilt, anterior tilt, abduction, adduction, internal rotation and external rotation (5, 10 and 15 degrees) when the cup was positioned in 45° inclination and 15° anteversion.

RESULTS

Sequencing leads to inaccuracy because the orientation in which the cup is positioned first is always in "true" and the second in "planar" dimension (Tables 1 and 2). When aiming within a proposed safe zone, positioning is more accurate when anteversion is applied before inclination. Table 1 shows an overestimation of true anteversion by 5.8° aiming at 45° inclination followed by 15° anteversion: (45 incl/15 av; 20.8-15= 5.8 degrees).

	PLAv 5°	PLAv 10°	PLAv 15°	PLAv 20°	PLAv 25°
Incl 50°	6.5°	13°	19.3°	25.4°	31.3°
Incl 45°	7.1°	14°	20.8°	27.2°	33.4°
Incl 40°	7.8°	15.3°	22.6°	29.5°	36°
Incl 35°	8.7°	17.1°	25°	32.8°	39.1°
Incl 30°	9.9°	19.4°	28.2°	36.1°	43°

Table 1. True anteversion as the result of first combining true inclination (Incl) followed by 5-25° planar anteversion (PLAv).

	PLAi 30°	PLAi 35°	PLAi 40°	PLAi 45°	PLAi 50°
Ant 5°	30.1°	35.1°	40.1°	45.1°	50.1°
Ant 10°	30. 4°	35.4°	40.4°	45.4°	50.4°
Ant 15°	30.9°	35.9°	41°	46°	51°
Ant 20°	31.6°	36.7°	41.8°	46.8°	51.7°
Ant 25°	32.5°	37.7°	42.8°	47.8°	52.7°

Table 2. True inclination as a result of first applying true anteversion (Ant) followed by 30-50° planar inclination (PLAi).

Movement	Degrees 0°	True inclination 45°	True anteversion 15°
Pelvic posterior tilt 	5° 10° 15°	44.4° 44.1° 44°	10.2° 5.2° 0°
Pelvic anterior tilt 	5° 10° 15°	45.8° 46.8° 48.1°	19.5° 23.6° 27.4°
Pelvic abduction 	5° 10° 15°	40° 35° 30°	16.4° 18.3° 20.8°
Pelvic adduction 	5° 10° 15°	50° 55° 60°	13.9° 13° 12.3°
Pelvic internal rotation 	5° 10° 15°	45.6° 45.9° 46°	10° 5° 0°
Pelvic external rotation 	5° 10° 15°	44.2° 43.2° 41.9°	20° 25° 30°

Table 3. Influence of pelvic motion for a left-sided cup. Targeting position: 45° true inclination (measured in a coronal plane) and 15° true anteversion (measured in a transverse plane).

Table 2 shows for the reverse sequence (anteversion followed by inclination) an overestimation of only 1° true cup inclination (15 av/45 incl; 46-45=1°). Selecting anteversion first affects inclination but will not lead to more than 3 degrees misinterpretation for the studied cup orientations. The traditional reversed sequence (inclination followed by anteversion) leads to more misinterpretation of true anteversion. As indicated in Table 1, we found that for certain combinations of inclination and anteversion true anteversion almost doubled the intended value. Pelvic orientation grossly influences true cup orientation. Table 3 shows that changes in rotation ranging from 5 to 15 degrees in any direction lead to misinterpretation of cup position with ranges of 1.1-15° anteversion and 0.6–15° inclination. Anteversion is mainly affected by posterior and anterior tilt, internal rotation and external rotation of the pelvis. Abduction and adduction influence mostly true inclination.

DISCUSSION

This study demonstrates that true cup positioning is influenced by sequencing and pelvic orientation. Quantifications were made in a modeling program initially designed for architectural, civil and mechanical engineers. This program is adequate for understanding the relationship between the orientation of a cup and the anatomical planes and axes. Lewinnek's safe zone is much debated but nevertheless most surgeons try to position their cups within this zone. Lewinnek defined his safe zone in true inclination (30-50) and true anteversion (5-25). Understanding the difference between true and planar helps the surgeon to understand why freehand cup positioning is inaccurate. Table 1 shows that the true cup anteversion can range from 1.5 to 18 degrees, depending on the amount of true inclination given. Table 2 shows that the mismatch between true and planar inclination is smaller if true anteversion is selected first. This can be explained by the smaller amount of degrees in anteversion according to Lewinnek's zone. According to this theoretical model, the best way to position the cup freehand, is by applying anteversion first, followed by planar inclination.

Malpositioning of components in THA is associated with decreased range of motion, luxation and increased wear. Increased wear of the conventional metal op polyethylene cup induces loosing of components due to particle disease and thereby shortens the implant's survival. Metal-on-Metal THA's were introduced as an alternative to the metal op polyethylene articulation. Although good short term results were reported, there is now increasing concern about the possible toxic effects of generated metal debris[10]. Although further studies are necessary to explain the generation of metal débris and failure mechanism of these articulations, malpositioning, especially high inclination, is thought to play an important role and thereby stressing the importance accurate positioning.

Malpositioning of the acetabular cup can be divided in patient- and surgeon related factors.

Patient related factors like pelvic tilt occurs in both the supine and in the lateral decubitus position. Lembeck et al. demonstrated that average pelvic tilt at rest was -4 in the lying position and -8 in the standing position, and ranged from -27 to +3, leading to increased risk of malpositioning by underestimating the amount of anteversion in the supine position. [11]

McCollum and Gray found that when a patient is placed in the lateral decubitus position, the lumbar lordotic curve is flattened, and the pelvis may be flexed as much as 35°. They noted that if the acetabular component was orientated in 20° of anteversion to the longitudinal axis of the body, when the patient stood, the lumbar lordosis would recur, the pelvis would extend, and the acetabulum could be retroverted by as much as 10°-15° 17,8. In the lateral decubitus position, the pelvis often adducts 10°-15° toward the foot, increasing the risk of vertical cup placement. [12] If the pelvis tilts posteriorly, the risk of decreased cup anteversion increases (table 3). Other patient related factors like obesity or distorted anatomy can contribute to malpositioning due to impediment of soft tissue or bone. Sequencing during cup implantation almost always occurs because it is nearly impossible to position the cup without manipulating in some degree to overcome the impediments.

Most patient related factors are hard to adjust in contrast to the surgeon related factors. Surgical exposure can be increased in case of obesity and for better identification of anatomical landmarks. Some authors state that the transverse acetabular ligament can be used as a reliable reference point for anteversion[13], but the reliability and reproducibility of this technique is still under debate. [14-16] Considering surgical approach, less anteversion can be given to the cup in the anterolateral approach versus the posterior lateral approach. Table 1 shows that the difference between true and planar anteversion is smaller for lower amounts of desired anteversion. The most accurate way for freehand cup positioning derived from table 1 and 2 is by using the anterolateral approach and placement of the cup by first selecting anteversion, followed by inclination. This statement is only valid if the pelvis is well positioned and no movement occurs during cup implantation, circumstances that are hard to obtain in everyday practice. The use of angled inserters are mostly referenced to the operating table or floor and therefore unreliable for the same reason. Rigid fixation of the pelvis is hard to achieve especially because, in our clinical experience, the pelvis tends to move while positioning the cup, due to levering of the femur. Asayama and colleagues found that the pelvis primarily tilts forward, averaging 14.57° anterior tilt in the horizontal plane. They noted that the pelvic motion primarily occurred while the Hohmann retractor was being applied to the femur to expose the acetabulum. [17] Beckman et al. conducted a systematic review to compile the best available evidence for the use of Computer Assisted Surgery (CAS). [18] They found that navigation reduced the variability in cup positioning and the risk of inserting the acetabular component beyond the safe zone, thereby reducing the number of outliers. Gandhi et al showed similar results in a meta-analysis consisting of 250 patients. [19] A more recent review of the literature confirms that, despite confusion in terminology of cup orientation, computer navigation leads to a "safer placement" and fewer dislocations than component positioning without navigation. [20]

Hence, navigation systems improve reliability and have more reproducible results. However, use of navigation systems also has its drawbacks, such as increased operation time, higher costs and a considerable learning curve. Compensation of costs by increasing survival due to better component orientation and the development of an easier to use system should overcome these drawbacks in the nearby future. There is thus a need for a method that combines the precision of computer-navigated cup insertion with the cost-effectiveness, time and simplicity of freehand positioning. Such a method should compensate for pelvic movement during surgery, avoid

sequencing by directly guiding the surgeon to the desired endpoint of the cup, and be based on the anatomical pelvic planes.
Surgeons should be aware that freehand cup positioning inevitably results in significant inaccuracy. This study shows that in clinical cases, where traditional instruments are used without navigation tools, the sequence in which inclination is selected first significantly leads to inaccuracy of the desired anteversion.

In conclusion, freehand positioning of the acetabular cup is inaccurate due to sequencing and pelvic movement. Patient- and surgeon related factors further influence this inaccuracy. Alternatives like Computer Assisted Surgery should be considered for more accurate cup positioning. This will increase implant survival, being of special importance due to aging of the population and the implantation of THA's in a growing group of younger patients.

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CHAPTER 4

Acetabular augmentation ring for recurrent dislocation of total hip arthroplasty: 60% stability rate after an average follow-up of 74 months

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ABSTRACT

Between 1988 and 2002, 47 patients (50 hips) were treated with acetabular shell augmentation arthroplasty for recurrent idiopathic dislocation of their total hip arthroplasty. Apparent causes for dislocation such as deep infection, component malposition, or polyethylene wear were excluded. Follow-up averaged 74 months (range, 12–178 months), and clinically, 30 hips (60%) did not present a subsequent dislocation at most recent follow-up. In five hips (10%), deep infection after the augmentation procedure necessitated removal of the entire prosthesis. In our opinion, this technique cannot be recommended as it has an unacceptable failure and high infection rate.

INTRODUCTION

Recurrent dislocation after total hip replacement is a disaster for patient and surgeon alike. Depending on the cause of the problem, several treatment options have been described in the literature. Conservative treatment with an above-knee spica brace or hip cast-brace has been reported to be successful in selected cases. Stewart described a 73% success rate of treatment with a hip cast-brace for hip prosthesis instability. [14] In cases of malposition of prosthetic components, revision arthroplasty is another well-accepted treatment. For patients with no apparent malpositioning, an acetabular augmentation ring can be a less invasive alternative treatment modality. This procedure, first described by Olerud and Karlström[12], is a relatively simple method attempting to prevent further dislocations, compared to acetabular shell and femoral stem revision. The aim of this retrospective study is to evaluate the results of the procedure.

MATERIALS AND METHODS

Between June 1988 and March 2002, 47 patients (50 hips) were treated with an acetabular shell augmentation ring for recurrent idiopathic dislocation of their total hip prosthesis at our hospital. All obvious causes for recurrent dislocation such as polyethylene wear, infection or component malposition were excluded. Shell orientation was estimated using the technique described by Widmer. [16] A normal inclination was defined between 30° and 50°, and anteversion between 5° and 25°. [9] End points for this study were re-luxation or revision surgery. All patients' radiographs and charts were reviewed. Augmentation was performed using the Waldemar Link anti-luxation ring (Fig 1). The appropriate-sized ring was fixed to the shell with malleolar screws in the position offering the most stability, depending on the anticipated direction of dislocation.

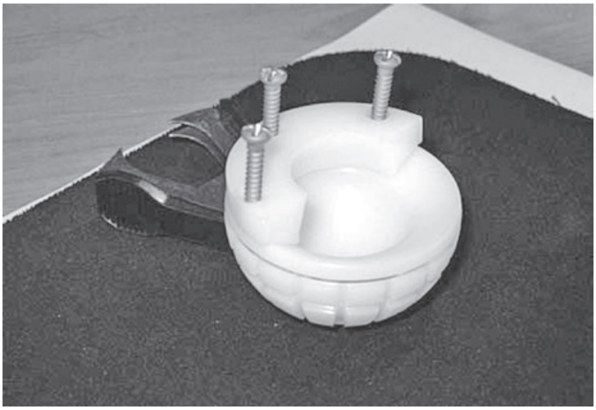

Figure 1. Acetabular augmentation ring partially fixed to the acetabular component of the dislocating total hip arthroplasty. The ring is fixed to the cup in the position offering the most stability, depending on the anticipated direction of dislocation.

STATISTICAL ANALYSIS

Survivorship free of subsequent dislocation was estimated with a Kaplan-Meier analysis. Comparison of continuous variables was done with the Mann-Whitney U test or, for categorical variables, with Chi-square testing.

RESULTS

Augmentation of the acetabular component was performed in 50 hips on 47 patients (12 males and 35 females). The average age was 75 years (range, 58–94 years) at the time of augmentation. Average follow-up was 74 months (range, 12–178 months). There were 27 right and 23 left hips treated after an average of 2.5 dislocations (range, 2–5). In 47 hips the surgical approach for the primary hip operation as well as the augmentation were posterolateral, and in the remaining three a lateral approach was used. Augmentation was performed an average of 27 months (range, 6–170 months) after the index operation. Thirty hips (60%) did not experience further dislocations after an average follow-up of 74 months after the ring augmentation procedure. Fifteen hips (30%) experienced subsequent dislocations after an average follow-up of 60 months (range, 2–126 months). Five hips (10%) developed a deep infection after an average follow-up of 16 months (range, 1–34 months), requiring removal of the hip prosthesis. Radiological, all hips that presented further dislocations showed broken screws of the augmentation ring (Fig. 2).

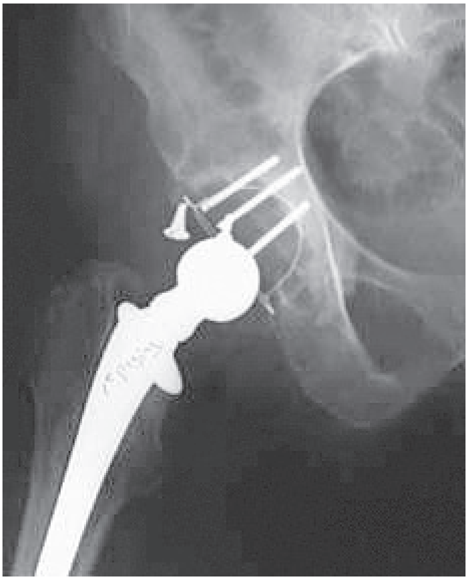

Figure 2. Redislocation. The component is displaced and there is interposition of the augmentation ring in the acetabulum. The patient was treated with a revision of the acetabular component.

Three hips showed broken screws on radiographs 1–5 years before they dislocated. In 44 of 50 hips the inclination and anteversion could be estimated. Inclination ranged from 30° to 69° with an average of 48°, and anteversion ranged from 5° to 47° with an average of 17°. Two out of 15 hips from the dislocation group were considered to be out of the safety zone regarding anteversion, as described by Lewinnek [9], and two out of 29 in the nondislocation group ($P = 0.42$). Inclination was out of the safety zone in two out of 15 of the dislocation group and four out of 29 in the nondislocation group ($P = 0.64$). All 15 patients with further dislocations underwent subsequent surgery (Table 1). Two of these patients developed a deep infection, which makes the total infection rate in our study 14% (7 patients).

Patient	2nd procedure	Outcome	Follow-up (months)
1	Cup revision	Stable	36
2	Cup revision	Stable	28
3	Cup revision	Stable	64
4	Cup revision	Stable	32
5	Cup revision with re-augmentation	Stable, broken screws after 18 months	139
6	Stem revision	Stable	26
7	Re-augmentation	Redislocation	54
8	Re-augmentation	Cup loosening, broken screws	62
9	Re-augmentation	Infection	53
10	Re-augmentation	Infection	27
11	Re-augmentation	Stable	30
12	Re-augmentation	Stable	48
13	Longer neck	Stable	34
14	Cup revision and longer neck	Stable	42
15	Stem revision	Stable	48

Table 1. Subsequent procedures after redislocation

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Figure 3 shows survivorship free of subsequent dislocations during follow-up. The survival rate after 5 years was 83% (95% confidence interval 77–89%) and after 10 years 44% (95% confidence interval 30–49%).

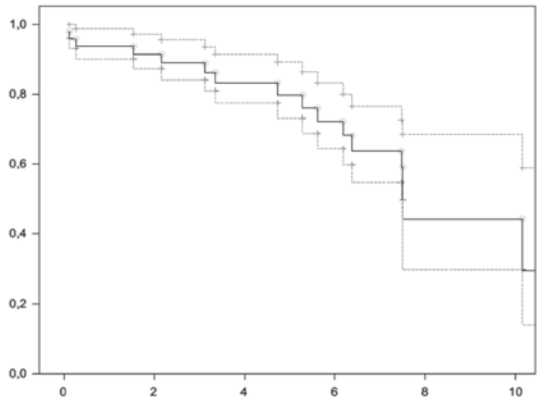

Figure 3. Kaplan-Meier survivorship free of subsequent dislocation and 95% confidence interval (dotted lines). Follow-up in years.

No significant relationship could be established with respect to sex, side operated on, age, interval from primary hip arthroplasty to augmentation, number of dislocations, or surgical approach and redislocation.

DISCUSSION

Our study reveals a high failure rate of 40% after acetabular augmentation for recurrent dislocation of total hip arthroplasties. Several studies have reported varying results of this procedure.[2, 10–12] To our knowledge, our study is the largest reported in the literature (Table 2).

			Outcome	
Author	N	FU months (range)	Success	Failure
Olerud et al. (1985)	6	(9-36)	6	0
Mogensen et al. (1986)	2	10 (7-13)	2	0
Reickerås (1988)	3	24	1	2
Graham et al. (1988)	3	NR	0	3
Gie et al. (1989)	10	12	7	3
Williamson et al. (1989)	3	14 (6-18)	0	3
Güngör et al. (1990)	13	12	12	1
Watson et al. (1991)	2	13 (7-18)	1	1
Bradbury et al. (1994)	16	35 (12-70)	14	2
Cohen et al. (1994)	9	25 (12-48)	5	4
Nicholl et al. (1999)	28	26 (0-108)	23	5
Charlwood et al. (2002)	20	24	20	0
Bosker et al. (2005)	50	74 (12-178)	30	20

NR: not reported; FU: follow-up

Table 2. Results from acetabular augmentation rings in the literature.

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Acetabular cup augmentation arthroplasty was first described by Olerud and Karlström[12], who used a segment cut from another polyethylene cup. They treated six patients successfully. The problem with these studies is the small number of patients and short follow-up, so they are difficult to compare with our results. We saw promising results in the first few years after augmentation, with an 83% success rate after 5 years, but the number of patients that redislocated continued to rise steadily over the years, dropping to a 43% survival rate after 10 years (Fig. 3). Although Olerud and Karlström[12] argued that the augmentation ring would be subjected to minimal stress, Watson et al.[15] saw screw breakage caused by metal fatigue causing brittle fracture, suggesting movement of the device relative to the acetabular shell. Habitual dislocation of a hip prosthesis is considered to be due mainly to cup malpositioning or to secondary polyethylene wear. Nevertheless, most of the acetabular components appeared to be within the safety zone of Lewinnek[9]. The six patients who were estimated to be outside the safety zone of acetabular orientation were equally distributed over the success and failure groups, so cup malposition did not appear to be a relevant factor in this study. In our group, seven patients (14%) ultimately lost their prosthesis due to infection after multiple revision procedures (augmentation and reaugmentation). This underscores the fact that habitual dislocation of a total hip prosthesis necessitating revision surgery is a very serious condition that can lead to significant morbidity. Strategies in treating habitual dislocation of a hip prosthesis include bracing[3], hip spica treatment[17], revision of one or both components, and acetabular augmentation. We feel that, in cases in which the alignment of the prosthesis components seems to be adequate[5] and there is no polyethylene wear, as on plain radiographs, acetabular augmentation arthroplasty could be considered. It must be realised that results deteriorate rapidly with time; therefore, it is appropriate to reserve the procedure for biologically older and less active patients. The main advantage of the acetabular augmentation technique is that it is a less demanding procedure compared to revision arthroplasty. However, the increased surface contact and possible friction between the acetabular shell and the augmentation ring may cause more polyethylene wear. The fact that the reconstruction becomes more constrained could also eventually lead to more rapid mechanical loosening of the shell in the bony acetabulum. Although this was also recognised by Watson[15], our data do not support this hypothesis.

CONCLUSION

Acetabular ring augmentation is an option for habitual dislocation of a hip arthroplasty in the absence of gross malalignment or polyethylene wear in elderly and less active patients. It is a less demanding procedure than revision arthroplasty but with poor long-term results. For this reason it should be reserved for patients in whom major surgery is contraindicated. With newer acetabular revision possibilities the role of this technique is very limited.

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CHAPTER 5

High incidence of pseudotumour formation after large-diameter metal-on-metal total hip replacement: a prospective cohort study

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ABSTRACT

Peri-articular soft-tissue masses or 'pseudotumours' can occur after large-diameter metal-on-metal (MoM) resurfacing of the hip and conventional total hip replacement (THR). Our aim was to assess the incidence of pseudotumour formation and to identify risk factors for their formation in a prospective cohort study. A total of 119 patients who underwent 120 MoM THRs with large-diameter femoral heads between January 2005 and November 2007 were included in the study. Outcome scores, serum metal ion levels, radiographs and CT scans were obtained. Patients with symptoms or an identified pseudotumour were offered MR imaging and an ultrasound-guided biopsy. There were 108 patients (109 hips) eligible for evaluation by CT scan at a mean follow-up of 3.6 years (2.5 to 4.5); 42 patients (39%) were diagnosed with a pseudotumour. The hips of 13 patients (12%) were revised to a polyethylene acetabular component with small-diameter metal head. Patients with elevated serum metal ion levels had a four times increased risk on developing a pseudotumour. This study shows a substantially higher incidence of pseudotumour formation and subsequent revisions in patients with MoM THRs than previously reported. Because most revision cases were identified only after an intensive screening protocol, we recommend close monitoring of patients with MoM THR.

INTRODUCTION

Approximately 750 000 total hip replacements (THRs) are performed annually. [1] Metal-on-metal (MoM) THRs were introduced for their purported advantages over conventional articulations, such as low rates of wear and increased stability. [2] MoM resurfacing arthroplasties and conventional THRs using a large size-modular femoral head have become increasingly popular during the last decade, especially in young, mobile patients. Based on a conservative estimate, approximately
500 000 current-generation MoM hip replacements, including resurfacing and THR, have been implanted during the last 15 years worldwide. [3] Favourable patient satisfaction, low rates of dislocation and wear and good survival has been reported at medium-term follow-up.[4] However, there have been reports of the formation of peri-articular masses in some patients, referred to as pseudotumours. [5] The term 'pseudotumour' appeared a century ago and was originally reserved for a neurological condition associated with the symptoms and signs of an intracranial tumour in the absence of an actual space-occupying lesion (pseudotumour cerebri). [6] Since then, it has been used to describe a variety of non-neoplastic non-infective lesions in various locations. The term is currently used in arthroplasty of the hip to denote a peri-articular mass caused by an immunological delayed hypersensitivity response to metal particles, characterised by a lymphocyte-dominated histological pattern. [7] A more specific term used is adverse reaction to metal debris (ARMD). [8] The term aseptic lymphocytic vasculitis-associated lesions (ALVAL) is reserved for the interpretation of histological findings. [9] Symptoms may vary, but characteristically include an unexplained discomfort in the region of the hip, sometimes accompanied by clicking or subluxation. [10] Occasionally on examination, a swelling of the upper leg or a lump in the inguinal region can be found. More serious symptoms include dislocation, nerve palsy[11] and fracture[12],depending on the location and size of the pseudotumour. When the diagnosis of pseudotumour is established and symptoms are troublesome[13], revision surgery is an option. The tumour is removed as radically as sensible and the arthroplasty is revised. The incidence of pseudotumours in retrospective studies after MoM THR varies between 1% and 4%.[14,15] These incidences are derived from symptomatic and revision cases, most likely underestimating the true incidence. The aims of this study were to establish the incidence of symptomatic and asymptomatic pseudotumours and to identify the risk factors for their formation in a prospective cohort of patients after a large-size modular femoral head MoM THR.

PATIENTS AND METHODS

We conducted a single-centre double-blind block-randomised controlled trial, after obtaining ethical approval. Patients who were eligible for THR were recruited between January 2005 and November 2007; all provided informed consent. Exclusion criteria included a body mass index (BMI) > 30 kg/m2, previous surgery on the ipsilateral hip or age > 75 years. A total of 119 patients with 120 consecutive primary uncemented MoM THRs were included in a separate randomised controlled trial investigating the effects of different surgical hip approaches. [16] The

Harris hip score (HHS)[17] was recorded at six weeks and one year post-operatively. The patient-centred Short-Form 36 (SF-36)[18] health survey was obtained pre-operatively and at six weeks and one year post-operatively. A Bi-Metric porous-coated uncemented stem with a metal-on-metal M2a-Magnum femoral head and ReCap acetabular component (Biomet, Warsaw, Indiana) were used in all patients. The modular head and acetabular component are high-carbon, as-cast (single heated) components. The system is modular, with increasing head size and concomitant larger shell size and the option to adapt the neck length using different-length tapers. The main components of the head and acetabular component are produced from a cobalt–chromium alloy containing a small proportion of molybdenum and carbon. The stem and taper are made of a titanium, aluminium and vanadium alloy. The radial clearance level of the M2a-Magnum articulation is maintained at 75 to 150 μm.[19] The acetabular component is 6 mm thick at the dome and an average of 3 mm thick at the rim. We used this prospective cohort of patients to investigate the incidence of pseudotumours and to identify potential risk factors for their occurrence, which required an adaptation to the original study protocol, for which ethical approval was obtained.

Definition

We defined a pseudotumour of the hip as a (semi)-solid or cystic peri-prosthetic soft-tissue mass with a diameter ≥ 2 cm which could not be attributed to an infection, malignancy, bursa or scar tissue. The diagnosis was based on CT evaluation and confirmed by MRI and/or ultrasound. A thickened capsule was recorded but not considered to constitute a pseudotumour.

Patients

Three patients who received a cemented polyethylene acetabular component in the original investigation were excluded from the study. Therefore, 116 patients (117 hips) were included. When reviewed post-operatively they were questioned about symptoms in the groin, buttock, thigh and leg, such as pain, swelling, discomfort, numbness, and sensations of subluxation and clicking. Pain was recorded on a visual analogue scale (VAS) ranging from no pain (0) to extreme pain (10). The HHS, SF-36 and Hip Disability and Osteoarthritis Outcome Score (HOOS)[20] questionnaires were completed at six weeks, one year and final follow-up (median 3.6 years (2.1 to 4.5)). The HOOS consists of five subscales: pain, other symptoms, function in daily living, function in sport and recreation (sport/rec) and hip-related quality of life (QOL). Standardised response categories were offered, with scores ranging from 0 to 4 for each item. A normalised score (100 indicating no symptoms and 0 indicating most severe symptoms) was calculated for each subscale. The results were plotted as an outcome profile. Patients were considered to be symptomatic if one or more of the previously described symptoms were reported at the follow-up. Patients were also questioned about their use of vitamin supplements and possible history of allergies. All patients underwent pelvic (pubis-centred) and hip (both hip and axially centred) radiographs, and the angle of inclination of the acetabular component was assessed. In addition, each patient underwent CT evaluation of the pelvis and knee to detect a peri-articular mass, if present, and to assess anteversion of the femoral component relative to the retrocondylar axis of the knee and anteversion of the acetabular component. Two radiologists (MFB, MM) evaluated all CT scans, and when the results did not match consensus was obtained. When a peri-articular mass was identified, its maximum dimensions were measured and MRI was performed and the patient was offered an ultrasound-guided biopsy of the mass. On MRI and/or ultrasound examination the pseudotumour was classified as mixed, solid or cystic. In the absence of such a mass, and when no symptoms were reported, the study ended and these patients returned to their regular follow-up schedule. If symptoms were present but no mass was identified on CT, an MR scan was performed. Laboratory analysis with atomic mass absorption spectrometry of serum levels of cobalt and chromium ions was performed during follow-up. Blood samples were collected according to recent guidelines.[21] We considered elevated concentrations of cobalt or chromium in the serum to be those > 5 μg/l. Serum levels of leucocytes, ESR, CRP, creatinine and urea were also analysed to screen for infection and renal impairment. Histological analysis was performed based on 16-gauge needle biopsies and, when applicable, cytological samples were evaluated by standard light microscopy. We evaluated the following parameters for risk factors: age, gender, diameter of the femoral component, side, surgical approach (anterolateral, posterolateral and minimally invasive for both groups), inclination and anteversion of the acetabular component, anteversion of the stem, combined anteversion of the acetabular component and stem, hip centre line–edge distance, metal ion levels > 5 μg/l, groin pain, clicking sensations, VAS score, HHS, SF-36, and known allergies to antibiotics or nickel. Vitamin supplements or other metal implants were regarded as confounding factors for the concentrations of metal ions in the serum. Patients who were found to have a peri-articular mass on the contralateral side were excluded from the analysis of serum ion levels.

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STATISTICAL ANALYSIS

The incidence of peri-articular masses in the study group was expressed as a percentage with 95% confidence intervals (CI). Non-parametric testing was conducted in ordinal or not normally distributed continuous variables, whereas parametric statistics were used in normal distributed variables. Based on logistic regression analysis, the potential risk factors of age, gender, acetabular component diameter, modular femoral head diameter, hip centre line–edge distance, side, operative approach, acetabular inclination and anteversion, stem anteversion, combined anteversion of the acetabular component and stem, metal ion levels > 5 μg/l, allergies, supplements, groin pain, renal impairment, stiffness and the presence of other implants, were initially studied univariately. Only variables that demonstrated an association of $p < 0.10$ in the univariate analysis were fitted in a multivariate logistic regression model. A best-subset stepwise forward procedure was followed to develop a prediction model for peri-articular mass. Only significant factors in the final regression model were considered predictors and presented with their odds ratio (OR). Multilevel analyses were used to demonstrate, if present, differences longitudinally in the SF6 and HHS scores between individuals with and without a peri-articular mass. Because our data for the SF-36 questionnaires and HHSs were repeatedly measured over time, repeated observations (level 1) were nested within subjects (level 2). Fixed and random intercepts were included in the longitudinal prediction models. Significance of the beta coefficient was based on the Wald test. Outcome scores were plotted to check for compliance with model assumptions in all linear regression models. Data were analysed with SPSS 18.0 (SPSS Inc., Chicago, Illinois) and MLwiN 2.22 software (Centre for Multilevel Modelling, Bristol, United Kingdom). For all tests, a two tailed significance level with a p-value < 0.05 was used.

RESULTS

Between May and November 2010, all 116 patients (117 hips) or their relatives were contacted. Three patients had died of unrelated causes and two were lost to follow-up. Four patients refused to participate in the trial, but did inform us that they had no symptoms from their hip. Therefore, 107 patients (108 hips) were available for review at a median follow-up of 3.6 years (2.1 to 4.5). The profile of the trial is shown in Figure 1, and the characteristics of the patients in Table I.

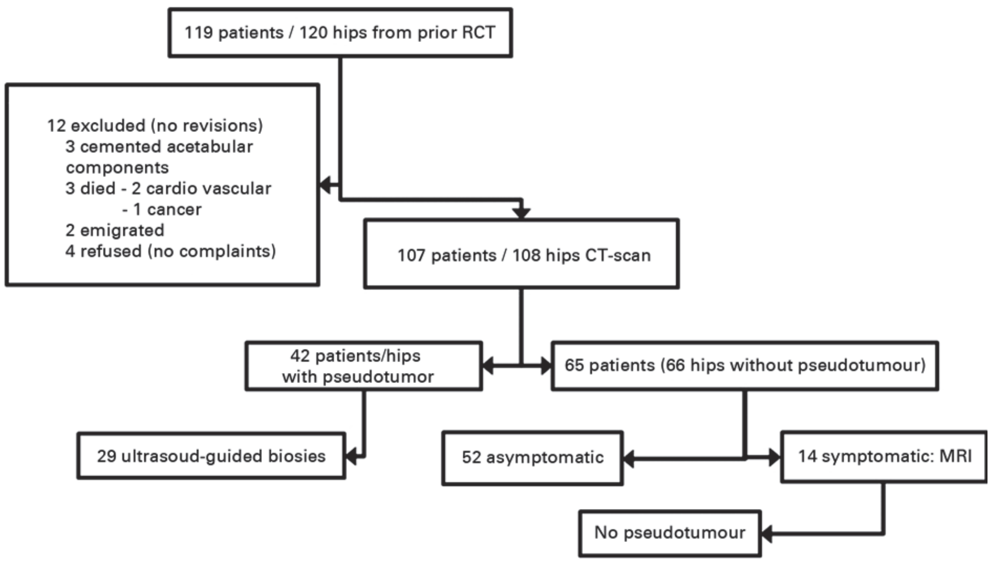

Figure 1. Flowchart showing the trial profile.

	Total (n=108)	Pseudotumour (n=42)	No pseudotumor (n=66)	Revisions (n=13)
Males (n, %)	52 (48)	16 (38)	38 (58)	4 (31)
Mean age (yrs) (range)	60 (38 to 72)	60 (39 to 72)	60 (38 to 71)	59
Follow-up(yrs) (range)	3.6 (2.1 to 4.5)	3.6 (2.1 to 4.5)	3.6 (2.6 to 4.5)	3.2 (2.1 to 4.9)
Symptoms (n, %)				
Swelling	6 (6)	4 (10)	2 (3)	4 (31)
Non-specific groin pain	32 (30)	19 (45)	13 (20)	11 (85)
Clicking sensations	24 (22)	13 (31)	11 (17)	7 (54)
Allergy (n, %)				
To antibiotics	4 (4)	4 (10)	-	2 (15)
To Nickel	9 (8)	4 (10)	5 (8)	1 (8)
Surgical approach (n, %)				
Classical	53 (49)	19 (45)	34 (52)	5 (38)
Posterolateral	56 (52)	23 (55)	33 (50)	6 (46)
Anterolateral	52 (48)	19 (45)	33 (50)	7 (54)
Minimal invasive	55 (51)	23 (55)	32 (49)	8 (62)
Median femoral head Ø (mm) (range)	46 (40 to 54)	46 (40 to 54)	46 (40 to 54)	45 (2)
Mean (SD) hip centre line-edge distance (mm)	18 (3)	18 (3)	18 (3)	17 (3)
Mean inclination angle of the acetabular component (°) (range)	48 (31 to 65)	47 (31 to 60)	49 (33 to 65)	49 (SD 8)
Mean anteversion angle of the acetabular component (°) (range)	11 (-9 to 58)	10 (-7 to 58)	11 (-9 to 35)	8 (SD 7) *
Mean anteversion of femoral component (°) (range)	11 (-25 to 40)	13 (-8 to 40)	10 (-25 to 33)	14 (SD 13) *
Mean combined anteversion (°) (range)	22 (-7 to 56)	23 (-7 to 50)	21 (-7 to 56)	23 (SD 14) **
Mean (SD) Maximum swelling on CT, (cm)	N/A	6 (2)	N/A	7 (4) *
Mean (SD) serum Cobalt (μg/l)	9 (17)	13 (22)	6 (11)	25 (38)*
Mean (SD) serum Chromium (μg/l)	8 (13)	10 (15)	7 (12)	20 (25)*

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	Total (n=108)	Pseudotumour (n=42)	No pseudotumor (n=66)	Revisions (n=13)
Mean outcome scores (range)				
HOOS	82 (14 to 100)	80 (24 to 100)	83 (14 to 100)	63 (40 to 72)*
SF36	80 (34 to 100)	78 (34 to 98)	81 (38 to 100)	60 (46 to 77)*
HHS	100 (93 to 100)	96 (89 to 100)	100 (96 to 100)	84 (66 to 91)*
VAS	1.5 (0 to 9)	2 (0 to 8)	1.2 (0 to 9)	3 (2 to 7)*
Revision (n, %)	13 (12)	13 (31)	0 (0)	

Table I. Patient characteristics and results of the 108 hip arthroplasties (107 patients). *values are based on 11 patients, excluding two patients previously revised.

We found a total of 42 pseudotumours in 42 patients. An additional four pseudotumours were found in the contralateral hip in patients with bilateral arthroplasties (n = 22), two of whom had bilateral pseudotumours. Because these had occurred in hips that were not included in the study, the rate of formation of a peri-articular mass was 42 of 108 hips (39% (95% CI 30% to 48%)). Multivariate analysis revealed that patients with serum
cobalt levels > 5 µg/l had a fourfold increased risk of developing a pseudotumour (OR 4.0; 95% CI 1.6 to 10.1). No other risk factors for developing a pseudotumour were identified (Table II).

Pseudo-tumor versus…	OR (95% CI)	P value
Age	1.01 (0.96 to 1.07)	0.75
Gender	2.21 (1.00 to 4.87)	0.05
cup size	0.87 (0.75 to 1.01)	0.06
Femoral head size	0.86 (0.75 to 0.999)	0.48
Hip centre line-edge distance	0.98 (0.85 to 1.12)	0.72
Side	0.48 (0.21 to 1.12)	0.09
lateral *versus* posterolateral approach	1.21 (0.56 to 2.63)	0.63
minimal invasive *versus* classical	0.78 (0.36 to 1.69)	0.53
inclination	0.96 (0.91 to 1.02)	0.17
anteversion	0.99 (0.94 to 1.03)	0.49
stem anteversion	1.03 (0.99 to 1.06)	0.18
combined cup/stem anteversion	1.01 (0.98 to 1.04)	0.49
Cobalt ion levels >5 µg/l	4.05 (1.63 to 10.06)	0.003
Chrome ion levels >5 µg/l	1.96 (0.87 to 4.41)	0.11

Pseudo-tumor versus…	OR (95% CI)	P value
Nickel allergy	1.28 (0.32 to 5.08)	0.72
Supplements	0.30 (0.03 to 2.64)	0.28
Groin pain	1.20 (0.997 to 1.44)	0.053
Serum creatinine	3.25 (0.29 to 37.01)	0.34
Stiffness	0.996 (0.98 to 1.02)	0.73
Other implants	0.53 (0.24 to 1.19)	0.12

Table II. Associations based on bivariate logistic regression analysis with their odds ratio (OR) and 95% confidence intervals (CI)

No relationship was found between the development of a pseudotumour and the size and position of the acetabular and/or the femoral component (Table II). The HHS, SF-36 (Table III) and HOOS scores ($p = 0.21$; Mann-Whitney U test) were not different in the pseudotumour or the non-pseudotumour groups.

Pseudotumor versus…	B coefficient (95% CI)	p-value
Short-Form 36	-1.57(-6.05 to 2.92)	0.50
Harris Hip Score	-2.74(-6.55 to 1.06)	0.16

Table III. Multilevel analysis. CI = confidence interval

The hips of two patients had already been revised. Histological analyses revealed ARMD, and per-operatively peri-articular masses were described in both patients, so they were merged into the pseudotumour group. Symptoms warranted a revision procedure in another 11 patients; the rate of revision rate was thus 12% (13 of 108). The details of the patients who underwent a revision are shown in Table I. Peri-operatively, at all revision procedures there was either an extensive black metallosis with peri-articular swelling and necrosis, or a large cystic or semi-solid tumour. There was extensive bone loss in all cases, mainly affecting the acetabular side. In four hips there was extensive corrosion of the taper–head interface, possibly contributing to the development of metal debris. In one patient the acetabular component was loose, but in all other cases it was firmly anchored. In two patients two or more per-operative biopsies produced positive microbiological cultures. These patients received antibiotics and there are no signs of active infection at present (after 1 and 1.1 years, respectively). There was a large variation in serum metal ion levels, ranging from 1 μg/l to 139 μg/l (mean 9.2 μg/l) for cobalt and from 0.7 μg/l to 90 μg/l (mean 7.5 μg/l) for chromium. Cobalt levels > 5 μg/l were found in 43 patients (40%) and chromium levels > 5 μg/l in 45 patients (42%). These ranges are illustrated in Figure 2.

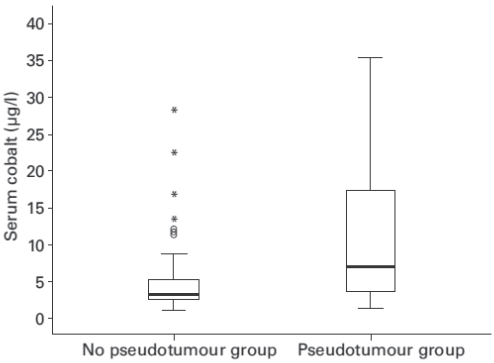

Fig. 2a

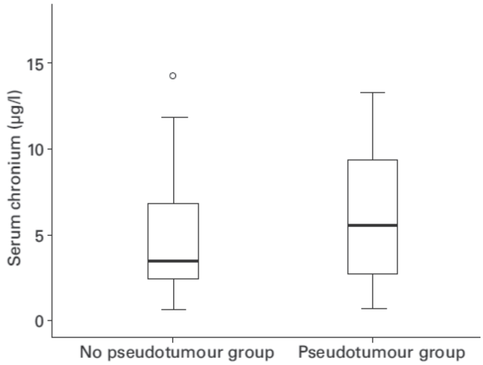

Fig. 2b

Figures 2a-b.
Box plots showing the serum levels of metal ions for a) cobalt and b) chromium. The boxes represent the median and interquartile range (IQR) and whiskers denote the range of data excluding outliers (°; values between 1.5 and 3 IQRs from the edge of the box) and extremes (*; values more than 3 IQRs from the box). Results beyond 40 µg/l and 15 µg/l for cobalt and chromium, respectively, are not displayed.

There was a strong correlation between cobalt and chromium levels (Spearman's $\rho = 0.827$; $p < 0.001$) and a significant relation between serum cobalt levels and the largest diameter of the pseudotumour (Spearman's $\rho = 0.361$; $p = 0.033$). Of the 42 pseudotumours, 21 were of the mixed type, 11 solid and ten cystic; their mean diameter was 6 cm (3 to 13).
Most were connected to the joint and located near or in the route of the surgical approach. Two pseudotumours extended into the abdominal space along the iliopsoas muscle. A total of 31 patients with a peri-articular mass on CT scanning underwent ultrasound-guided biopsy. Two patients who were receiving thromboembolic prophylaxis did not undergo needle biopsy, and in five hips the retrieved material was not suitable for analysis; this left 24 patients in whom a cytological analysis could be made. In these, a non-specific mixture of histiocytes, peri-vascular lymphocyte aggregates, necrosis and metal debris was identified.

DISCUSSION

Recently, concern has been raised about the formation of a peri-articular mass around a MoM hip arthroplasty which is referred to as a pseudotumour. In April 2010 the British Orthopaedic Association issued an alert to its members concerning large-sized femoral head MoM hip arthroplasty[22], and in May 2011 the American Food and Drug Administration ordered the post-market surveillance of MoM hip replacement systems from 21 companies.[23] Our study revealed a 39% incidence of pseudotumours after a large-sized femoral head MoM THR. Furthermore, in 13 patients (12% of the total; 31% of patients diagnosed with a pseudotumour) symptoms warranted revision surgery. One cross-sectional study reported a prevalence of asymptomatic pseudotumours of 4% (seven of 158) with comparable follow-up to our study.[15] In that report, three types of resurfacing arthroplasty of the hip were studied with a response rate of 75%, where ultrasound was used as the screening modality. Although effective in diagnosing pseudotumours, ultrasound is operator dependent.

Our original RCT was designed to evaluate the effects of minimally invasive surgical approaches on patient-related outcome measures (PROMs)[16],which supplement our subsequent screening protocol. All patients underwent a CT scan and, in case of a suspicious lesion, MRI. The images produced by both modalities were independently assessed by two radiologists. For additional histological investigation an ultrasound-guided biopsy was offered to all patients with a suspicious lesion. A systematic review of the literature on MoM hip resurfacing reported a mean survival of about 97% after 3.6 years, based on 10 000 hip replacements.[24] These results are significantly better than the 88% survival in our study with MoM large-head THRs. However, before we conducted this study only two of our patients had undergone revision. This amounts to a comparable survival rate of 98%. It was not until the trial protocol was implemented and additional CT scan evaluations and serum metal ion levels were obtained that the requirement for addition revisions was identified. A patient with discomfort in the groin, a clicking sensation, adequate range of movement and a radiologically well-positioned prosthesis without signs of loosening would be scored as an excellent result. The fact that clinical scores did not differ between the pseudotumour and non-pseudotumour groups reflects the insidious course that pseudotumour formation takes. Symptoms emerge slowly and are generally initially mild and often have little impact on patient-reported outcome scores. When symptoms of swelling, pain in the groin and clicking become sufficient to warrant revision, a sizeable pseudotumour with extensive local-tissue destruction may already be present.

Several papers on MoM resurfacing hip arthroplasty report component malposition, smaller femoral head/acetabular components and female gender (possibly related to smaller head size) as risk factors for the formation of a pseudotumour.[25,26] Other possible risk factors are allergies to antibiotics and nickel.[14] An association between pseudotumour and elevated levels of serum cobalt and chromium has also been established.[15] In our study, we investigated many potentially relevant parameters, but no single risk factor was identified other than a fourfold increase in the risk of developing a pseudotumour in patients with serum cobalt levels > 5 μg/l. The median head size of 46 mm in our study is small, especially compared with other studies using a resurfacing arthroplasty.[27] The true incidence of pseudotumour formation after MoM resurfacing arthroplasty of the hip remains largely unclear, but the reported incidence is significantly lower than in our series with a conventional stemmed MoM THR.[27] We encountered extensive corrosion on the taper and trunion in some revision cases contributing to the formation of metal debris, and it may be that well-positioned components are still associated with the increased production of debris from this junction. This may also explain why the association between pseudotumour formation and malposition of components was not established in our study.

We believe that the CT scanning used to detect the presence of a peri-articular mass, despite scattering artefacts caused by the large metal implant, provides diagnostic images with the added benefit of allowing the measurement of anteversion of the acetabular and femoral components. [28] CT scanning was preferred over ultrasound as a screening modality because it is less operator dependent. CT is also more readily available than metal artefact reduction scanning (MARS) MRI. [29] In order to exclude false positive cases, we undertook MR imaging to confirm a positive CT scan for pseudotumour, and to minimise the risk of false negative results we also obtained MRI scans in all four symptomatic cases with negative CT scans. In all cases MRI confirmed the diagnosis suggested by the CT scans. We found a large range of serum metal ion levels, and levels > 5 μg/l were found in over 40% of the patients. The additional MoM interfaces at the taper–head junction or taper–taper adaptor–head junctions in MoM THR are the probable explanation for an increased formation of metal debris with this arthroplasty. This is despite being manufactured from high-carbon, as-cast, single heated cobalt–chromium alloy, which has been shown to provide enhanced protection against abrasive wear and reduced wear rates compared to multiple heat-treated materials. [30] The low clearance of the implant is thought to be associated with increased wear due to reduced fluid film formation. [31] Histological analysis revealed a mixed infiltration of histiocytes and peri-vascular lymphocytes with metal debris. Generally, our 16-gauge needle biopsies were too small, with insufficient tissue to be able to reliably calculate the appropriate ALVAL score. [32] This analysis requires samples collected during revision surgery. In addition, the histology in the biopsies did not appear to be specific to MoM arthroplasties, as the infiltration pattern is also found in conventional metal-on-polyethylene THRs, albeit rather less extensively. [33] The relevance of asymptomatic pseudotumours remains unclear. However, as pseudotumours have been reported to become symptomatic up to 15 years post-operatively[12] and considering our short follow-up, the high rate of pseudotumour formation and the accompanying local soft-tissue destruction at the time of revision found in our patients is a cause for great concern.

This study shows that there is a substantially higher incidence of pseudotumour formation and subsequent revision in our series with the Biomet M2a-Magnum/ReCap MoM THR than previously reported in other studies on large-diameter modular femoral head MoM conventional THR or resurfacing hip arthroplasties. We are unaware of any other published study involving MoM hip arthroplasties which has examined all its patients with CT/MR scanning. Because most revisions in symptomatic patients were identified only after applying a comprehensive screening protocol, we recommend close monitoring of all patients with a MoM hip arthroplasty.

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CHAPTER 6

Pseudotumor formation and serum ions after large head metal-on-metal stemmed total hip replacement. Risk factors, time course and revisions in 706 hips

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ABSTRACT

Although metal-on-metal may offer benefits over conventional bearings in total hip arthroplasty, generated debris can lead to adverse local tissue reactions and systemic effects. In this study the incidence, time course and risk factors for pseudotumor formation were analysed after large femoral head metal-on-metal stemmed total hip arthroplasties. Furthermore, the relevance of serum metal ions is investigated and revisions accounted for.

All patients treated in our clinic with large head metal-on-metal stemmed total hip arthroplasties were contacted and screened. CT scan examination, serum metal ions and conventional X-rays were obtained. Symptoms associated with pseudotumors were recorded.

After a median follow-up of 3 years, 706 hips were screened in 626 patients. There were 228 pseudotumors (32.3%) in 219 patients (35.0%). Pseudotumor formation significantly increased after prolonged follow-up. Independent risk factors for the presence of pseudotumor were: aspecific pain, cobalt ≥ 4 μg/l, and swelling. Seventy-six hips (10.8%) were revised in 73 patients (11.7%), risk factors being younger age at follow-up, aspecific pain, cobalt ≥ 4 μg/l, and swelling. The best cut-off point for both cobalt and chromium was 4 μg/l (sensitivity 57.3% and 53.9%, specificity 71.0% and 65.6%).

This study shows a dramatic increase of pseudotumors in patients treated with large head metal-on-metal total hip arthroplasties after prolonged follow-up. A high incidence of pseudotumors was confirmed. Associated risk factors for pseudotumor formation are of limited importance. Cobalt and chromium should be regarded as poor predictors for the presence of pseudotumor leaving cross-sectional imaging as the main screening tool during follow-up.

INTRODUCTION

Large head metal-on-metal (MoM) bearings for total hip arthroplasty (THA) have purported advantages over conventional articulations such as lower wear rates, increased range of motion and increased stability which has made them a popular solution in the young and active patient with osteoarthritis of the hip.[1,2] Although good clinical results and survival have been reported at medium-term follow-up[3], serious adverse reactions to metal debris (ARMD) leading to early failure and the formation of pseudotumors as well as systemic toxicity of increased serum levels of chromium (Cr) and cobalt (Co) have been described.[4-6] Since 2010, metal-on-metal hip articulations have been on increased scrutiny from governmental regulatory agencies and national and international societies leading to alerts, advices and post marketing surveillance up to outright discontinuation of metal-on-metal devices.[7-9] Metal debris is thought to be generated by the articulation and/or the taper adapter interface depending on the model of prosthesis used. The exact mechanism of local and systemic metal release is yet not fully understood. Pseudotumors can be granulomatous or cystic lesions, neither infective nor neoplastic, which develop in the vicinity of the total hip arthroplasty. They can be large or small in size with or without communication to the joint. The lesion is supposedly progressive. It can cause pain, swelling, pressure effects, subluxation, bone and soft tissue destruction and can as well be asymptomatic. Revision arthroplasty is advised in case of symptoms and/or tissue destruction.[10]
We previously reported on a smaller prospectively followed subset of our patients and found a very high incidence of pseudotumors.[6] In the present study we applied a comprehensive screening protocol to all our patients to confirm the high incidence of pseudotumors and identify risk factors for pseudotumor formation. The time course of pseudotumor formation and revision rate due to ARMD was assessed. Finally, we aimed to establish an optimal cut-off point for metal ion serum levels as a predictor of presence of local tissue reactions in patients treated with large head metal-on-metal total hip arthroplasty.

PATIENTS AND METHODS

From January 2005 to July 2010 a Bi-Metric porous-coated uncemented stem with a metal-on-metal M2a-Magnum femoral head and ReCap acetabular component (Biomet, Warsaw, Indiana) was used in our facility. It was applied in relatively young and active patients, accounting for about 15% of all our THAs in that period. The modular head and acetabular component are high-carbon, as-cast (single heated) components. The system is modular, with increasing head size and concomitant larger shell size and the option to adapt the neck length using different length taper adaptors. The main components of the head and cup are produced from a cobalt–chromium alloy containing a small proportion of molybdenum and carbon. The stem, taper and taper adapter are made of a titanium, aluminium and vanadium alloy. The radial clearance level of the M2a-Magnum articulation is maintained at 75 to 150 μm.[11] The acetabular component is 6 mm thick at the dome and approximately 3 mm at the rim.
After obtaining ethical approval, all patients treated with the implant were contacted and invited to participate in the study and in hospital screening. This study population includes

the subset of 120 patients of which we have reported in a previous publication.[6] Patients were questioned about symptoms in the groin, buttock, thigh and leg, such as pain, swelling, discomfort, numbness, and sensations of subluxation and clicking. Pain was also recorded on a visual analogue scale (VAS) ranging from no pain (0) to extreme pain (10). Patients were questioned about their use of vitamin supplements and possible history of allergies. All patients underwent pelvic (pubis centered) and hip (both hip and axially centered) radiographs. The angle of inclination of the acetabular component and center line–edge distance (wedge, covering distance) were assessed. In addition, each patient underwent CT evaluation of the pelvis and knee to detect peri-articular masses. Also, anteversion of the femoral component relative to the retrocondylar axis of the knee and anteversion of the acetabular component was measured on a CT-scan. Two radiologists (MFB, MM) independently evaluated all CT scans for the presence of pseudotumor, obtaining consensus when results did not match. We defined a pseudotumor as a (semi-)solid or cystic peri-prosthetic soft-tissue mass with a diameter ≥ 2 cm that could not be attributed to infection, malignancy, bursa or scar tissue.[6] Laboratory analysis with atomic mass absorption spectrometry of serum levels of cobalt and chromium ions was performed at the time of CT evaluation. Blood samples were collected according to recent guidelines.[12] Serum levels of leucocytes, ESR, CRP, creatinine and urea were also analysed to screen for infection and renal impairment. In this study the radiological follow-up ended at the time of latest CT evaluation, the clinical (revision) follow-up ended in April 2013.

STATISTICAL ANALYSIS

Analyses of survival included the computation of hazards ratios and the estimation of survival functions. Kaplan-Meyer procedure was used to estimate survival curves. Based on a backward selection procedure, Cox proportional hazards regression analysis was conducted to identify significant risk factors for pseudotumor and revision (p in/out = 0.05).

Differences in follow-up time were tested using Mann-Whitney U test. Pearson correlation coefficients were used for collinearity analyses. Receiver Operating Characteristics (ROC) curves were constructed to define the best cut-off point for serum levels with the highest cumulative sensitivity and specificity of cobalt and chromium. A two-sided p-value <0.05 was considered to be significant.

RESULTS

From January 2005 to July 2010 a total of 643 patients were treated with 723 MoM total hip arthroplasties. At the time of CT-follow-up, 5 patients had died and 12 patients refused further follow-up (3 were terminally ill, 9 for other reasons). A total of 626 patients with 706 hips were available for review. Of these patients, 15 were not eligible for follow-up because hip revision surgery had already been performed. Metal ion levels were not obtained in these and two additional patients. The trial profile is shown in Figure 1.

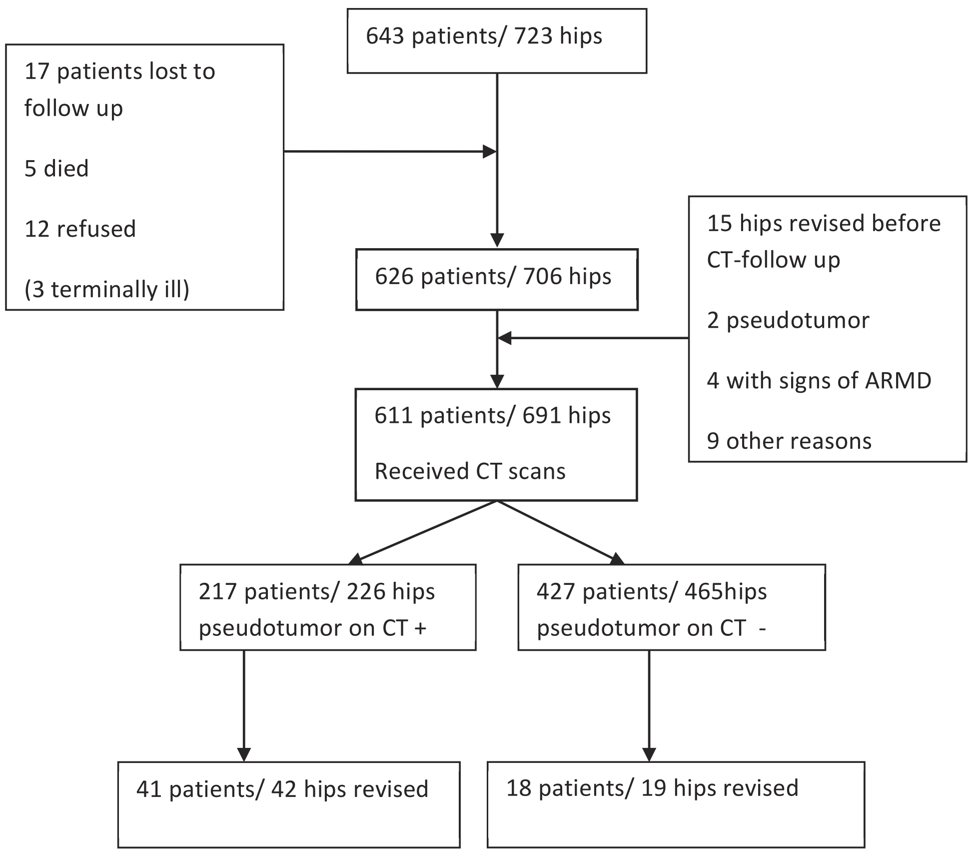

Figure 1. Trial profile.

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Patient and implant characteristics with bivariate risk factor analyses for pseudotumor formation and revision are show in Tables 1a and 1b.

	Total N=706	Pseudo-tumor N=228	No pseudo-tumor N=478	p-value	Revision N=76	No revision N=630	p-value
Patients							
Men	315 (45%)	81 (36%)	234(49%)	<0.01	18 (25%)	297 (47%)	<0.01
Women	391 (55%)	147 (64%)	244 (51%)		58 (76%)	333 (53%)	
Side right	390 (55%)	132 (58%)	258 (54%)	0.35	46 (61%)	344 (55%)	0.37
Bilateral MoM	160 (23%)	51 (22%)	109 (23%)	0.82	20 (26%)	140 (22%)	0.54
Approach							
Anterolateral	168 (24%)	65 (29%)	103 (22%)	0.17	24 (32%)	144 (23%)	0.12
Posterolateral	538 (76%)	163 (71%)	375 (78%)		52 (68%)	486 (77%)	
Mean age at follow up / years (range)	62 (21 to 79)	63 (21 to 79)	62 (42 to 74)	0.49	60 (42 to 74)	62 (21 to 79)	<0.01
Mean BMI (range)	27.8 (18 to 46)	27.7 (18 to 45)	27.8 (18 to 46)	0.91	28.1 (19 to 43)	27.8 (18 to 46)	0.47
Median follow up	3.0 (0.3 to 6.1)	3.5 (0.6 to 6.1)	2.8 (0.3 to 5.5)	<0.01	3.8 (0.5 to 7.4)	5.4 (2.8 to 8.3)	<0.01
Symptoms							
Swelling	18 (3%)	13 (6%)	5 (1%)	<0.01	8 (11%)	10 (2%)	<0.01
Non-specific groin pain	178 (25%)	94 (41%)	84 (18%)	<0.01	60 (79%)	118 (19%)	<0.01
Clicking sensations	158 (23%)	69 (30%)	90 (19%)	<0.01	31 (41%)	128 (20%)	<0.01
Allergy n= (%)							
To antibiotics	44 (6%)	16 (7%)	28 (6%)	0.27	7 (9%)	37 (6%)	0.14
To nickel	39 (6%)	18 (8%)	21 (4%)	0.26	5 (7%)	34 (5%)	0.81
Vitamin supplements	63 (9%)	20 (9%)	43 (9%)	0.56	5 (7%)	58 (9%)	0.42
Renal failure	18 (2.5%)	5 (2.2%)	13 (2.7%)	0.62	1 (1%)	17 (3%)	0.51
Mean serum cobalt / µg/l (range)	6.6 (0.3 to 176.8)	11.0 (0.8 to 176.8)	4.5 (0.3 to 153.2)	<0.01	20.8 (0.3 to 176.5)	5.2 (0.4 to 153.2)	<0.01
<4	422 (61%)	97 (43%)	325 (70%)	<0.01	18 (29%)	404 (64%)	<0.01
≥4	270 (39%)	130 (57%)	140 (30%)		45 (71%)	225 (36%)	
Mean serum chromium / µg/l (range)	5.9 (0.2 to 93.6)	8.7 (0.3 to 93.6)	4.5 (0.2 to 89.7)	<0.01	16.1 (0.2 to 93.6)	4.9 (0.3 to 89.7)	<0.01
Mean Visual analogue Scale (VAS) for pain (range)	1.2 (0 to 9)	1.7 (0 to 9)	1.0 (0 to 9)	<0.01	3.6 (0 to 9)	0.9 (0 to 8)	<0.01

Table 1a. Patient characteristics.

	Total N=706	Pseudo-tumor N=228	No pseudo-tumor N=478	p-value	Revision N=76	No revision N=630	p-value
Mean femoral head diameter / mm (range)	47.0 (36 to 58)	47.0 (38 to 58)	47.0 (36 to 56)	0.62	45.9 (38 to 58)	47.1 (36 to 56)	<0.01
≤46 mm	374 (53%)	118 (52%)	256 (54%)	0.56	55 (72%)	319 (51%)	<0.01
>46 mm	332 (47%)	110 (48%)	222 (46%)		21 (28%)	311 (49%)	
Mean hip centre line-edge distance / mm (range)	16.6 (7 to 25)	16.6 (10 to 24)	16.6 (7 to 25)	0.02	16.1 (8 to 24)	16.6 (7 to 25)	0.17
Mean inclination acetabulum / ° (range)	47.8 (18 to 80)	47.5 (22 to 72)	48.0 (18 to 80)	0.04	50.5 (32 to 80)	47.5 (18 to 68)	<0.01
≤ 45 °	258 (37%)	83 (36%)	175 (37%)	0.18	25 (33%)	233 (37%)	0.59
> 45 °	448 (63%)	145 (64%)	303 (63%)		51 (67%)	397 (63%)	
≤ 50 °	401 (57%)	135 (59%)	266 (56%)	0.04	35 (46%)	366 (58%)	0.06
> 50 °	305 (43%)	93 (41%)	212 (44%)		41 (54%)	264 (42%)	
Mean anteversion acetabular component / ° (range)	12.5 (-17 to 45)	13.4 (-17 to 43)	12.1 (-17 to 45)	0.08	7.8 (-17 to 37)	13.0 (-17 to 45)	<0.01
0 - 20°	518 (77%)	154 (69%)	364 (80%)	0.04	42 (72%)	476 (77%)	0.40
<0 or >20°	159 (23%)	70 (31%)	89 (20%)		16 (28%)	143 (23%)	
Mean anteversion femoral component / ° (range)	11.5 (-22 to 51)	10.7 (-22 to 36)	11.9 (-22 to 45)	0.83	12.2 (-16 to 40)	11.4 (-22 to 51)	0.40
0-20°	471 (70%)	162 (72%)	309 (69%)	0.87	43 (72%)	428 (70%)	0.03
<0 or >20°	204 (30%)	62 (28%)	142 (31%)		17 (28%)	187 (30%)	
Mean combined anteversion / ° (range)	23.9 (-29 to 73)	24.0 (-29 to 72)	23.8 (-9 to73)	0.22	18.8 (-29 to 50)	24.3 (-9 to 73)	<0.01
20 - 40°	346 (52%)	113 (51%)	233 (53%)	0.84	23 (42%)	323 (53%)	0.18
<20 or >40°	316 (48%)	109 (49%)	207 (47%)		32 (58%)	284 (47%)	

Table 1b. Implant characteristics.

There were 228 pseudotumors (32.3%) in 219 patients (35.0%). The median follow-up of the entire cohort was 3.0 (0.3-6.1) years where CT-scan indicated the end of follow up. When

a pseudotumor was present, follow-up was significantly longer (median 3.5 versus 2.8 years, $p<0.01$).
Seventy-six hips (10.8%) have been revised in 73 patients (11.7%) after a median period of 5.3 (1.0-8.3) years.

Kaplan-Meyer plots for estimating survival are shown in Figures 2a (pseudotumor free survival) and 2b (revision free survival).

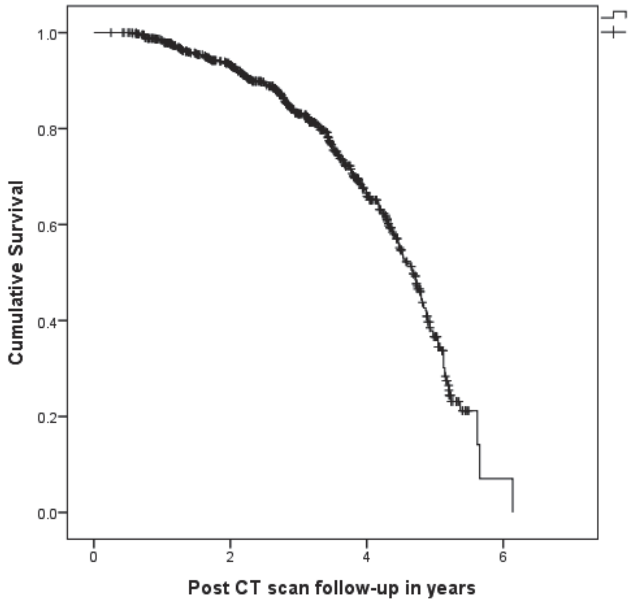


Figure 2a. Pseudotumor-free survival at CT follow-up (Cox regression plot).

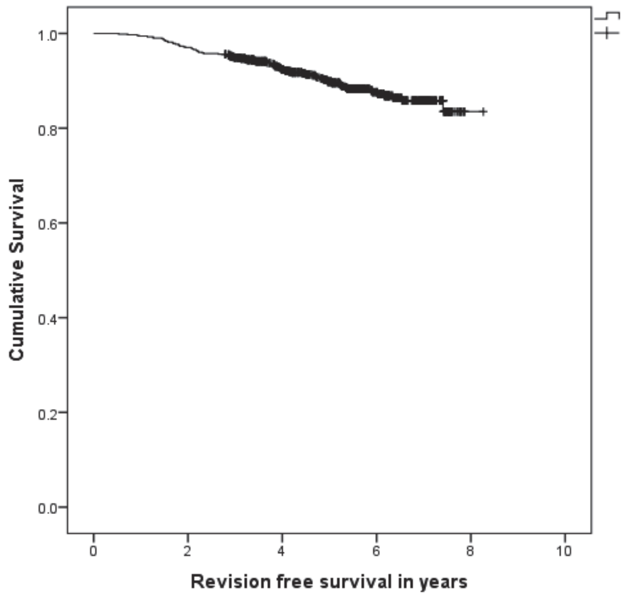


Figure 2b. Revision-free survival (Cox regression plot).

Multivariate risk factor analyses identified the following independent risk factors for the presence of a pseudotumor: aspecific pain, cobalt ≥ 4 µg/l, and swelling (Table 2a).

Risk Factor	Hazard Ratio	95% Confidence Interval	P value
Aspecific Pain	2.01	1.51-2.67	<0.01
Cobalt ≥ 4	1.36	1.03-1.80	0.03
Swelling	1.82	1.02-3.27	0.04

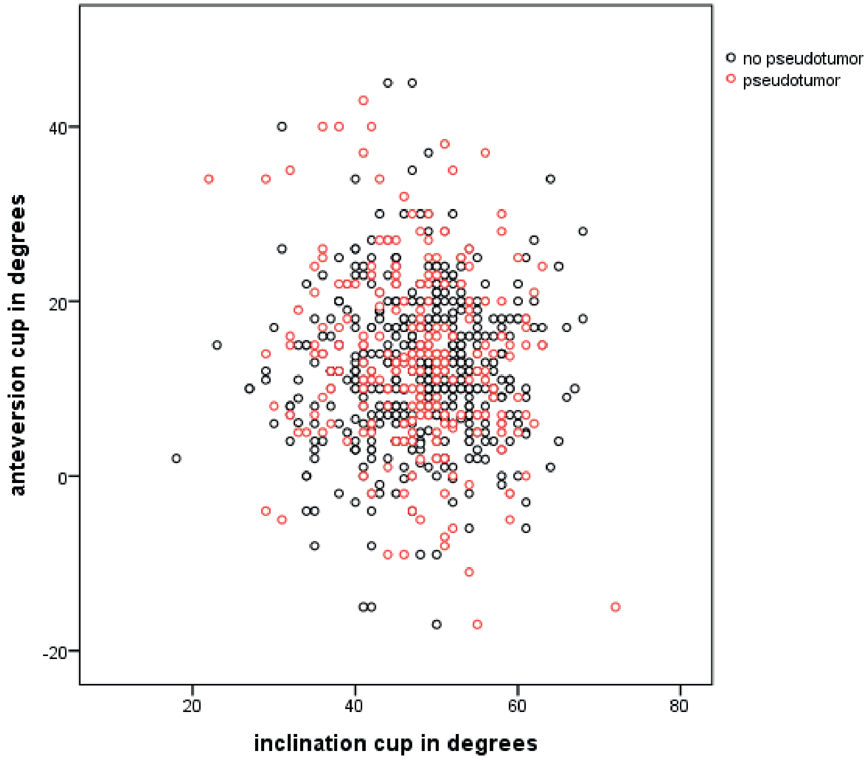
Table 2a. Significant risk factors for pseudotumor presence after multivariate cox regression analysis

Significant risk factors for revision are: younger age at follow-up, aspecific pain, cobalt ≥ 4 µg/l, and swelling (Table 2b).

Risk Factor	Hazard Ratio	95% Confidence Interval	P value
Age at Follow-up	0.95	0.92-0.98	<0.01
Aspecific Pain	10.15	5.52-18.69	<0.01
Cobalt ≥ 4	2.77	1.57-4.88	<0.01
Swelling	2.22	1.03-4.75	0.04

Table 2b. Significant risk factors for revision after multivariate cox regression analysis.

No clear relation between acetabular component orientation and pseudotumor formation



could be observed (Figure 3).

Figure 3. Scatter plot showing acetabular component orientation for patients with and without pseudotumor.

Collinearity analysis revealed that cobalt and chromium levels were highly associated (Pearson's r=0.932, p=0.000). We found 4 µg/l to be the "best" cut-off point for both serum cobalt and serum chromium (sensitivity 57.3% and 53.9%, specificity 71.0% and 65.6%).

DISCUSSION

This study shows a dramatic increase of pseudotumors in patients treated with large head metal-on-metal total hip arthroplasties after prolonged follow-up. A high incidence of pseudotumors was found after performing a specific and extensive screening protocol for all patients (symptomatic and asymptomatic) with a metal-on-metal THA. Associated risk factors for pseudotumor formation seem of limited importance. Independent risk factors for the presence of a pseudotumor are aspecific pain, cobalt ≥ 4, and swelling.

Cobalt and chromium should be regarded poor predictors for pseudotumor presence leaving cross sectional imaging as the main screening tool during follow-up. Each of these statements will be discussed in the following paragraphs.

Pseudotumors

Most literature about pseudotumors is based on symptomatic patients or revision series and studied resurfacing implants.[13-15] Generally, a much lower incidence of pseudotumors (0.10%-0.15%) is reported in these case series. An explanation for the high incidence in our study could be that we performed a specific and extensive screening protocol for all patients (symptomatic and asymptomatic) with a metal-on-metal THA. A more comparable incidence of 25-61% is found in other more recent studies investigating both asymptomatic and symptomatic patients.[16-18]

Implant design could also contribute to the difference in incidence between studies. Various models of metal-on-metal THAs can generate different amounts of wear probably influencing the occurrence of metal debris associated problems. A large femoral head (36mm and more), as used in our patients, is considered to be a risk factor for developing ARMD, due to the elevated risk of taper wear and edge loading.[2]

The definition of a pseudotumor, as stated in our study, might as well contribute to the high incidence. We believe that a lesion as small as 2 cm in diameter that cannot be explained by other causes, can be accurately diagnosed on CT as a pseudotumour.[6] Although associated with implant failure, the clinical relevance of the asymptomatic lesions, especially the smaller ones, is still subject to discussion. Longer follow-up of these smaller lesions is needed. In accordance, a similar study using MRI found an incidence of pseudotumors in well-functioning metal-on-metal hip prostheses of 61%. As a result less clinical importance is assigned to fluid filled lesions on Mars MRI. They emphasize that the natural history and longitudinal imaging findings of these lesions should be more fully analysed to prove their significance.[17]

We used CT to detect the presence of a periarticular mass. We believe that CT, despite scattering artifacts caused by the large metal implant, provides adequate diagnostic images with the important added benefit that it allows measurement of femoral anteversion (relative to the retrocondylar axis of the knee) and acetabular component anteversion.[19] A CT scan is less expensive and more readily available than metal artifact reduction scanning (MARS) MRI, which reduces the susceptibility of artefacts due to the large metal implants. The radiation caused by CT scanning seems of relative importance because new protocols have reduced the total amount needed for adequate imaging. Furthermore patients exposed are generally of older age, a relative less vulnerable group. CT scanning was preferred over ultrasound (US) as screening modality, because the produced US images are operator dependent with more interobserver bias. Ultrasound can, however, be helpful in separating solid from fluid filled swellings as this distinction is less clear on CT. Finally, in contrast to ultrasound, stored CT-images are easily reproduced and thus compared with future studies, and, therefore, CT constitutes a better instrument for follow-up.

The fact that pseudotumor-free survival steadily declines over time emphasizes the necessity for an intensive extended follow-up protocol of all patients treated with the metal-on-metal implant. The results of this and other screening studies suggest that imaging techniques must be performed in all patients and probably repeated.[6,16, 17, 18]

In accordance to our study, several authors found that patients with pseudotumors often present with pain or discomfort.[10, 20] One study found that the first clinical sign of a pseudotumor was usually pain, which led to radiographic examination and detection of lesions around the prosthetic stem.[21] Other studies have identified osteolytic areas as a precursor to pseudotumors.[22] Osteolysis was much more frequently found on CT scans than on X-rays in our study, adding a possible additional benefit to CT as a screening device .

Associations of cup malposition with increased release of metal wear debris [23-25] and with increased component wear rates and pseudotumor formation have been reported. [26, 27] Cup position in our study however could not be pointed out as an independent risk factor. This is in line with several other publications suggesting pseudotumors are also common in patients with asymptomatic MoM THA[28] and in patients with low metal ion levels and a well-positioned cup. [29, 30] A substantial fraction of our acetabular components were placed outside Lewinnek's safe zone (for stability) or outside any other arbitrary set desired range of inclination and anteversion. This is in line with literature on free hand cup positioning.[31] Pseudotumors almost equally occurred in well and malpositioned cups. Cup positioning was within Lewinnek's safe zone in 50% (111) of the pseudotumor group and in 45% (205) of the group without pseudotumors. Furthermore, in different ranges for combined anteversion (cup plus stem) a risk factor could not be identified. This and the comparable results of similar studies[29, 30] might indicate that the orientation of components plays a less important role in pseudotumor formation than previously suggested. One explanation might be that most literature about malposition comes from resurfacing studies and therefore applies less to MoM total hip arthroplasties. Another explanation could be the somewhat randomly chosen safe zones in our study. We could not identify any literature concerning safe zones for anteversion of the cup and stem related to implant wear and therefore loosely based our safe zones on anatomical averages.

Several other risk factors for pseudotumors, as described in literature (female gender, swelling, clicking sensations and femoral head size), [27, 32] could not be confirmed as an independent risk factor for developing a pseudotumor in our multivariate analysis.

The Kaplan-Meyer plot for pseudotumor formation dramatically demonstrates that almost all our patients will have developed a pseudotumor in about six years. Considering this, identifying risk factors for pseudotumor formation seems of limited clinical importance. Obviously, since the Kaplan-Meyer plot is an estimation based on patients with a broad range of follow-up, the actual incidence of detectable pseudotumors has to be confirmed in a future follow-up of our cohort of patients.

Revisions

The revision rate in our series was 10.8% at a median follow-up of 5.3 years, increasing over time. Risk factors for revision were: younger age at follow-up, aspecific pain, cobalt ≥ 4, and swelling. Some confounding by indication should be assumed when considering these risk factors. Pain combined with presence of a pseudotumor on CT was the main indication for revision.

During revision the acetabular component was replaced by a polyethylene cup and the large metal head by a 28mm metal or ceramic head. In some cases the femoral component had to be revised, because the taper adapter was corroded to the femoral taper. As much as sensible the pseudotumour was excised with the intent not to endanger neurovascular structures. In addition to the peri-articular swelling, a mixture of soft tissue and bone necrosis was observed. In most cases, abundant metallosis (black) with a thin walled cystic dark pigmented swelling was noticed but also a cystic non pigmented (white) often thick walled swelling filled with a milky chylous or clear fluid was encountered. Substantial acetabular bone loss, requiring bone grafts, with metal debris on the backside of the acetabular component was often encountered in patients revised for ARMD. Although revision is considered to be the indicated treatment if symptoms are severe, the patient should be explained thoroughly about the associated risks. Periprosthetic fractures, dislocation, poor post-operative function, significant blood loss and infection are all well-known complications, especially in well-fixed prosthetic components.

Early detection of pseudotumors is important because it is generally agreed that if revision surgery is performed in patients before substantial soft tissue damage has occurred, the outcome is likely to be better.[33] If substantial tissue damage has occurred, than revision surgery is associated with poor function and more complications. [34]

Metal ions

6

Serum cobalt and chromium levels were mutually related. Although metal ions were on average higher when a pseudotumor was present, they are a poor predictor for the presence of a pseudotumor in our study population (sensitivity 57.3% and 53.9%, specificity 71.0% and 65.6%).

We tried to identify if there was a value of serum metal ions below which the presence of a pseudotumor was unlikely. A very high sensitivity would be required. For cobalt, an appropriate threshold value would be 1 μg/l (sensitivity 98.0%, specificity 10.6%). Using this threshold, cobalt would have saved the need for 47 of 609 CTs (8%) and we would still have missed 3 pseudotumors.

In literature threshold values of metal ions grossly range between 2 and 19 μg/l.[35, 36]

Although associated with ARMD (especially in Co-values >20 μg/L),[35] ion levels are still considered to be unreliable predictors of periarticular soft tissue damage and should not be used in isolation as surgical intervention triggers.[37]

Although its use for predicting the presence of a pseudotumor is limited, it still can be of value. A (sudden) increase of serum metal ions is reported to be associated with implant failure. [38] Furthermore, several studies report about toxic effects of prolonged elevated serum metal ion exposure. Health risks that are related to chronically elevated blood cobalt concentrations induced by abnormal wear and corrosion of the metal-on-metal prosthesis are: hypothyroidism, polyneuropathy, impairment of cranial nerves II and VIII and cardiomyopathy. [39] Others report concerns about carcinogenicity, hypersensitivity and fetal exposure in pregnant women. [40-42] Another report compared well-functioning MoM Hip Resurfacings with conventional THAs, 8 years after surgery in asymptomatic patients. Chronic exposure to low elevated metal concentrations in patients with MoM hip resurfacings may have systemic effects and long-term epidemiological studies in large populations, such as those available through joint registries are needed. [43]

CONCLUSION AND RECOMMENDATIONS

This study shows a very high incidence of pseudotumors in patients treated with large head metal-on-metal total hip arthroplasty at short term follow-up. Time course analysis estimates that the fair share of our patients is likely to develop a pseudotumor in the near future. Several risk factors for developing a pseudotumor were identified, but considering that almost all patients ultimately seem to become affected, their clinical relevance is limited. Cobalt and chromium are poor predictors for pseudotumor presence.

We recommend an annual follow-up of all patients subjected to a large diameter femoral head metal-on-metal total hip arthroplasty for as long as the prosthesis is in situ. Routine X-rays and imaging techniques like MARS MRI or CT should be performed and probably repeated to assess pseudotumor formation in all patients. Further research is needed to show if and when the intensified follow-up can be returned to a more routine schedule.

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CHAPTER 7

The relation between titanium taper wear and cobalt-chromium bearing wear in large head metal on metal total hip prostheses - A retrieval study

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ABSTRACT

Revision of hip implants due to adverse tissue reactions to metal debris has been associated with wear and corrosion of the metal-on-metal bearing articulation or the modular taper interface. Bearing articulation wear is increased in conditions of poor lubrication which can lead to high friction moments that may also cause corrosion at the taper interface. This suggests that wear of the bearing and the taper interface should occur simultaneously, which was investigated in this study.

43 large diameter cobalt-chrome bearings of the same design implanted with a titanium stem using a titanium adapter were retrieved at revision by a single centre. Volume change of bearing and taper surfaces was assessed using a coordinate measurement machine and assigned to "severe" (titanium oxide deposition rate > $0.1mm^3$/year on the female adapter taper) and "slight" corrosion groups. Serum ion and tissue metal concentrations were determined for 43 and 12 specimens, respectively.

47 % of the bearing surfaces exhibited edge wear with combined head and cup wear rates above 1 mm^3/year. "Severe" taper corrosion was observed in 30 % of the retrievals. Corrosion at the tapers was observed either as material deposition or removal and titanium oxide was also found penetrating into the original taper surface. The overall bearing wear rate was significantly higher in the "severe" than in the "slight" taper corrosion group (7.2 ± 9.0 mm^3/year vs. 2.9 ± 6.6 mm^3/year, respectively, $p=0.013$). Serum metal ion concentrations were better indicators of wear than tissue sample concentrations.

The increased bearing articulation wear and serum metal ion concentrations in cases with taper interface corrosion supports the hypothesis that increased friction in the joint articulation is one of the factors responsible for simultaneous articulation and taper damage. However, independent taper or bearing damage were also observed suggesting that other factors are involved.

INTRODUCTION

National Joint Registry data have shown increased revision rates for large diameter metal-on-metal (MoM) hip replacement bearings compared to other material couplings.[1] Metal wear debris accumulates in adjacent tissues and also enters the lymphatic and blood systems. Soft tissue reactions to metal debris are described variously as: metallosis[2], aseptic lymphocytic vasculitis-associated lesions (ALVAL)[3,4], metal allergies[5] or sensitivities[6,7] and mass formation (pseudotumors)[8-10]. Systemic toxicity has been described in terms of cobaltism[11], with severe sensory disturbance, and has even led to a fatal case of cardiomyopathy[12]. Modular MoM implants provide flexibility regarding offset and angle but introduce an additional load bearing taper interface between head and stem.[13] This interface is prone to corrosion, which is currently an extensively discussed clinical problem.[9,14-17]

The interface between head and stem has been intensively analysed but the mechanisms responsible for wear debris generation and the relation between bearing articulation wear and taper wear remains unclear.[18-21] Two different female (inner) head taper wear patterns have been demonstrated for retrieved cobalt chrome heads on titanium stems: An asymmetric wear pattern was explained by toggling loads, while an axisymmetric wear pattern was explained by rotation and subsidence onto the stem.[19] Negligible titanium (Ti) stem taper wear was observed compared to wear of the cobalt-chromium (CoCr) female head taper and the joint surfaces. Similar results have been observed by several groups.[18,20,21] Bearing articulation wear occurs in conditions of poor lubrication which can simultaneously lead to high friction moments. This might cause the corrosion observed at taper interfaces. It is therefore hypothesized that increased taper wear is related to an increase in bearing wear. This was investigated in revised large diameter MoM hip implants of a with a Ti-Ti taper connection, which is relatively uncommon in primary hip arthroplasty. [22,23]

MATERIAL AND METHODS

Patients

43 revised large-diameter modular MoM prostheses of a single design were available for analysis (Biomet modular M2a Magnum™; Biomet, Warsaw, IN, US; Figure 1).

Figure 1. The Bi-MetricTM stem with the M2a MagnumTM components (Biomet, Warsaw, USA), which were used in all analysed cases. The four taper and bearing surfaces analysed for wear and deposit are highlighted in red (stem taper, female adapter taper, head and cup articulation).

Implantation had been performed via an anterolateral or posterolateral approach. All implantations and revisions were performed in a single clinic between 2010 and 2012 (Isala, Department of Orthopedic Surgery, Zwolle, The Netherlands). The clinical performance of this cohort has been reported previously.[10] Retrievals were from 30 females and 13 males, with 27 from the right side and 16 from the left (Table 1).

Patient ID	Gender	Age at revision	In vivo time	Side	Approach Lateral =1 Postero-lateral =2	BMI	Pain = 1 Tumor = 2 Other tissue reaction = 3 Metallosis = 4 Loosening stem or cup = 5	MOM unilat = 1 MoM bilat = 2 MoM and conven.THA = 3 MoM bilat and TKA bilat = 4 MoM and conven.THA and unilat TKA =5
1	Female	62	5 years and 4 months	Right	1	26	1	1
2	Male	69	4 years and 9 months	Left	1	28	2	2
3	Female	66	2 years and 10 months	Right	2	29	2	2
4	Female	64	3 years and 10 months	Right	1	27	1	3
5	Male	44	1 year and 6 months	Left	2	24	5	1
6	Female	70	3 years and 1 month	Left	1	19	2	3
7	Female	68	5 years and 0 months	Left	2	24	2	1
8	Male	63	3 years and 2 months	Right	2	29	2	3
9	Female	68	1 year and 10 months	Left	2	40	1	1
10	Male	50	2 years and 7 months	Right	2	28	1	3
11	Female	58	2 years and 2 months	Left	2	26	2	3
12	Female	65	2 years and 1 month	Right	2	29	2	3
13	Female	56	0 years and 11 months	Right	2	36	1	2
14	Female	52	3 years and 4 months	Right	2	31	2	3
15	Male	62	4 years and 2 months	Left	2	29	2	5
16	Female	59	5 years and 2 months	Right	2	25	2	2
17	Female	75	4 years and 11 months	Right	2	24	5	4
18	Female	70	1 year and 3 months	Left	2	29	2	2

Patient ID	Gender	Age at revision	In vivo time	Side	Approach Lateral =1 Postero-lateral =2	BMI	Pain = 1 Tumor = 2 Other tissue reaction = 3 Metallosis = 4 Loosening stem or cup = 5	MOM unilat = 1 MoM bilat = 2 MoM and conven.THA = 3 MoM bilat and TKA bilat = 4 MoM and conven.THA and unilat TKA =5
19	Female	56	2 years and 11 months	Left	1	24	2	1
20	Male	65	4 years and 8 months	Left	1	30	1	3
21	Female	69	4 years and 4 months	Right	2	28	3	2
22	Female	67	4 years and 5 months	Left	2	32	5	1
23	Female	43	5 years and 3 months	Right	2	26	5	2
24	Female	58	2 years and 11 months	Left	2	40	2	3
25	Female	70	6 years and 2 months	Left	1	31	1	5
26	Male	66	2 years and 5 months	Left	1	22	2	1
27	Male	54	2 years and 10 months	Right	2	24	5	3
28	Female	62	1 year and 5 months	Right	1	31	1	1
29	Female	56	6 years and 5 months	Right	2	28	2	2
30	Male	65	4 years and 10 months	Right	2	30	2	1
31	Female	58	3 years and 1 month	Right	1	26	1	1
32	Female	64	3 years and 11 months	Right	1	24	1	3
33	Male	56	1 year and 8 months	Left	1	27	2	1
34	Male	46	2 years and 2 months	Left	2	27	4	3
35	Male	68	6 years and 6 months	Right	2	26	2	1
36	Female	63	2 years and 10 months	Right	1	23	2	1

Patient ID	Gender	Age at revision	In vivo time	Side	Approach Lateral =1 Postero-lateral =2	BMI	Pain = 1 Tumor = 2 Other tissue reaction = 3 Metallosis = 4 Loosening stem or cup = 5	MOM unilat = 1 MoM bilat = 2 MoM and conven.THA = 3 MoM bilat and TKA bilat = 4 MoM and conven.THA and unilat TKA =5
37	Female	55	4 years and 8 months	Right	2	22	2	2
38	Female	67	3 years and 8 months	Right	2	43	1	1
39	Female	64	4 years and 1 month	Right	2	24	2	2
40	Female	60	3 years and 2 months	Right	2	28	1	2
41	Male	69	6 years and 3 months	Right	2	29	2	1
42	Female	64	4 years and 11 months	Right	2	31	2	2
43	Female	57	1 year and 9 months	Right	2	35	3	1

Table 1. Demographic and surgical data.

Mean patient age at revision was 61.5 years (43 to 75 years) and mean time to revision was 3.7 years (1.0 to 6.5 years). Mean body mass index (BMI) at revision was 28.2 kg/m^2 (19 to 43 kg/m^2). Cup inclination was measured on AP radiographs and cup anteversion were measured on CT images of the pelvis. Indications for revision were pseudotumor (23 cases), pain (12), loosening of stem or cup (5), other tissue reaction (2) and metallosis (1). To reduce surgery related morbidity, stems were left in situ where possible.

14 porous coated collarless uncemented stems were retrieved (Bi-Metric™, Biomet, Warsaw, IN). This type of femoral stem (Ti6Al4V) was used in all investigated patients. The M2a Magnum bearing articulation consists of a monoblock press-fit cobalt chrome molybdenum cup articulating against a cobalt chrome molybdenum head, which is mounted on the stem taper via a titanium alloy (Ti6Al4V) taper adapter (Figure 1). Head diameter ranged from 40 to 54 mm and nominal head offsets from -6 to +6 mm, defined by the position of the taper adapter on the stem.

Blood samples

Prior to revision, blood samples were taken from all patients, according to MacDonald et al.[24] Serum cobalt and chromium ion concentrations were measured by atomic mass absorption spectrometry. Leucocytes, ESR, CRP, creatinine and urea were analysed to rule out infection and kidney disorders. External causes of high serum metal concentrations, such as impaired kidney function and use of vitamin supplements were traced.

Tissue samples

During revision surgery, tissue samples from 12 patients were taken to determine Co, Cr and Ti concentrations. Samples were freeze-dried and crushed with a scalpel. 100 mg samples were digested by microwaves (ELAN DRC II and Optima7000DV ICP-OES, PerkinElmer, Inc. Waltham, MA, USA). Two samples were taken from the solution, separately investigated and the results averaged.

Surface analysis

Four surfaces (stem taper, adapter female taper, head and cup bearing articulations; Figure 1) were measured using a coordinate measurement machine (BHN805 with a 2 mm diameter ruby tip, 2μm accuracy, Mitutoyo, Japan). Negative deviations from estimated unworn geometries (perfect sphere or cone assumed) were interpreted as material loss corresponding to wear, as described in detail previously.[19,25,26] By using the same estimated unworn geometries material deposition was determined by positive deviations from the estimated unworn geometries (Figure 2).

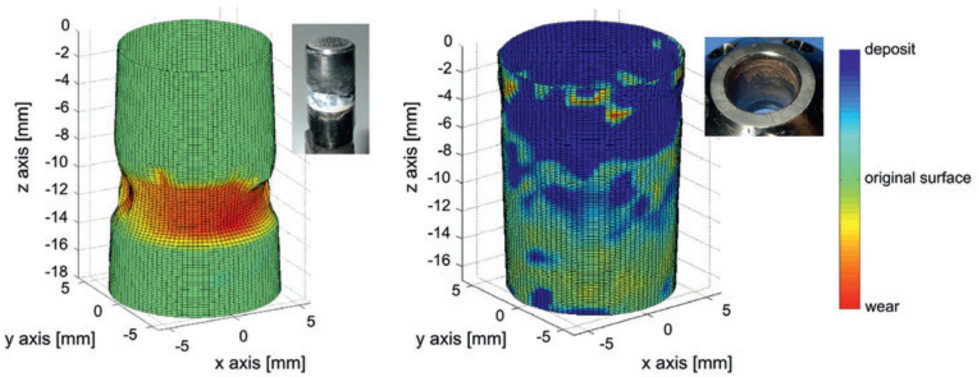

Figure 2. Wear plots of a stem taper and female adapter taper with corresponding images. In both plots, the green area represents the estimated original surface, red and blue areas wear and deposit, respectively. Wear is directed towards the component and is defined as the negative deviation from the estimated original surface; deposit is directed away from the component in the opposite direction and is defined as the positive deviation from the estimated original surface.

In a few cases scratches due to disassembly during revision surgery were observed. These regions were neglected from the subsequent analysis. The male (outer) adapter taper and female head taper were analysed only visually, since these components had been dissembled in only eight of the retrievals and had become damaged.

Groups

Retrieved components were firstly grouped according to the material deposit rate on the female adapter taper: a "severe" taper corrosion group with a deposition of >0.1 mm^3/year and otherwise "slight" (Figure 3).

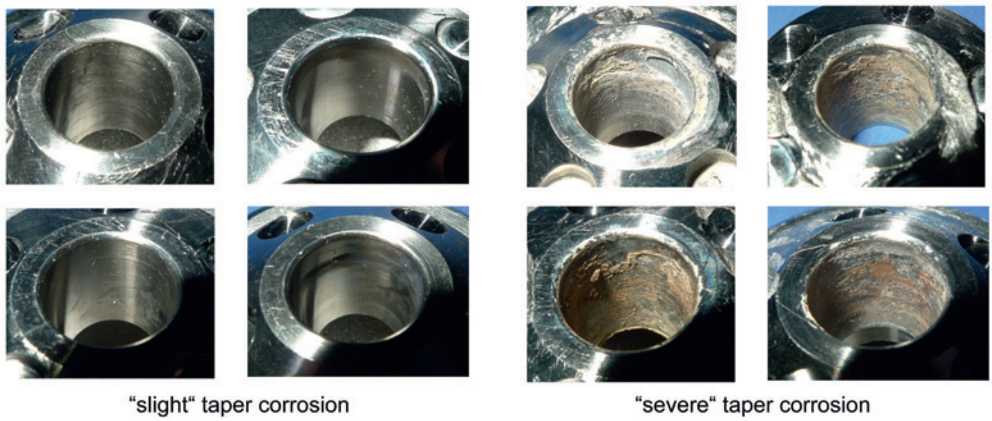

Figure 3. Representative examples of the female adapter taper for the two corrosion groups ("slight" and "severe" taper corrosion). The distal surfaces of the female adapter tapers with the taper directed into the head are shown.

Components were also grouped based on observed edge wear patterns, according to an accumulated head and cup wear rate of > 1 mm^3/year, defined as "edge" wear, otherwise "no edge". Finally, retrievals were grouped according to the position of the cup with respect to Lewinnek´s safe range defined as "in" for 30-50° inclination and 5-25° cup anteversion, otherwise "out".[27]

Statistics

On the basis of Shapiro-Wilk tests for normality, either a non-parametric Mann-Whitney test, a one-way analysis of variance or a linear regression was performed to analyze the data (α=0.05, PASW Statistics 18, Chicago, IL, USA).

Source of Funding

There was no external funding source.

RESULTS

Explants

The bearing surfaces exhibited no wear visually, but marginal scratches. Of all 43 heads, the Ti adapter was still assembled in the CoCr head in 35 samples. In three cases the adapter without head was still attached to the stem and was removed carefully (Figure 4).

Figure 4. Example for an adapter still connected to the stem after revision (left). After disassembly, severe corrosion was visible on the stem taper and the female adapter taper (right). The distal part of the female adapter taper (middle right) showed thicker oxide layers than the proximal part (bottom right).

Severe corrosion, with an oxide layer covering both taper surfaces, more or less entirely, was visible after disassembly of these samples. Oxide layer damage was observed mostly at the distal taper interface.

The female adapter tapers showed traces of discoloration, scratches and corrosion products (Figure 3). Thirty (70 %) female adapter tapers exhibited "slight" corrosion and 13 (30%) "severe" corrosion. Material loss from this surface was observed visually, as well as a material gain in the form of a titanium oxide deposition. The stem tapers also showed either mild corrosion (9 of 14) or heavy corrosion (5 of 14) by qualitative inspection (Figure 5).

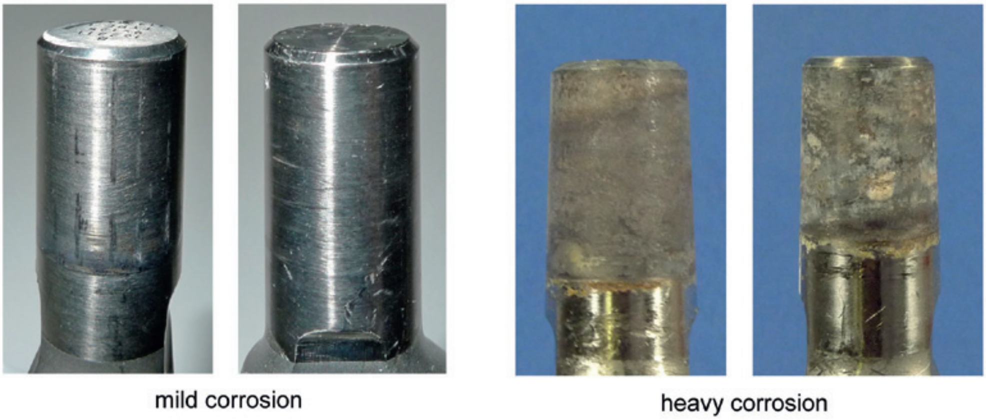

Figure 5. Representative examples of stem tapers with mild and heavy corrosion.
The male adapter and female head interfaces (8 disassembled) only showed slight signs of corrosion but some major scratches arising from the disassembly procedure (Figure 6).

Figure 6. Representative examples of the male (outer) adapter tapers (top row) and the corresponding female head tapers (bottom row). Most adapter tapers exhibited serious disassembly marks which did not allow surface analysis.

Bearing analysis

Almost half of the components (20/43) exhibited “edge” wear (Table 2, Figure 7). Metal ion concentrations in the tissue were significantly higher in the “edge” group than in the “no edge” group only for Cr ($p=0.042$). Combined cup and head wear rate correlated highly with the serum ion concentrations (adj $r^2 = 0.47$ for Co and 0.61 for Cr, $p < 0.001$ for both). The orientation of the components was not significantly different for the “edge” and the “no-edge” groups (Table 2).

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		n	edge mean ± sd	n	no edge mean ± sd	
Gender	(female / male)	20	15/5	23	15/8	p=0.486
Time in situ	[years]	20	4.0 ± 1.6	23	3.3 ± 1.4	p=0.149
Head wear rate	[mm^3/year]	20	5.1 ± 6.7	23	0.4 ± 0.3	p<0.001
Cup wear rate	[mm^3/year]	20	3.5 ± 4.5	23	0.04 ± 0.1	p<0.001
Co concentration serum	[µg/l]	20	37.1 ± 38.0	23	10.5 ± 22.9	p<0.001
Cr concentration serum	[µg/l]	20	28.6 ± 27.5	23	9.3 ± 15.0	p<0.001
Co concentration tissue	[mg/kg]	4	59.9 ± 43.1	8	110 ± 279.9	p=0.089
Cr concentration tissue	[mg/kg]	4	729.9 ± 397.6	8	211.9 ± 449.4	p=0.042
Ti concentration tissue	[mg/kg]	4	456.3 ± 613.4	8	1215.3 ± 3112.0	p=0.396
Inclination	[°]	20	52.4 ± 9.6	23	49.4 ± 8.4	p=0.258
Anteversion	[°]	20	8.8 ± 10.7	23	7.3 ± 7.8	p=0.620
Lewinnek's safe range	[in/out]	20	7/13	23	9/14	p=0.780

Table 2. Wear, metal ion concentrations and orientations for the two bearing groups (please note different units for serum and tissue concentrations).

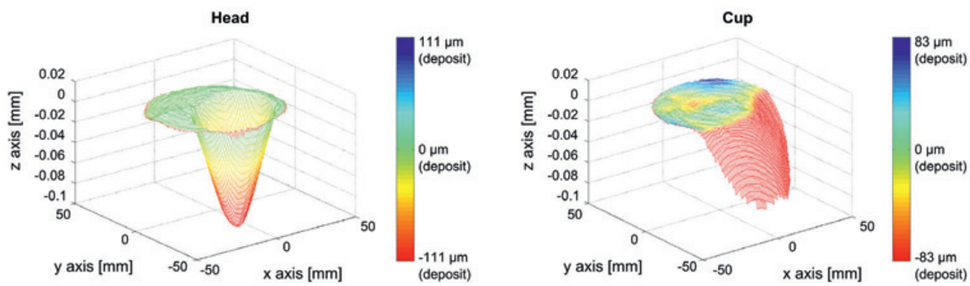

Figure 7. Bearing wear plots for patient #10, who exhibited the most bearing wear of all samples. The distinct edge wear patterns on the head ("hole" close to the equator) and cup surfaces ("edge" worn off) can be seen.

Taper analysis

Female patients were represented significantly more frequently than male patients in the "severe" corrosion group (12:1, p=0.035) (Table 3). There were no significant differences in any other patient characteristics between the "slight" and "severe" corrosion groups (head size, head offset, BMI).

		n	slight mean ± sd	n	Severe Mean ± sd	
Gender	(female/ male)	30	18/12	13	12/1	p=0.035
Time in situ	[years]	30	3.5 ± 1.6	13	3.9 ± 1.2	p=0.456
Stem taper wear rate	[mm^3/ year]	9	0.02 ± 0.05	5	1.28 ± 1.84	p=0.007
Stem taper deposit rate	[mm^3/ year]	9	0.02 ± 0.05	5	0.47 ± 0.45	p=0.007
Inner adapter taper wear rate	[mm^3/ year]	30	<0.001 ± 0.0004	13	0.46 ± 1.29	p<0.001
Inner adapter taper deposit rate	[mm^3/ year]	30	0.02 ± 0.02	13	0.91 ± 0.64	p<0.001
Cr concentration serum	[µg/l]	30	12.0 ± 15.1	13	32.7 ± 32.7	p=0.019
Co concentration serum	[µg/l]	30	15.2 ± 23.9	13	40.5 ± 44.9	p=0.024
Cr concentration tissue	[mg/kg]	6	226.5 ± 459.3	6	542.5 ± 499.8	p=0.065
Co concentration tissue	[mg/kg]	6	13.9 ± 15.6	6	172.6 ± 311.1	p=0.041
Ti concentration tissue	[mg/kg]	6	237.6 ± 535.3	6	1687.0 ± 3541.8	p=0.093
Inclination	[°]	30	49.8 ± 9.1	13	53.2 ± 8.6	p=0.267
Anteversion	[°]	30	7.2 ± 8.3	13	9.8 ± 11.1	p=0.391

Table 3. Wear, metal ion concentrations and orientations for the two taper corrosion groups (please note different units for serum and tissue concentrations).

All taper wear/deposit volumes and ion concentrations were clearly elevated in the "severe" taper wear group, most of them significantly (Table 3). Wear volume of the stem taper was strongly related to wear volume of the female taper of the adapter (adj $r^2 = 0.965$, $p < 0.001$; Figure 8).

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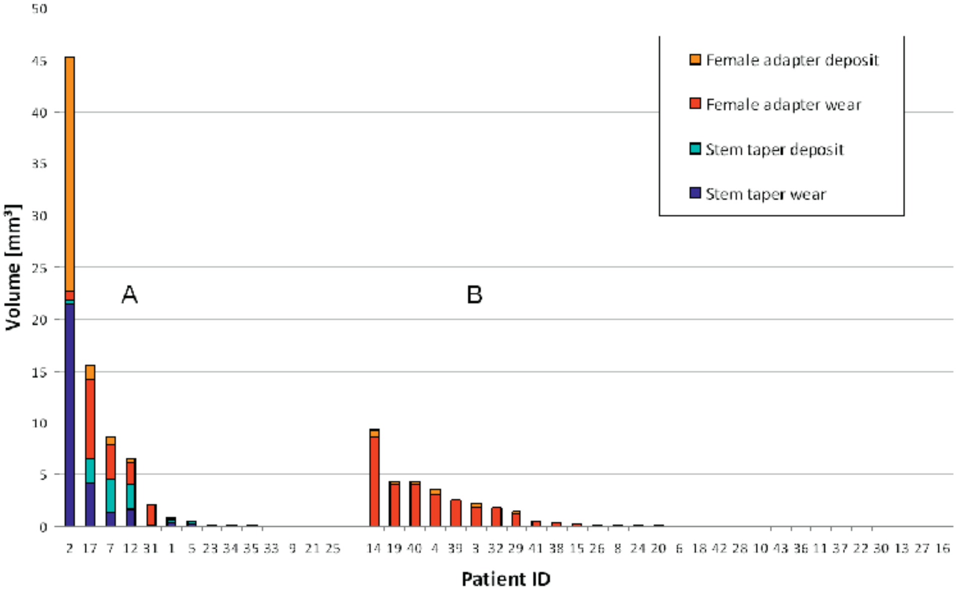

Figure 8. Wear and deposition rate of stem and/or adapter tapers. Since only 14 stems were available, data is displayed for explants with (A) and without stem (B).

However, there was no association of wear volume of the stem taper with deposition volume on the female taper of the adapter ($p=0.614$, Figure 8) and similarly, there was no association of wear volume on the female taper of the adapter with deposit volume on the stem taper ($p=0.994$). Also, there was no association between the wear volume and the deposition volume for the female taper of the adapter ($p=0.765$, Figure 8), or for the stem taper ($p=0.729$). The maximum measured wear volumes were 21.5 mm^3 for the stem taper and 22.6mm^3 for the female taper of the adapter. The maximum deposition volumes were 1.3 mm^3 for the stem taper and 7.7 mm^3 for the female taper.

Relation between taper and bearing wear

Explants with "edge" wear were more frequently observed in the "severe" taper corrosion group: 8 of 13 bearing surfaces (~62 %) in the "severe" group vs. 12 of 30 bearing surfaces (40 %) in the "slight" corrosion group ($p = 0.193$). This was also reflected by the wear rates: combined head and cup rate was significantly higher in the "severe" taper wear group ("severe": 7.2 ± 9.0 mm^3/year vs. "slight": 2.9 ± 6.6 mm^3/year, $p=0.012$; (Figure 9). The variation, however, was very large in both groups This arises from 5/23 samples demonstrating "severe" taper corrosion despite being in the "no edge" wear group and 12/20 samples demonstrating "slight" taper corrosion despite being in the "edge" wear group.

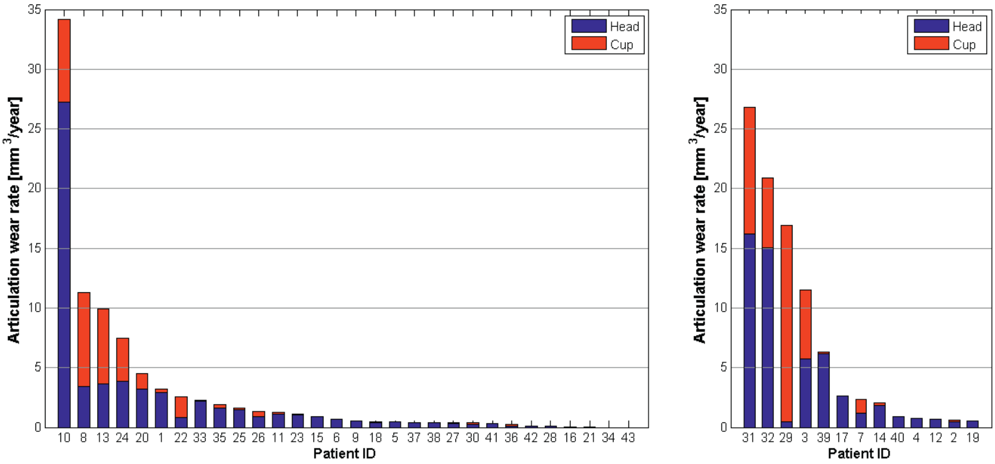

Figure 9. Wear rates for head (blue bars) and cup (red bars) sorted by combined wear rate for "slight" (left) and "severe" (right) taper corrosion.

Serum ion concentrations showed significant differences between both taper and both bearing wear groups (Table 2, Table 3) and also significant interactions (Figure 10): In the "edge" wear group, the ion concentrations were significantly higher for samples with "severe" than with "slight" taper corrosion whereas in the "no edge" group, no differences between taper corrosion groups were observed (Cr: taper corrosion group p=0.024, edge wear p=0.02, interaction p=0.025; Co: taper corrosion group p=0.068, edge wear p=0.02, interaction p=0.032).

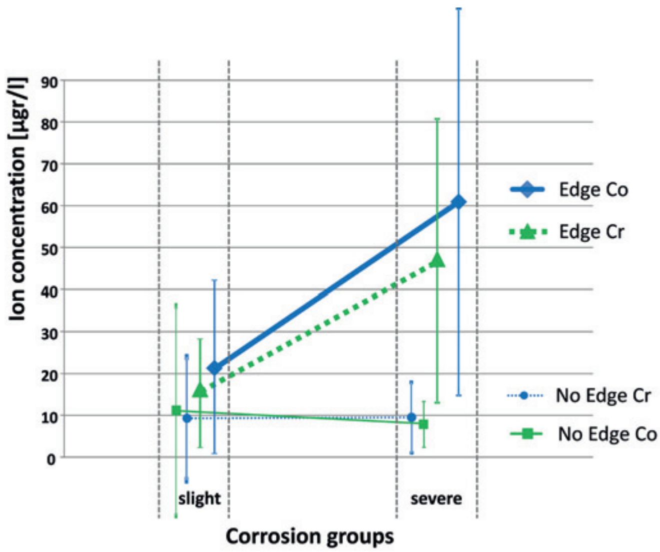

Figure 10. Serum metal ion concentrations for the two corrosion and the two taper wear groups.

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DISCUSSION

Wear or corrosion of the modular junction between stem and head has been reported as one of the causes for hip implant failure[9,14-17]. The current increase in the implication of corrosion in implant failure has been related to the re-introduction of large diameter metal-on-metal bearings.[28,29] The bearing components themselves are cobalt chrome and are usually fixed directly to a cobalt chrome or titanium stem. The use of a titanium adapter in the design of the current retrievals has demonstrated a rather different corrosion mode for the less common titanium-titanium material combination. Differentiation between volumetric material changes at the bearing articulation and at the taper interface was studied for this implant design to investigate the failure mechanism.

The 43 adapter components were separated visually into groups of slight and severe corrosion. The latter group revealed an irregular crumbly oxide layer penetrating into the female taper adapter and stem taper, and with some material loss, as well as deposit. Massive material loss at the stem taper reached 21.5 mm^2 in one case (Figure 2), in which also the female adapter taper wear was very high (22.6 mm^3) but deposit on the female adapter was low (0.8 mm^3). Such corrosion might be clinically dangerous but could not be verified in this study. Serum titanium ions were not measured and no tissue sample was available. There were no significant associations between wear and deposit volumes for the stem or for the adapter, and it is noted that material may have been lost during removal of the adapter from the stem in revision surgery. The more common cobalt chrome tapers have been shown to be prone to galvanic and fretting corrosion,[30,31] possibly facilitated by high friction moments in metal bearings in conditions of poor lubrication. Revision rates of such bearings have been found to increase with bearing diameter[1], which increases joint friction moments.[32] This mechanism provides the basis for the hypothesis tested in this study, but uniquely for a Ti-Ti taper interface. The significantly higher bearing wear rate and ion concentrations observed in the “severe” taper corrosion group supports the study hypothesis.

Mechanical loading introduces cyclic local relative motion between modular components.[33] The resulting frictional shear can generate wear particles, as well as remove the protective oxide layer, revealing the metal alloy of the bulk material, which is highly reactive, and corrodes as it comes into contact with fluid, releasing metal ions.[14] The titanium interfaces in the current study appear to corrode by progressive oxidation radially from the surface, resulting in a bulk oxide layer of increasing thickness on both sides of the interface, with local crumbling. In contrast to cobalt chrome components, fretting is unlikely to be involved since this would only affect the surface. Instead, progressive corrosion into the depth of the material must occur due to disruption of the bulk material and contact with the joint fluid. A small difference in taper angle between adapter and stem tapers is found in most implants, either due to design or manufacturing tolerances. The resulting gap, as well as the channels due to surface profiles, may both accelerate corrosion by increasing the fluid circulation to the interface. These factors do not explain the severe corrosion observed for some explants in the current study, since the implant investigated has a smooth surface and matching taper angles.

Assuming the fluid could enter the gap either passively or pumped due to the bending under joint loading, the individual local conditions in the patient's hip may account for some variation in the extent of corrosion observed. The composition and volume of the joint fluid itself may dictate how corrosive the environment for bearing surfaces becomes, both for the taper interfaces and for the bearing surfaces. The clinical implications of titanium ion concentrations are much less well studied and documented than cobalt and chrome, however, titanium ions are not yet thought to be as aggressive clinically.[35,36] Vanadium, which is one of the components of the stem and adapter Ti-alloy, is a potentially negative factor which has not been investigated in detail and should be included in future analyses.[37]

A recent study showed that the volume of material loss from the taper surfaces does not correlate with the occurrence of pseudotumors, but no differentiation between CoCr and Ti was performed.[21] Major oxidation of the titanium tapers as seen in some retrievals in the current study clearly reduces the cross sectional area and can lead ultimately to taper fracture, as observed in a modular hip stem.[38] It is noted that some cases of severe corrosion of the female taper of the adapter occurred without any wear of the bearing surface (Figure 9), suggesting that friction moments due to compromised joint lubrication are only one factor for taper corrosion. An explanation could be that the tapers were assembled differently, for example with regard to assembly force, thereby varying mechanical stability.[33,39,40] Such a variation may be related to the technique of the 15 different surgeons involved in primary implantation of the retrieved samples.

The clinical consequence of wear and corrosion of cobalt chrome taper components appears to be similar to the effect of bearing wear. In the current study, a large proportion of the implants (47%) presented with edge wear, which has been related to high revision rates in similar studies.[25,26,41,42] Edge wear has been related to cup orientation outside the safe range according to Lewinnek.[27] This was not confirmed in the current study, suggesting that cup position is not a unique factor in compromising lubrication, and that other factors must be involved.

Applying serum ion concentration thresholds associated with metallosis (Co>19 μg/l and Cr> 17 μg/l)[43], 13 (30 %) and 12 (28 %) patients presented with elevated cobalt and chromium levels, respectively. Thus, the majority of implants was revised for other reasons than elevated ion concentrations. Since the interface between the titanium adapter and the cobalt chrome head was not assessed, this interface cannot be ruled out as an ion source, particularly since cobalt chrome corrodes preferentially to titanium.[19,21] Disassembly of this interface was not possible. Another study limitation is that only 14 stems were available for assessment. Also, 63 % of the patients had additional implants, which could have contributed to the high ion concentrations (Table 1).

The ion thresholds applied have been suggested as a useful indicator for metallosis. However, corresponding metal concentrations in the tissues were not found to correlate with serum concentrations, indicating that tissue samples give a very local estimate of ion and particle concentrations, but not a representative estimate of the systemic exposition. For example, a sample with a high Ti concentration in tissue (1330 mg/kg) showed only a minor deposit on the female adapter sleeve.

Serum metal ion concentrations were shown to be good estimates for bearing wear and also for taper corrosion, due to its demonstrated association with bearing wear. Ion concentrations measured in tissues were not as useful. Patient factors, operative technique and implant design all remain potential origins for the problems observed, as no single factor can be identified to explain such implant failure.[41,42] In future studies, Ti and possibly Vanadium concentrations in blood or serum should be determined as they could be one of the missing pieces of information.

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CHAPTER 8

General discussion

For as long as surgical procedures are performed, complications are described. Therefore it remains a challenge in modern orthopaedics to decrease their incidence. Although infection, thrombosis, peri-operative fractures, among many others, are all serious complications, it is the author's opinion that malposition of components in THA is probably the most important pitfall. It enhances dislocation and wear, it limits ROM, reduces implant survival and increases the necessity for re-operation with its associated risks. This thesis describes several pitfalls that contribute to some of the well-known complications. The first part of this thesis describes how freehand cup positioning results to malpositioning and subsequently in (recurrent) dislocation. The second part describes how a new innovative solution was introduced to address some of the described pitfalls, but unfortunately as a consequence, created new ones. The general discussion will end with the main findings of this thesis and recommendations for further research.

TRADITIONAL

The accuracy of freehand cup positioning

Based on a retrospective cohort of 300 THA's, Lewinnek defined his safe zone.[1] He stated that within this zone dislocation rates are reduced from 6.1% to 1.5%. Freehand cup placement within this zone is difficult because of the relative narrow range. Saxler studied 105 patients who received a THA using freehand positioning of the acetabular cup. He found only 27/105 cups (26%) implanted within the limits of the safe zone.[2] In another study, DiGoa et al found only 22% of their cups placed correctly, even by the use of a special alignment guide.[3] We have demonstrated in chapter 2, that 70.5% of our cups, implanted freehand, were placed within Lewinnek's safe zone. Although our results seem better, an unacceptable amount of outliers of about 30% remains. Because of our findings and those of others, we conclude that freehand cup positioning is inaccurate. In the next part we will try to explain why this method is inaccurate. Several authors investigated the influence of pelvic motion in the supine and lateral decubitus on cup position. Lembeck et al. demonstrated that pelvic tilt changes in the supine to standing position, lead to increased risk of malpositioning by underestimating the amount of anteversion in the supine position.[4] McCollum and Gray found that when a patient is placed in the lateral decubitus position, the lumbar lordotic curve is flattened, and therefore the pelvis is flexed. They noted that if the acetabular component was orientated in 20° of anteversion to the longitudinal axis of the body, when the patient stood, the lumbar lordosis would recur, the pelvis would extend, and the acetabulum could easily be retroverted.[5] Besides flexion, the pelvis also adducts in the lateral decubitus position, increasing the risk of vertical cup placement.[5] Besides patient positioning, pelvic movement during the procedure can significantly contribute to inaccuracy in freehand cup positioning as shown in chapter 3. In an ideal situation the pelvic would not move during the procedure, but in reality movement almost always occurs. Asayama noted that the pelvic motion primarily occurred while the Hohmann retractor was being applied to the femur to expose the acetabulum.[6] Chapter three also shows how sequencing further contributes to inaccuracy of cup positioning. It demonstrates how the first selected cup position influences the second due to its planar orientation. Derived from the data in chapter 3, positioning the cup by applying anteversion first, followed by setting inclination is more accurate than vice versa. Understanding this phenomenon, the "problems" of improper positioning and pelvic movement during the procedure explain why freehand cup positioning is inaccurate.

The significance of Lewinnek's safe zone

Complication registrations in our facility during the study period showed a dislocation rate of about 1.7%. This is much lower than expected, based on Lewinnek's article, published in 1978.[1] If freehand cup positioning is inaccurate, and placement beyond Lewinnek's safe zone leads to an increased dislocation rate, than why did we have such a low dislocation rate? The clinical relevance of the safe zone can therefore be questioned. The transverse acetabular ligament (TAL) is a recent discussed anatomic structure, used as a reference point in freehand positioning, that might enhance more precise cup placement. Abe et al found the ligament to be a good guide for determining cup orientation but stated that TAL has large individual variations.[7] Viste et al. found in a cadaveric study that TAL seems to be a specific reference for each patient, but in many cases outside the safe zone as described by Lewinnek.[8] Because of these statements and the low dislocation rate in our cohort, we suggests that an universal safe zone for all patients is unlikely. The natural orientation of the acetabulum and femoral neck seem to differ among patients and reconstruction of the joint should restore both these anatomies as close as possible.

From Lewinnek to Widmer?

Although cup position is important, stability of a total hip prosthesis depends on both cup and stem orientation. Widmer shows that the cup and neck should be oriented relative to each other in order to prevent cup-to-neck impingement.[9] Because the orientation of the natural acetabular opening in the human pelvis can vary from anteversion to retroversion, and inclination from lower to higher degrees, the stem position should be adjusted accordingly. Widmer states that even extreme but compliant positions of the components can be accepted in order to obtain good component fixation and long-term stability, as long as the morphology of the proximal femur and the pelvis allows the stem and the cup to be placed in complementary orientations. Hence, the relative positioning of the components is more important than the absolute positioning with regard to bony landmarks. This goal is best achieved when the second component is intentionally oriented relative to the first component. The surgeon may follow the "stem first" concept, where the cup is positioned relative to the stem after the trial stem has been implanted. Because we believe that the cup and neck should be oriented relative to each other, accordingly, in order to prevent cup-to-neck impingement, the "stem first" is an interesting concept that could be an alternative to Lewinneks safe zone.

Argumentation for augmentation?

Dislocation is a devastating complication associated with THA. Its aetiology is multivariate but malposition of components seems to be one of the most causative factors. There are several treatment options for recurrent dislocation. Conservative treatment mainly consists of (Spica) cast bracing. Although good results are reported [10,11], newer studies show little benefit from this treatment.[12,13] Although invasive treatment by revisional surgery might give better results in component malposition, the risk for (more) severe complications is increased.
The procedure is associated with prolonged operating time, increased blood loss and poor postoperative mobility. It is therefore highly demanding and significant increases patient morbidity and mortality. The surgeon is faced with an ethical dilemma between the patients' health and quality of life.
The acetabular augmentation ring was introduced as a less invasive procedure to address recurrent dislocation. It was first described by Olerud and Karlström.[14] They treated six patients successfully, followed by Nicholl who had 5 failures in 28 patients.[15] Although promising, with increased use and follow-up more reports of screw breakage, re-dislocation and infection were reported. [16] We analysed results of the augmentation ring as used in our clinic. We encountered screw breakage, infection and re-dislocation. The results are poor and we therefore feel that the technique has limited use. Patients in whom major surgery is contra-indicated and who have cups without gross malalignment or polyethylene wear seem to be the only group that could benefit from this technique.

The role of Computer Assisted Surgery

Computer Assisted Surgery (CAS) found its way into the operating theatre and is now entering its second decade of use. Although good results are reported in spine and knee surgery, the benefit still does not outweigh the suggested disadvantages in total hip arthroplasty. Computer navigation may improve the accuracy of prosthesis positioning but, despite its obvious advantage with respect to reducing asymmetric wear, this has not yet been shown to have a clinical benefit. [17,18] Navigation leads to increased surgical time, elevated costs and operative complexity.[17] Some discussion as to whether the combination of Computer Assisted Surgery with a minimally invasive approach can help to improve outcomes is on-going. At present greater quality designed studies and the mastering of this surgical technique is required before such techniques can be formally analysed.[18,19] We therefore feel that CAS is a promising new development, but it has to evolve further to address the present drawbacks before it can be used on a large scale.

INNOVATIVE

The introduction of MoM

To address the complications caused by malposition like dislocation, wear and ROM (as stated earlier), industries developed a new articulation, and introduced Metal-on-Metal. The articulation was more stable than the conventional polyethylene bearing because of decreased wear rates and the possibility to use bigger diameter femoral heads. Good short term results were described and especially the Resurfacing Total Hip Arthroplasty gained popularity in young and active patients, because of its bone preserving design. Low dislocation rates were reported and based on a conservative estimate, approximately 500 000 current-generation MoM hip replacements, including resurfacing and THR, have been implanted during the last 15 years worldwide.[20]

Serious adverse events

In April 2010 the British Orthopaedic Association issued an alert to its members concerning large-sized femoral head MoM hip arthroplasties.[21] The alert followed various reports about the formation of pseudotumors, associated with metal debris generated by the Metal-on-Metal articulation. Pseudotumors, although assumed to be benign, are associated with dislocation, nerve palsy [22] and fracture [23] depending on the location and size of the tumor. Several studies report toxic effects of prolonged elevated serum metal ion exposure like hypothyroidism, polyneuropathy, impairment of cranial nerves II and VIII and cardiomyopathy. [24] Others report concerns about carcinogenicity, hypersensitivity and fetal exposure in pregnant women.[25-26] If symptoms are severe, revision seems to be the only option to halt the process, unfortunately with poor functional outcomes in many patients. Because of the adverse events described above, the Dutch Orthopaedic Association has ordered its members to halt further implantation of Metal-on-Metal devices, until further evidence is available.

Incidence of pseudotumors

The incidence of pseudotumors in retrospective studies after MoM THR varies between 1% and 4%.[28,29] These incidences are derived from mostly symptomatic and revision cases, therefore likely underestimating the true incidence. Chapter 5 dramatically illustrates an extreme high incidence of 39% in our series. Two possible explanations for the difference are discussed. First, we performed a specific and extensive screening protocol for all patients (symptomatic or asymptomatic) with a metal-on-metal THA. The second explanation is the definition of a pseudotumor, as stated in our study. We believe that a lesion as small as 2 cm in diameter, that cannot be explained by other causes, can be accurately diagnosed on CT as a pseudotumor.[30] Although associated with implant failure, the clinical relevance of the asymptomatic lesions, especially the smaller ones, is still subject to discussion. Longer follow-up of these smaller lesions is needed. Chapter 6 confirms the high incidence in all our treated patients.

Risk factors

Known risk factors for pseudotumors are young women, small diameter femoral heads[31], pain and elevated serum metal ions.[29] Although in our study several new risk factors were identified and others confirmed, they seem of relative clinical importance, because the vast majority of our patients will develop a pseudotumor in due time. Furthermore, serum cobalt and chromium should be regarded poor predictors for pseudotumor presence leaving cross sectional imaging as the main screening tool during follow-up. Once again we should emphasize that longer follow-up is needed to confirm the worrisome findings. Most reported incidences and risk factors concerned resurfacing hip prostheses. Implant design could therefore also contribute to the difference in incidence.[32] Various models of metal-on-metal THA's can generate different amounts of wear probably influencing the occurrence of metal debris associated problems. A large femoral head (36mm and more), as used in our patients, is considered to be a risk factor for developing ARMD, due to the elevated risk of taper wear and edge loading.

Corrosion and bearing wear

Chapter 7 demonstrates, in a retrieval study, that there is a relation between titanium taper wear and cobalt-chromium bearing wear in the large head metal-on metal-total hip prostheses. A different corrosion mode for the less common titanium-titanium interface might eventually lead to overload of the neck of the stem, which could result in fracture of the taper (figure). Although in many cases the stem is well fixed, if revision is indicated, removal of the stem should be considered. Bearing wear is believed to have caused many of the pseudotumors in the retrievals. Further research is necessary to confirm our findings and to study the toxicological effects of the released metal ions.

MAIN FINDINGS OF THE THESIS

- Freehand cup positioning is an inaccurate technique resulting in a high rate of cup malpositioning.
- Cup positioning is more accurate when anteversion is applied before inclination for various orientations within Lewinnek's safe zone.
- Results of acetabular augmentation arthroplasty deteriorate rapidly through time; therefore, it is appropriate to consider it as a salvage procedure for the biologically infirm and less active patients.
- The incidence of pseudotumor formation and revisions in our large cohort of metal-on-metal total hip arthroplasties is substantially higher than previously reported.
- The true incidence of pseudotumors can only be determined after deploying an extensive screening protocol.
- The most important risk factor for developing a pseudotumor in large head metal-on-metal stemmed total hip arthroplasties appears to be time.
- Wear of the modular titanium taper interface is related to wear at the bearing articulation in large head metal-on-metal stemmed total hip arthroplasties.

RECOMMENDATIONS FOR FURTHER STUDIES

One of the most intriguing questions might be if there really exists a safe zone for cup placement. Although much cited, Lewinnek's safe zone is still questionable. With newer 3D imaging techniques en better pre-operative planning, this question can be answered by further studies with sufficient follow-up. We should however recognize that both cup and stem play an important role in prosthesis stability and generated wear.

Positioning of the pelvis perpendicular to the operating table, preventing any per-operative movement, would enhance more accurate freehand cup positioning. To our knowledge no such devises are yet available. Alternatives for better patient immobilization on the operating table should be examined.

CAS seems a promising technique. Although reducing the number of outliers of malpositioned cups, there are still improvements to be made. Further research is needed to reduce operating time, reduce the complexibility, reduce costs and increase its accuracy, before it can be used on a large scale.

Pseudotumors associated with metal-on-metal implants are worrisome. Their incidence varies and might be related to implant design. Prolonged follow-up of patients treated with metal-on-metal devices is needed to learn about their clinical course and about effects of prolonged toxic metal ion exposure. All patients should be thoroughly examined with imaging studies. Until more is known about the adverse effects seen in metal-on-metal devices, implantation should be discouraged.

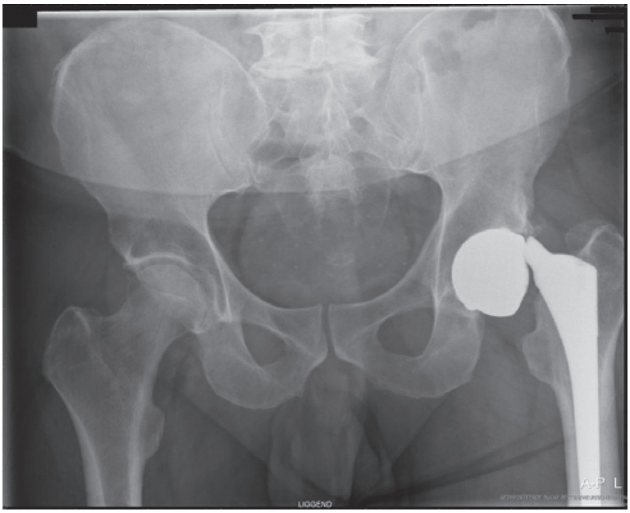

Figure. X-ray showing spontaneous fracture of the taper in a Metal-on-Metal big femoral head arthroplasty six years after implantation.

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CHAPTER 9

Summary & Samenvatting

SUMMARY

This thesis focusses on pitfalls in traditional and innovative hip replacement surgery.
The first part (traditional) of the thesis focusses on several well-known problems encountered in total hip arthroplasty: the inaccuracy of freehand cup implantation and recurrent dislocation. The degree of inaccuracy is demonstrated and discussed, furthermore an alternative treatment option for recurrent dislocation using an augmentation ring is investigated.
The second part (innovative) discusses the recently recognised problems associated with the metal-on-metal bearing.

TRADITIONAL:

Chapter 2: The inaccuracy of freehand cup positioning.

Design and rationale: a prospective study was designed to assess the accuracy of freehand cup positioning. Peroperative estimated abduction and anteversion of 200 acetabular components (placed by three orthopaedic surgeons and nine residents) were compared with measured outcomes (according to Pradhan) on postoperative radiographs.
Main results: 70.5% Of cups were placed within Lewinnek's safe zone (5-25° anteversion and 30-50° abduction). Only 21.5% of cups were placed within 10-20° anteversion and 35-45° abduction.
Considering peroperative estimation of cup placement, there was a mean difference of 5.5 and 5.4 degrees between estimated and actual placement as measured on the postoperative radiograph for anteversion and abduction respectively. There is a tendency to underestimate both abduction and anteversion. Orthopaedic surgeons are superior to their residents in estimating abduction of the acetabular component, suggesting a learning curve.
Discussion: although illustrating the inaccuracy of freehand cup positioning, we should realise that an important potential flaw in this study might be that anteversion was calculated on standardized X-rays.
Variations in pelvic flexion-extension during imaging can be responsible for variations in anteversion up to -26° to +10°. Therefore, in our study, special attention was given for optimal positioning of the pelvis to minimize rotation and tilt before the X-ray was taken.
Conclusion and recommendations: we conclude that free hand cup positioning results in a high rate of cup malposition. Peroperative estimates of cup placement are inaccurate.
For a more precise cup placement alternatives like guidance tools or Computer Assisted Surgery (CAS) techniques should be considered.

Chapter 3: Is there still a place for freehand cup positioning? The inaccuracy of freehand cup positioning explained by a theoretical model.

Design and rationale: the previous described inaccuracy of freehand cup positioning is further investigated. One of the goals, described in this chapter, was to find contributing factors to explain why freehand cup positioning is inaccurate. The definitions of planar- and true cup dimensions are introduced. Understanding the difference between planar and true explains how sequencing leads to an inaccurate estimation of the true cup position.
A 3D modelling program was used to predict true cup position after first applying inclination and subsequently anteversion and vice versa. The influence of pelvic motion on cup position during placement was calculated.
Main results: cup positioning is more accurate when anteversion is applied before inclination.
Inclination followed by anteversion leads to overestimation of true anteversion, ranging from 1.5 to 18 degrees, for various orientations within Lewinnek's safe zone. Slight pelvic movement (5–15° in any direction) leads to misinterpretation of cup position with ranges of 1.1–15° anteversion and 0.6–15° inclination.
Conclusion and recommendations: the study illustrates factors contributing to inaccuracy of freehand cup placement. Due to sequencing and improper preoperative patient positioning and/ or pelvic movement, accurate freehand cup placement is almost impossible to achieve.

Chapter 4: Acetabular augmentation ring for recurrent dislocation of total hip arthroplasty: 60% stability rate after an average follow-up of 74 months.

Design and rationale: this chapter describes a retrospective study that investigates the results of an acetabular augmentation ring for recurrent dislocation of a total hip arthroplasty. It was used in our clinic as a less invasive alternative to revisional surgery.
Main results: forty-seven patients (50 hips) were treated with acetabular shell augmentation arthroplasty for recurrent idiopathic dislocation. Follow-up averaged 74 months (range 12–178 months), and clinically, 30 hips (60%) did not present a subsequent dislocation at most recent follow-up. In five hips (10%), deep infection after the augmentation procedure necessitated removal of the entire prosthesis. Seven patients (14%) ultimately lost their prosthesis due to infection after multiple revision procedures (augmentation and re-augmentation). Although cup malposition did not appear to be a relevant factor in this study, potential drawbacks are the calculation of anteversion on X-rays and missing data about stem version.
Conclusion and recommendations: in cases without excessive malpositioning of components, acetabular augmentation arthroplasty could be considered. It must be realised that results deteriorate rapidly with time; therefore, it is appropriate to reserve the procedure for biologically older and less active patients.

INNOVATIVE:

The second part of the thesis describes the pitfalls of large head metal-on-metal stemmed total hip replacements.

Chapter 5: High incidence of pseudotumour formation after large-diameter metal-on-metal total hip replacement: a prospective cohort study.

Design and rationale: chapter 5 investigates the incidence of pseudotumor formation after large-diameter metal-on-metal total hip replacement in a prospective cohort study.
A total of 119 patients with 120 MoM THAs with large-diameter femoral heads were included in the study. Outcome scores, serum metal ion levels, radiographs and CT scans were obtained. Patients with symptoms or an identified pseudotumor were offered MRI and an ultrasound-guided biopsy.
Main results: there were 108 patients (109 hips) eligible for evaluation by CT scan at a mean follow-up of 3.6 years (2.5 to 4.5); 42 patients (39%) were diagnosed with a pseudotumor. The hips of 13 patients (12%) were revised to a polyethylene acetabular component with small-diameter metal head. Patients with elevated serum metal ion levels had a four times increased risk on developing a pseudotumor.
Conclusion and recommendations: the study shows a substantially higher incidence of pseudotumor formation and subsequent revisions in patients with MoM THAs than previously reported. Because most revision cases were identified only after an intensive screening protocol, close monitoring of patients with MoM THA is strongly recommended.

Chapter 6: Pseudotumor formation and serum ions after large head metal-on-metal stemmed total hip replacement. Risk factors, time course and revisions in 706 hips.

Design and rationale: chapter 6 describes the results of all patients treated with large-diameter MoM THA's in our clinic. The incidence, time course and risk factors for pseudotumor formation are analysed. Furthermore, the relevance of serum metal ions was investigated and revisions described.
Main results: the median follow-up was 3 years. Seven hundred-six hips were screened in 626 patients. Two hundred twenty eight pseudotumors (32.3%) were diagnosed in 219 patients (35.0%), thereby presenting a comparable incidence as described in chapter 5.
Pseudotumor formation significantly increased after prolonged follow-up. Isolated risk factors for the presence of pseudotumor were: aspecific pain, cobalt ≥ 4 μg/l and swelling.
Seventy-six hips (10.8%) were revised in 73 patients (11.7%), risk factors being younger age at follow-up, aspecific pain, cobalt ≥ 4 μg/l and swelling. The best cut-off point for both cobalt and chromium was 4 μg/l (sensitivity 57.3% and 53.9%, specificity 71.0% and 65.6%).
Conclusion and recommendations: this study confirms the previously found high incidence of pseudotumors in patients treated with large-head MoM THA's. Although several risk factors are

confirmed, their importance seems limited because the vast majority of patients will develop a pseudotumor in the course of time. Cobalt and chromium are poor predictors for pseudotumor presence, therefore making radiological follow-up indispensable.

Chapter 7: The relation between titanium taper wear and cobalt-chromium bearing wear in large head metal on metal total hip prosthesis - A retrieval study.

Design and rationale: chapter 7 describes a retrieval study that investigates the possible relation between wear of the modular titanium taper interface and wear at the bearing articulation. Forty-three large diameter cobalt-chrome bearings mounted on a titanium stem using a titanium adapter were retrieved. Bearing and taper surfaces were assessed using a coordinate measurement machine for wear and corrosion.

Main results: thirteen adapter interfaces (30%) presented severe corrosion, 30 (70%) mild or little corrosion. Severe corrosion was visible on the stem taper and the inner adapter tapers and an oxide layer covered the entire contact area. There was a significant difference in metal ion concentrations between heavy and light taper corrosion groups. Edge wear has been related to cup orientation outside the safe range according to Lewinnek. This was not confirmed in this study, suggesting that cup position is not a unique factor in compromising lubrication, and that other factors must be involved. Sixty-two percent of the implants with severe taper corrosion and 40% with mild taper corrosion demonstrated edge loading. Serum metal ion concentrations were shown to be good estimates for bearing wear and also for taper corrosion, ion concentrations measured in tissues were not as useful.

Conclusion and recommendations: corrosion of the taper interface is directly related to wear of the bearing surfaces due to disrupted tribology. The study presents a different corrosion mode for the less common titanium-titanium interface that might eventually lead to overload of the neck of the stem resulting in fracture of the taper. Bearing wear may have caused many of the pseudotumor formations in these retrievals.

SAMENVATTING

Dit Proefschrift bespreekt "valkuilen" in traditionele en innovatieve totale heup chirurgie. Het proefschrift bestaat uit twee delen. Het eerste deel (traditioneel) bespreekt de onnauwkeurigheid van "freehand" cup positioneren en een alternatieve behandeling van recidiverende heupluxaties middels een augmentatiering. Het tweede (innovatieve) deel gaat in op de recentelijk beschreven problemen, geassocieerd met metaal-op-metaal (MoM) articulaties.

TRADITIONEEL:

Hoofdstuk 2: de onnauwkeurigheid van "freehand" cup positioneren.

Design en rationale: een prospectieve studie werd opgezet om de nauwkeurigheid van "freehand" cup positioneren te analyseren. De peroperatief ingeschatte inclinatie en anteversie van 200 cups (geplaatst door drie orthopedisch chirurgen en negen assistenten) werd postoperatief vergeleken met op röntgenfoto's gemeten waarden (volgens Pradhan).
Resultaten: 70.5% van de cups stonden binnen de safe zone van Lewinnek (5-25° anteversie en 30-50° inclinatie). Slechts 21.5% van de cups stond binnen 10-20° anteversie en 35-45° inclinatie.
Het mediane verschil tussen meten en plaatsen voor respectievelijk anteversie en inclinatie bedroeg 5.5 versus 5.4 graden. Er blijkt een tendens te bestaan om zowel anteversie als inclinatie te onderschatten. Orthopedisch chirurgen zijn beter in het schatten van inclinatie van de cups dan assistenten, zodat er sprake kan zijn van een learning curve.
Discussie: anteversie werd op röntgenfoto's berekend. Variatie in flexie en extensie van het bekken, kan een röntgenologisch verschil in anteversie geven van -26 tot 10°. Om deze reden werd speciale aandacht besteed aan het positioneren van het bekken en het voorkomen van bewegingen voordat de opname werd gemaakt.
Conclusie en aanbevelingen: het "freehand" positioneren van de cup in het acetabulum resulteert in een hoog aantal malposities. Peroperatieve inschatting van cup positie is onbetrouwbaar. Voor meer betrouwbare cup positionering, moeten alternatieven zoals computer navigatie systemen (CAS) worden overwogen.

Hoofdstuk 3: Is er nog plaats voor het "freehand" cup positioneren? De onnauwkeurigheid van "freehand" cup positionering verklaard middels een theoretisch model.

Design en rationale: de hiervoor beschreven onnauwkeurigheid van "freehand" cup positioneren wordt in dit hoofdstuk verder onderzocht. De definities van planar- en true cup dimensies worden geïntroduceerd. Het verschil tussen true en planar verklaart hoe sequencing bijdraagt aan het onnauwkeurig inschatten van cup positie. Middels software om 3D modellen te ontwerpen werd de ware cup positie berekend nadat eerst inclinatie, gevolgd door anteversie werd toegepast en vice versa. Tevens werd de invloed van (peroperatieve) bekken bewegingen op de cup positie berekend.

Resultaten: "freehand" cup positioneren is betrouwbaarder indien eerst anteversie wordt ingesteld en daarna inclinatie. Indien eerst inclinatie wordt gekozen, gevolgd door anteversie, resulteert dit in een overschatting van de ware anteversie, met een range van 1.5 tot 18 graden, voor verschillende oriëntaties binnen Lewinnek's safe zone. Beweging van het bekken (5-15° in iedere richting) leidt tot misinterpretatie van de cup positie met ranges van 1.1-15° anteversie en 0.6-15° inclinatie.

Conclusie en aanbevelingen: deze studie demonstreert factoren welke bijdragen tot de onnauwkeurigheid van "freehand" cup positioneren. Sequencing, de moeilijkheid van het goed positioneren van de patiënt en peroperatieve (bekken) bewegingen maken het nauwkeurig plaatsen van een cup praktisch onmogelijk.

Hoofdstuk 4: De augmentatiering als behandeling voor recidiverende luxaties na een totale heup arthroplastiek: 60% succesvol na een gemiddelde follow-up van 74 maanden.

Design en rationale: dit hoofdstuk beschrijft een retrospectieve studie waarin de resultaten van de behandeling van recidiverende heupluxaties middels een augmentatiering werden onderzocht. De augmentatiering werd in onze kliniek gebruikt als een minder invasief alternatief voor revisie chirurgie.

Resultaten: zevenenveertig patiënten (50 heupen) werden voor recidiverende idiopathische heupluxatie behandeld met een augmentatiering. De gemiddelde follow-up bedroeg 74 maanden (12-178 maanden). Dertig heupen (60%) ondergingen geen nieuwe episode van luxatie ten tijde van de meest recente follow-up. Bij 5 heupen (10%) ontstond een "diepe" infectie ten gevolge van de procedure, waardoor extractie van de prothese noodzakelijk was. Cup malpositie kon niet worden aangetoond als een oorzakelijke factor voor (re)dislocatie. Zeven patiënten (14%) ondergingen uiteindelijk extractie van hun prothese als gevolg van infectie door meerdere revisie procedures (augmentatie en re-augmentatie). Een belangrijke tekortkoming in de studie is de beperkte betrouwbaarheid van het berekenen van cup anteversie op röntgenfoto's en het ontbreken van gegevens over de oriëntatie van de steel.

Conclusie en aanbevelingen: bij patiënten zonder extreme malpositie van componenten, kan een augmentatiering worden overwogen. Gerealiseerd moet worden dat de resultaten van deze behandeling snel verslechteren na langere follow-up. Het is daarom aan te raden om de behandeling van recidiverende heup luxaties middels een augmentatiering te reserveren voor de biologisch oudere, minder actieve en kwetsbare patiënt.

INNOVATIEF:

Het tweede deel van het proefschrift behandelt de MoM totale heup prothese en onderzoekt en bediscussieert de daaraan geassocieerde complicaties.

Hoofdstuk 5: Hoge incidentie van pseudotumoren bij de grote koppen metaal-op-metaal totale heup prothese: in een prospectief cohort.

Design en rationale: in dit hoofdstuk wordt middels een prospectief onderzoek de incidentie van pseudotumoren bij grote koppen metaal-op-metaal totale heupprothesen (MoM THA's) onderzocht. Honderdnegentien patiënten met 120 MoM THA's werden geïncludeerd. Pijnscores, PROMS, serum metaal ionen, röntgenfoto's en CT-scans werden verkregen. Bij symptomen of bij een gediagnosticeerde pseudotumor op CT werd een aanvullende MRI-scan en echogeleide biopsie aangeboden.
Resultaten: honderdacht patiënten (109 heupen) waren beschikbaar voor analyse middels een CT scan met een mediane follow-up van 3.6 (2.5-4.5) jaar; bij 42 patiënten (39%) werd een pseudotumor gediagnosticeerd. Bij 13 patiënten (12%) werd de heup gereviseerd naar een metaal-op-polyethyleen articulatie. Patiënten met verhoogd serum metaal ionen hadden een vier maal hogere kans op een pseudotumor.
Conclusie en aanbevelingen: de studie toont een substantieel hogere incidentie van pseudotumoren en revisies bij patiënten met MoM THA's dan eerder in de literatuur werd gerapporteerd. Omdat de meeste revisie-indicaties pas werden gesteld na het uitvoeren van een uitvoerig screeningsprotocol, wordt een strenge, jaarlijkse controle van patiënten behandeld met MoM THA's sterk aanbevolen.

Hoofdstuk 6: Pseudotumoren en serum metaal ionen bij de grote koppen metaal-op-metaal totale heup prothese. Risicofactoren, beloop en revisies in 706 heupen.

Design en rationale: hoofdstuk 6 beschrijft de resultaten van alle patiënten waarbij in onze kliniek de grote koppen metaal-op-metaal totale heup prothese (MoM THA) werd geplaatst. Incidentie, beloop en risicofactoren voor het ontwikkelen van pseudotumoren werden geanalyseerd. De relevantie van serum metaal ionen werd onderzocht en revisies beschreven.
Resultaten: de mediane follow-up bedroeg 3 jaar. Zevenhonderd en zes heupen werden geanalyseerd in 626 patiënten. Tweehonderd achtentwintig pseudotumoren (32.2%) werden gediagnosticeerd bij 219 patiënten (35.0%), daarmee werd een vergelijkbare incidentie gevonden als eerder beschreven in hoofdstuk 5. De incidentie steeg bij langere follow-up. Risicofactoren voor pseudotumoren zijn: aspecifieke pijn, cobalt ≥ 4µg/l en zwelling.
Zes en zeventig heupen (10.8%) werden bij 73 patiënten (11.7%) gereviseerd. Risicofactoren voor revisie zijn: lagere leeftijd ten tijde van follow-up, aspecifieke pijn, cobalt ≥ 4µg/l en zwelling. De beste afkapwaarden voor zowel cobalt als chroom bedroeg 4 µg/l (sensitiviteit 57.3% en 53.9%, specificiteit 71.0% en 65.6%).
Conclusie en aanbevelingen: de studie bevestigt de eerder door ons beschreven hoge incidentie

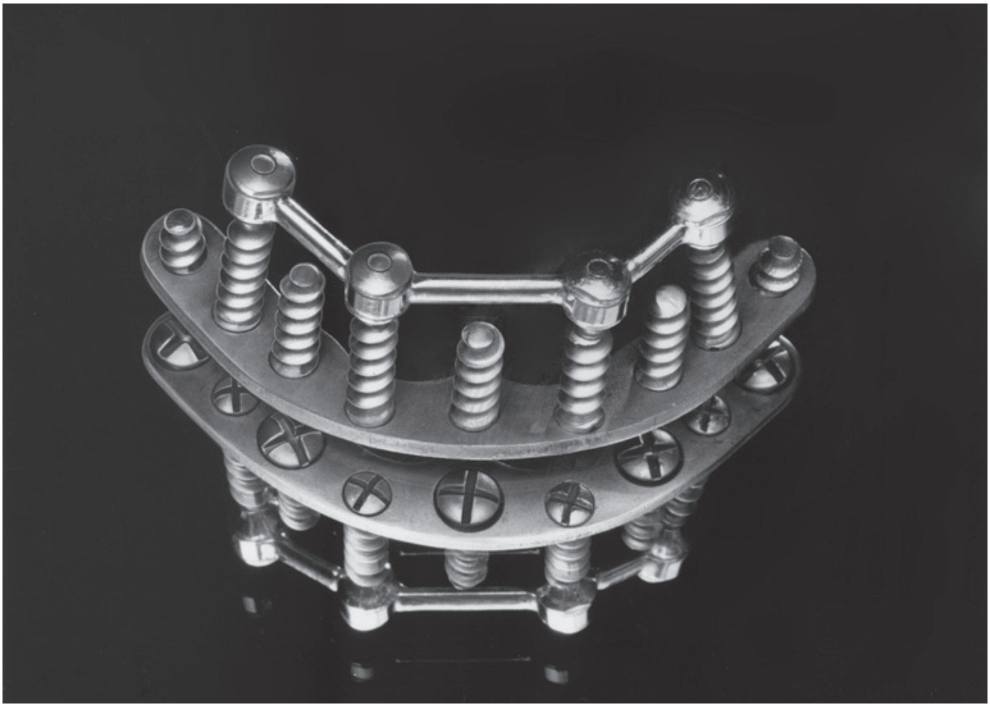
van pseudotumoren bij patiënten, behandeld met de grote koppen MoM THA's. De klinische relevantie van gevonden risicofactoren lijkt beperkt omdat de overgrote meerderheid van de patiënten uiteindelijk een pseudotumor ontwikkelt bij het verstrijken van tijd. Cobalt en chroom zijn zwakke voorspellers voor de aanwezigheid van een pseudotumor zodat follow-up middels beeldvorming onmisbaar is.

Hoofdstuk 7: De relatie tussen titanium taper wear en cobalt-chroom bearing wear in grote koppen metaal-op-metaal totale heup prothesen. Een retrieval studie.

Design en rationale: hoofdstuk 7 beschrijft een retrieval studie welke de mogelijke relatie tussen wear ter plaatse van de titanium taper interface en de articulatie onderzoekt. Drie en veertig grote koppen metaal-op-metaal articulaties, gemonteerd op een titanium steel middels een titanium adapter, werden onderzocht. Het oppervlak van de articulatie en taper werd geanalyseerd voor wear en corrosie.
Resultaten: dertien adapter interfaces (30%) toonden ernstige corrosie, 30 (70%) mild of weinig corrosie. Ernstige corrosie was zichtbaar op de taper en het binnen oppervlak van de adaptoren, een oxide laag besloeg het gehele oppervlak. Er was een significant verschil in metaal ion concentraties tussen de ernstig en lichte taper corrosie groep. Edge wear wordt toegeschreven aan cup malpositie (Lewinnek), dit werd echter niet door onze bevindingen ondersteund. Wij vermoeden dat cup positie slechts een van de factoren is, welke lubricatie van de articulatie beïnvloedt. Twee en zestig procent van de implantaten met ernstige taper corrosie en 40% met milde taper corrosie vertoonden ook edge loading. Serum metaal ion concentraties zijn goede indicatoren voor articulatie wear en taper corrosie, dit in tegenstelling tot de ion concentraties gemeten in weefsels.
Conclusie en aanbevelingen: taper corrosie is gerelateerd aan wear van de articulatie, ten gevolge van verstoorde tribologie. De studie demonstreert een "nieuw" corrosie mechanisme bij de minder conventionele titanium-titanium interface, hetgeen uiteindelijk kan leiden tot overbelasting van de taper en zodoende mogelijk uiteindelijk het breken daarvan. Wear ter plaatse van de articulatie was waarschijnlijk de grootste oorzaak van de pseudotumoren.

ADDENDUM

DANKWOORD



The innovative Bosker TMI system

Promotor prof. dr. S.K. Bulstra,
Beste Sjoerd. Met veel plezier denk ik terug aan onze gesprekken, meestal in de regen, bij het rokershokje voor het UMCG. Onder het genot van een nat geregende sigaret stuurde jij mij feilloos de juiste kant op als het onderzoekstechnisch eens tegen zat. Met veel bewondering heb ik gezien hoe je in het drukke "professor bestaan" altijd de tijd kon vinden om op te leiden en promovendi te begeleiden. Je gevoel voor rechtvaardigheid en menselijkheid hebben voor mij bijgedragen tot een plezierige ervaring in het tot stand komen van dit proefschrift.

Copromotor dr. C.C.P.M. Verheyen,
Beste Cees. Toen ik als arts assistent onderzoeker in 2005 begon, had ik weinig tot geen verstand van wetenschappelijk onderzoek. Door jouw enthousiasme, begeleiding en kritische houding ben ik gegroeid wat uiteindelijk vorm heeft gekregen in dit proefschrift. Ik ben je dankbaar voor al het begrip, geduld en aansturen van het onderzoek, op soms moeilijke momenten. Zonder jou was dit boek niet realiseerbaar. Naast het onderzoek heb je mij opgeleid tot orthopedisch chirurg waar ik goede herinneringen aan heb. Ook onze reizen naar congressen en de avonturen die we daar beleefden, zal ik nooit vergeten. Net als de ritten naar Kampen in Porsche, Aston Martin en Corvette.

Copromotor dr. H.B. Ettema,
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Mijn mede auteurs,
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niet alleen publicaties, maar ook meer inzicht in de metaal-op-metaal geassocieerde problemen. Beste Mario, dank voor het vele reizen tussen het AMC en de Isala Klinieken. Jouw onbetwiste expertise op radiologisch gebied, heeft ons zeer geholpen bij het tot stand komen van onze publicaties en inzichten. Dear Florian, Nicholas and Michael, thank you very much for your important contribution to the analysis of the titanium-titanium taper-taper adapter interface. We enjoyed working together and sharing our different expertises on a challenging but difficult subject.

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Maatschap orthopedie Isala Klinieken te Zwolle,
C. van Egmond, dr. H.B. Ettema, dr. A.J.M. Janus, dr. A.K. Mostert, dr. N.J.A. Tulp, dr. C.C.P.M. Verheyen, dr. R.G. Zuurmond en destijds dr. R.A.A. Bots en dr. J.J. Rondhuis. Beste Cees, Harmen, Guus, Adriaan, Niek, Kees, Rutger, Robert en Jorco. Hartelijk dank voor het mogelijk maken van het onderzoek dat in jullie praktijk heeft plaats gevonden. De problematiek rondom de metaal heupen heeft op een bijzondere manier op ons allen indruk gemaakt. Gedurende mijn opleiding heb ik met een ieder, naast een collegiale, ook een vriendschappelijke band opgebouwd, welke ik zal koesteren.

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Lieve dames, een goed secretariaat is onmisbaar voor elke orthopedische praktijk, maar ook voor goed onderzoek. Jullie inbreng is van groot belang geweest voor het slagen van dit proefschrift. De extra taken die jullie kregen toebedeeld rondom de metaal-heup-problematiek, werden moeiteloos door jullie opgenomen. Naast deze taken, kregen jullie ook te maken met (door de re-call) ongerust geworden patiënten. Het eerste contact met deze patiënten verloopt vaak via jullie en het omgaan met dergelijke situaties verlangt zelfbeheersing en professionaliteit. Ik prijs jullie dan ook om deze eigenschappen.

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Beste Martin, dank voor je adviezen en sturing bij het tot stand komen van dit proefschrift.

Secretariaat orthopedie van het Universitair Medisch Centrum Groningen,
Lieve Els en Yvonne, voor de "hard werkende" jonge orthopeed i.o. promovendus en vader was het in de grote academie een verademing om zo nu en dan door jullie bemoederd te worden.

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Hartelijk dank voor de plezierige samenwerking. Door de re-call was het soms nodig dat jullie trial patiënten zagen. Ik dank jullie voor het begrip en geduld dat soms nodig was. Jullie hebben bijgedragen tot het completeren van de data, zodat statistiek mogelijk was.

Jon Goosen,
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Mijn Broer,
Beste Robbert, als broertje keek ik vroeger altijd met bewondering naar jouw sportieve talenten. Nu bewonder ik je als chirurg. Jouw bescheiden karakter en zorgzaamheid maken je tot de beste broer die men kan hebben.

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Lieve papa en mama, jullie liefdevolle opvoeding heeft mij gemaakt tot wie ik ben. Jullie geloof en vertrouwen in mij (in tegenstelling tot dat van de vele leraren) hebben geleid tot het behalen van het VWO om zodoende uiteindelijk geneeskunde te kunnen gaan studeren. Ik kan jullie niet genoeg bedanken voor de plezierige jeugd en warme herinneringen die altijd bij mij zullen blijven, dank voor alle liefde die ik heb genoten en nog steeds ontvang!

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Mijn liefde voor jou kent geen grenzen. Jij bent mijn steun en toeverlaat! Jij hebt in belangrijke mate bijgedragen tot dit proefschrift, zowel als medeauteur als statisticus. Je bent het beste en het mooiste wat ik heb meegenomen uit mijn studie geneeskunde. Ik ben je oneindig dankbaar voor je liefde en geduld! Maar vooral voor wie je bent en het geluk dat we vinden in onze lieve kinderen Mieke, Hans en Sjoerd.

Always yours!
Bart

CURRICULUM VITAE

Bart Hans Bosker werd in Groningen geboren op 22 juni 1974. Na zijn middelbare schooltijd start hij eerst met de studie rechtsgeleerdheid aan de universiteit van Groningen om later met de studie geneeskunde in 1996 aan te vangen. In 2004 behaalt hij zijn arts examen. Gedurende deze periode leert hij Marloes van Rossum kennen met wie hij trouwt in 2008. Gedurende zijn keuze-coschappen in Zwolle raakt hij geënthousiasmeerd voor de orthopedie. In 2005 begint hij als arts onderzoeker in de Isala Klinieken te Zwolle, onder supervisie van dr C.C.P.M. Verheyen. In 2005 wordt hij aangenomen voor de opleiding tot orthopedisch chirurg, welke aan zal vangen in 2007. In het tussenliggende jaar is hij AGNIO chirurgie in de Isala Klinieken. Na zijn vooropleiding start hij in 2009 met de opleiding tot orthopedisch chirurg onder supervisie van dr C.C.P.M. Verheyen. In 2011 vervult hij een jaar van zijn opleiding in het Universitair Medisch Centrum Groningen onder supervisie van professor dr S.K. Bulstra. Uiteindelijk rondt hij zijn opleiding af in 2013 tot orthopedisch chirurg. Gedurende zijn opleiding werd hij vader van drie kinderen: Mieke, Hans en Sjoerd.
Na een periode te hebben gewerkt in Zwolle als orthopeed, zal hij vanaf januari 2014 beginnen als fellow primaire- en revisie totale heup en knie prothesiologie in de Sint Maartenskliniek te Nijmegen, onder begeleiding van dr G.G. van Hellemond.

The international rank order of publications in major clinical orthopaedic journals from 2000 to 2004

Bart H Bosker
Cees C.P.M. Verheyen

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INTRODUCTION

Publications in peer-reviewed journals are the most important determinant by which research is rated and funding awarded. In this study, the publication rate in orthopaedic surgery of individual countries was scored in selected clinical journals in order to identify those which are making the principal contributions to the development of the orthopaedic discipline. A total of 15 major clinical orthopaedic journals was selected. All articles with abstracts were scored for the country of the corresponding author through a bibliometric search in Medline/PubMed over a period of five years (2000 to 2004). The total number of publications, the number adjusted for size of population and the impact factor of the journal were assessed for each country. A total of 13 311 articles were scored, of which 92% were generated by 15 countries with 47.4% by the United States followed by Japan (8.0%) and the United Kingdom (7.3%). Corrected for population size, eight smaller European countries led this ranking with Sweden, Switzerland and Finland at the top, with the United States in their midst in sixth place. Japan and Finland scored the highest mean impact factor. This observational study demonstrates that the United States is the most productive country in absolute number of publications in the selected clinical orthopaedic journals, and when normalised for population size, the smaller European countries with a high proficiency in English were most successful. Our objective was to identify the countries which generate knowledge and progress in orthopaedic surgery and consider the factors that enabled them to be major contributors.

METHODS

The major clinical orthopaedic journals were selected and ranked by the senior author (CCPMV) from the 'orthopaedics' category of journals established by the Institute for Scientific Information as searched in April 2005.[1] He chose to add the American Journal of Sports Medicine to that list. The 15 journals with the highest impact factor were chosen. The Medline/PubMed Journals Database[2] was searched for these journals, and all articles with an abstract, as indicated in the 'limits' function in PubMed, were selected. The country of the corresponding author was used as the source nation for the article. Countries with fewer than 50 publications during the period tested were excluded. The mean impact factor for the period of review was calculated, as were the totals for each journal and country. For the calculation of publications per million inhabitants, the 2005 national population data were derived from the UN Population Information Network.[3] The domestic expenditure on research as percentage of the gross domestic product was taken as an indicator for the amount of national research funding.

RESULTS

There was a total of 13 311 articles with abstracts in the 15 chosen journals during the period of the review. All the selected journals were in English, 11 from the United States and four from Europe. The figures for the top 15 journals and countries are shown in Table I, in which the ranking order is determined by impact factor for the journals and by the total number of publications for the countries. The 15 countries listed account for 92% of the total number of articles, the first five countries for 71.9% and the United States by itself for 47.4%. The contribution from the United States was the highest in *Orthopedic Clinics of North America* (89.5%) and the American volume of *the Journal of Bone and Joint Surgery* (69.1%). The United Kingdom was responsible for 7.3% of the total scored articles. Its share in the British volume of the *Journal of Bone and Joint Surgery* was 37.7% of the 974 publications. Of these 367 articles, England had the highest share with 324 (88.2%), followed by Scotland with 38 (10.4%), Northern Ireland with four and Wales with one. Sweden scored 23.6% of the papers in the *Acta Orthopedica Scandinavica*, now *Acta Orthopaedica*.

TABLE I Top 15 Countries* Ranked according to Total of Publications in Clinical Orthopedic Journals (2000-2004)

	IF† Mean	Publ Total	US	JP	UK	GE	CA	SE	NL	CH	TR	KO	AU	FR	IT	FI	AT
Spine	2,17	2409	1049	337	124	97	144	58	81	23	57	48	58	52	25	55	15
Am J Sports Med	2,13	713	443	42	17	36	14	24	13	20	-	4	23	4	8	22	3
J Bone Joint Surg Am	2,08	1034	719	42	26	24	55	10	15	21	3	19	9	18	9	8	10
J Bone Joint Surg Br	1,51	928	73	119	321	55	29	31	30	35	10	30	34	29	13	6	27
Arthroscopy	1,49	1012	472	109	40	64	21	13	14	13	31	64	10	16	40	5	20
Eur Spine J	1,24	537	57	21	46	80	32	47	51	42	23	4	9	26	13	12	7
Clin Orthop	1,23	2188	1408	164	51	81	80	28	31	45	14	39	19	34	27	13	33
Knee Surg Sp Tr Arthrosc	1,13	407	42	21	31	65	4	34	13	17	62	5	12	8	30	6	4
Orthop Clin North Am	1,00	257	230	-	1	2	8	1	-	-	-	-	7	-	-	-	-
Acta Orthop Scand	0,99	483	21	38	22	47	4	114	34	11	12	7	7	6	8	24	10
J Arthroplasty	0,97	1019	523	68	127	21	64	30	20	20	2	15	23	11	14	6	13
J Shoulder Elbow Surg	0,95	435	206	43	29	25	14	7	6	18	2	1	21	17	5	6	4
J Orthop Trauma	0,92	541	306	24	23	31	32	6	9	21	14	11	1	3	3	2	2
J Pediatric Orthop	0,70	645	381	19	33	6	34	-	4	3	23	23	19	16	7	7	3
Foot Ankle Int	0,62	651	385	23	31	34	13	4	11	18	28	10	27	1	11	7	5
Total Publications		13259	6315	1070	922	668	548	407	332	307	281	280	279	241	213	179	156
(Ranking)			(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)
Publ/10E6 Inhabitants			21,2	8,4	15,5	8,1	17,0	45,0	20,4	41,3	3,8	5,9	13,8	4,0	3,7	34,1	19,0
(Ranking)			(6)	(16)	(11)	(17)	(9)	(1)	(7)	(2)	(21)	(19)	(13)	(20)	(22)	(3)	(8)

* US: United States, JP: Japan, UK: United Kingdom, GE: Germany, CA: Canada, SE: Sweden, NL: Netherlands, CH: Switserland, TR: Turkey, KO: South Korea, AU: Australia, FR: France, IT: Italy, FI: Finland, AT: Austria.

† Mean Impact Factor over 2000-2004.

Table 1. Top 15 countries ranked according to total of publications in clinical orthopedic journals (2000 to 2004).

TABLE II Ranking Countries according to Publications, Impact Factor and Research Spending

	Publications/ 10E6 (Ranking)		Total Publications (Ranking)		Mean Impact Factor (Ranking)		Research spending (%GDP*) (Ranking)	
Sweden	45,0	(1)	407	(6)	1,36	(17)	4,27	(2)
Switzerland	41,3	(2)	307	(8)	1,35	(18)	2,63	(7)
Finland	34,1	(3)	179	(14)	1,58	(1)	3,40	(3)
Norway	23,6	(4)	109	(20)	1,54	(3)	1,62	(16)
Denmark	21,7	(5)	118	(18)	1,33	(19)	2,19	(11)
United States	21,2	(6)	6315	(1)	1,44	(9)	2,82	(6)
Netherlands	20,4	(7)	332	(7)	1,49	(5)	1,94	(13)
Austria	19,0	(8)	156	(15)	1,39	(13)	1,34	(18)
Canada	17,0	(9)	548	(5)	1,50	(4)	1,85	(15)
Israel	16,8	(10)	113	(19)	1,25	(22)	4,90	(1)
United Kingdom	15,5	(11)	922	(3)	1,41	(11)	1,90	(14)
Ireland	14,5	(12)	60	(23)	1,24	(23)	1,17	(19)
Australia	13,8	(13)	279	(11)	1,42	(10)	1,53	(17)
Greece	9,2	(14)	102	(21)	1,38	(14)	0,67	(22)
Belgium	9,0	(15)	94	(22)	1,33	(20)	1,96	(12)
Japan	8,4	(16)	1070	(2)	1,58	(1)	3,09	(4)
Germany	8,1	(17)	668	(4)	1,40	(12)	2,50	(8)
Taiwan	6,2	(18)	142	(16)	1,46	(7)	2,45	(9)
South Korea	5,9	(19)	280	(10)	1,45	(8)	2,96	(5)
France	4,0	(20)	241	(12)	1,48	(6)	2,20	(10)
Turkey	3,8	(21)	281	(9)	1,31	(21)	0.64	(23)
Italy	3,7	(22)	213	(13)	1,38	(15)	1,07	(20)
Spain	2,9	(23)	125	(17)	1,36	(16)	0,96	(21)

Table II. ranks the publications per million inhabitants and establishes the position of each country. The data for domestic expenditure on research are listed as a percentage of the gross domestic product and are from 2002 or the last available year. [4-6]

DISCUSSION

The United States has traditionally led the rankings in the output of publications in each of the 20 fields of science defined by the Institute for Scientific Information, and consequently also in clinical medicine overall[1]. It is therefore not surprising that the same country also tops the ranking for total publications in major clinical orthopaedic journals. In similar recent studies of high-ranked journals in other medical specialties, their mean percentage was 37 (24 to 48). [7-14] When corrected for the size of population, the smaller western European countries (ranks 1 to 5, 7, 8) outrank the others, with the United States in their midst. The sixth place of the United States with clinical orthopaedic papers is substantially higher than their rank of 13 in the comparable list of publications in clinical medicine (1992 to 2002).[15] Some major western European countries perform rather poorly. France, Italy, Spain and Germany are low in lists normalised for population size in both clinical medicine and orthopaedics, as is Japan. Germany has some fine orthopaedic journals published in the native language such as *Zeitschrift für Orthopädie und ihre Grenzgebiete, Der Unfallchirurg* and *Der Orthopäde* with impact factors of approximately 0.50, but not sufficient to qualify for selection in the present study. We chose 15 major clinical orthopaedic journals since a broader selection would include a larger number of articles which will never be cited and therefore lack scientific impact. Narrowing the selection enhances the scientific quality of the selected papers but this disqualifies mainstream contributions. Many important contributions to orthopaedics are in publications which are not specific to orthopaedics and may be ranked higher than any journal in our list. The number of citations in top journals might be a more sensitive marker of scientific impact than the impact factor and the number of publications. However, it is hard to assess, and there is also a potential selection bias. We, therefore, decided to use the mean impact factor as an autonomous indicator of the prestige of a journal. Its limitations are acknowledged when used to compare large series but it has become an influential tool within the scientific world to evaluate research and award funding.[16]

We originally planned to relate the total of clinical orthopaedic publications to the number of orthopaedic surgeons practising in a country, but it was not possible to construct such a list. It could also be argued that the number of scientists working in musculoskeletal research should also be included.

The editorial process differs in the selected journals. Peer-reviewed journals such as both the American and British volumes of *the Journal of Bone and Joint Surgery* and *Acta Orthopaedica* are treated identically to those such as *Clinical Orthopaedics and Related Research* and *Orthopedic Clinics of North America* which have a relatively large number of invited manuscripts. It may be suggested that our findings are merely a reflection

of the preference of editorial boards to select manuscripts written in proper English. Apart from the evident factor of size of population, national funding capacity and proficiency in English may also be important factors in the ranking.[17]

The gross domestic expenditure on research as a percentage of gross domestic product was used as a determinant for the national funding capacity. Norway, Denmark, The Netherlands and Austria do well in clinical orthopaedic publications corrected for population size with relatively modest research funding, particularly when contrasted with Israel, Japan, Germany, Taiwan, South Korea and France. This finding contradicts the study from Man et al[17], who stated that publication output in major medical journals is linked to research funding at a national level. Their paper also suggested that proficiency in English may be an important determinant for publication in English-language medical journals. It is remarkable that five European countries where English is not the native language outrank all five where it is. The poor proficiency in English of the Mediterranean countries, as well as Japan, may partly explain their lower scores in publications corrected for population size. We are aware of only one other article that focuses on the ranking of countries with respect to publications in orthopaedic literature (1991 to 2001) which, in particular analysed the share of Japan.[18]

The selection of journals and articles was different from ours in that the top seven orthopaedic journals from the Institute for Scientific Information list were picked and it was not limited to articles with an abstract on Medline/PubMed. It therefore included editorials, letters to the editor and case reports. It focused on total production only, not taking population size into account.

The conclusions from our study cannot be strict or definitive. However, it is obvious that, as in all other fields of science, the United States is the most productive country in terms of absolute number of publications (47.4%) in the selected clinical orthopaedic journals. When corrected for population size, the smaller European countries with a high proficiency in the English language were most successful.

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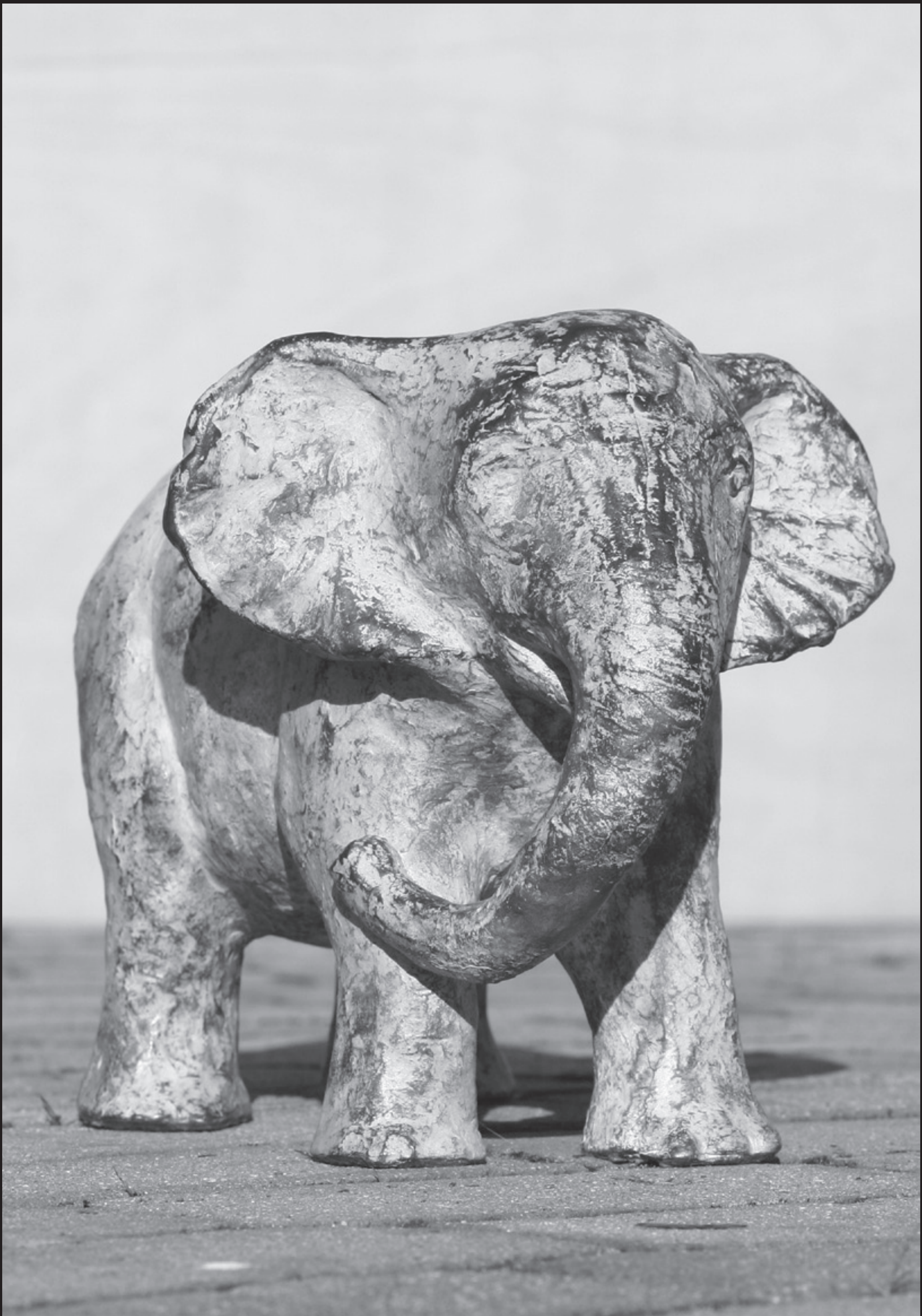

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