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Treatment of Pseudotumors After Metal-on-Metal Hip Resurfacing Based on Magnetic Resonance Imaging, Metal Ion Levels and Symptoms

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ABSTRACT

Peri-prosthetic pseudotumor formation can be a severe complication following Metal-on-Metal hip resurfacing arthroplasty (MoMHRA), with limited data on the optimal management of this complication. The aims of this study were (1) to evaluate the prevalence and severity of pseudotumors in a consecutive cohort of 248 MoMHRA (214 patients, mean follow-up 4.6 years, range: 1 – 8.2), and (2) to present a clinical guideline for their treatment based on severity grading with Metal Artefact Reduction Sequence Magnetic Resonance Imaging, metal ion levels and symptoms. Pseudotumor prevalence was 36.3%: 61 mild, 25 moderate and four were graded severe. Five revisions followed, all in symptomatic patients with elevated metal ion levels. Pseudotumor severity grading allowed us to be conservative with revision surgery for mild and moderate MoM disease.

Recently controversies occur on the benefit of metal on metal arthroplasty (MoM), due to an increasing number of studies on pseudotumors occurrence next to these types of hip replacements [1–3]. Adverse peri-prosthetic soft tissue reactions following MoM hip arthroplasty can include metallosis, Asymptomatic Lymphocyte Vasculitis-Associated Lesions (ALVAL) or pseudotumor formation [4]. Pseudotumors, defined as a solid or fluid mass which has developed in the peri-prosthetic soft tissue [5], are considered a severe complication of these MoM implants, which may cause pain, swelling, deep vein thrombosis and extensive soft tissue damage [6–8]. Interestingly, not all MoM prostheses seem to develop these pseudo tumor sequelae, and a debate exists on the prevalence of these pseudotumors, which ranges from less than 1% to 39% [9,10]. Currently the only treatment option in case of pseudotumors is revision surgery, during which the MoM articulation is replaced by a non-MoM articulation. However, outcome of revision surgery for pseudotumor is poor compared to MoM revision surgery for other reasons [11]. Incomplete pseudotumor resection and recurrence of pseudotumor, both a reason for re-operation, is reported by Liddle et al [12] while de Steiger et al found infection to be a major cause for re-revision surgery in MoM hip arthroplasty [13].

In clinical practice, symptoms (both general health as well as local at the hip region) and metal ion levels are also used next to MARS-MRI pathology about the hip, to guide not only surgical treatment, but also follow up of these patients, despite that controversy exists on the validity of these variables [2,14–16]. Furthermore, only poor consensus exists on detection of these MoM pseudotumors [2,17,18]. The aim of this study was to evaluate the prevalence and severity of pseudotumors in a consecutive cohort of MoM hip resurfacings using MARS-MRI. Secondly, a clinical guideline for the treatment of these MoM pseudotumors will be presented based on pseudotumor severity as graded with MARS-MRI, combined with metal ion levels and symptoms.

Patients and Methods

A consecutive cohort of 258 patients (296 MoM hip resurfacing procedures) who had surgery between September 2004 and November 2011. The MoM prosthesis in all patients was the ReCap resurfacing hip (Biomet, Bridgend, South Wales, UK). Data was prospectively collected as part of an Investigational Device Exemption study for this specific MoM hip resurfacing design (Registration: NCT00603395), before surgery, 6 weeks and one year post-surgery and yearly thereafter. Clinical outcomes and radiographs were collected per protocol from 2004 onwards. The study protocol was extended in 2011 to include baseline cross-sectional imaging (MARS-MRI or ultrasound) and metal-ion blood analysis for each patient

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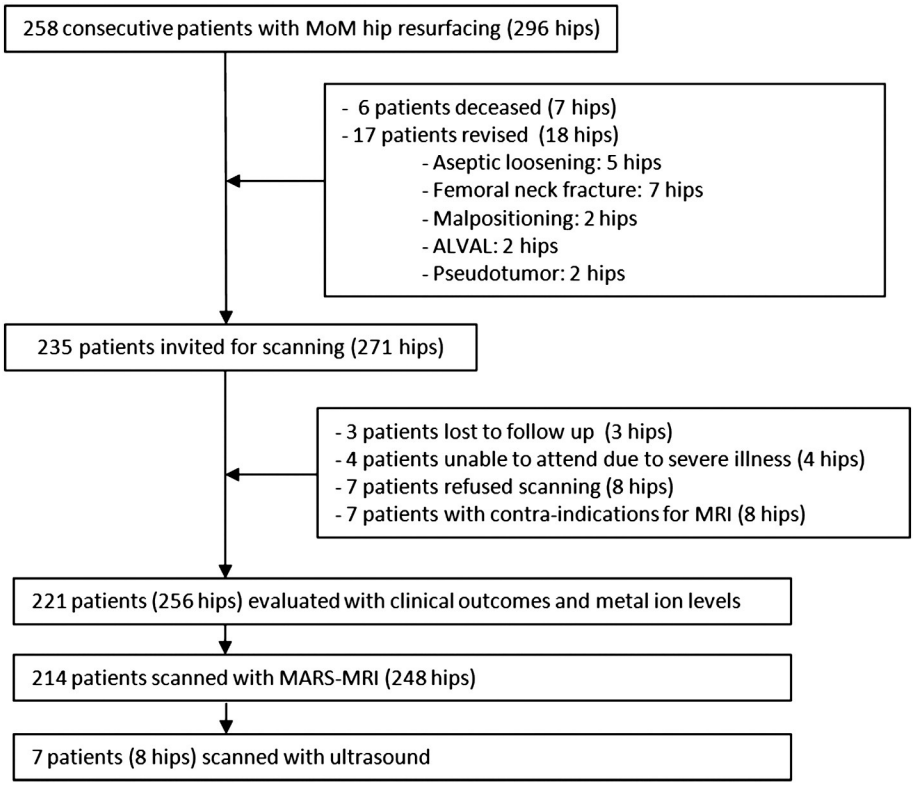

Fig. 1. Study Flow.

scheduled for follow up, as a response to the concerns raised on adverse reactions to metal debris.

Forty-one patients had a bilateral MoM hip implant, two of these had a different design contra lateral hip resurfacing from another hospital, one received a contra lateral MoM Total Hip Arthroplasty (THA) in our hospital. These three MoM hips were excluded from analyses, all other bilateral cases (n = 38) were analysed as separate cases. At the last follow-up in 2012, 17 patients (18 hips) had been revised of which details were published before [19]. After excluding 21 patients (23 hips) for reasons explained in Fig. 1, pseudotumor prevalence using MARS-MRI could be evaluated in 214 patients (248 hips). Mean age of the 235 invited patients was 53.7 years (range, 31–76), mean follow up was 4.6 years (range: 1 – 8.2). In seven patients (8 MoM hips) a contra-indication for MRI was present, these patients were examined using ultrasound examination of the hip area. Ultrasound examinations were performed in supine, prone and left or right side position with different planes (coronal, transversal and saggital) to detect hydrops and/or peri-articular masses and fluid collections; if needed duplex ultrasound was used to differentiate between vascular and non vascular lesions.

Clinical examination was done using the Oxford Hip Score (OHS) [20] and physical examination (i.e. hip Range of motion, groin swelling and palpation tenderness). Patients were also questioned about their general health. Since public awareness existed on possible general symptoms of the MoM, questions on symptoms which could be attributed to the MoM implant, were nevertheless posed: "Did general health changed since their hip surgery" in a dichotomous way. Special notice was given to symptoms derived from the NHS advise on follow-up for MoM patients: chest pain or shortness of breath, numbness or weakness, changes in vision or hearing, fatigue, feeling cold or weight gain [21].

An anterior-posterior radiograph of the pelvis and a lateral hip were made annually. At the latest follow up, particular attention was given to radiolucency, evidence of peri-articular masses and peri-prosthetic bone resorbtion. Radiographs were scored for position of the prosthesis (i.e. inclination of the cup, neck thinning etc). Blood serum samples were collected and assessed on cobalt and chromium concentrations. Samples were collected in metal-free vacutainers; the first 5 mL blood was discarded to eliminate metal contamination from the needle. Tubes were stored at 2-8 °C and sent to an external laboratory (Ziekenhuis Groep Twente, Hengelo, the Netherlands) for analysis. The metal ion levels in serum blood were determined using Atomic Absorption Spectrophotometry (AAS) analysis. The Medicines and Healthcare products Regulatory Agency (MHRA) statutory body that regulates resurfacing devices in the UK advocates 7 parts per billion (ppb) for chromium and cobalt after MoM hip arthroplasty as a

Table 1
MARS-MRI Scan Parameters.

	TE ms)	TR (ms)	TI (ms)	Slice Thickness	FOV (mm)	Matrix	BW (HZ/pixel)	Coil
Coronal PDW	30	3000		2,5	230 × 197	328 × 220	435	sense body 16 ch
Coronal STIR	40	8645	130	2,5	230 × 198	256 × 168	437	sense body 16 ch
Transverse PDW	30	3576		3	240 × 199	344 × 198	437	sense body 16 ch
Transverse	40	105000	130	3	280 × 198	280 × 152	435	sense body 16 ch
Sagittal STIR	40	9570	130	3	230 × 230	256 × 189	438	sense body 16 ch

Table 2
Anderson Classification [Anderson 2011] [13].

Grade	Description	Criteria
A	Normal or acceptable	Normal post-op appearances including seromas and small haematomas
B	Infection	Fluid-filled cavity with high signal T2 wall; inflammatory changes in soft tissues, ± bone marrow oedema
C1	Mild MoM disease	Periprosthetic soft tissue mass with no hyperintense T2W fluid signal or fluid-filled peri-prosthetic cavity; either less than 5 cm maximum diameter
C2	Moderate MoM disease	Peri-prosthetic soft tissue mass/fluid-filled cavity greater than 5 cm diameter or C1 lesion with either of following: (1) muscle atrophy or edema in any muscle other than short external rotator or (2) bone marrow edema: hyperintense on STIR
C3	Severe MoM disease	Any of the following: (1) fluid-filled cavity extending through deep fasci, (2) a tendon avulsion, (3) intermediate T1W soft tissue cortical or marrow signal, (4) fracture

safe upper limit [22]. All MARS-MRI examinations were performed on a 1,5 T MRI (Philips Medical Systems, Best, The Netherlands). Scan parameters are listed in Table 1.

MARS-MRI images were judged by one experienced musculoskeletal radiologist and validated by a second radiologist. If patients had 2 cysts observed on MRI, the maximum diameters of both were added up. In case of disagreement consensus was reached by discussion. Pseudotumour findings were classified according to the grading system described by Anderson (Table 2), which has a good interobserver reliability ($\kappa = 0.78$, 95% confidence intervals: 0.68–0.88) [18]. We defined pseudotumors to be asymptomatic if patients scored no pain on the OHS pain question and if the total OHS score was less than 19 [20]. Our study was approved by the Institutional Review Board (IRB nr. 08.013, 18th December 2008).

Statistical Analysis

Descriptive statistics were used to report patient characteristics, clinical outcomes and radiographic measurements the including number of (asymptomatic) pseudotumors detected with MRI scanning. Serum metal ion data are non-normally distributed, therefore median with interquartile ranges (IQR) were used. Normally distributed data are represented as mean and range. A priori sub analyses were planned on the odds ratios for pseudotumor prevalence based on gender, unilateral or bilateral MoM implants, cup inclination angle (55^0 or higher was considered a cut-off point for too steep), component size (femoral component less than 50 mm was considered small), neck thinning (neck thinning versus no neck thinning), and elevated blood metal ion levels. The Pearson correlation coefficient between cup inclination and both chromium and cobalt serum levels was determined. The significant level α is defined as .05. All statistics were carried out using SPSS19.0 software (SPSS Inc., Chicago, Illinois).

Results

Pseudotumors Identified with MARS-MRI

In 90 hips (85 patients) pseudotumors were detected at MARS-MRI (36.3%, Table 3). The mean follow-up of these patients was 4.8 years (range: 1.0-8.2). No pseudotumors were detected in the seven patients scanned with ultrasound. There were no significant risk groups identifiable (Table 4) and there were 80 pseudotumors visible on MRI in patients with low chromium or cobalt levels (Tables 5 and 6).

Table 3
Pseudotumor Severity Grading.

	C1	C2	C3	Total
Total (n)	61 (23.8%)	25 (9.8%)	4 (1.6%)	90 (35.2%)
Symptomatic (n)	11 (4.3%)	8 (3.2%)	2 (0.8%)	20 (7.8%)
Silent (n)	50 (19.5%)	17 (6.6%)	2 (0.8%)	70 (27.3%)

Table 4
Odds Ratio's for Pseudotumour Prevalence.

	OR (95% CI)	P
Female	0.91(0.5 – 1.64)	0.74
Unilateral MoM	1.25 (0.61-2.55)	0.06
Femoral head < 50 mm	1.3 (0.78-2.2)	0.30
Cup inclination angle of < 550	0.94 (0.53-1.66)	0.83
General symptoms present	0.71 (0.35-1.45)	0.35
Femoral neck thinning	1 (0.6-1.67)	0.10

Fluid Collections Not Graded as MoM Disease

There were 41 cases of fluid-filled cysts observed on MR images which were graded normal (Anderson grade 'A'). The mean size of these cysts was 26 mm (range: 8–62).

Metal Ion Levels

Median chromium and cobalt values were 1.82 ppb (IQR: 1.1-3.2) and 1.47 ppb (IQR: 1.1-2.40), but increased per pseudotumor severity group (Table 7). Eight patients had chromium and cobalt levels > 7 ppb, another five patients had chromium values of > 7 ppb but cobalt values of < 7 ppb. No patients with cobalt values of > 7 ppb had Chromium values < 7 ppb. Bilateral patients had median chromium and cobalt levels of respectively 2.92 ppb (IQR: 1.82-4.46) and 2.35 ppb (IQR: 1.65-3.49) compared to 1.51 ppb (IQR: 0.98-2.19) and 1.29 ppb (IQR: 0.94-1.71) for unilateral patients. The Pearson correlation between acetabular cup inclination angle and chromium blood-levels was 0.22 ($p < 0.001$). See Fig. 2A. The Pearson correlation between acetabular cup inclination angle and cobalt blood-levels was 0.19 ($p = 0.002$). See Fig. 2B

Symptoms

Pain in or around the hip area (as a domain of the Oxford Hip score), was reported in 23.6% (n = 60) of all 256 cases, ranging from slight (n = 32, 12.6%), mild (n = 16, 6.3%), moderate (n = 9, 3.5%) or marked (n = 3 hips, 1.2%). A wide variety of general symptoms were reported by 44 of all 221 patients (19.9%) and ranged from poor vision, general fatigue, hypertension and other cardiovascular diseases to skin disease, strength loss, weight loss and stomach aches. General health symptoms as specified in the NHS advice on MoM implants are given in Table 8. Eleven patients reported other cardiovascular symptoms than chest pain, such as hypertension or coronary bypass surgery. Another six patients reported tinnitus.

Plain Radiographs

In none of the 221 patients, plain radiographs were indicative for MoM disease. The contrast between plain radiographs and MARS MRI is seen in Fig. 3A and B.

Table 5
2 × 2 Table for Chromium Level and Pseudotumor Occurrence.

	No pseudotumor	Pseudotumor
Chromium <7 ppb	161	80
Chromium >7 ppb	4	11

Table 6
2 × 2 Table for Cobalt Level and Pseudotumor Occurrence.

	No pseudotumor	Pseudotumor
Cobalt <7 ppb	163	84
Cobalt >7 ppb	2	7

Revision Case Description

Severe MoM Disease

Of the four patients with a C3 pseudotumor, two were revised and one is scheduled for revision surgery. Besides a C3 pseudotumor these patients presented with either symptoms and/or metal ion levels > 7 ppb. In both revision cases a large, fluid filled cyst was excised, which was thick-walled in one patient. Post operative histopathology confirmed metallosis for each revised pseudotumor. In both cases an uncemented THA with a ceramic-on-polyethylene bearing was inserted. Metal ion levels dropped significantly 6 weeks after revision surgery (a 20-fold decrease in one patient and a 10-fold decrease in the other patient).

One patient who was without general or hip symptoms and had metal ion levels < 7 ppb, was treated conservatively. This patient was hesitant to undergo revision surgery and pseudotumor evaluation, including MRI and metal ion levels, is scheduled after six months.

Moderate MoM Disease

One patient was revised for a C2 pseudotumor with mild hip pain but no general symptoms, during which a fluid-filled cyst was excised. ALVAL was confirmed with post-operative histopathology. For one other patient with a C2 pseudotumor, mild hip pain but no general symptoms, revision surgery is scheduled. Repeated MR scanning and metal ion sampling with an interval of six months was scheduled for all non-revised patients with a C2 pseudotumor.

Mild MoM Disease

We revised no patients for a C1 pseudotumor, and no revisions are pending for this reason. One patient with elevated metal ion levels (13.7 and 8.88 respectively) had no pain the first five post-operative years, but developed increasing pain around the hip during the last two years, which is now moderate. The observed pseudotumor had a maximum 49 mm diameter (>50 mm will classify as a C2 pseudotumor). Repeated MR scanning and metal ion sampling was scheduled for all patients with a C1 pseudotumor with a time interval of one year.

Total MoM Disease in our Cohort

Before this study, two patients were revised for persistent pain who post-operatively had histopathological evidence of ALVAL to metal debris and two patients were revised for pseudotumor diagnosed with MARS-MRI following our pilot study. Combined with the 90 pseudotumors detected with MR scanning, this results in 94 cases of MoM disease (36.7%) in our total cohort of 256 hips (excluding deceased, lost to follow up and unwilling patients). Until now, 7 hips were revised and 2 revisions are pending Mom disease (3.5%).

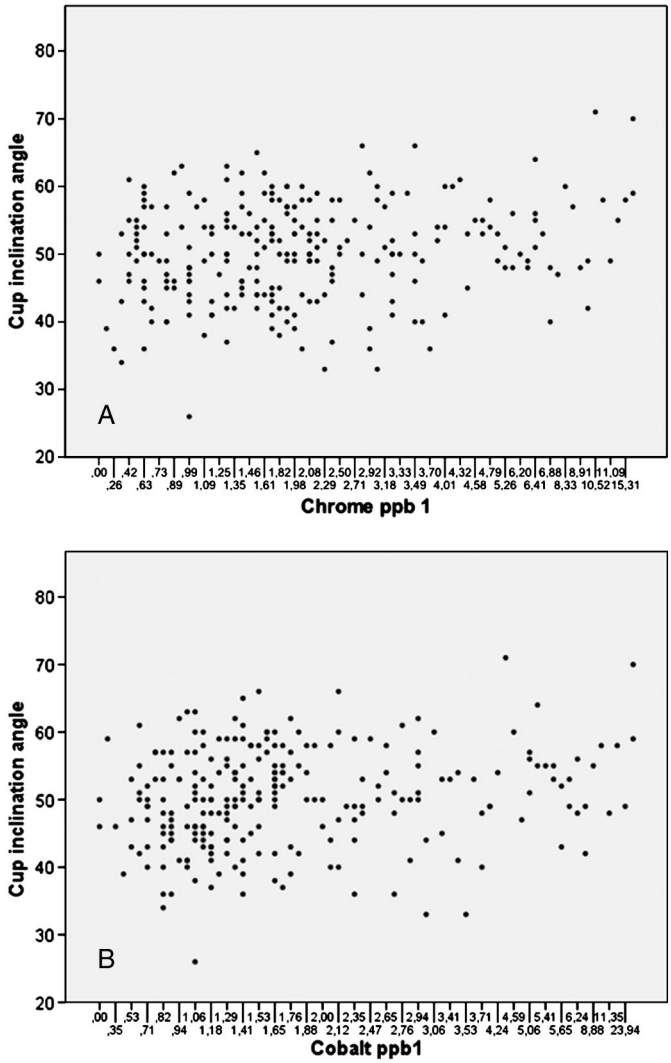

Fig. 2. A.Chromium levels versus cup inclination. B. Cobalt levels versus cup inclinication.

Follow-up of Patients without a Pseudotumor on MR Scanning

Patients without a pseudotumor seen with MR scanning are followed up yearly with a clinical examination and metal ion levels.

Discussion

MRI screening a complete cohort of MoM hip arthroplasty patients, we found a high prevalence of pseudotumors, the majority (70/90) asymptomatic. Other authors have confirmed the high prevalence (up

Table 7
Details per Pseudotumor Severity.

Anderson Score	Male/Female (n)	Bilateral (%)	FU (YR) Mean (Range)	Acetabular Inclination(°) Mean (Range)	Neck Thinning (%) Mean (Range)	Silent (%)	Chromium ppb Median (IQR)	Cobalt ppb Median (IQR)
A	113/43	22.7	5.1 (1.0-8.2)	50 (27–71)	2.1 (0–18.5)	n/a	1.82 (1.0-2.89)	1.41 (1.1-2.05)
C1	44/14	15.5	4.6 (1.1-8.2)	50 (38–66)	1.74 (0–8.7)	82	1.72 (1.25-3.15)	1.29 (1.03-2.09)
C2	17/6	21.7	4.6 (2.1-7.7)	57 (55–60)	2.1 (0–9.5)	68	3.18 (1.25-5.56)	2.47 (1.24-4.97)
C3	2/2	25	5.5 (3.3-7.7)	55 (46–70)	2.6 (0–9)	50	6.41 (2.42-42.35)	5.06 (1.86-60.56)

Table 8
Reporting of General Health Symptoms According to NHS Advice on MoM Implants.

Symptoms	N (%)
Chest pain/shortness of breath	4 (1.5%)
Numbness/weakness	5 (2.0%)
Change in vision/hearing	3 (1.2%)
Fatigue	8 (3.1%)
Feeling cold	0 (0%)
Weight gain	0 (0%)

to 30%) of asymptomatic pseudotumors in MoM patients, although screening for pseudotumors is generally advised if symptoms are present food and drug administration or if the serum metal ions levels are above a certain threshold (UK) [22,23]. Based on our results and from previous reports, we believe that commonly used follow up methods (clinical examination and plain radiographs) will give a gross underestimation of (asymptomatic) pseudotumors in MoM hip arthroplasty. This conventional approach might result in late surgery for pseudotumor, increasing the risk of poor outcome of revision surgery. The early and low-threshold use of cross-sectional imaging might prevent this. In the discussion about the clinical value of both symptomatic and asymptomatic pseudotumors the true incidences

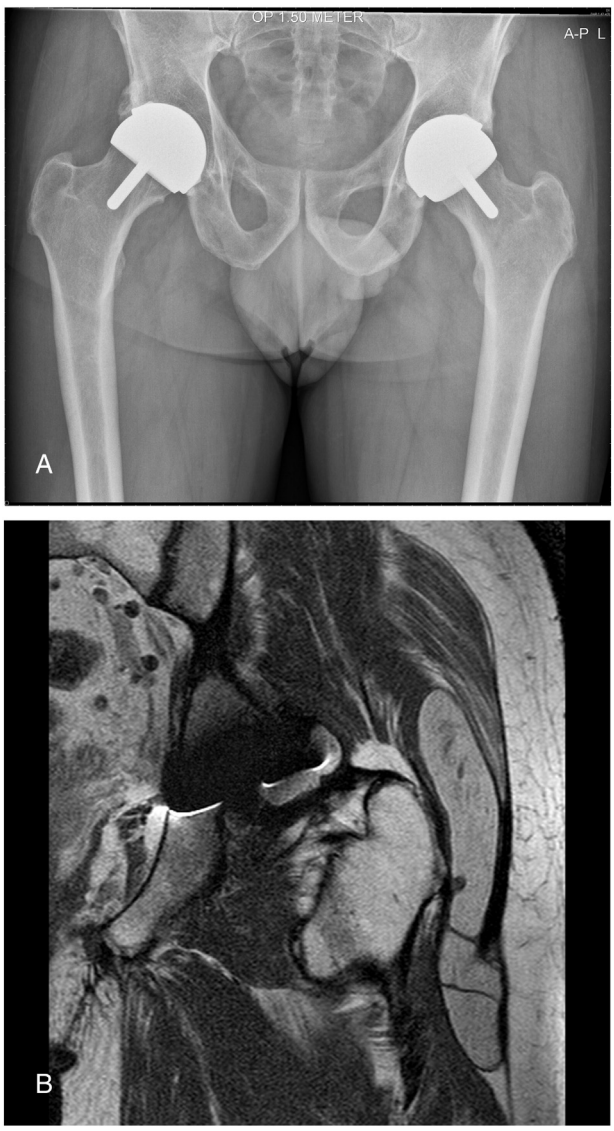

Fig. 3. A. Plain radiograph in patient with C3 pseudotumor. B. PDW MARS-MRI in same patient.

are important facts to know. Furthermore, only 13 patients (5.9%) had metal ion levels > 7 ppb, the latter also a threshold to initiate MRI screening. This confirms that ion levels do not correlate with visualized adverse local tissue reaction, either noted at the time of revision or on MRI. As for the usefulness of metal ions levels to detect pseudotumors, MacNair found a pseudotumor prevalence of 24% in patients with normal metal ion levels [16] and Matthies found that patients revised with pseudotumors had similar whole-blood metal ion levels to those who were not revised [24]. These findings, together with the findings of our study, underline the importance of cross-sectional imaging in MoM patients. The high prevalence of up to 30% or more of asymptomatic pseudotumors in MoM hip arthroplasty, does raise ethical concerns both for the patients as well as for society [25,26]. However, there is little knowledge about the clinical relevance of these silent pseudotumors and the natural course of pseudotumors. Further, there is no validated follow-up for detected pseudotumors. We propose a conservative approach for mild to moderate pseudotumors (Anderson grade C1 and C2) which are asymptomatic and have normal metal ion levels. Since there is no clear consensus on the optimal treatment of pseudotumors, and revision surgery of these pseudotumors result in poor outcome [11–13], future studies with multiple follow-up time points including cross-sectional imaging are needed to validate the optimal management of pseudotumors. Until the optimal management of conservatively treated pseudotumors is established, we suggest that cross-sectional imaging is repeated every six months until lesion stability is confirmed. This will provide new insight in the yet unknown natural history of conservatively treated pseudotumors, while at the same time minimizing the burden for both patients and for society (economic costs). The management of pseudotumors after MoM hip resurfacing is hindered at this moment since only a few, unvalidated, qualitative grading systems exist [2,17,18]. Although the interrater reliability of the Anderson grading system is good ($\kappa = 0.78$, 95% confidence intervals: 0.68–0.88) [18], the clinical validation of this grading system is still limited. This is also the case for other published pseudotumor grading systems [2,17]. The importance of a validated management of pseudotumors is stressed even more since it is estimated that more than a million large diameter MoM implants were inserted worldwide [27]. Using a validated quantitative pseudotumor grading system would also prevent an overly aggressive surgical treatment of pseudotumors. We advocate an approach of conservative policy with intensified follow up if a moderate to mild (Anderson class C1 or C2) pseudotumor at MRI is present with low metal ion levels (< 7 ppb) and no symptoms. We based revision surgery of pseudotumors primarily on pseudotumor appearance on MRI (Anderson grade C3), and secondly on metal ion levels (> 7 ppb) and symptoms.

Limitations

Since our study is cross-sectional in design, no conclusions on the development of pseudotumors throughout follow-up can be made. The natural course of adverse reactions to metal debris is unclear, but based on two studies Fary et al suggested the likelihood of progression [15]. Sequential MR scanning will be needed to evaluate any change in pseudotumor size, shape and location.

Despite the problems with these MoM implants some authors still claim they are useful in the correct setting and if the implant is correct [10]. But, this approach is only possible when all risk factors for pseudotumor formation are well understood. We found an increased risk (however not significant) in men, for smaller components and for unilateral MoM hip resurfacing. In previous studies, female patients and age <40 years were found as risk factors for pseudotumors [20].

A second limitation is, that a small number of patients did not have MR scanning due to contra-indications or unwillingness to participate. However, the complete follow up of MARS-MRI, metal ion levels and hip and general symptoms of the remaining, consecutive

series of this large cohort with a single hip resurfacing design has not been presented before. One has to keep in mind that the amount of wear depends on details of each specific resurfacing design such as acetabular arc of cover and clearance, thereby limiting the ability to extrapolate our results to other resurfacing designs [28,29].

In conclusion, although prevalence of pseudotumors in a single design MoM hip resurfacing is high, the majority of these patients having subclinical appearance of the pseudotumors, and chromium and cobalt levels < 7 ppb. In contrast to guidelines from national orthopedic boards, we believe that clinical examination and plain radiographs only have a limited role in the detection of pseudotumors. On the other hand, only a small number of pseudotumors is graded severe on MRI. For now, this allows us to be conservative in the management of detected pseudotumors. Data on the future development of mild to moderate pseudotumors is however lacking and there is a clear need for studies presenting multiple follow up points with cross-sectional imaging of these type of pseudotumors.

References

1. Canadian Hip Resurfacing Study Group. A survey on the prevalence of pseudotumors with metal-on-metal hip resurfacing in Canadian academic centers. J Bone Joint Surg Am 2011;93-A(Suppl 2):118.
2. Hart AJ, Satchithananda K, Liddle AD, et al. Pseudotumors in association with well-functioning metal-on-metal hip prostheses: a case–control study using three-dimensional computed tomography and magnetic resonance imaging. J Bone Joint Surg Am 2012;94-A:317.
3. Wynn-Jones H, Macnair R, Wimhurst J, et al. Silent soft tissue pathology is common with a modern metal-on-metal hip arthroplasty. Acta Orthop 2011;82:301.
4. Langton DJ, Jameson SS, Joyce TJ, et al. Early failure of metal-on-metal bearings in hip resurfacing and large-diameter total hip replacement: A consequence of excess wear. J Bone Joint Surg Br 2010;92-B:38.
5. Pandit H, Vlychou M, Whitwell D, et al. Necrotic granulomatous pseudotumours in bilateral resurfacing hip arthoplasties: evidence for a type IV immune response. Virchows Arch 2008;453:529.
6. Memon AR, Galbraith JG, Harty JA, et al. Inflammatory pseudotumor causing deep vein thrombosis after metal-on-metal hip resurfacing arthroplasty. J Arthroplasty 2013;28(1):197.e9, http://dx.doi.org/10.1016/j.arth.2012.02.014 [Epub 2012 Apr 11].
7. Shahrdar C. Pseudotumor in large-diameter metal-on-metal total hip articulation. J Arthroplasty 2011;26(4):665.e21.
8. Watters TS, Eward WC, Hallows RK, et al. Pseudotumor with superimposed periprosthetic infection following metal-on-metal total hip arthroplasty: a case report. J Bone Joint Surg Am 2010;92(7):1666.
9. Bosker BH, Ettema HB, Boomsma MF, et al. High incidence of pseudotumour formation after large-diameter metal-on-metal total hip replacement: a prospective cohort study. J Bone Joint Surg Br 2012;94-B:755.
10. Murray DW, Grammatopoulos G, Gundle R, et al. Hip resurfacing and pseudotumour. Hip Int 2011;21:279.
11. Grammatopolous G, Pandit H, Kwon YM, et al. Hip resurfacings revised for inflammatory pseudotumour have a poor outcome. J Bone Joint Surg Br 2009;91:1019.
12. Liddle AD, Satchithananda K, Henckel J, et al. Revision of metal-on-metal hip arthroplasty in a tertiary center. Acta Orthop 2013;84(3):237.
13. de Steiger RN, Miller LN, Prosser GH, et al. Poor outcome of revised resurfacing hip arthroplasty. Acta Orthop 2010;81:72.
14. Van Der Straeten C, Grammatopoulos G, Gill HS, et al. The 2012 Otto Aufranc Award: The Interpretation of Metal ion Levels in Unilateral and Bilateral Hip Resurfacing. Clin Orthop Relat Res 2013;471:377.
15. Fary C, Thomas GE, Taylor A, et al. Diagnosing and investigating adverse reactions in metal on metal hip implants. BMJ 2011;343:d7441.
16. Macnair RD, Wynn-Jones H, Wimhurst JA, et al. Metal ion levels not sufficient as a screening measure for adverse reactions in metal-on-metal hip arthroplasties. J Arthroplasty 2013;28:78.
17. Hauptfleisch J, Pandit H, Grammatopoulos G, et al. A MRI classification of periprosthetic soft tissue masses (pseudotumours) associated with metal-on-metal resurfacing hip arthroplasty. Skeletal Radiol 2012;41:149.
18. Anderson H, Toms AP, Cahir JG, et al. Grading the severity of soft tissue changes associated with metal-on-metal hip replacements: reliability of an MR grading system. Skeletal Radiol 2011;40:303.
19. van der Weegen W, Hoekstra HJ, Sijbesma T, et al. Hip resurfacing in a district general hospital: 6-year clinical results using the ReCap hip resurfacing system. BMC Musculoskelet Disord 2012;13:247.
20. Kalairajah Y, Azurza K, Hulme C, et al. Health outcome measures in the evaluation of total hip arthroplasties–a comparison between the Harris hip score and the Oxford hip score. Arthroplasty 2005;20:1037.
21. Ref: http://www.nhs.uk/Conditions/Hip-replacement/Pages/Metal-on-metalimplants.aspx. Accessed 2012 Nov 18.
22. No authors listed. Medicines and Healthcare products Regulatory Agency: medical device alert: all metal-on-metal (MoM) hip replacements, 2012 (MDA/2012/036) http://www.mhra.gov.uk/home/groups/dts-bs/documents/medicaldevicealert/con155767.pdf. Accessed 2012 Dec 13.
23. FDA Safety Communication: Metal-on-Metal Hip Implants. Date Issued: Jan. 17, 2013. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm335775.htm . Accessed 2013 Jan 22.
24. Matthies AK, Skinner JA, Osmani H, et al. Pseudotumors are common in well-positioned low-wearing metal-on-metal hips. Clin Orthop Relat Res 2012;470(7):1895.
25. Kwon YM, Ostlere SJ, McLardy-Smith P, et al. "Asymptomatic" pseudotumors after metal-on-metal hip resurfacing arthroplasty: prevalence and metal ion study. J Arthroplasty 2011;26(4):511.
26. Williams DH, Greidanus NV, Masri BA, et al. Prevalence of pseudotumor in asymptomatic patients after metal-on-metal hip arthroplasty. J Bone Joint Surg Am 2011;93-A:2164.
27. Cohen D. How safe are metal-on-metal hip implants? BMJ 2012;28:344.
28. Langton DJ, Joyce TJ, Jameson SS, et al. Adverse reaction to metal debris following hip resurfacing: the influence of component type, orientation and volumetric wear. J Bone Joint Surg Br 2011;93(2):164.
29. Prosser GH, Yates PJ, Wood DJ, et al. Outcome of primary resurfacing hip replacement: evaluation of risk factors for early revision. Acta Orthop 2010;81(1):66.