The Journal of Arthroplasty 31 (2016) 146–151

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

How Should We Follow-Up Asymptomatic Metal-on-Metal Hip Resurfacing Patients? A Prospective Longitudinal Cohort Study

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ARTICLE INFO

Article history:
Received 25 May 2015
Accepted 11 August 2015

Keywords:
asymptomatic
blood metal ions
follow-up
hip resurfacing
metal-on-metal
ultrasound

ABSTRACT

Current surveillance for metal-on-metal hip resurfacing (MoMHR) patients is not evidence based. This study established changes that occurred in 152 asymptomatic MoMHRs using repeat ultrasound and patient-reported outcomes. Factors associated with (1) ultrasound progression and (2) developing new pseudotumors were analyzed. Patients underwent repeat assessments 4.3 years later. Ultrasound progression was observed in 19% (n = 29), with 10% (n = 15) developing new pseudotumors. Key predictors of ultrasound progression included high blood cobalt ($P = .00013$) and chromium ($P = .00065$), and high initial ultrasound grade ($P = .003$) and volume ($P = .036$). No asymptomatic MoMHRs with initially normal metal ions (<2 μg/L) and normal ultrasounds (33% of cohort) developed new pseudotumors. This patient subgroup does not require repeat follow-up within 5 years.

Numerous metal-on-metal (MoM) hip arthroplasty designs have experienced high failure rates due to pseudotumors [1,2]. Patients developing these problems often require revision surgery. As lesions can be destructive with significant bone and muscle damage, outcomes after revision can be poor [3,4]. To identify patients with pseudotumors early, regulatory authorities have published guidance regarding the regular follow-up of MoM hip patients [5–7].

Presently, there is no consensus on how to follow up asymptomatic MoM hip resurfacing (MoMHR) patients, with this patient subgroup being the most difficult to manage clinically [8,9]. European guidance recommends annual follow-up with radiographs and blood metal ions in these patients. However, the US Food and Drug Administration guidance recommends annual clinical review, whereas the Medical and Healthcare Products Regulatory Agency in the United Kingdom recommend reviewing asymptomatic MoMHR patients according to local protocol. Recent work has demonstrated that worldwide MoM hip follow-up guidance is neither evidence based nor financially sustainable, with most protocols lacking the sensitivity to detect asymptomatic pseudotumors [10].

Most MoMHR patients remain asymptomatic and do not develop pseudotumors [11,12]. However, a small but significant number of asymptomatic patients do develop pseudotumors [8,9,13], and it is important to identify these individuals early in order to prevent bone and soft tissue damage. At present, there is no clear guidance as to which parameters should be used to distinguish asymptomatic MoMHR patients who can be safely discharged and need not be subjected to repeated investigations from those asymptomatic MoMHR patients who need monitoring. Decisions regarding which asymptomatic MoMHR patients require monitoring, at what intervals, and how frequently such follow-up should be repeated require well-designed prospective longitudinal cohort studies. At present, very few such studies exist involving MoMHR patients, with most reporting on serial magnetic resonance imaging (MRI) at short-term follow-up in small cohorts [14,15]. Ultrasound is another commonly used and recommended modality for cross-sectional imaging in MoM hip patients [5,16]. It has many advantages over MRI: it is cheaper, faster to perform, and not affected by metal artifact. Furthermore, ultrasound is sensitive when screening for pseudotumors [16] with results comparable to MRI [17], and recent work suggests that ultrasound has a role in the surveillance of asymptomatic pseudotumors [18].

This article reports on a prospective cohort of 152 asymptomatic MoMHRs who were comprehensively assessed between 2007 and 2008 [8]. Ultrasound and patient-reported outcomes were repeated at a mean of 4.3 years since initial assessment and at a mean of 8.2 years since primary MoMHR. The present study aimed to assess factors associated with (1) ultrasound finding progression and (2) developing new pseudotumors. This information will assist in risk stratifying patients,

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to http://dx.doi.org/10.1016/j.arth.2015.08.007.

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http://dx.doi.org/10.1016/j.arth.2015.08.007

thereby allowing recommendations to be devised for the follow-up of asymptomatic MoMHR patients.

Patients and Methods

Between 2007 and 2008, we performed an ethically approved prospective cohort study involving 201 asymptomatic MoMHRs in 158 patients (mean age, 56.0 years; 61% male) [8]. This study was designed to determine the prevalence of pseudotumors in asymptomatic patients after MoMHR, given little was known about this clinical entity at the time. Therefore, asymptomatic MoMHR patients participating in this initial study were assessed at variable time points from their index arthroplasty, although all patients were assessed at a minimum of 3 years from MoMHR. In 2007/2008, all patients completed an Oxford Hip Score (OHS) and the University of California, Los Angeles (UCLA) activity score questionnaire. Patients were also investigated using hip radiographs, blood metal ions, and hip ultrasound. Details about this initial patient cohort and the investigations performed have been described previously [8]. In 2012/2013, these patients underwent repeat hip ultrasound examination and completed a further OHS and UCLA score questionnaire. The OHS was scored from 0 (worst outcome) to 48 points (best outcome) [19], and the UCLA activity scores were from 1 (wholly inactive) to 10 (regular participation in impact sports) [20].

Repeat investigations were performed in 152 of the asymptomatic MoMHRs (122 patients) at a mean of 4.3 years (range, 3.2-5.0 years) from the initial assessment (Table 1). The mean duration from MoMHR implantation to final follow-up was 8.2 years (range, 6.2-12.4 years). Forty-nine MoMHRs in 36 patients from the initial cohort were not recruited to the present study for the following reasons: death (4 hips in 3 patients), revision to a total hip arthroplasty (16 hips in 13 patients), declined to participate, or did not attend scheduled ultrasound appointments (29 hips in 20 patients). The demographics for these 49 MoMHRs as well as the results of their initial assessment are summarized (Table 2).

Mean time from initial assessment to revision for the 16 revised MoMHRs was 2.5 years (range, 0.4-4.4 years), and the mean time from primary MoMHR to revision was 6.6 years (range, 3.1-9.4 years).

Table 1
Summary of the Study Cohort.

	152 Hips in 122 Patients
Gender, male/female	99 (65%)/53 (35%)
Age at first ultrasound (y), mean (range)	60.7 (33.3 to 74.7)
Patients with unilateral or bilateral MoM hips, unilateral/bilateral	92 (75%)/30 (25%)
Hip resurfacing design	
Birmingham Hip Resurfacing (Smith & Nephew, Warwick, UK)	82 (54%)
Conserve Plus (Wright Medical, Memphis, TN)	64 (42%)
Recap (Biomet, Bridgend, UK)	6 (4%)
Time between hip resurfacing and first ultrasound (y), mean (range)	3.9 (3.0 to 7.4)
Time interval between repeat ultrasounds (y), mean (range)	4.3 (3.2 to 5.0)
Acetabular component position	
Inclination (°), mean (range)	46.2 (21.3 to 65.5)
Anteversion (°), mean (range)	15.9 (2.0 to 33.0)
Blood metal ion concentration (μg/L), median (IQR)	
Cobalt	2.3 (1.5 to 4.2)
Chromium	2.4 (1.3 to 4.9)
OHS (0-48 scale)	
Median (IQR)	
- 2007/2008 score	47.0 (45.0 to 48.0)
- 2012/2013 score	46.0 (42.8 to 48.0)
Mean (range)	
- Change in score	−0.9 (−17 to 7)
UCLA score (1-10 scale), mean (range)	
- 2007/2008 score	7.2 (3 to 10)
- 2012/2013 score	7.2 (2 to 10)
- Change in score	0.1 (−4 to 5)
Hips with pseudotumors revised after repeat ultrasound	4 (3%)

The indications for the 16 MoMHR revisions were symptomatic pseudotumor (n = 14), dislocation (n = 1), and femoral component loosening (n = 1). All hips were revised to a non-MoM bearing. The 14 revisions for symptomatic pseudotumor all had blood metal ions above 2 μg/L and abnormal ultrasound imaging when assessed in the initial study (Table 2). The mean pseudotumor volume on initial ultrasound was 48.5 cm^3 (6.8-135.2 cm^3), with 50% (n = 7) cystic in nature, 36% (n = 5) mixed, and 14% (n = 2) solid lesions. All pseudotumors were confirmed both intraoperatively and on histopathologic examination. At latest follow-up, the mean postrevision OHS was 31.4 (range, 11-48). Fifteen revised MoMHRs remain in situ, with 1 pseudotumor patient subsequently undergoing re-revision for recurrent dislocation within 8 months of the revision procedure.

The same experienced musculoskeletal radiologist performed all ultrasound examinations in the initial study and the 2012 study. Ultrasound imaging (Sonoline Antares; Siemens Medical Solutions, Malvern, PA) was performed following verbal patient consent using a standard technique, which encompasses a systematic approach to assess the anterior, medial, lateral, and posterior hip regions. This examination technique is recommended by the European Society of Skeletal Radiology and is widely used for examining the hip joint [21], and allows for the assessment of a range of pathologies associated with hip arthroplasty [22].

The radiologist graded all scans and measured volumes of any lesions present. In each instance, the radiologist was blinded to all clinical information. Each ultrasound scan was assigned to one of four grades: (1) normal, (2) bursa (psoas bursa, trochanteric bursa/thickening), (3) pathological effusion, and (4) pseudotumor. A small amount of intra-articular fluid was considered normal, but when the depth of fluid exceeded 15 mm at the anterior joint line, this was classified as a pathological effusion. Simple fluid collections in the anatomical psoas or trochanteric bursa were classified as such, but complex bursal collections with evidence of communication with the hip joint were classified as pseudotumors. A pseudotumor was defined as a cystic, solid, or mixed mass with evidence of communication with, but extending beyond the confines of, the anatomical hip joint. When lesions were present, the volume (product of the maximum recorded dimension in each of three orthogonal planes in centimeters), consistency (solid, cystic, or mixed), and location were recorded for each lesion.

Outcomes of interest were (1) the proportion of MoMHRs with progression of ultrasound findings between repeat scans and (2) the proportion of MoMHRs developing new pseudotumors between repeat ultrasounds. Hips were considered to have progression of ultrasound findings between repeat scans if at least one of the following criteria were present: (1) an increase in ultrasound scan grade, (2) an increase in lesion volume but no change in ultrasound grade, (3) change in pseudotumor consistency from liquid to solid, and/or (4) need for revision surgery. Progression of pseudotumors to a solid consistency has been associated with adverse outcomes [3,23]; therefore, this change was deemed to be clinically significant. All MoMHRs not meeting these criteria after repeat ultrasound examination were considered to have no evidence of progression.

Statistical analysis

All statistical analyses were performed using the R library [24]. Either the median and interquartile range (IQR) or the mean and range were used depending on data distribution. For paired analyses, change in volume between ultrasound scans was assessed using a paired *t* test, and change in grade between scans was assessed using a Wilcoxon signed rank test. To assess factors associated with progression of ultrasound findings and the development of new pseudotumors, statistical tests were chosen to reflect the exposure variable and data distribution. These included unpaired *t* tests (age, acetabular inclination and anteversion, time from primary MoMHR to first scan, time between repeat scans, change in OHS, UCLA score, initial lesion volume), the

Table 2
Summary of 2007-2008 Data for 49 MoMHRs in 36 Patients That Were Excluded From the 2012 Study.

	Revised Before 2012 (n = 16)	Died (n = 4)	Declined to Participate (n = 29)
Gender, male/female	2 (12%)/14 (88%)	4 (100%)/0 (0%)	20 (69%)/9 (31%)
Age at 2007/2008 ultrasound (y), mean (range)	59.2 (39.2-73.1)	66.4 (61.6-70.2)	60.6 (40.8-73.8)
Patients with unilateral or bilateral MoM hips, unilateral/bilateral	10 (77%)/3 (23%)	2 (67%)/1 (33%)	11 (55%)/9 (45%)
Hip resurfacing design			
BHR	10 (63%)	1 (25%)	18 (62%)
Conserve	4 (25%)	3 (75%)	11 (38%)
Recap	2 (12%)	0 (%)	0 (0%)
Time between hip resurfacing and 2007/2008 ultrasound (y), mean (range)	4.1 (3.0-5.8)	3.9 (3.4-5.2)	4.7 (3.0 to 7.1)
Acetabular component position			
Inclination (°), mean (range)	47.0 (34.7-55.3)	39.4 (37.9-40.8)	45.5 (30.1-64.0)
Anteversion (°), mean (range)	16.5 (5.1-34.3)	16.2 (14.9-17.5)	13.9 (7.2-20.8)
Blood metal ion concentration (μg/L), median (IQR)			
Co	6.3 (4.7-13.3)[a]	0.9 (0.9-1.0)	1.6 (1.3-2.7)
Cr	7.1 (3.8-19.6)[a]	1.3 (1.1-1.5)	1.5 (1.2-2.4)
Ultrasound grade 2007/2008			
1	2 (13%)	2 (50%)	26 (90%)
2	0 (0%)	2 (50%)	3 (10%)
3	1 (6%)	0 (0%)	0 (0%)
4	13 (81%)	0 (0%)	0 (0%)
OHS (0-48 scale), 2007/2008, median (IQR)	41.0 (35.0-46.5)	48.0 (48.0-48.0)	47.0 (44.0-48.0)
UCLA score (1-10 scale), 2007/2008, mean (range)	5.6 (3-8)	8.5 (7-10)	7.3 (1-10)

BHR, Birmingham Hip Resurfacing; Co, cobalt; Cr = chromium.
[a] For the 14 hip revisions performed for symptomatic pseudotumor, blood metal ion concentrations in 2007/2008 were as follows: median (IQR): cobalt = 10.7 μg/L (5.9-14.3 μg/L) and chromium = 11.6 μg/L (6.3-24.4 μg/L), and mean (range): cobalt = 14.5 μg/L (2.9-64.1 μg/L) and chromium = 15.8 μg/L (2.1-45.2 μg/L).

Wilcoxon rank sum test (OHS, blood cobalt and chromium concentrations), and χ^2 test with Yates correction (gender, MoMHR design, bilateral MoMHRs, grade of first ultrasound scan). The level of significance was set at $P < .05$. Diagnostic test characteristics with respective 95% confidence intervals were calculated for various clinical scenarios relating to the results of the initial investigations (ie, normal initial ultrasound with low blood metal ions, normal initial ultrasound alone, and low blood metal ions alone).

Results

Change in Grade and Volume Between Repeat Ultrasound Scans

Changes in grade that occurred between repeat ultrasound scans are summarized (Table 3). An increase in grade between scans was seen in 17% (n = 25) of hips, 80% (n = 122) had no grade change, and 3% (n = 5) had a decrease in grade. There was a significant increase in ultrasound grade between repeat scans ($P = .00018$). The mean change in lesion volume between scans for all 152 MoMHRs was an increase of 5.9 cm^3 by the second scan (range, −21.8 to 392 cm^3), which was significant ($P = .0058$). For each initial ultrasound scan grade, the risk of any progression in findings and the risk of developing new pseudotumors 3.2 to 5.0 years later were as follows, respectively: grade 1, 12% (13/110) and 4% (4/110); grade 2, 39% (9/23) and 35% (8/23); grade 3, 43% (3/7) and 43% (3/7); and grade 4, 33% (4/12) and not applicable.

Progression of Ultrasound Findings

Evidence of any progression in findings between repeat scans occurred in 19% (n = 29) of hips. Of those with progression, 25 hips had grade increases, with the other 4 hips having an increase in lesion volume (increase of between 19 and 286 cm^3) with no grade increase. One of these 29 hips also experienced pseudotumor progression from liquid to solid. Four of these 29 hips have been revised to date. The remaining 81% (n = 123) of MoMHRs in this cohort had no evidence of progression between repeat ultrasounds. Five factors were significantly associated with progression of ultrasound findings between repeat scans (Table 4): high blood cobalt concentration ($P = .00013$), high blood chromium concentration ($P = .00065$), decrease in OHS, ($P = .043$), high initial ultrasound scan volume ($P = .036$), and high initial ultrasound scan grade ($P = .003$).

Table 3
Change in Ultrasound Grade Between Scans in 152 MoMHRs.

Ultrasound Grade 2007/2008	Total number of hips (%)	Ultrasound Grade 2012/2013			
		1	2	3	4
Total number hips (%)	152 (100)	102 (67)	17 (11)	6 (4)	27 (18)
1	110 (72)	97 (64)	6 (4)	3 (2)	4 (3)
2	23 (15)	3 (2)	11 (7)	1 (1)	8 (5)
3	7 (5)	2 (1)	0 (0)	2 (1)	3 (2)
4	12 (8)	0 (0)	0 (0)	0 (0)	12 (8)

Development of New Pseudotumors

New pseudotumors developed in 10% (n = 15) of the cohort (Table 3). The median volume of these new lesions was 18.0 cm^3 (IQR, 6.8-35.6 cm^3). Median (IQR) cobalt and chromium concentrations for this subgroup were 3.8 μg/L (2.6 μg/L to 9.8 μg/L) and 3.9 μg/L (2.4-8.2 μg/L), respectively. The mean (range) acetabular component inclination and anteversion for MoMHRs developing new pseudotumors were 44.7° (range, 27.8°-57.0°) and 15.0° (range, 2.7°-30.3°), respectively.

Analysis demonstrated that high blood cobalt concentration ($P = .006$) and high blood chromium concentration ($P = .023$) were significantly associated with developing new pseudotumors. All other factors analyzed in Table 4 were found to be nonsignificant (P values ranging from .074 to .955) for developing new pseudotumors.

The results of the initial assessment (2007/2008) in hips with a pseudotumor on ultrasound in 2012 (n = 27) were compared with the results in hips revised for symptomatic pseudotumor (n = 14). Hips revised for pseudotumor had significantly higher blood cobalt ($P = .02$) and chromium ($P = .02$) concentrations, and significantly lower OHS ($P = .007$) and UCLA ($P = .003$) scores.

Diagnostic Test Characteristics for Clinical Scenarios

In light of the factors significantly associated with progression of ultrasound findings between repeat scans and those factors associated with developing new pseudotumors, three clinical scenarios were formulated and the diagnostic test characteristics for these scenarios were assessed. The optimal diagnostic test characteristics for identifying both MoMHRs with no evidence of progression of ultrasound findings

Table 4
Factors Associated With Progression of Ultrasound Findings Between Repeat Imaging.

Factor	Hips With Progression (n = 29)	Hips Without Progression (n = 123)	*P*
Gender			
Female	12 (41%)	41 (33%)	.548
Male	17 (59%)	82 (67%)	
Age at first ultrasound (y), mean (range)	62.2 (52.7-74.7)	60.3 (33.3-73.1)	.237
Unilateral or bilateral MoM hips			
Bilateral	11 (38%)	49 (40%)	1.00
Unilateral	18 (62%)	74 (60%)	
Hip resurfacing design			
BHR	14 (48%)	68 (55%)	.756
Conserve	14 (48%)	50 (41%)	
Recap	1 (4%)	5 (4%)	
Time between hip resurfacing and first ultrasound (y), mean (range)	3.9 (3.0-7.4)	3.9 (3.0-7.0)	.947
Time interval between repeat ultrasounds (y), mean (range)	4.2 (3.2-5.0)	4.4 (3.2-5.0)	.080
Acetabular inclination (°), mean (range)	47.2 (27.8-62.6)	46.0 (21.3-65.5)	.501
Acetabular anteversion (°), mean (range)	14.8 (2.7-32.0)	15.3 (2.0-33.0)	.783
Blood cobalt concentration (μg/L), median (IQR)	3.8 (2.6-6.3)	2.0 (1.3-3.6)	.00013[a]
Blood chromium concentration (μg/L), median (IQR)	4.1 (2.5-7.5)	2.0 (1.2-3.9)	.00065[a]
Initial OHS (0-48 scale), median (IQR)	47.0 (45.0-48.0)	47.0 (45.0-48.0)	.775
Change in OHS, mean (range)	−3.6 (−10 to 5)	−0.3 (−2 to 7)	.043[a]
Initial UCLA score (1-10 scale), mean (range)	6.9 (4-9)	7.3 (3-10)	.208
Change in UCLA score, mean (range)	−0.1 (−3 to 4)	0.1 (−4 to 5)	.534
Initial scan volume (cm^3), mean (range)	5.9 (0-60.0)	1.4 (0-100.0)	.036[a]
Initial scan grade			
1	13 (45%)	97 (79%)	.003[a]
2	9 (31%)	14 (11%)	
3	3 (10%)	4 (3%)	
4	4 (14%)	8 (7%)	

[a] Statistically significant ($P < .05$).

(Table 5), and MoMHRs not developing new pseudotumors (Table 6) were obtained for asymptomatic MoMHRs with low initial blood cobalt and chromium levels (<2 μg/L) and normal initial ultrasound scans (grade 1) (n = 50; 33% of current cohort). The diagnostic test characteristics for having no evidence of progression of ultrasound findings on repeat examination for this subgroup were as follows: sensitivity, 40%; specificity, 97%; positive predictive value (PPV), 98%; negative predictive value (NPV), 27%; positive likelihood ratio (LR+), 11.6; and negative likelihood ratio (LR−), 0.6. The diagnostic test characteristics for not developing new pseudotumors in this subgroup were as follows: sensitivity, 37%; specificity, 100%; PPV, 100%; NPV, 15%; LR+, infinity; and LR− 0.6.

Discussion

Although the management of asymptomatic MoMHR patients has proved to be difficult, little evidence is available regarding the serial cross-sectional imaging changes that occur in relation to these implants [14,15,18]. Previous studies performing serial imaging in MoMHR patients have involved small cohorts (4-53 hips) with short-term follow-up between repeat imaging (mean of 0.7-2.2 years), and also have not uniformly included asymptomatic patients only [14,15,18].

The present study represents the largest cohort of MoMHR patients (n = 152) investigated with repeat ultrasound within 5 years of initial assessment. Although there were significant increases in ultrasound grade and volume between repeat scans, it was observed that asymptomatic MoMHR patients with normal initial blood metal ion levels (<2 μg/L) and normal ultrasound imaging had very little risk of progression of ultrasound findings, and no risk of developing new pseudotumors within 5 years of initial assessment. These findings are of clinical importance to guide the follow-up of asymptomatic MoMHR patients, given that current protocols are not evidence based, with most lacking the sensitivity to detect asymptomatic pseudotumors [10].

Serial ultrasound imaging was effective for identifying the development and progression of abnormalities around MoMHRs, including pseudotumors. This suggests that ultrasound is a useful clinical tool for the surveillance of MoMHR patients, and supports the findings of a smaller longitudinal study which observed ultrasound was effective in the short-term for monitoring the natural history of asymptomatic pseudotumors around MoM hips [18]. In the present study, the risk of any progression in ultrasound findings (33%-43%) and the risk of developing new pseudotumors (35%-43%) in MoMHRs with an abnormal initial ultrasound (grades 2, 3, or 4) were higher than those in hips with normal (grade 1) initial scans (12% risk of progression

Table 5
Diagnostic Test Characteristics for Asymptomatic MoMHRs Having no Evidence of Progression of Ultrasound Findings on Repeat Examination for 3 Different Clinical Scenarios.

	Normal Initial Ultrasound and Initial Blood Metal Ions <2 μg/L	Normal Initial Ultrasound Alone	Initial Blood Metal Ions <2 μg/L Alone
No. of hips (% of cohort)	50 (33)	110 (72)	62 (41)
Sensitivity	40 (31-49)	79 (70-85)	48 (39-57)
Specificity	97 (80-100)	55 (36-73)	90 (72-97)
PPV	98 (88-100)	88 (80-93)	95 (85-99)
NPV	27 (19-37)	38 (24-54)	29 (20-40)
LR+	11.6 (1.6-80.2)	1.8 (1.2-2.7)	4.6 (1.6-13.8)
LR−	0.6 (0.5-0.7)	0.4 (0.3-0.6)	0.6 (0.5-0.7)

All diagnostic test characteristic values are provided as percentages with 95% confidence intervals provided in brackets.

Table 6
Diagnostic Test Characteristics for Asymptomatic MoMHRs Not Developing New Pseudotumors for 3 Different Clinical Scenarios.

	Normal Initial Ultrasound and Initial Blood Metal Ions <2 μg/L	Normal Initial Ultrasound Alone	Initial Blood Metal Ions <2 μg/L Alone
No. of hips (% of cohort)	50 (33)	110 (72)	62 (41)
Sensitivity	37 (29-45)	77 (69-84)	44 (35-52)
Specificity	100 (75-100)	73 (45-91)	87 (58-98)
PPV	100 (91-100)	96 (90-99)	97 (88-99)
NPV	15 (9-23)	26 (14-42)	14 (8-24)
LR+	Infinity (N/A)	2.9 (1.2-6.7)	3.3 (0.9-12.1)
LR−	0.6 (0.6-0.7)	0.3 (0.2-0.4)	0.6 (0.5-0.8)

All diagnostic test characteristic values are provided as percentages with 95% confidence intervals provided in brackets.

and 4% risk of new pseudotumors). It is therefore recommended that asymptomatic MoMHR patients with abnormal initial ultrasounds remain under surveillance. Although worldwide authorities provide guidance on how to follow up asymptomatic MoMHR patients [5–7], our data suggest that this subgroup requires review within 5 years of initial assessment. However, the exact timing of this review will depend on a number of factors including the nature of the imaging abnormality, blood metal ion levels, and implant track record [25].

Factors associated with any progression in findings between repeat ultrasound scans were related to blood metal ions (high initial cobalt and chromium concentrations) and the initial ultrasound (high initial scan grade and volume). Only high initial blood cobalt and chromium concentrations were associated with developing new pseudotumors. Although factors such as female gender, acetabular component malposition, and HR design have been observed to be risk factors for pseudotumor formation in previous studies [26–29], they were not associated with ultrasound progression or new pseudotumor development in this longitudinal cohort.

The 10% of MoMHRs developing new pseudotumors all had initial blood cobalt and/or chromium concentrations greater than 2 μg/L, as did all 14 hips revised for symptomatic pseudotumors prior to the repeat assessment. This ion threshold has previously been considered the acceptable upper limit of a well-functioning MoMHR [6,30]. However, these new pseudotumors developed from all possible types of initial ultrasound scan, that is, those that were normal (grade 1), had bursal pathology (grade 2), and had pathological effusions (grade 3). This suggests that all asymptomatic MoMHR patients, including those with normal initial ultrasound scans, have a theoretical risk of developing new pseudotumors when blood metal ion concentrations are greater than 2 μg/L. It is recommended that these patients remain under clinical surveillance.

The optimal diagnostic test characteristics for identifying both MoMHRs with no evidence of progression of ultrasound findings and those not developing new pseudotumors were obtained for asymptomatic MoMHRs with low initial blood cobalt and chromium levels (<2 μg/L) and normal initial ultrasound scans (grade 1; 33% of the current cohort). This subgroup of patients had very little risk of progression of ultrasound findings and no risk of developing new pseudotumors within 5 years of initial assessment.

Determining the optimal diagnostic test characteristics for a screening test depends on numerous factors, which includes the condition being screened for [31]. The short-term outcomes after revision for pseudotumors have largely been poor [32], which has led regulatory authorities to issue follow-up guidance to detect problems early [5–7]. In our cohort, asymptomatic MoMHRs with low initial blood cobalt and chromium levels (<2 μg/L) and normal initial ultrasound scans had almost perfect specificities and PPVs for identifying MoMHRs with no evidence of progression (Table 5), and 100% specificity and PPV for identifying hips not developing new pseudotumors within 5 years (Table 6). Furthermore, the LR+ values were high (11.6 for no ultrasound progression and infinity for not developing new pseudotumors), with a LR+ of greater than 10 considered a large and conclusive increase in the likelihood of disease [33]. We therefore recommend that asymptomatic MoMHR patients with both low initial blood metal ion levels (<2 μg/L) and normal ultrasound scans can be safely removed from regular clinical follow-up for the first 5 years from initial assessment. Using ultrasound alone or blood metal ions alone did not provide as good diagnostic test characteristics compared to when these investigations were combined (Tables 5 and 6). Therefore, our data provides further evidence that a comprehensive baseline assessment in all asymptomatic MoMHR patients using blood metal ions and cross-sectional imaging is important.

The financial implications of releasing asymptomatic MoMHR patients with normal blood metal ion levels (<2 μg/L) and normal ultrasound imaging from regular follow-up are significant. A recent financial analysis of MoM hip follow-up using various worldwide protocols [10] estimated that follow-up costs for all asymptomatic MoMHR patients recorded in the UK National Joint Registry (29 795 hips) was £8 283 010 ($13 735 495) per year when using current European guidance [6]. In the present study, 33% of asymptomatic MoMHR patients were in the subgroup which could be released from regular follow-up for the first 5 years from initial assessment. Therefore, the potential cost savings made by not reviewing this subgroup of patients for the next 5 years is more than £13 600 000 ($22 551 520). These are huge savings, and given that the cost of a MoM hip revision for pseudotumor has been estimated at £10 000 ($16 582) per case in the UK, this would cover 1360 revision procedures.

A more conservative estimate of cost savings for asymptomatic MoMHR follow-up can be obtained by assuming a worse-case scenario. If all 49 MoMHRs in 36 patients from the initial cohort not recruited to the present study were assumed to not satisfy our new recommendations for release from follow-up for 5 years (ie, assume all 49 hips had blood metal ions of ≥2 μg/L and/or abnormal initial ultrasound imaging), then 25% (50/201) of asymptomatic MoMHRs would still be eligible for release from follow-up rather than 33% (50/152). The potential cost savings made by not reviewing this smaller subgroup of patients for the next 5 years still remains significant (> £10 300 000, or $17 079 460).

This study has certain limitations. It is suspected that our findings are not applicable to large-diameter MoM total hip arthroplasties or MoMHR designs other than those studied here, especially the Articular Surface Replacement (De Puy, Leeds, United Kingdom), which was recalled in 2010 due to its high failure rate [34]. Serial ultrasound was repeated within 5 years of initial assessment, and therefore, our findings only apply to patients undergoing repeat cross-sectional imaging within this period. Further studies are needed to assess the natural history of asymptomatic MoMHRs at extended follow-up. An experienced musculoskeletal radiologist performed and assessed all ultrasound scans. Given that ultrasound is operator dependent, it is possible that less experienced radiologists would not obtain the same results. It is suspected that MRI could be used in centers without adequate experience to perform and interpret ultrasound imaging around MoMHRs. Finally, the definition for pseudotumor has evolved since it was first described in 2008 [35]. In this study, a strict definition was used, and abnormalities were only classified as pseudotumors if there was communication with the hip joint. We have also clearly documented other pathology such as bursal lesions or pathology confined to the joint, with this approach recommend by other authors [22]. Broader definitions for pseudotumors and/or classification of extra-articular lesions as pseudotumors have been used previously [36,37]; therefore, this must be considered when interpreting our results.

Conclusions

It is proposed that all asymptomatic MoMHR patients undergo a comprehensive baseline assessment, which includes blood metal ions and cross-sectional imaging. Asymptomatic MoMHR patients with normal blood metal ion levels (<2 μg/L) and normal ultrasound imaging (33% of the current cohort) have very little risk of progression of ultrasound findings (2%) and no risk of developing new pseudotumors (0%) within 5 years of initial assessment. We therefore recommend that this patient subgroup does not require repeat follow-up within 5 years of initial assessment. This will result in considerable financial savings and allow follow-up resources to be concentrated toward those MoM hip patients requiring further review, investigation, and/or revision surgery. Annual follow-up for all asymptomatic MoMHR patients currently recommended by European guidance [6] is costly and unnecessary. Longitudinal studies beyond 5 years of initial assessment are required to guide the most appropriate follow-up regimen for asymptomatic MoMHR patients in the long term.

Acknowledgments

The authors would like to thank The Royal College of Surgeons of England and The Arthritis Research Trust, who have provided one of the authors with funding in the form of a surgical research fellowship.

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