The Journal of Arthroplasty 33 (2018) 2906–2911

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Primary Arthroplasty

Indications for MARS-MRI in Patients Treated With Articular Surface Replacement XL Total Hip Arthroplasty

James W. Connelly, BA [a], Vincent P. Galea, BA [a], Inari Laaksonen, MD, PhD [a, b], Sean J. Matuszak, BA [a], Rami Madanat, MD, PhD [a, b, c], Orhun Muratoglu, PhD [a, b], Henrik Malchau, MD, PhD [a, b, *]

[a] Harris Orthopaedic Laboratory, Department of Orthopaedic Surgery, Massachusetts General Hospital, Boston, Massachusetts
[b] Department of Orthopaedic Surgery, Harvard Medical School, Boston, Massachusetts
[c] Department of Orthopaedics and Traumatology, Helsinki University Hospital, Helsinki, Finland

ARTICLE INFO

Article history:
Received 17 January 2018
Received in revised form
9 April 2018
Accepted 9 April 2018
Available online 19 April 2018

Keywords:
metal-on-metal
adverse local tissue reaction
MARS-MRI
Articular Surface Replacement XL
total hip arthroplasty

ABSTRACT

Background: The purpose of this study was to identify which patient and clinical factors are predictive of adverse local tissue reaction (ALTR) and to use these factors to create a highly sensitive algorithm for indicating metal artifact reduction sequence magnetic resonance imaging (MARS-MRI) in Articular Surface Replacement (ASR) XL total hip arthroplasty patients. Our secondary aim was to compare our algorithm to existing national guidelines on when to take MARS-MRI in metal-on-metal total hip arthroplasty patients.

Methods: The study consisted of 137 patients treated with unilateral ASR XL implants from a prospective, multicenter study. Patients underwent MARS-MRI regardless of clinical presentation at a mean of 6.2 (range, 3.3-10.4) years from surgery. Univariate and multivariate analyses were conducted to determine which variables were predictive of ALTR. Predictors were used to create an algorithm to indicate MARS-MRI. Finally, we compared our algorithm's ability to detect ALTR to existing guidelines.

Results: We found a visual analog scale pain score ≥ 2 (odds ratio [OR] = 2.53; $P = .023$), high blood cobalt (OR = 1.05; $P = .023$), and male gender (OR = 2.37; $P = .034$) to be significant predictors of ALTR presence in our cohort. The resultant algorithm achieved 86.4% sensitivity and 60.2% specificity in detecting ALTR within our cohort. Our algorithm had the highest area under the curve and was the only guideline that was significantly predictive of ALTR ($P = .014$).

Conclusion: Our algorithm including patient-reported pain and sex-specific cutoffs for blood cobalt levels could predict ALTR and indicate MARS-MRI in our cohort of ASR XL metal-on-metal patients with high sensitivity.

Level of Evidence: Level II, diagnostic study.

Metal-on-metal (MoM) hip implants have seen a significant decline in their utilization because of reports of metal bearing–related complications and high failure rates [1]. Although there is a strong consensus that there is no role for large-headed MoM total hip arthroplasty (THA) in the future, there is an urgent need for establishing an accurate and reliable protocol for the follow-up of the more than 1 million MoM THAs that were implanted and are still in situ [2]. Adverse local tissue reaction (ALTR) is a common cause of implant failure leading to revision in MoM implants [3]. Identification of ALTR is a crucial aspect in establishing a protocol for the follow-up of patients treated with MoM THA.

ALTR has a severity spectrum ranging from mild aseptic lymphocyte-dominated vasculitis-associated lesions to inflammatory lesions with periprosthetic tissue masses (pseudotumors) and necrosis [4]. Previous literature has demonstrated that ALTR rates in MoM THA may be as high as 69% [5]. In addition, ALTR rates have been shown to be similar between symptomatic and asymptomatic patients [5–8], which makes diagnosing ALTR more difficult and

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 https://doi.org/10.1016/j.arth.2018.04.021.

This study was supported by the Harris Orthopaedic Laboratory, Massachusetts General Hospital, Boston, Massachusetts and DePuy Orthopaedics, Warsaw, Indiana.

* Reprint requests: Henrik Malchau, MD, PhD, Orthopedic Department, Massachusetts General Hospital, 55 Fruit Street, GRJ 1126, Boston, MA 02114-2696.

https://doi.org/10.1016/j.arth.2018.04.021
0883-5403/

confounds follow-up protocols for MoM THA patients. Metal artifact reduction sequence magnetic resonance imaging (MARS-MRI) is the gold standard for diagnosing ALTR [3,9]. Currently, there are no universally accepted guidelines on when a patient with an MoM implant should undergo a MARS-MRI. The availability of MARS-MRI is often limited and, from a cost perspective, conducting MARS-MRI on all patients with MoM implants is not feasible.

Our primary objective was to determine which patient demographic and clinical factors are predictive of ALTR in a cohort of patients treated with MoM THA and use these prognostic variables to create an effective algorithm to prescreen patients for MARS-MRI. Our secondary aim was to compare our algorithm to existing national guidelines on when to take MARS-MRI in other MoM THA patients.

Methods

Patients

The study cohort consisted of 137 patients treated with Articular Surface Replacement (ASR) XL THA (DePuy Orthopaedics, Warsaw, IN) from a larger, prospective, multicenter study. Patients were enrolled in the study after the recall of the ASR Hip System by the manufacturer in 2010 with the aim of creating clinical follow-up guidelines. Sixteen centers enrolled a total of 1721 patients (1950 hips) to be followed annually for 6 years. The protocol for the study has been detailed in previous publications [10–12]. The current cohort consists of patients from the 3 sites that performed MARS-MRI on all patients regardless of clinical presentation. Bilateral patients and patients with ASR hip resurfacing arthroplasty were excluded for the present analysis. Patient-reported outcome measures (PROMs), whole blood metal ion levels for cobalt (Co) and chromium (Cr), anteroposterior and lateral plain radiographs, and MARS-MRI were collected at a postoperative office visit. MARS-MRIs were obtained at a mean of 6.2 (range, 3.4-10.4) years from index surgery. All information was collected within 6 months of the clinical visit. Patient demographics and clinical data are summarized in Table 1. Informed consent was obtained from all patients, and the study was approved by the institutional review board.

Table 1
Summary of Patient Demographics, Clinical, Blood Metal Ion, and Radiographic Analysis Data.

Parameter	Value
N	137
Male:female	72:65
Age at surgery (y)[a]	62 ± 11
Time to MARS-MRI (y)[a]	6.2 ± 1.6
Blood cobalt (ppb)[b]	3.1 (1.4-8.1)
Blood chromium (ppb)[b]	1.7 (0.9-3.7)
Serum Co/Cr ratio[b]	1.6 (1.2-2.4)
HHS[b]	89 (80-96)
VAS pain[b]	1.0 (0.5-2.0)
VAS satisfaction[b]	1.5 (0.5-3.0)
EQ-5D weighted index[b]	0.80 (0.69-1.00)
Any acetabular radiolucency[c]	32.8
Any femoral radiolucency[c]	31.1
Any acetabular osteolysis[c]	5.2
Any femoral osteolysis[c]	11.8

Co, cobalt; Cr, chromium; EQ-5D, EuroQol-5D; HHS, Harris Hip Score; MARS-MRI, metal artifact reduction sequence magnetic resonance imaging; N, number of hips; VAS, visual analog scale.
[a] Descriptive statistic is given as mean and standard deviation.
[b] Descriptive statistic is given as median and interquartile range.
[c] Descriptive statistic is given as percentage.

Radiological Assessment

MARS-MRI assessment was performed by one of the authors with 4 years of experience reviewing MARS-MRI, who was trained and validated by a musculoskeletal radiologist with more than 10 years of experience reviewing MARS-MRI. The MARS-MRI reviewer was blinded to previous clinical results. Anderson classification, which has the highest intraobserver and interobserver reliability of the currently used systems, was used [13,14]. Based on this classification, a mild ALTR (C1) is defined as a periprosthetic soft tissue mass with no hyperintense T2W fluid signal or a fluid-filled periprosthetic cavity less than 5 cm in maximal diameter. A moderate ALTR (C2) is a periprosthetic soft tissue mass or fluid-filled cavity greater than 5 cm in diameter. C1 lesions with either (1) muscle atrophy or edema in any muscle other than short external rotators or (2) bone marrow edema hyperintense on short tau inversion recovery sequences are also considered moderate ALTR (C2). Severe ALTRs (C3) displayed any of the following features: fluid-filled cavities extending through deep fascia, a tendon avulsion, intermediate T1W soft tissue cortical or marrow signal, or fracture [14].

The plain anteroposterior radiographs were assessed for bony changes at the acetabulum-implant interface using mDesk software (RSA Biomedical, Umeå, Sweden) by 5 trained and validated orthopedic surgeons with at least 5 years clinical experience. The Charnley/DeLee zones [15] were used to define lesion location. Radiolucency was defined as a lesion with a clear sclerotic border less than 2 mm from the implant surface. Any lesion with a border greater than 2 mm from the surface was categorized as osteolysis. Inter-reader reliability was strong (Kappa coefficients >0.9).

Statistical Analysis

The primary outcome was ALTR presence. Anderson classifications of C2 and C3 severity were considered ALTR positive, and C1 and nonexistent ALTR were considered ALTR negative. Univariate tests were conducted to determine associations between ALTR presence and all relevant demographic and clinical variables including radiolucency, osteolysis, sex, age at surgery, MARS-MRI time from surgery, femoral head size, blood metal ion levels, Co/Cr ratio, and all PROM measures. For these tests, age, blood metal ion levels, MARS-MRI time from surgery, Harris Hip Score, and EuroQol-5D index were defined as continuous variables. Sex, femoral head size ($\geq$52 mm and <52 mm for men and $\geq$48 mm and <48 mm for women), clinically relevant visual analog scale (VAS) pain scores ($\geq$2 and <2), VAS satisfaction ratings ($\geq$2 and <2), and ALTR presence were categorized as binary groups. The Mann-Whitney *U* test was used for continuous, non-normally distributed variables. A Student's *t* test was used for continuous, normally distributed variables. Chi-squared analysis was used for categorical variables.

Based on our univariate results, multivariate logistic regression analysis was performed taking into consideration age, blood Co levels, MARS-MRI time from surgery, sex, femoral head size, and clinically significant VAS pain while using ALTR presence as the dependent variable. Blood Co levels, Cr levels, and Co/Cr ratio were considered in separate binary logistic regressions to avoid collinearity in predictor variables. Variables that proved significant in the multivariate model were included in the algorithm. A P value < .05 was considered significant.

Clinically useful cutoff values of all predictive variables were determined for each sex using receiver-operating characteristic (ROC) analysis with ALTR presence as the outcome variable. We used continuous versions of predictive variables in ROC analysis to determine the most sensitive and specific cutoff values possible for our algorithm. The Youden index, which maximizes the balance of

Table 2
Summary of Existing National Guidelines for When to Take MARS-MRI in MoM THA Patients.

Guideline	Co (ppb)	Cr (ppb)	Symptoms
National MoM THA 1 [18]	>7	>7	Any pain
National MoM THA 2 [17]	≥5	≥5	Any pain

If any condition in the guideline is fulfilled, then MARS-MRI is indicated.
Co, cobalt; Cr, chromium; MoM, metal-on-metal; MARS-MRI, metal artifact reduction sequence magnetic resonance imaging; THA, total hip arthroplasty.

sensitivity and specificity, was used to determine cutoff values [16]. We then crafted decision trees for predicting ALTR in ASR XL patients using all possible configurations of our ROC-generated cutoff values. We considered the decision tree algorithm that achieved the highest sensitivity in predicting ALTR in our ASR XL patients for subsequent analyses.

ROC analysis with ALTR presence as the outcome variable was performed using our novel algorithm as well as 2 existing national guidelines for when MARS-MRI should be taken in MoM THA patients (Table 2) [17,18]. One national guideline had separate guidelines for the ASR Hip System and for other large-head MoM THA systems [17]. For this guideline, only the large-head MoM THA version was used for ROC analysis, because the ASR-specific guideline recommended MARS-MRI in all cases. The proposed algorithm and the previously established guidelines were applied to our data set and compared by using area under the curve, sensitivity, and specificity. Statistical analyses were performed using SPSS, version 24.0.

Results

Forty-four (32.1%) of all 137 ASR XL patients were ALTR positive in our cohort. In the univariate analysis, clinically relevant VAS pain ($P = .040$), blood Co levels ($P = .003$), and Co/Cr ratio ($P = .010$) were significantly associated with being ALTR positive. Blood Cr, radiographic radiolucency or osteolysis, and the other collected PROMs were not significantly associated with ALTR presence in the univariate analysis (Table 3). The multivariate analysis yielded clinically relevant VAS pain (odds ratio [OR] = 2.221; $P = .044$), high blood Co levels (OR = 1.053; $P = .015$), and male gender (OR = 2.371; $P = .028$) as independent predictors of ALTR presence (Table 4).

Based on ROC analysis, VAS pain cutoff values were determined to be 1.0 for both males (46.4% sensitivity, 65.9% specificity) and females (56.3% sensitivity, 71.4% specificity). Blood Co level cutoffs were determined to be 2.40 ppb for men (75.0% sensitivity, 59.1% specificity) and 4.00 ppb for women (68.8% sensitivity, 59.2% specificity). The novel algorithm based on these cutoffs indicated MARS-MRI for any patients having blood Co levels above their sex-specific cutoff values, self-reported pain above 1.0 on a VAS scale, or both (Fig. 1).

When applied to our patient cohort, our algorithm indicated a total of 94 (68.6%) patients for MARS-MRI, successfully identifying 38 of 44 (86.4%) patients with ALTR. Of those with ALTR, 6 (13.6%) had high pain only, 16 (36.4%) had high ions only, 16 (36.4%) had both high pain and high ions, and 6 (13.6%) had neither high pain nor high ions based on our algorithm's cutoffs. When compared with the 2 existing national guidelines via ROC analysis (Fig. 2), our algorithm was the only guideline better than chance alone at predicting ALTR in our cohort of ASR XL patients ($P = .014$) (Table 5). The proposed algorithm displayed the highest area under the curve, at 0.631 (95% confidence interval, 0.535-0.726) of the 3 considered guidelines. The Finnish Arthroplasty Association guideline showed comparable sensitivity to our algorithm, but its predictive ability did not reach statistical significance ($P = .084$) in our cohort. Similarly, the Medicines and Healthcare Products Regulatory Agency guidelines achieved similar specificity to our algorithm but did not achieve statistical significance either ($P = .216$).

Table 3
Univariate Test Results and Descriptive Statistics for Demographic and Clinical Variables in Relation to ALTR.

Variable	ALTR+	ALTR−	*P* Value
Male gender[a]	28 (64%)	44 (47%)	.074
Large femoral head size (≥52 mm for men, ≥ 48 mm for women)[a]	12 (27%)	27 (29%)	.831
Age at surgery (y)[b]	63 ± 13	62 ± 10	.486
MRI time from surgery (y)[b]	6.3 ± 1.7	6.1 ± 1.6	.688
Co (ppb)[c]	4.1 (2.2-12.3)	2.3 (1.3-6.4)	.009[d]
Cr (ppb)[c]	2.5 (1.1-4.2)	1.5 (0.9-3.5)	.057
Co/Cr[c]	1.7 (1.3-3.8)	1.4 (1.1-2.2)	.036[d]
HHS[c]	86 (77-93)	90 (80-96)	.085
EQ-5D index[c]	0.80 (0.64-1.00)	0.80 (0.69-1.00)	.613
VAS satisfaction (≥2 and <2)[a]	22 (50%)	39 (42%)	.375
VAS pain (≥2 and <2)[a]	19 (43%)	22 (24%)	.020[d]
Any acetabular radiolucency[a]	17 (39%)	27 (30%)	.317
Any femoral radiolucency[a]	14 (34%)	23 (29.5%)	.602
Any acetabular osteolysis[a]	1 (2%)	6 (7%)	.283
Any femoral osteolysis[a]	7 (17%)	7 (9%)	.193

ALTR, adverse local tissue reaction; Co, cobalt; Cr, chromium; EQ-5D, EuroQol-5D; HHS, Harris Hip Score; MRI, magnetic resonance imaging; VAS, visual analog scale.
[a] Descriptive statistic is given as number and percentage.
[b] Descriptive statistic is given as mean and standard deviation.
[c] Descriptive statistic is given as median and interquartile range.
[d] Denotes a statistically significant *P* value.

Discussion

Several national guidelines currently exist on when to take MARS-MRIs in MoM THA patients. However, there is no clear consensus on how MoM THA patients should be followed. The need for an updated, evidence-based guideline has been emphasized in recent literature [19]. In addition, implant-specific factors must be considered especially in cases of recalled implants, such as the ASR XL. Such guidelines are crucially important to screen high-risk patients while not burdening patients and health-care providers with costly MARS-MRIs when pathologic findings are unlikely. Our analyses showed pain, elevated blood Co levels and male gender to be predictive of ALTR presence in ASR XL patients. We constructed a highly sensitive and specific algorithm for when to obtain MARS-MRIs in ASR XL patients based on these prognostic variables. When applied to our study cohort, our algorithm outperformed existing national guidelines and was the only guideline capable of significantly predicting ALTR.

Although pain plays a key role in clinical decision-making, there is little statistical evidence in previous literature showing that pain is associated with ALTR or metal ion levels. In fact, several studies

Table 4
Multivariate Test Results for Demographic and Clinical Variables in Relation to ALTR.

Variable	*P* Value	Odds Ratio	95% Confidence Interval
Male gender	.034[a]	2.371	1.067-5.266
Age at surgery (y)	.426	1.016	0.978-1.055
MRI time from surgery (y)	.883	1.019	0.789-1.317
Large head size	.488	0.733	0.304-1.765
VAS pain ≥2	.023[a]	2.529	1.136-5.628
Cobalt (ppb)	.023[a]	1.050	1.007-1.094

ALTR, adverse local tissue reaction; MRI, magnetic resonance imaging; VAS, visual analog scale.
[a] Denotes a statistically significant *P* value.

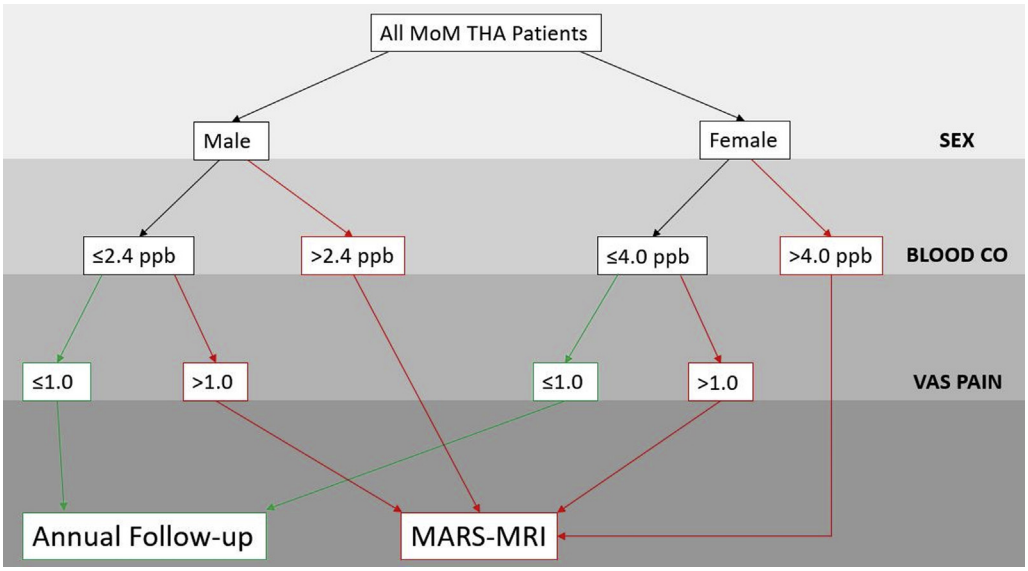

Fig. 1. Proposed decision tree algorithm for when to take MARS-MRI in patients treated with ASR XL THA.

have shown that ALTR prevalence in asymptomatic patients may range from 5% to 68% [7,20–22]. Our results show that higher pain is predictive of ALTR incidence. However, of patients in our cohort with ALTR, 22 (50.0%) reported pain at or below 1 on a VAS, supporting previous literature's findings that ALTR can still occur in asymptomatic patients. Although 50.0% of our patients with ALTR reported pain below our cutoff, inclusion of pain in our algorithm clearly improved our model when taken into consideration with blood Co levels. In addition, VAS pain is a simple measure that can be performed at outpatient visits, which makes it a very useful screening tool. Our results suggest that pain should be considered when deciding whether to conduct soft tissue imaging on ASR XL patients.

Previous literature has shown a connection between blood Co and Cr levels and ALTR formation in MoM THA [8,23–25]. There are, however, several studies showing that metal ion levels are not reliable predictors of ALTR [26,27]. One study consisting of patients with modular neck stems and metal-on-polyethylene bearings indicated Co/Cr ratio as a predictor of ALTR [28], but findings from a study considering MoM THA showed no association between the Co/Cr ratio and ALTR [29]. Only Co remained a significant predictor of ALTR in our multivariate analysis, although in our univariate

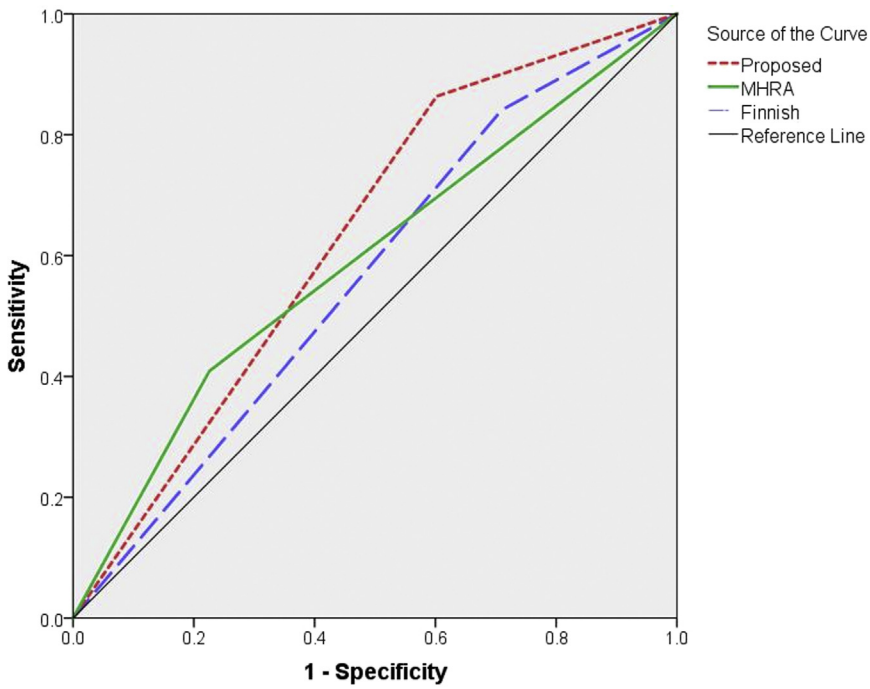

Fig. 2. Receiver-operating characteristic (ROC) curves demonstrating the diagnostic power (sensitivity and specificity) of our proposed algorithm compared to existing national guidelines for when to take MARS-MRI.

Table 5
ROC Curve AUC, Sensitivity, and Specificity of Existing Guidelines and the Proposed Decision Tree Algorithm.

Guideline	AUC (95% Confidence Interval)	*P* Value	Sensitivity	Specificity
Proposed	0.631 (0.535-0.726)	.014[a]	0.864	0.398
National MoM THA 1 [18]	0.566 (0.465-0.666)	.084	0.841	0.290
National MoM THA 2 [17]	0.592 (0.487-0.696)	.216	0.409	0.774

AUC, area under the curve; MoM, metal on metal; ROC, receiver-operating characteristic; THA, total hip arthroplasty.
[a] Indicates a statistically significant *P* value.

analysis both Co and Co/Cr ratio were significantly associated with ALTR. Blood Cr levels were not associated with the presence of ALTR in our cohort. Thus, blood Co levels were a necessary consideration in our algorithm.

Our finding that male gender increases the likelihood of developing moderate to severe ALTR conflicts with the findings reported in some previous literature [30]. This is emphasized by the difference between the sexes observed in our ROC analyses with Co as a predictor of ALTR. The lower threshold for men (2.40 ppb) than for women (4.00 ppb) suggests males may be more sensitive to high Co levels than females. This finding, however, may be confounded by higher early revision rates for females with ASR hip implants [31,32]. This could mean that, compared with men, more women with poorly performing ASR XL implants were revised before our follow-up at a mean of 6.2 years after index surgery. In addition, it should be noted that whole blood Co levels may not be perfectly reflective of Co levels in the joint fluid. Previous studies have shown only moderate correlation in Co levels between blood and joint fluid. Previous studies did not investigate sex differences in joint fluid Co levels [33,34].

Our proposed algorithm for when to take MARS-MRIs in ASR XL patients considers VAS pain, blood Co levels, and sex. To be indicated for MARS-MRI, the patient must have Co above their sex-specific cutoff value, VAS pain greater than 1.0, or both. Patients with Co below the sex-specific cutoffs and pain below 1.0 were considered low risk for ALTR and were not indicated for MARS-MRI. Patients not indicated for MARS-MRI are still recommended for annual blood metal ion testing and PROMs. Using our algorithm, 94 (68.6%) patients were indicated for MARS-MRI and we successfully identified 38 of 44 (86.4%) patients with ALTR in our cohort.

A perfect diagnostic model would have 100% sensitivity and 100% specificity. However, in complicated real-world models, such diagnostic accuracy is unrealistic. We aimed to maximize sensitivity and specificity to capture as many patients with ALTR as possible while also minimizing the number of MARS-MRIs given to patients without ALTR. When applied to our ASR XL patient cohort and compared with existing national guidelines for MoM THA [17,18], our proposed algorithm was the only guideline with the statistically significant ability to predict ALTR. One national guideline has an additional clause recommending at least one MARS-MRI on all ASR hip arthroplasty patients [17]. Compared with this conservative approach, our model reduced the number of MARS-MRIs required to diagnose a similar proportion of ALTRs in our study cohort.

Eighteen patients (22.7% of ALTR positive, 8.6% of ALTR negative) from the present study cohort have been revised since the time of their MARS-MRI. The remaining patients are being followed up closely and will provide valuable longitudinal data on ALTR change. In the future, additional longitudinal studies should be conducted to investigate how these ALTRs change over time and if these changes are associated with changes in blood metal ion levels or pain. We also found the Co/Cr ratio to be significant in the univariate analysis. Therefore, additional research should be conducted to clarify the role of Co/Cr in ALTR formation in MoM THA patients. Finally, as we have used our cohort to test the external validity of other MRI algorithms, future studies should seek to validate the reliability of our algorithm in another cohort of MoM THA patients.

Our study had some limitations. First, our cohort consisted of unilateral ASR XL patients only. Generalization to other implant types should be done with caution given the ASR XL's unique design among MoM THA implants. This also complicates the comparison of our results to other recommendations, which are guidelines for all MoM THA devices. Furthermore, we developed our algorithm and tested it on the same cohort of patients, and thus, our algorithm has not been validated. Another limitation of our study is that patients in our cohort were a mean of 6.2 (range, 3.3-10.4) years from the index surgery at the time of MARS-MRI. This means that our study cohort consisted of only relatively well-performing implants compared with the many ASR XL implants that were revised the first few years after being implanted. It is important to note that although revision rates for ALTR as high as 39% have been published for the ASR XL [30], the majority of ASR XL implants are still in situ worldwide. When considering a recalled implant, such as the ASR XL, relevant guidelines must follow the in situ population. Therefore, as more patients are revised and the in situ population shrinks, analyses such as ours must be revisited to maximize the efficiency and accuracy of the follow-up guidelines. Similarly, national guidelines should be revised annually based on the most current literature.

In conclusion, we determined that pain on a VAS, blood Co levels, and male gender were predictive of ALTR in MARS-MRI of ASR XL patients at midterm follow-up. We used these predictive measures to craft a decision tree algorithm that could predict ALTR and indicate MARS-MRI in our cohort of ASR XL MoM patients with high sensitivity and moderate specificity.

Acknowledgments

The authors would like to thank the Harris Orthopaedic Laboratory and DePuy Orthopaedics for enabling this study. They also thank the Finnish Arthroplasty Association, Dr Ola Rolfson, and Dr Viktor Lindgren for their efforts in radiographic analysis. Finally, they thank Dr Hollis Potter for her MARS-MRI analysis training efforts.

References

[1] AOANJRR (2016) hip and knee arthroplasty - 2016 supplementary report. In: Metal on metal bearing surface conventional hip arthroplasty; 2017.
[2] Bozic KJ, Kurtz S, Lau E, Ong K, Chiu V, Vail TP, et al. The epidemiology of bearing surface usage in total hip arthroplasty in the United States. J Bone Joint Surg Am 2009;91:1614–20. https://doi.org/10.2106/JBJS.H.01220.
[3] Wiley KF, Ding K, Stoner JA, Teague DC, Yousuf KM. Incidence of pseudotumor and acute lymphocytic vasculitis associated lesion (ALVAL) reactions in metal-on-metal hip articulations: a meta-analysis. J Arthroplasty 2013;28:1238–45. https://doi.org/10.1016/j.arth.2013.03.027.
[4] Campbell P, Ebramzadeh E, Nelson S, Takamura K, De Smet K, Amstutz HC. Histological features of pseudotumor-like tissues from metal-on-metal hips. Clin Orthop Relat Res 2010;468:2321–7. https://doi.org/10.1007/s11999-010-1372-y.
[5] Chang EY, McAnally JL, Van Horne JR, Statum S, Wolfson T, Gamst A, et al. Metal-on-metal total hip arthroplasty: do symptoms correlate with MR imaging findings? Radiology 2012;265:848–57. https://doi.org/10.1148/radiol.12120852.
[6] Wynn-Jones H, Macnair R, Wimhurst J, Chirodian N, Derbyshire B, Toms A, et al. Silent soft tissue pathology is common with a modern metal-on-metal hip arthroplasty. Acta Orthop 2011;82:301–7. https://doi.org/10.3109/17453674.2011.579518.
[7] Hart AJ, Satchithananda K, Liddle AD, Sabah SA, McRobbie D, Henckel J, 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;94:317–25. https://doi.org/10.2106/JBJS.J.01508.
[8] Sutphen SA, MacLaughlin LH, Madsen AA, Russell JH, McShane MA. Prevalence of pseudotumor in patients after metal-on-metal hip arthroplasty evaluated with metal ion analysis and MARS-MRI. J Arthroplasty 2016;31:260–3. https://doi.org/10.1016/j.arth.2015.07.011.
[9] Matharu GS, Mansour R, Dada O, Ostlere S, Pandit HG, Murray DW. Which imaging modality is most effective for identifying pseudotumours in metal-on-metal hip resurfacings requiring revision. Bone Joint J 2016;98-B:40–8. https://doi.org/10.1302/0301-620X.98B1.36746.
[10] Madanat R, Hussey DK, Donahue GS, Potter HG, Wallace R, Bragdon C, et al. Early lessons from a worldwide, multicenter, followup study of the recalled articular surface replacement hip system. Clin Orthop Relat Res 2016;474:166–74. https://doi.org/10.1007/s11999-015-4456-x.
[11] Donahue GS, Lindgren V, Galea VP, Madanat R, Muratoglu O, Malchau H. Are females at greater risk for revision surgery after hip resurfacing arthroplasty with the articular surface replacement prosthesis? Clin Orthop Relat Res 2016;474:2257–65. https://doi.org/10.1007/s11999-016-4860-x.
[12] Hussey DK, Madanat R, Donahue GS, Rolfson O, Bragdon CR, Muratoglu OK, et al. Scoring the current risk stratification guidelines in follow-up evaluation of patients after metal-on-metal hip arthroplasty: a proposal for a metal-on-metal risk score supporting clinical decision-making. J Bone Joint Surg Am 2016;98:1905–12. https://doi.org/10.2106/JBJS.15.00685.
[13] van der Weegen W, Brakel K, Horn RJ, Wullems JA, Das HP, Pilot P, et al. Comparison of different pseudotumor grading systems in a single cohort of metal-on-metal hip arthroplasty patients. Skeletal Radiol 2014;43:149–55. https://doi.org/10.1007/s00256-013-1755-8.
[14] Anderson H, Toms AP, Cahir JG, Goodwin RW, Wimhurst J, Nolan JF. Grading the severity of soft tissue changes associated with metal-on-metal hip replacements: reliability of an MR grading system. Skeletal Radiol 2011;40:303–7. https://doi.org/10.1007/s00256-010-1000-7.
[15] DeLee JGCJ. Radiological demarcation of cemented sockets in total hip replacement. Clin Orthop Relat Res 1976;121:20–32.
[16] Youden WJ. Index for rating diagnostic tests. Cancer 1950;3:32–5. https://doi.org/10.1002/1097-0142(1950)3.
[17] MHRA. Metal-on-metal (MoM) hip replacements - updated advice with patient follow ups. MDA/2012/036. MDA/2012/036 2017. 2012. https://assets.publishing.service.gov.uk/media/5954ca1ded915d0baa00009b/MDA-2017-018_Final.pdf.
[18] FAA (2017) Finnish Arthroplasty Association's recommendations for the follow up of patients with metal on metal hip arthroplasty. 2017. http://www.suomenartroplastiayhdistys.fi/files/faa_mom_fu_recommendations.pdf.
[19] Matharu GS, Mellon SJ, Murray DW, Pandit HG. Follow-up guidance for metal-on-metal hip replacement patients should be updated. Int Orthop 2015;39:609–10. https://doi.org/10.1007/s00264-015-2667-0.
[20] Kwon YM, Ostlere SJ, McLardy-Smith P, Athanasou NA, Gill HS, Murray DW. "Asymptomatic" pseudotumors after metal-on-metal hip resurfacing arthroplasty: prevalence and metal ion study. J Arthroplasty 2011;26:511–8. https://doi.org/10.1016/j.arth.2010.05.030.
[21] Nawabi DH, Hayter CL, Su EP, Koff MF, Perino G, Gold SL, et al. Magnetic resonance imaging findings in symptomatic versus asymptomatic subjects following metal-on-metal hip resurfacing arthroplasty. J Bone Joint Surg Am 2013;95:895–902. https://doi.org/10.2106/JBJS.K.01476.
[22] Williams DH, Greidanus NV, Masri BA, Duncan CP, Garbuz DS. Prevalence of pseudotumor in asymptomatic patients after metal-on-metal hip arthroplasty. J Bone Joint Surg Am 2011;93:2164–71. https://doi.org/10.2106/JBJS.J.01884.
[23] Bosker BH, Ettema HB, Boomsma MF, Kollen BJ, Maas M, Verheyen CC. High incidence of pseudotumour formation after large-diameter metal-on-metal total hip replacement: a prospective cohort study. J Bone Joint Surg Br 2012;94:755–61. https://doi.org/10.1302/0301-620X.94B6.28373.
[24] Bayley N, Khan H, Grosso P, Hupel T, Stevens D, Snider M, et al. What are the predictors and prevalence of pseudotumor and elevated metal ions after large-diameter metal-on-metal THA? Clin Orthop Relat Res 2015;473:477–84. https://doi.org/10.1007/s11999-014-3824-2.
[25] Bosker BH, Ettema HB, van Rossum M, Boomsma MF, Kollen BJ, Maas M, et al. Pseudotumor formation and serum ions after large head metal-on-metal stemmed total hip replacement. Risk factors, time course and revisions in 706 hips. Arch Orthop Trauma Surg 2015;135:417–25. https://doi.org/10.1007/s00402-015-2165-2.
[26] Griffin WL, Fehring TK, Kudrna JC, Schmidt RH, Christie MJ, Odum SM, et al. Are metal ion levels a useful trigger for surgical intervention? J Arthroplasty 2012;27:32–6. https://doi.org/10.1016/j.arth.2012.03.020.
[27] Hjorth MH, Stilling M, Soballe K, Bolvig LH, Thyssen JP, Mechlenburg I, et al. No association between pseudotumors, high serum metal-ion levels and metal hypersensitivity in large-head metal-on-metal total hip arthroplasty at 5-7-year follow-up. Skeletal Radiol 2016;45:115–25. https://doi.org/10.1007/s00256-015-2264-8.
[28] Kwon YM, Tsai TY, Leone WA, Liow MH. Sensitivity and specificity of metal ion levels in predicting "pseudotumors" due to taper corrosion in patients with dual taper modular total hip arthroplasty. J Arthroplasty 2017;32:996–1000. https://doi.org/10.1016/j.arth.2016.08.040.
[29] Fehring TK, Carter JL, Fehring KA, Odum SM, Griffin WL. Cobalt to chromium ratio is not a key marker for adverse local tissue reaction (ALTR) in metal on metal hips. J Arthroplasty 2015;30:107–9. https://doi.org/10.1016/j.arth.2015.02.049.
[30] Reito A, Puolakka T, Elo P, Pajamaki J, Eskelinen A. High prevalence of adverse reactions to metal debris in small-headed ASR hips. Clin Orthop Relat Res 2013;471:2954–61. https://doi.org/10.1007/s11999-013-3023-6.
[31] Jameson SS, Baker PN, Mason J, Porter ML, Deehan DJ, Reed MR. Independent predictors of revision following metal-on-metal hip resurfacing: a retrospective cohort study using national joint registry data. J Bone Joint Surg Br 2012;94:746–54. https://doi.org/10.1302/0301-620X.94B6.29239.
[32] Langton DJ, Sidaginamale RP, Joyce TJ, Natu S, Blain P, Jefferson RD, et al. The clinical implications of elevated blood metal ion concentrations in asymptomatic patients with MoM hip resurfacings: a cohort study. BMJ Open 2013;3. https://doi.org/10.1136/bmjopen-2012-001541.
[33] Davda K, Lali FV, Sampson B, Skinner J, Hart J. An analysis of metal ion levels in the joint fluid of symptomatic patients with metal-on-metal hip replacements. J Bone Joint Surg Br 2011;93:738–45. https://doi.org/10.1302/0301-620X.93B6.25804.
[34] Reito A, Parkkinen J, Puolakka T, Pajamäki J, Eskelinen A. Diagnostic utility of joint fluid metal ion measurement for histopathological findings in metal-on-metal hip replacements. BMC Musculoskelet Disord 2015;16:393. https://doi.org/10.1186/s12891-015-0851-4.