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Original Research

Metal-on-Metal Total Hip Arthroplasties: Why Do They Fail?

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ABSTRACT

Background: Metal sensitivity reaction is a major concern in painful failed metal-on-metal (MoM) total hip arthroplasty (THA), but it may not be the dominant failure mode. We investigated revised MoM THAs for failure etiologies, operative indications, and clinical outcomes.
Methods: Ninety consecutive revised MoM THAs were reviewed. Preoperative evaluation included inflammatory markers, metal ion levels, radiographs, metal artifact reduction sequence magnetic resonance imaging, synovial fluid analysis, and operative histopathology. Outcome measures included advanced imaging and laboratory findings, revision etiology, and clinical outcomes.
Results: Metal sensitivity reactions (MSRs) accounted for 36% of MoM failures, with 64% of MoM THA being revised for non-MSR-related etiologies. Failure etiologies not related to MoM bearing articulation included prosthetic joint infection (14%), aseptic loosening (13%), isolated abductor failure (7%), periprosthetic fracture (3%), recurrent dislocation (3%), symptomatic heterotopic ossification (3%), mechanical failure (1%), and angiosarcoma (1%). Additionally, 18% of patients had painful MoM THA with no identifiable failure etiology; of these patients, 69% had continued pain following revision. Patients with large periarticular fluid collections had an odds ratio of 19.2 (P =< 0.0001) of having MSR. Cobalt (Co) levels were statistically higher in patients with MSR compared to non-MSR-related failures ($P = .034$). Chromium (Cr) ion levels and the Co/Cr ratio did not predict MSR.
Conclusions: The majority of revised MoM THAs did not have MSR. Large periarticular fluid collections and elevated Co levels were highly predictive of MSR. Painful MoM THA without an identifiable failure etiology resulted in a high incidence of persistent pain following revision.

Introduction

Early- and intermediate-term results of contemporary metal-on-metal (MoM) total hip arthroplasties (THAs) were promising. [1] However, the 2011 Australian Orthopaedic Association National Joint Replacement Registry Annual Report demonstrated an alarming 9.4% and 10.4% failure rate at 7 years for MoM THA with head sizes >32 mm and 40 mm, respectively. Failures at 10 years were due to aseptic loosening (3.9%), prosthetic joint infection (1.4%), and metal sensitivity reaction (MSR) (1.0%). [2] The potential for MoM bearing-related complications and failures has increased physician and patient concerns. High-profile MoM implant recalls and relentless "bad hip" legal advertisements at the height of those recalls increased patient anxiety driving them to seek evaluations.

The potential for MSR in MoM bearing hips has been raised for decades. [3,4] MSR is thought to be a result of a lymphocyte-dominated immune response generated by the metal debris from implant wear, categorizing this response as a delayed type IV hypersensitivity reaction. [5,6] Additionally, there is evidence that patients may possess a genetic predisposition to these MSR. [7] This can cause extensive bone and soft tissue destruction, leading to early failure from osteolysis, aseptic loosening, potential instability, and persistent pain. [5,8] Clinical follow-up of patients with a MoM THA can present challenges for the orthopaedic surgeon, especially in discerning the etiology if they have pain. Somewhat complex

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strategies have been proposed with the efficacy of some of the diagnostic work-up being controversial. [9,10] Blood cobalt (Co) and chromium (Cr) ion levels are frequently utilized to follow these patients, but their utility is under debate. [11-14] There is some support for monitoring asymptomatic patients with Co ion levels alone or using implant-specific blood metal ion thresholds. [15,16] However, in cases of asymptomatic patients with clinically and radiographically confirmed well-functioning prostheses, the United States Food and Drug Administration (2019) does not suggest routine checks of blood metal ion levels. [17] Additionally, the 2012 American Academy of Orthopaedic Surgeons (2023) information statement on current concepts with MoM THA notes insufficient evidence to provide a worrisome threshold value of metal ion levels in the blood and should not be used as an independent metric for revision surgery. [18] Utilizing metal artifact reduction sequence (MARS) magnetic resonance imaging (MRI) in the workup of painful MoM hips has been shown to be effective in determining an MSR. [19-21] The purpose of this study was to evaluate the preoperative work-up used for patients with revision MoM THA and to investigate failure etiologies, operative indications, and clinical outcomes.

Material and methods

This retrospective, institutional review board-approved analysis consisted of 90 consecutive revised painful MoM THA (51 women and 39 men) with an average age of 59.8 ± 13.2 years, between July 1st, 2010, and December 31st, 2018. All procedures were performed by the same fellowship-trained adult reconstruction specialist at a tertiary care facility. Revision of MoM hip resurfacings was excluded. Preoperative, operative, and postoperative medical records were reviewed for revision etiology, implants revised, clinical outcomes, and incidence of litigation regarding their MoM THA. Main outcome measures included blood ion levels and advanced imaging findings, revision etiology, and resolution of pain following revision surgery.

Clinical analysis

Preoperative testing consisted of plain film radiographs, MARS MRI, inflammatory markers (erythrocyte sedimentation rate and C-reactive protein), complete blood count with differential, and Co and Cr blood ion levels.

MARS MRIs were reviewed by a specialist musculoskeletal radiologist for the presence or absence of periarticular effusions and/or fluid extending through deep fascial planes. Synovial fluid analysis was performed when indicated (elevated inflammatory markers, clinical signs of infection, or MRI findings of periarticular fluid collection). Intraoperative tissue samples were analyzed for the presence of MSR by a board-certified pathologist utilizing the aseptic lymphocytic vasculitis-associated lesions scoring criteria proposed by Campbell et al. [5]

Data analyses

Laboratory data are expressed as median (Q1-Q3) values for non-normally distributed data and mean (standard deviation) for normally distributed data. In order to evaluate the predictive value of prerevision laboratory and imaging studies, results were made binary, comparing patients with MSR and patients without MSR. A Wilcoxon-Mann-Whitney test was used to determine statistical significance for all laboratory results. An odds ratio was used for the MRI results. A secondary analysis was performed on the subgroup of patients excluding septic revisions and a case of angiosarcoma. All statistical analysis was performed using SPSS version 22.0 (IBM Armonk, NY) at a significance level of $\alpha = 0.05$.

Results

Ten different etiologies contributed to MoM THA failures. (Table 1) MSR accounted for 36% (32/90), while 64% (58/90) of patients were without MSR and failed secondary to other etiologies. Eighteen percent (16/90) of patients revised for a persistently painful MoM THA had no identifiable failure etiology. All cups were correctly positioned in the patients revised for recurrent dislocations, and there were no overlapping diagnoses between patients with MSR and those with a preoperative diagnosis of aseptic loosening or recurrent dislocation. Implants revised were recorded. (Table 2)

Laboratory results

A total of 71 samples of Co and 69 samples of Cr blood ion levels were obtained. Cobalt ion levels for patients with MSR and non-MSR etiologies were 6.3 (3.9-14.4) ug/L and 3.8 (1.4-10.2) ug/L, respectively; ($P = .034$). Chromium ion levels for MSR and non-MSR were 3.4 (1.4-13.4) ug/L and 2.5 (0.9-7.5) ug/L, respectively; ($P = .173$). Cobalt/chromium ratio was 1.6 (1.1-3.2) for MSR and 1.2 (0.8-1.8) for non-MSR, ($P = .207$).

For a secondary analysis, a total of 61 samples of Co and 58 Cr blood ion levels were obtained. Cobalt ion levels were 6.3 (3.9-14.4) ug/L in MSR group and 3.8 (1.9-11) ug/L in non-MSR group, respectively; ($P = .048$). Chromium ion levels for MSR and non-MSR were 3.4 (1.4-13.4) ug/L and 2.8 (1.6-8.2) ug/L, respectively; ($P = .696$). Cobalt/chromium ratio was 1.6 (1.1-3.2) for MSR and 1.1 (0.8-1.6) for non-MSR, ($P = .125$).

MRI results

Seventy-one patients obtained MARS MRIs prior to revision MoM THA (79%). Thirty patients had large (>5 cm) periarticular effusions or fluid extending through deep fascia. (Fig. 1) Twenty-three of 30 patients with these MRI findings were determined to have MSR by intraoperative histology (77%). The odds ratio for patients with large periarticular effusions or fluid extending through deep fascia planes on MRI having MSR was 19.2 (P =< 0.0001). Similarly, in secondary analysis of aseptic cases and cases without diagnosed tumor, the odds ratio was 38.3 ($P < .0001$).

Clinical results

Average patient follow-up was 22.0 ± 15.5 months. Pain resolution following revision THA was achieved in 84% (27/32) of patients with MSR and 57% (33/58) of patients with non-MSR MoM-related failure at the latest follow-up. Pain resolution was

Table 1
Revision diagnoses for patient cohort.

Diagnosis	# Patients (%)
Metal sensitivity reaction (MSR)	32 (35.6)
Prosthetic joint infection	13 (14.4)
Unknown	16 (17.8)
Aseptic loosening	12 (13.3)
Isolated abductor failure	6 (6.7)
Periprosthetic fracture	3 (3.3)
Recurrent hip dislocations	3 (3.3)
Heterotopic ossification (HO)	3 (3.3)
Mechanical failure	1 (1)
Angiosarcoma	1 (1)

Table 2
Revised implants by manufacturer.

Revised implants	# Patients
M2 (Biomet, Warshaw, IN)	5
Cormet (Corin, Tampa, FL)	1
Summit Pinnacle Ultamet (Depuy, Warsaw, IN)	57
SROM Pinnacle Ultamet (Depuy, Warsaw, IN)	7
Corail Pinnacle Ultamet (Depuy, Warsaw, IN)	2
Prodogy Pinnacle Ultamet (Depuy, Warsaw, IN)	2
SROM ASR (Depuy, Warsaw, IN)	1
Summit ASR (Depuy, Warsaw, IN)	4
SROM Pinnacle Bantam (Depuy, Warsaw, IN)	1
Synergy BHR (Smith & Nephew, Memphis, TN)	3
Pinnacle Ultamet (Smith & Nephew, Memphis, TN)	1
Metasul Durom (Zimmer, Warsaw, IN)	6

obtained in 5/16 (31%) of patients with an unknown diagnosis. Overall, revision resolved hip pain in 66% (59/90) of patients with failed MoM THA, with pain resolution varying with revision diagnosis. Litigation was pursued in 20% (18/90) of patients regarding their MoM THA, of which 33% (6/18) of those patients had an MSR.

Discussion

Contemporary MoM bearing THA provides evidence of good long-term survivorship ranging from 93% to 96% in some studies. [22,23] However, the presence of MSR resulting in significant soft tissue damage and bone loss has raised physician concern for this risk in their patients with a painful MoM THA, with and without a diagnosable cause for their symptoms. Similarly, anxiety has affected patients with MoM THA because of implant recalls and negative media attention. In our cohort of 90 revised MoM THA, we found that the majority of failure etiologies were not specific to the MoM bearing surface, with only 36% of patients having MSR. Eighteen percent (16/90) of patients had a painful MoM THA with no identifiable failure etiology; of these patients, 69% (11/16) had continued pain following revision. Ideally, if we have testing with high sensitivity, revision with poor prognosis for pain relief may be avoided.

Metal ion levels are frequently obtained by surgeons to monitor patients with MoM THA. Systemic effects from elevated metal ions from orthopaedic implants have been debated in previous studies. [14,24,25] Van Lingen et al. (2013) looked at patients with serum cobalt ion concentrations ranging from 18 to 153 μg/L and found no signs or symptoms of neurologic dysfunction, cardiomyopathy, renal, or thyroid dysfunction. [25] The Food and Drug Administration does not recommend routine checking of blood metal ion levels in asymptomatic patients. Additionally, there has been debate over the correlation between increased systemic ion levels and MSRs. [11,12] The American Academy of Orthopaedic Surgeons (2023) information statement suggests that an isolated increase in metal ion levels should not serve as a clinical recommendation to revise patients with MoM THA. [18] In our case series, Cr levels were not a predictor of MSR. However, Co levels were statistically higher in patients with MSR compared to patients without MSR. A recent study (2021) showed that increased Co ions lead to inflammatory processes and adverse local tissue reactions. [26] Previous reports (2017, 2019, and 2014) found Co/Cr ratio to be associated with adverse reactions to metal debris. [16,27,28] Our study could not corroborate those findings as we demonstrated no difference in the Co/Cr ratio between patients with and without MSR. However, these findings suggest that an increased Co level should trigger further evaluation with an MARS MRI study.

As MARS MRIs are increasingly implemented in management protocols, several studies (2011, 2012) have explored the correlation between MRI findings and adverse reactions to metal debris, investigating adjacent musculature and neurovascular disease involvement, osteolysis, synovitis, and bone marrow changes. [19,20,29] Moreover, Nawabi et al. (2014) reported a sensitivity and specificity of 94% and 87% when using a predictive model on MRI to diagnose aseptic lymphocytic vasculitis-associated lesion consistent with MSR. [30] We found that MRI findings provided the most significant insight to diagnosing MSR preoperatively. Twenty-three out of 30 (77%) patients with MSR who had MRIs available for review had large periarticular effusions or fluid extending through deep fascial planes. Seven patients with non-MSR-related etiologies had these MRI findings. Of these 7, 4 were diagnosed with prosthetic joint infections, 1 patient had a fracture hematoma, 1 case of aseptic loosening, and 1 case of a hematoma from recurrent instability. Our data suggests that patients with large periarticular fluid collections or fluid extending past deep fascial planes on MRI supports concern for a poorly functioning MoM THA. We advocate for hip arthrocentesis for synovial fluid analysis in patients with these MRI findings.

Sixty-five percent of the patients in our cohort were revised for etiologies not specifically related to the MoM bearing articulation. Seven of these patients were revised at the time of addressing extraarticular pathology, at which time it was decided to concurrently exchange the MoM bearing to a non-MoM bearing articulation. This included 3 patients with heterotopic ossification causing severe pain and significant limitation in range of motion and 4 patients with isolated abductor failure who failed conservative treatment and were without evidence of MSR. All 7 of these patients had a head liner exchange to metal or ceramic on highly cross-linked polyethylene at the time of heterotopic ossification resection or abductor tendon repair/reconstruction.

After extensive work-up, 18% of the patients in this cohort had no identifiable cause for their painful MoM THA. This leads one to question if the negative publicity surrounding MoM implants and increased call for litigation against these manufacturers affected

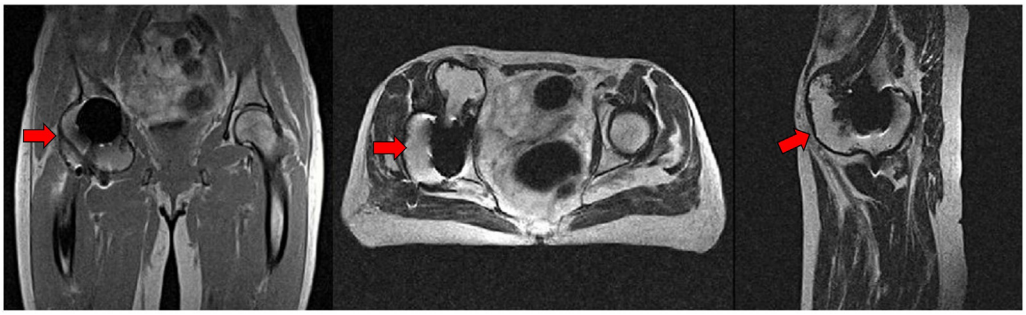

Figure 1. Large periarticular fluid collection extending past deep fascial plains seen in an anterior-posterior, cross-section, and sagittal view.

patient satisfaction and increased their desire for revision. Twenty percent of patients in our series pursued legal action regarding their MoM THA. It was difficult to discern if any true correlation existed between patients revised for a painful MoM THA with no identifiable etiology and the 31% (5/16) incidence of litigation in this subset of patients. It is also disconcerting that 69% (11/16) of the revised patients with pain of unknown etiology continued to have pain through the latest follow-up visit. Revisions may not ameliorate the patients' pain and symptoms when there is no clear etiology of pain or failure and raise concern about the efficacy of operating on these patients. If choosing to operate on patients without a clear etiology for their pain, expectations need to be adjusted, as pain is likely to persist.

This study has limitations. As with any retrospective analysis, data may be missing or unobtainable. Only 71 MRIs were available for 90 hips for review, either secondary to an MRI not being indicated or not having access to review imaging if obtained at a remote location. Another limitation is that the pathology and MRI analysis were performed by a single pathologist and musculoskeletal radiologist, respectively. Therefore, an interclass correlation coefficient to combat the degree of subjectiveness that each grading criterion encompasses could not be produced.

Conclusions

Despite study limitations, this study provides useful information regarding appropriate diagnostics that can guide a surgeon's treatment algorithm when working up a painful MoM THA. As a direct result of this study, MARS MRI is obtained for all symptomatic patients who have previously undergone MoM THA in our practice. We suggest stratifying the patient's risk and ruling out any other possible etiology before revising a patient with possible MoM failure. The presence of large periarticular effusions and/or fluid extending through deep fascial planes was found to be highly predictive of MSR and may serve as a reliable indication that a patient will need a revision. If choosing to operate on patients with pain of unknown etiology, expectations need to be adjusted, as persistent pain is likely.

Study type

Therapeutic Level IV Retrospective Case Series.

Conflicts of interest

K. A. Gustke receives royalties from Stryker MAKO; is a speaker bureau of Stryker MAKO; is paid consultant of Stryker MAKO; has stock options in Zimmer; and receives research support from Stryker MAKO and Zimmer. P. Simon receives research support and financial support from ENOVIS and is a Chair of the Research Committee of the American Shoulder and Elbow Surgeons. T. L. Bernasek receives royalties from DePuy and A Johnson & Johnson Company; is a speaker bureau of DePuy and A Johnson & Johnson Company; is a paid consultant of DePuy and A Johnson & Johnson Company; receives research support from Corin U.S.A., DePuy, and A Johnson & Johnson Company; and is a board/committee member of Florida Orthopaedic Society. All other authors declare no potential conflicts of interest.

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CRediT authorship contribution statement

T. Kyle Stoops: Writing – review & editing, Writing – original draft, Investigation, Data curation, Conceptualization. **Josué G. Layuno-Matos:** Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Data curation. **Peter Simon:** Writing – review & editing, Writing – original draft, Resources, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Kenneth A. Gustke:** Writing – review & editing, Writing – original draft, Supervision, Resources, Conceptualization. **Thomas L. Bernasek:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Conceptualization.

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