Gender is a Significant Factor for Failure of Metal-on-Metal Total Hip Arthroplasty

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Abstract: Metal-on-metal (MoM) articulations offers low wear, larger head size, and increased stability. Reports of early failure are troubling and include failure of ingrowth and metal articulation problems such as metallosis, hypersensitivity, pseudotumor, and unexplained pain. This study investigates the survivorship of modern MoM articulations by gender. We reviewed 1589 primary MoM THA in 1363 patients, with minimum 2-year follow-up for 1212 hips. Follow-up averaged 60 months. There were 643 female patients and 719 male patients. The incidence of cup revision was significantly higher in women than in men (8.2% vs 2.7%; $P = .0000$), as was incidence of aseptic loosening (4.3% vs 1.1%; $P = .0006$), and failure for metal-bearing complications (2.2% vs 0.6%; $P = .0126$). There appear to be gender factors influencing the success of MoM THA, which may include hormonal, anatomic, or functional differences.
Keywords: total hip arthroplasty, metal-on-metal, pseudotumor, hypersensitivity, gender difference.

The greatest controversy in total hip arthroplasty (THA) today is the bearing. Despite numerous long-term satisfactory results, conventional polyethylene was plagued by wear-induced osteolysis and both early and late dislocation. These 2 factors have been the driving force in the search for an optimal bearing. Current material choices include highly cross-linked polyethylene, ceramic-on-ceramic bearings, and metal-on-metal (MoM) bearings.

Metal-on-metal articulations offer a very attractive alternative and have a long record of use. Metal-on-metal devices are self-polishing and are associated with a very low wear rate [1]. With MoM, large heads have enhanced tribologic behavior and thus less wear than smaller MoM articulations and are favored because of the increased stability afforded [2]. Clinical results of the so-called second-generation MoM with short to midterm follow-up have demonstrated excellent survivorship [3]. However, there have been increasing reports and growing concerns surrounding implant design–related failures, metallosis, pseudotumors, and hypersensitivity occurring in patients with MoM THA (Fig. 1) [4-7]. Clearly not all MoM systems are created equal. Variables include metallurgy, specifically carbon content, method of fabrication, surface finish, and heat treatment. A second variable is geometry, which encompasses clearance, sphericity, functional articular arc, and head size. Another variable is the acetabular component design, specifically monoblock vs modular construction, cup wall thickness, and fixation surface.

As bearing couples advance, so do the possible failure modes associated with these bearings. To date, there is no definitive test or even definition of metallosis, hypersensitivity, or early aseptic failure in MoM THA [8]. Studies have attempted to define these conditions by immunologic responses. Others have defined these based on pathological findings at the time of revision surgery. Mechanical factors have also been associated with early failure and hypersensitivity symptoms. In particular, vertical cup placement and smaller cup sizes have been shown to correlate with increase local and serum metal ions, cup loosening, pseudotumor formation, and acute lymphocytic vascular–associated lesions [9-12]. Because of the lack of a clear definition and the unknown denominator in most series, the true prevalence of

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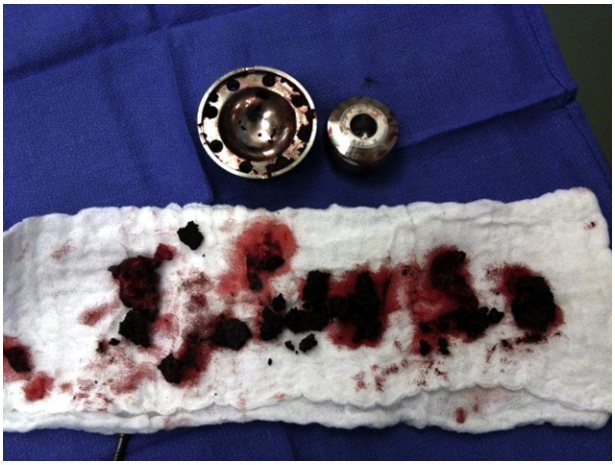

Fig. 1. Tissue is shown from a pseudotumor debrided during revision of the acetabular component in a 42-year-old female patient with failure secondary to metal complication at 6.5 years postoperatively.

hypersensitivity/metallosis occurring in patients with a MoM THA is unknown.

Our experience with MoM articulations commenced in 1996. In review of our series, we noted that early failure was more common in women. Other studies have noted this as well [4,13-15]. The purpose of the current study is to investigate the minimum 2-year survivorship of second-generation MoM articulations as it relates to gender.

Methods

A retrospective review of all primary THA performed at our institution from 1996 to 2006 identified 1589 THA in 1363 patients with MoM bearings (Table 1). Of the 1367 patients, 719 (52.8%) were male (848 hips; 53.4%) and 643 (47.2%) were female (741 hips; 46.6%). The average age at the time of surgery was 57.4 (19-88) years old. The diagnosis for hip arthroplasty was osteoarthritis in 1224 (77.0%), avascular necrosis in 162 (10.2%), developmental dysplasia in 71 (4.5%), posttraumatic arthritis in 40 (2.5%), rheumatoid arthritis in 32 (2.0%), and slipped capital femoral epiphysis in 16 (1.0%) with acute fracture (9), ankylosing spondylitis (3), osteopetrosis (1), and Paget disease (1) comprising the remaining 1% of patients.

Table 1. Patient Demographics and Results by Gender

Parameter	Overall	Male	Female	*P*
No. of THA	1589	850	745	
No. of patients	1363	721	646	
Average age (y)	57.4	56.6	58.4	.0012
Average height (in)	67.6	70.3	64.5	.0000
Average weight (lb)	204.4	221.7	184.5	.0000
Average body mass index (kg/m^2)	31.4	31.5	31.2	.4858
THA, minimum 2-y follow-up	1212 (76%)	627 (74%)	585 (79%)	.0294
Average follow-up (mo)	60.2	60.3	60.2	.9776
Failure mode				
Aseptic loosening	32 (2.6%)	7 (1.1%)	25 (4.3%)	.0006
Metal complication	17 (1.4%)	4 (0.6%)	13 (2.2%)	.0126
Dislocation	1 (0.1%)	0 (0.0%)	1 (0.2%)	.4819
Infection	10 (0.8%)	5 (0.8%)	5 (0.9%)	.2459
Cup well fixed	5 (0.4%)	1 (0.2%)	4 (0.7%)	.1394
Total overall	65 (5.4%)	17 (2.7%)	48 (8.2%)	.0000

Three different MoM implant designs were used during this time frame (Table 2). The first, the M^{2}a-Taper (Biomet, Warsaw, Ind), was a titanium (Ti) shell with porous plasma-sprayed (PPS) coating mated with a cobalt chromium (CoCr) tapered insert of 28- or 32-mm inner diameter. The second design, the M^{2}a-38 (Biomet), was a CoCr monoblock shell with Ti-PPS surface coating, a standard head diameter of 38 mm, and wall thickness increasing with outer diameter. The third, the Magnum (Biomet), was a resurfacing style monoblock cup of CoCr with Ti-PPS surface coating and a constant wall thickness of 3 mm for an effective outer diameter 6 mm larger than the femoral head, with head sizes available from 40 to 60 mm. The distribution between male and female patients remained similar among the different designs.

Minimum 2-year follow-up was available for 1212 THA (76%) in the overall series (Table 1). Of the 1212 THA with minimum 2-year follow-up, 584 (48%) were in female patients and 628 (52%) were in male patients. From the follow-up data, patients who required reoperation of the hip for any reason were considered failures. Reason for failure was noted for each of these patients including acetabular loosening, metal complication, dislocation, infection, and other reason for failure with a well-fixed cup. Surgical information including acetabular component size, cup design, and head size were recorded.

A radiographic assessment was also done to measure the inclination (abduction) angle of the acetabular component (Fig. 2). Measurements were done by a blinded observer (M.J.L.) using a calibrated picture archiving and communication system (Stryker, Inc, Rutherford, NJ). The angle between the inferior aspect of the ischium and the face of the acetabular component was measured using the Cobb angle tool.

A statistical analysis of the data was done to determine if there were any significant differences between men and woman. A χ^2 test was used to compare failure between men and women and for the different modes of failure. A 2 tailed Student *t* test was performed to compare differences in mean acetabular component sizes, head sizes, and angle of inclination between men vs women, and failures vs nonfailures. Survivorship was stratified by gender and revision for any reason, aseptic loosening (or failure of ingrowth), and metal-bearing–related failure using the Kaplan-Meier method and χ^2 analysis. Power to detect a difference was greater than 80% at $P = .05$ with

Table 2. Results by MoM Design and Gender

	M^2a-Taper		M^2a-38		Magnum	
	Male	Female	Male	Female	Male	Female
No. of THA	180	172	408	342	260	227
THA, minimum 2-y follow-up	157	143	302	275	169	166
Failure mode						
Metal complication	1 (0.6%)	2 (1.2%)	**2 (0.5%)**	**9 (2.6%)** *	1 (0.4%)	2 (0.9%)
Acetabular loosening	**0**	**5 (2.9%)** †	**4 (1.0%)**	**16 (4.7%)** ‡	3 (1.2%)	4 (1.8%)
Cup well fixed	0	1 (0.6%)	1 (0.2%)	2 (0.6%)	0	0
Dislocation	0	1 (0.1%)	0	0	0	0
Infection	0	2 (1.2%)	4 (1.0%)	2 (0.6%)	1 (0.4%)	1 (0.4%)
Total aseptic	**1 (0.6%)**	**9 (5.3%)** §	**7 (1.7%)**	**27 (7.9%)** ‖	4 (1.5%)	6 (2.6%)
Total overall	**1 (0.6%)**	**11 (6.4%)** ¶	**11 (2.7%)**	**29 (6.3%)** #	5 (1.9%)	7 (3.1%)

Boldface type in table indicates a statistically significant difference in values between male and female.
* $P = .01584$.
† $P = .0237$.
‡ $P = .0017$.
§ $P = .0014$.
‖ $P = .0000$.
¶ $P = .0003$.
# $P = .0004$.

the numbers available. All confidence intervals were calculated to the 95% level. Statistical significance was determined at P equals or less than .05.

Results

The average follow-up was 60 (24-178) months. Of the 1212 hips with 2 year follow-up, there were 65 (5.4%) failures. The average time to failure was 47 months. The failures were then analyzed by gender and mode of failure. Of the 65 failures, 49 (77%) were due to either aseptic loosening or metal complications. Forty-eight (74%) of the failures were in women. There was statistically higher incidence in failure for women vs men both overall as well as in failures for metal complications and aseptic loosening (Table 1). The data were further analyzed to determine if there was a difference in these modes of failure among the 3 cup designs (Table 2). In all 3 designs, there was a trend toward increased failure in women, which reached statistical significance for metal complications in the M^2a-38 and aseptic loosening in the M^2a-Taper and M^2a-38.

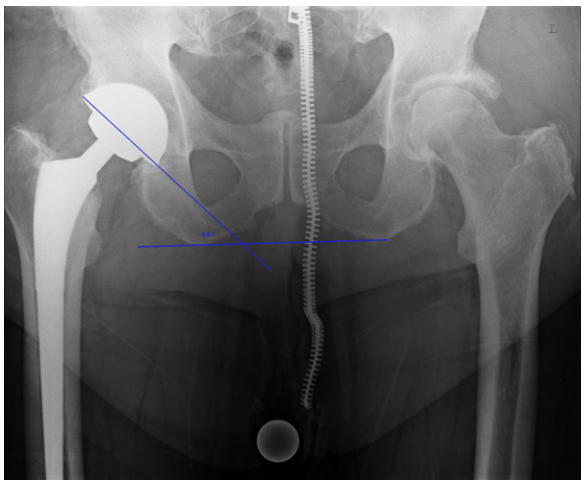

Fig. 2. The acetabular inclination (abduction angle) was measured referencing a transischial line and was performed on a calibrated picture archiving and communication system (Stryker, Inc.; Rutherford, NJ).

The average inclination angle was 44° (range, 24°-62°). Average acetabular component diameter was 55 mm (range, 46-70 mm). The average head diameter was 40 mm (range, 28-60 mm). These data were also stratified by gender (Table 3) and further analyzed to determine if there was an association with failure. In comparing all failures to nonfailures, there was a higher inclination angle in both overall failures (46.3° vs 44.1°; $P = .0061$) and failure due to metal complication (47.9° vs 44.3°; $P = .0119$). When analyzing further angle of inclination by gender for failures vs nonfailures, there was no significant difference in women for any failure mode but a higher inclination angle in men with failure due to metal complication (49.5° vs 43.3°; $P = .0423$). Head size was smaller in failures for women and larger in failures for men, but this was not statistically significant. A χ^2 analysis was performed to evaluate inclination angle less than or equal to 45° compared with inclination angle greater than 45° for both men and women failures and survivors. There was a statistically significant ($P = .0249$) correlation for overall failures and metal complication/loosening failure in men with an inclination angle greater than 45° but not for women (Table 3).

Discussion

This study examines the 15-year experience of a single center using MoM articulations in primary THA. Overall, our experience with MoM articulations has yielded a 94.6% survivorship at an average of 60-month follow-up. Of the 65 failures, 75% were associated with aseptic loosening or metal complications. There was one failure

Table 3. Implant Parameters by Gender and Survival

Parameter	Male			Female		
Inclination angle (deg)	43.4			45.3		.0003
Average cup diameter (mm)	57.3			52.6		.0000
Average head diameter (mm)	40.5			38.8		.0000
	Failed	Nonfail	*P*	Failed	Nonfail	*P*
Revision for any reason						
Inclination angle (deg)	45.9	43.2	.0789	46.6	45.1	.1073
% of THA >45°	70.1	9.7	.0000	53.3	46.0	.3755
Revision, loosening or metal complication						
Inclination angle (°)	45.7	43.3	.1916	46.3	45.2	.2918
% of THA >45°	81.8	10.8	.0000	47.2	47.4	.1431
Revision, metal complication						
Inclination angle (°)	49.5	43.3	.0426	46.8	45.3	.3283
% of THA >45°	100.0	10.9	.0002	43.8	46.6	.1967
Odds ratio for failure with inclination angle >45°	4.2			1.0		

due to dislocation in this MoM group in a patient with a 28-mm head. Despite the success of MoM articulations in improving stability and eliminating the risk of polyethylene osteolysis, we cannot overlook the adverse soft tissues reactions that occur with these devices. These reactions have ranged from unexplained groin pain to aseptic loosening to large cystic and fibrotic pseudotumors [14]. Unfortunately, these pseudotumors represent a devastating complication and reconstructive challenge (Fig. 1) [4]. The incidence in our series was low at 1.3%, whereas others have suggested that as many as 5% of patients will fail secondary to adverse soft tissue reactions.

The incidence of such complications increased in this series, when examined by gender. The incidence of metal-related complications was significantly higher ($P = .0126$) in women (2.2%) than in men (0.6%), with an increased odds ratio of 5.0. Aseptic loosening was also significantly higher ($P = .0006$) for women (4.3%) compared with men (1.1%). As we have learned more about metal-related complications, it is possible that some of the failures early in the series that were attributed to aseptic loosening may have been related to metallosis and hypersensitivity. In most of the articles published to date, female patients tend to have a higher incidence of adverse soft tissue reactions than male patients. There is little information, however, as to why. Possible reasons have been proposed such as differences in anatomy, which relates to implant sizes, range of motion, impingement, functional differences, hormonal factors, preoperative sensitization to metal from jewelry, among others [4,13,14,15].

The surgical technique of implantation has been shown to correlate with incidence of adverse tissue reactions. Several recent studies have associated metal-related complications with implant design and component placement. Vertical placement of components and excessive anteversion have been associated with increased metal ion production and therefore increased adverse soft tissue reactions. De Haan et al [10] have described the significance of the functional articular arc in MoM components. Vertical placement or a high inclination angle and excessive anteversion decrease the amount of bearing arc available for coverage. This can result in a smaller amount of coverage laterally over the head, leading to edge loading and increased metal wear [11,12,16]. This effect is magnified with decreased hemisphericity in some cup designs and in smaller cup and head sizes that may be more commonly used in female anatomy.

We analyzed our data to see whether the gender difference could be explained by differences in component size and inclination angles between men and women. In this series, women did have significantly smaller cups and heads than men. However, when women who failed were compared with women survivors, there was no significant difference in size. In this series, women did have a higher inclination angle than in men, but there was no statistical significance for women when comparing the inclination angle in failures and survivors. Higher inclination angles were observed in male failures due to metal complications. The χ^2 analysis demonstrated a significant increase in failure for men with an inclination angle more than 45°, but this was not true for women (Table 3). From these data, it does not appear that differences in survivorship between genders can be fully explained by smaller sizes of components used in women or inclination angle. The data suggest that failures in men are more dependent on inclination angle than in women. The analysis is limited in that we did not measure cup anteversion and calculate the specific articular surface arcs of the different cup designs in each patient. Also, 3 different cup designs were used during this time frame. The individual designs were analyzed, and statistical significance for gender differences in metal-related complications was shown in design 2, and there remained a trend toward increased failure in women in

designs 1 and 3. With these limitations aside, this suggests that for women, there are other more significant factors than cup placement and implant design and size that predispose them to metal complications.

The definition and knowledge of the exact incidence of adverse tissue reaction secondary to MoM articulations are needed. There is a need to determine which patients will benefit from MoM articulations and those patients who will not succeed with MoM. As we continue to learn more about the etiology and immunologic processes that lead to these reactions, we may gain more insight into these factors and help identify risks of complications in female patients. Despite our reported success with MoM articulations, we currently proceed with caution. We currently have expanded our contraindications to include avoiding this device in female patients because there has been a higher incidence of adverse tissue reactions reported in female patients.

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