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CLINICAL RESEARCH

Do Ion Levels In Hip Resurfacing Differ From Metal-on-metal THA at Midterm?

A. Moroni MD, L. Savarino BSc, M. Hoque PhD, M. Cadossi MD, N. Baldini MD

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Abstract

Background Metal-on-metal Birmingham hip resurfacing (MOM-BHR) is an alternative to metal-on-metal total hip arthroplasty (MOM-THA), especially for young and/or active patients. However, wear resulting in increased serum ion levels is a concern.

Questions/purposes We asked whether (1) serum chromium (Cr), cobalt (Co), and molybdenum (Mo) concentrations would differ between patients with either MOM-BHR or MOM-THA at 5 years, (2) confounding factors such as gender would influence ion levels; and (3) ion levels would differ at 2 and 5 years for each implant type.

Patients and Methods Ions were measured in two groups with either MOM-BHR (n = 20) or MOM-THA (n = 35) and a mean 5-year followup, and two groups with either MOM-BHR (n = 15) or MOM-THA (n = 25) and a mean 2-year followup. Forty-eight healthy blood donors were recruited for reference values.

Results At 5 years, there were no differences in ion levels between patients with MOM-BHR or MOM-THA. Gender was a confounding factor, and in the MOM-BHR group at 5 years, Cr concentrations were greater in females compared with those of males. Mean ion levels were similar in patients with 2 and 5 years of followup for each implant type. Ion levels in patients were sevenfold to 10-fold higher than in controls.

Conclusions As the metal ion concentrations in the serum at 5 years were in the range reported in the literature, we do not believe concerns regarding excessive metal ion levels after MOM-BHR are justified.

Level of Evidence Level III, therapeutic study. See the Guidelines for Authors for a complete description of level of evidence.

Each author certifies that he or she has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.
Each author certifies that his or her institution approved the human protocol for this investigation and that all the investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.
This work was performed at the Rizzoli Orthopaedic Institute.

A. Moroni (✉), M. Hoque, M. Cadossi
Department II of Orthopaedics and Traumatology, Bologna University, Rizzoli Orthopaedic Institute, Via G. C. Pupilli 1, 40136 Bologna, Italy
e-mail: a.moroni@ior.it

L. Savarino, N. Baldini
Laboratory for Orthopaedic Pathophysiology and Regenerative Medicine, Rizzoli Orthopaedic Institute, Bologna, Italy

N. Baldini
Department of Orthopaedics and Traumatology, Rizzoli Orthopaedic Institute, Bologna, Italy

Introduction

During the last decade, there has been an increase in the use of MOM-BHR, especially for young, active patients. MOM bearings have been reintroduced in orthopaedics because they exhibit reduced wear and osteolysis compared with standard metal-on-polyethylene bearings [2, 9, 21, 33]. This is important in young, active patients because the increased level of function exposes the implant to greater cumulative mechanical stress. In comparison to standard THA, MOM-BHR offers several advantages including femoral bone stock preservation, wider ROM, better functional outcomes, and lower rates of dislocation [1]. The latter is attributable to the increased stability offered by a large-diameter head which, unlike a smaller-diameter prosthetic head, replicates the size of the patient's original femoral head.

Although MOM-THA is in widespread use [24], concerns remain regarding wear and corrosion of the bearing surfaces and the subsequent increase in serum metal ion levels [2, 8, 10, 18, 28]. All metal implants corrode at a rate which is determined partly by their surface area [4]. For this reason, the introduction of large-diameter MOM bearings, as used in MOM-BHR, has prompted even more concern [5]. However, the large diameter and low radial clearance of MOM bearings are key factors in reducing dry contact and hydrodynamic pressures and important in improving lubrication performance [25]. The better lubrication regime observed with large-diameter MOM bearings with low clearance allows for a thicker fluid film which completely separates the articular surfaces, generating less wear [22, 35]. Despite the increased surface area available for corrosion [19, 40], the potentially reduced surface wear may diminish the production of metal ions. Nonetheless, concerns have been raised regarding increased postoperative serum metal ion concentrations [20]. A previous study of Cr, Co, and Mo values in patients treated with either MOM-BHR or MOM-THA showed higher serum metal ion levels in both groups compared with those of control subjects but no differences between the two implant groups at a followup of 2 years [27]. The same comparison has not been made at medium term, and confounding factors, such as gender, time of followup, and age in association with implant type have not been considered. In addition, discordant results have been reported concerning the wear rate of MOM bearings with time. An in vitro study showed a period of increased wear during the early run-in period, followed by much lower steady-state levels [36], but a clinical study contradicted this finding and showed an increasing trend in metal ion levels in blood or its fractions with time [31].

We asked whether (1) at a mean 5 years of followup serum ion concentrations would differ between patients with either MOM-BHR or MOM-THA, (2) whether confounding factors, in association with implant type, could have an effect on ion levels; and (3) metal ion levels would differ in patients with the same implants at 2 and 5 years of followup.

Patients and Methods

We performed an observational cross-sectional study and retrospectively created five groups of patients who were matched for femoral head diameter, acetabular component inclination angle [38], activity level, and body mass index: (1) Group A consisted of 20 patients who had unilateral MOM-BHR (Smith and Nephew, Memphis, TN, USA), with a minimum followup of 55 months (average, 58 months; range, 55–63 months); (2) Group B consisted of 35 patients who had Metasul® MOM-28-mm-THA (Zimmer, Warsaw, IN, USA) with a minimum followup of 48 months (average, 56 months; range, 48–66 months); (3) Group C consisted of 15 patients with the same unilateral MOM-BHR bearings as patients in Group A but with a minimum followup of 15 months (average, 24 months; range, 15–33 months); (4) Group D consisted of 25 patients with the same unilateral 28-mm-diameter THA bearings as in Group B but with a minimum followup of 14 months (average, 26 months; range, 14–38 months); and (5) Group E consisted of 48 healthy blood donors who were not receiving medication and who did not have metal implants (Table 1). Only five of the patients who had MOM-BHR who were followed up at 2 years (Group C) returned for a followup visit at 5 years (Group A), and only 15 of the patients who had MOM-THA who were followed up at 2 years (Group D) returned for a 5-year followup visit (Group B). It therefore was necessary to recruit additional patients for the current medium-term study. We excluded patients with infection, malignancy, bilateral hip implants, radiographic signs of loosening, osteolysis, and environmental or occupational chemical exposure. Patients were questioned regarding prescription drugs, alcohol intake, smoking history, and chronic occupational exposure to hazardous substances. Ingestion of prescription or nonprescription drugs containing metal ions, such as vitamin B12, were considered exclusion factors, as was renal impairment. None of the patients fell into these categories. The criteria used for the interview were reported previously [29]. We performed a pretest power analysis to determine sample sizes. For the effect size, we considered previous data concerning the MOM-BHR group at 2 years in comparison with control subjects, taking into account the fact that a difference had been found between the two groups. We used the means and two standard deviations of both groups and found that a sample size of 27 in each group gave a power of 71%. Consequently, the study was underpowered. One outlier in Group A was excluded from the statistical comparison between groups as the patient complained of severe hip pain and we thought that the high ion levels potentially could be associated with component loosening; CT showed no pseudotumors and a patch test was performed to exclude a hypersensitivity response to the implant. The clinical study was approved by the Institutional Ethics Committee on Human Research and the subjects signed informed consent forms to participate in the study.

The MOM-BHR was manufactured from a cast, high-carbon Co-Cr alloy. In Group A, the mean head diameter was 47 mm ± 7 mm (51 mm ± 5 mm and 40 mm ± 3 mm

Table 1. Profile of patients

Variable	Group A (20)	Group B (35)	Group C (15)	Group D (25)	Group E (48)
Gender					
Males	11	19	8	11	37
Females	9	16	7	14	11
Age (years)					
Mean ± standard error of mean (median)	53 ± 2 (54)	60 ± 2 (61)	49 ± 12 (44)	48 ± 8.5	42 ± 2 (40)
Range	30–65	41–79	26–75	30–64	20–71
Diagnosis					
Osteoarthritis	14	30	7	20	
Congenital hip dysplasia	3	1	6	4	
Rheumatoid arthritis			1		
Trauma	1	4	1		
Necrosis	2			1	
Followup (months)					
Mean ± standard error of mean (median)	58 ± 2.5 (57)	56 ± 5.5 (56)	24 ± 4.2 (24)	26 ± 4.4 (25)	
Range	55–63	48–66	15–33	14–38	
Bone mass index					
Mean ± standard error of mean (median)	28 ± 1 (27)	25 ± 0.6 (25)	29 ± 2 (28)	25 ± 0.7 (25)	
Range	22–37	22–30	24–40	22–30	
Activity level					
Mean ± standard error of mean (median)	7 ± 0.4 (6)	6.3 ± 0.3 (6)	8 ± 0.5 (8)	7 ± 0.4 (7)	
Range	5–10	4–8	6–10	4–10	
Cup inclination angle					
Mean ± standard error of mean (median)	46 ± 2.2 (45)	42 ± 2.1 (41)	40 ± 3.6 (41)	42 ± 1.3 (42)	
Range	30–60	28–58	28–61	31–58	
Harris hip score					
Mean ± standard error of mean (median)	95 ± 4.3 (95)	93 ± 4.3 (93)	95 ± 6.5 (100)	91 ± 5.2 (90)	
Range	88.3–100	80–98	83.5–100	80–100	

Group A = MOM-HR at 5 years; Group B = MOM-28-mm-THA at 5 years; Group C = MOM-HR at 2 years; Group D = MOM-28-mm-THA at 2 years; and Group E = control subjects.

in males and females, respectively; $p = 0.003$). The acetabular component was fixed without cement, whereas the femoral component was cemented. The Metasul® MOM-28-mm-THA (Zimmer) acetabular component consisted of a titanium (Ti) shell with an ultrahigh-molecular-weight polyethylene insert, containing a Co-Cr alloy liner. The Co-Cr alloy head was assembled on an uncemented, Ti alloy, femoral stem (Zimmer). The acetabular and femoral components were implanted without cement.

Followups were scheduled at 1, 3, and 6 months postoperatively and once a year thereafter. The Harris hip score (HHS) [16] was assessed at each followup and plain radiographs of the treated hip also were taken. At the 2- and 5-year followups, blood samples were obtained from the antecubital veins of fasting subjects using a disposable intravenous cannula. The blood was collected in metal-free Vacutainers (Becton Dickinson and Co, Meylan, France). To avoid contamination from the needle, the first 5 mL of blood withdrawn was discarded. Serum was separated by centrifugation at 400× *g* for 10 minutes at 4°C. Ion content was measured using a graphite furnace atomic absorption spectrometer (GFAAS) equipped with double background correction Deuterium/Zeeman (Thermo Fisher ICE4000; Thermo Fisher, Cambridge, UK).

Environmental and sampling contamination was avoided when determining ion content by using a dedicated room with efficient fume extraction and temperature monitoring. A clean bench area was reserved for solution preparation. Every item used from the time of sampling until analysis was regarded as a potential source of contamination, and was used only after soaking in 2% HNO_3 in twice-distilled and deionized water, followed by thorough rinsing in twice-distilled and deionized water. Each item then was checked using a nitric acid leach test to ensure that it did not contain detectable amounts of the relevant trace elements. Calibration was performed by applying the standard addition method and by using certified standard solutions at three concentrations for each element (NIST). Specimens were diluted with 0.1 vol. % HNO_3 and 0.05 vol. % Triton X100 (Santa Cruz Biotechnology, Inc., Heidelberg, Germany) and analyzed as 15-μL aliquots in triplicate. For Cr and Co analysis, magnesium nitrate was added as a matrix modifier. The accuracy and precision of the method was validated using SRM 1598 NIST human serum for all the elements. Additionally, UTAK® (UTAK Laboratories Inc., Valencia, CA, USA) normal and high-range trace elements were used for Cr. Test repeatability was ensured by rejecting ion levels with a relative standard deviation greater than 10%. All the results were expressed as nanograms per milliliter (equivalent to micrograms per liter and parts per billion). The sensitivity of the method was established by using detection limits for sample matrix, ie, 0.06 ng/mL for Cr, 0.08 ng/mL for Co, and 0.83 ng/mL for Mo. All ion levels below the detection limits were assigned detection level values.

We determined differences in serum ion concentrations between two groups of patients with either MOM-BHR or MOM-THA at 5 years followup using the Mann-Whitney U test; the general linear model (GLM) multivariate analysis was used to evaluate whether confounding factors, such as gender, time of followup, and age, in association with implant type, could influence serum ion concentrations; furthermore, the comparison between males and females in the MOM-BHR group at 5 years was made using the Mann-Whitney U test, calculated according to the exact test for small samples. Finally, the Mann-Whitney U test was used to determine whether the levels of metal ions in patients with the same type of implant were similar at 2 and 5 years. Data were analyzed using StatView 5.0.1.0 software (SAS Institute, Inc, Cary, NC). SPSS software (SPSS, Inc., Chicago, IL, USA) was used to apply the GLM and the Mann-Whitney U test, calculated according to Fisher's exact test.

Results

We found no differences in mean Co, Cr, and Mo levels between patients in Groups A and B (Table 2).

Time of followup and age did not affect ion values. On the contrary, the association between gender and implant type influenced ($p = 0.02$) Cr levels at 5 years followup; females had greater ($p = 0.013$; power of test, 69%) Cr levels compared with males (Table 3).

We found no differences between mean serum ion levels in patients with MOM-BHR at 2 years followup and those at 5 years followup (Group A versus Group C), or between the mean serum ion levels in patients with MOM-THA at 2 years followup and those at 5 years followup (Group B versus Group D) (Table 2). Ion levels in patients were

Table 2. Comparison of ion levels between groups

Ion	Group A	Group B	Group C	Group D	Group E	p Value Group A versus Group B	p Value Group A versus Group C	p Value Group A versus Group E	p Value Group B versus Group D
Chromium	2.26 ± 2.15 (1.63)	1.96 ± 2.11 (1.19)	2.18 ± 1.92 (1.53)	1.76 ± 1.70 (1.16)	0.25 ± 0.17 (0.28)	0.13	0.64	< 0.001	0.93
	0.49–10.47	0.06–8.00	0.69–7.24	0.22–6.6	0.06–0.67				
Cobalt	1.13 ± 1.19 (0.72)	1.44 ± 1.61 (0.86)	1.17 ± 2.28 (0.55)	1.35 ± 1.28 (0.98)	0.29 ± 0.03 (0.27)	0.48	0.14	< 0.001	0.67
	0.30–5.60	0.08–7.31	0.08–8.96	0.34–5.32	0.08–0.86				
Molybdenum	0.84 ± 0.03 (0.83)	Less than DL	0.90 ± 0.14 (0.83)	0.97 ± 0.27 (0.83)	Less than DL	0.43	0.07	0.23	0.06
	0.83–0.96		0.83–1.30	0.83–1.73					

Ion values were expressed as nanograms per milliliter (mean ± standard deviation, median value, minimum-maximum range); Mann-Whitney test used for all comparisons; DL = detection limit.

Table 3. Differences in chromium, cobalt, and molybdenum levels in patients with MOM-BHR at 5 years

Metal	Males	Females	p Value
Chromium	1.44 ± 0.54 (1.30) 0.88–2.47	3.17 ± 2.89 (2.36) 0.49–10.47	0.013
Cobalt	0.82 ± 0.58 (0.63) 0.30–2.27	1.47 ± 1.60 (1.20) 0.30–5.60	0.18
Molybdenum	0.85 ± 0.04 (0.83) 0.83–2.27	0.83 ± 0.01 (0.83) 0.83–0.84	0.72

Ion values expressed as nanograms per milliliter (mean ± standard deviation, median value, minimum-maximum range; Mann Whitney U test, Exact test for small samples used for all comparisons.

sevenfold to 10-fold greater than in control subjects. In particular, at medium term, Cr and Co values were greater ($p < 0.001$) in patients who had MOM-BHR and MOM-THA than in control subjects.

Discussion

Modern metal-on-metal hip resurfacing is considered an alternative to THA, especially for young and/or active patients. Theoretical and experimental studies, however, suggest metal wear may increase serum metal ion levels, which would be a cause for concern, particularly in the long term. A previous short-term study suggested that there were no differences in metal ion concentrations between large-diameter MOM-BHR bearings and small-diameter MOM-THA bearings [27]. Data from the same comparison at medium term are lacking. Furthermore, some authors have reported conflicting results regarding wear rate with time in MOM bearings [6, 31]. We therefore asked whether (1) at a mean 5-year followup serum ion concentrations would differ between two groups of patients with either MOM-BHR or MOM-THA, (2) whether confounding factors, such as gender, in association with implant type, could have an effect on ion levels; and (3) metal ion levels would differ in patients with the same implants at 2 and 5 years followup.

We acknowledge several limitations of our study. First is the small number of subjects enrolled. The pretest analysis gave relatively low power (71%); moreover, we split patients by gender, and two smaller subpopulations were created. To address these small subpopulations we used a statistical test for small samples and 69% power was calculated. Second, we were unable to perform a longitudinal study because only five of the patients who had MOM-BHR and 15 of the patients who had MOM-THA and who were studied at short term could be assessed at medium term. Consequently, additional patients who had been treated with these types of prostheses were recruited for the current medium-term study. Thus, our data are cross-sectional rather than longitudinal; moreover, the study is underpowered and, therefore, the data less persuasive. Nonetheless, we found what we believe are plausible trends, and we were able to show that (1) ion levels in patients who had MOM-BHR and MOM-THA are similar at 5 years, (2) ion levels in patients who had MOM-BHR are similar at 2 and 5 years; and (3) ion levels in patients who had MOM-BHR and MOM-THA are greater than in control subjects. Third, clinical interpretation of high ion levels is difficult because the in vivo threshold limit is still unknown. International and national working groups are discussing the reference values to be set for hazardous occupational toxicants in body fluids and biologic tolerance values for occupational exposure [13, 23, 26]. Studies reporting local or systemic damage caused by metal ion elevation are scarce [12, 30, 37]. Some authors have suggested a possible sensitizing effect of Cr and Co ions, but without evidence of a correlation between ion concentrations and exposure [14, 15].

At a followup of 5 years, we found ion concentrations in patients with MOM-BHR were similar to those in patients who had MOM-THA. Although there are no published reports which directly compare ion levels in patients with MOM-BHR or MOM-THA, our data are in the range previously reported. Some authors have evaluated ion levels, but the studies either had short-term followup or they were not comparative studies of MOM-BHR versus MOM-THA (Table 4) [3, 5, 11, 17, 27, 29, 34, 38, 39]. In addition, we found time of followup and age had no influence on serum ion levels, whereas gender in association with implant type influenced Cr levels, with females who had MOM-BHR showing an increase in Cr levels compared with males who had MOM-BHR. Our results confirm those reported by Vendittoli et al. [38], who evaluated blood ion concentrations in patients with MOM Durom hip resurfacing (Zimmer, Winterthur, Switzerland). Concerns have been raised regarding a substantially greater failure rate in females treated with MOM-BHR compared with males [7, 32]. Vendittoli et al. [38] suggested that female gender contributed to higher metal ion levels with resurfacing implants. They proposed that the difference in ion levels between genders may be secondary to differences in metal ion metabolism, such as different lean body mass, cellular or extracellular storage, or renal excretion. Another possible explanation for the gender difference could be the different hip anatomy and biomechanics between genders. However, there is no evidence to substantiate these hypotheses.

Finally, we found that mean ion levels were similar at 2 and 5 years in patients with either type of prosthesis. These results are not in agreement with those reported by Daniel et al. [6], who reported a decreasing trend in Cr blood

Table 4. Literature comparison of metal ion levels in patients with MOM-THA

Study	Analysis	Implant	Type of study	Time	Samples and ion values
Back et al. [3]	ICP-MS AAS	BHR	Prospective	Preoperative, 3, 6, 9 months, 1, and 2 years	Serum, mean values, nmol/L, 2 years Co: 31.8; Cr: 67.9
Clarke et al. [5]	ICP-MS	BHR Cormet 2000 Ultima	Retrospective	7–56 months (median, 16)	Serum, median values, nmol/L BHR/Cormet, 2000 Co: 38, Cr: 53 Ultima, Co: 22, Cr: 19
Daniel et al. [6]	ICP-MS	BHR	Prospective	Preoperative, 5 days, 2, 6 months, 1, 2, 4, 6 years	Whole blood, mean values, ng/mL 1 year, Co: 1.26; Cr: 2.41 4 years, Co: 1.21; Cr: 1.12 6 years, Co: 1.17; Cr 1.11
Garbuz et al. [11]	ICP-MS	Durom resurfacing Metasul	Prospective randomized	Preoperative, 2 months, 1, and 2 years	Serum, median values, ng/mL, 2 years Metasul, Co: 5.8; Cr: 2.9 Durom resurf., Co: 0.54; Cr: 0.8
Hart et al. [17]	ICP-MS	MOM resurfacing (type not specified)	Prospective	Not specified	Whole blood, median values, ng/mL Co: 4.5; Cr: 3.0
Moroni et al. [27]	AAS	BHR, Metasul (monolateral and bilateral)	Retrospective	2 years	Serum, mean values, ng/mL BHR, Co: 1.4; Cr: 2.3 Metasul, Co: 1.7; Cr: 1.3
Savarino et al. [29]	AAS	Metasul	Retrospective	14-38 months (median, 25)	Serum, mean values, ng/mL Co: 1.3; Cr: 1.7
Skipor et al. [34]	AAS	Resurfacing Conserve® Plus	Prospective	Preoperative, 3, 6, 12 months	Serum, mean values, ng/mL, 12 months Co: 1.1; Cr: 1.8
Vendittoli et al. [38]	ICP-MS	THR and Durom resurfacing system	Prospective randomized clinical trial	Preoperative, 3, 6, 12, 24 months	Mean values, ng/mL, 24 months Whole blood, Co: 0.6; Cr: 1.4 Serum, Co: 1.4; Cr: 1.4 Erythrocytes, Co: 0.8; Cr: 1.0
Witzleb et al. [39]	AAS	BHR and Metasul	Retrospective	3, 12, 24 months	Serum, median values, ng/mL, 24 months BHR, Co: 4.3; Cr: 5.1 Metasul, Co: 1.7; Cr: 1.22
Current study	AAS	BHR, Metasul (monolateral)	Retrospective	2 and 5 years	Serum, mean values, ng/mL 2 years Metasul, Co: 1.3; Cr:1.8, BHR Co: 1.2; Cr: 2.2 5 years Metasul, Co: 1.4; Cr:1.9, BHR Co: 1.1; Cr: 2.3

levels with time in patients with MOM-BHR implants. However, a precise comparison with our data was not possible. Daniel et al. [6] reported results obtained from whole blood, whereas our data come from serum.

Our cross-sectional study shows that patients with MOM-BHR or MOM-THA had a similar metal ion content at a mean followup of 5 years. In addition, contrary to the study by Daniel et al. [6], we found that ion levels were similar in patients who had MOM-BHR at 2 and 5 years followup. Patient age did not influence ion concentrations, but female gender was a determinant of increased serum Cr content in patients who had MOM-BHR. Although the systemic effects of an increase in serum metal ions are unknown [38], the elevation observed in females merits consideration during implant selection. The clinical relevance of the fact that the metal ion concentrations in patients who had MOM-BHR and MOM-THR were sevenfold to 10-fold greater compared with concentrations in the control subjects remains unclear. As the metal ion concentrations in the serum at 5 years were in the range reported in the literature, concerns regarding excessive metal ion levels after MOM-BHR are not justified.

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