

Comparing 1-year and 10-year whole blood metal ion results following Birmingham hip resurfacing for osteoarthritis

Scott J. Watt Kearns, BSc
Jonathan Bourget-Murray, MD,
CM
Kelly Johnston, MD
Jason Werle, MD

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Correspondence to:

J. Werle
Suite 335, 401 9th Ave. SW
Calgary, AB T2P 3C5
jason.werle@albertahealthservices.ca

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Background: Patients with metal-on-metal hip arthroplasty may develop adverse reactions to metal debris that can lead to clinically concerning symptoms, often needing revision surgery. As such, many regulatory authorities advocate for routine blood metal ion measurement. This study compares whole blood metal ion levels obtained 1 year following Birmingham Hip Resurfacing (BHR) to levels obtained at a minimum 10-year follow-up.

Methods: A retrospective chart review was conducted to identify all patients who underwent a BHR for osteoarthritis with a minimum 10-year follow-up. Whole blood metal ion levels were obtained at final follow-up in June 2019. These results were compared with patients' metal ion levels at 1 year.

Results: Of the 211 patients who received a BHR, 71 patients (54 males and 17 females) had long-term metal ion levels assessed (mean follow-up 12.7 ± 1.4 yr). The mean cobalt and chromium levels for patients with unilateral BHRs (43 males and 13 females) were 3.12 ± 6.31 µg/L and 2.62 ± 2.69 µg/L, respectively; for patients with bilateral BHRs (11 males and 4 females) cobalt and chromium levels were 2.78 ± 1.02 µg/L and 1.83 ± 0.65 µg/L, respectively. Thirty-five patients (27 male and 8 female) had metal ion levels tested at 1 year postoperatively. The mean changes in cobalt and chromium levels were 2.29 µg/L ($p = 0.0919$) and 0.57 µg/L ($p = 0.1612$), respectively.

Conclusion: Our results suggest that regular metal ion testing as per current regulatory agency guidelines may be impractical for asymptomatic patients. Metal ion levels may in fact have little utility in determining the risk of failure and should be paired with radiographic and clinical findings to determine the need for revision.

Contexte : Il arrive que les patients ayant subi une arthroplastie de la hanche métal sur métal développent des réactions indésirables aux débris métalliques qui causent des symptômes cliniques préoccupants, et souvent requièrent une reprise de l'intervention. C'est pourquoi de nombreux organismes de réglementation plaident pour que la mesure des ions métalliques dans le sang total soit intégrée aux examens de routine. Cette étude compare les taux d'ions métalliques obtenus 1 an après l'installation d'une prothèse Birmingham Hip Resurfacing (BHR) aux taux obtenus lors d'un suivi après 10 ans au minimum.

Méthodes : Un examen rétrospectif des dossiers a été effectué pour identifier tous les patients ayant reçu une prothèse BHR dans le cadre d'un traitement pour l'arthrose et un suivi après au moins 10 ans. Le taux d'ions métalliques dans le sang total a été mesuré lors d'un suivi final en juin 2019. Ces résultats ont été comparés aux taux d'ions métalliques obtenus un an après l'intervention.

Résultats : Des 211 patients ayant reçu la prothèse BHR, 71 patients (54 hommes et 17 femmes) ont fait l'objet d'une évaluation de leurs taux d'ions métalliques à long terme avec un intervalle de suivi moyen de 12,7 ans et un écart-type (ÉT) de ± 1,4 an. Les taux moyens de cobalt et de chrome chez les patients porteurs d'une prothèse BHR unilatérale (43 hommes et 13 femmes) étaient de 3,12, ÉT de ± 6,31 µg/L et de 2,62, ÉT de ± 2,69 µg/L, respectivement; chez les patients porteurs de 2 prothèses BHR (11 hommes et 4 femmes), les taux moyens de cobalt et de chrome étaient de 2,78, ÉT de ± 1,02 µg/L et de 1,83, ÉT de ± 0,65 µg/L, respectivement. Trente-cinq patients (27 hommes et 8 femmes) avaient obtenu leurs taux d'ions métalliques 1 an après l'intervention. Le changement moyen des mesures de cobalt et de chrome était de 2,29 µg/L ($p = 0,0919$) et de 0,57 µg/L ($p = 0,1612$), respectivement.

Conclusion : Nos résultats suggèrent que la mesure régulière des taux d'ions métalliques, conformément aux directives actuelles des organismes de réglementation, n'est peut-être pas commode dans les cas de patients asymptomatiques. En fait, elle pourrait être de peu d'utilité dans l'évaluation du risque d'échec et devrait être considérée conjointement aux résultats radiographiques et cliniques pour déterminer la nécessité d'une nouvelle intervention.

Hip resurfacing arthroplasty (HRA) provides an alternative to conventional total hip arthroplasty (THA) for young patients with debilitating hip arthritis. In fact, there is compelling evidence that HRA improves return to high-level activities and sports in young active men.¹ This is clinically relevant as younger patients have reported decreased satisfaction owing to the imposed limitations following a THA.^{1,2} The Birmingham Hip Resurfacing (BHR) system has excellent functional outcomes and offers a viable treatment option with a revision rate at 10 years comparable to conventional THA.³⁻⁵

As with any metal-on-metal (MoM) hip arthroplasty, there is ongoing concern regarding production of metal (cobalt and chromium) wear debris. Although most patients with MoM hip arthroplasty have well-functioning hips, a subset of patients will develop adverse reactions to metal debris. This can lead to clinically concerning symptoms, often needing revision surgery, with a subsequent high risk of poor outcome.⁶⁻⁸ Furthermore, these debris may have systemic effects involving multiple organ systems.⁹⁻¹¹

In an attempt to recognize these complications early, several regulatory agencies have developed recommendations for follow-up of patients with MoM hip arthroplasty. The Medicines and Healthcare Products Regulatory Agency (MHRA) advocates for routine whole blood metal ion measurement for all patients with an MoM prosthesis.¹² Currently, they recommend that all asymptomatic patients with a BHR undergo metal ion testing at 1 year postoperative, 7 years postoperative, and every 3 years thereafter. Despite the lack of scientific evidence,¹³ the MHRA has determined whole blood metal ion levels of 7 µg/L or more (119 nmol/L cobalt or 134.5 nmol/L chromium) in 1 or both metals to indicate the need for closer follow-up and cross-sectional imaging.¹² However, the sensitivity and specificity of this threshold have been shown to be 52% and 89%, respectively.¹⁴

Although whole blood metal ion measurement has been recognized as a valuable screening tool for adverse reactions to metal debris,^{15,16} little is known about their dynamic change over time. Tribological and clinical studies have described a characteristic wear pattern of MoM HRA with an initial “run-in period,” followed by a lower-wear situation known as “steady state.”¹⁷ How the wear evolves during the steady state is not completely understood, especially in asymptomatic patients.

The purpose of this study was to compare whole blood metal ion levels obtained 1 year postoperative to levels obtained beyond 10 years in a cohort of patients who received a BHR for osteoarthritis.

METHODS

Study design

We retrospectively studied consecutive patients who received a BHR (Smith & Nephew Orthopaedics Ltd,

Warwick, UK) for osteoarthritis with a minimum 10-year follow-up. All procedures were performed by a single nondesigner fellowship-trained arthroplasty surgeon (J.W.) at a Canadian university hospital between 2003 and 2009. For the purpose of this study, only patients with an underlying diagnosis of osteoarthritis were included for analysis. We included patients who agreed to return to clinic for long-term follow-up in June 2019 and to have their whole blood metal ions tested. To be eligible for this study, patients were required to have healthy renal function (creatinine < 120 µmol for males and < 110 µmol for females) to ensure adequate metal ion clearance.

A retrospective review of electronic medical records from the senior surgeon's practice was performed to identify all patients who satisfied the inclusion criteria. We identified 243 consecutive BHRs, which were performed in 211 patients. These patients were contacted by telephone and offered an in-person follow-up appointment.

All patients' follow-up appointment in clinic occurred in June 2019, at which time we obtained written informed consent from all participants. All patients were given a requisition for a blood test to assess whole blood metal ion levels and were asked to have the test done as soon as possible. To ensure accuracy and reliability of our results, all metal ion measurements reported in this study were from a single recognized Canadian laboratory. This is paramount in the interpretation of results, as differences in absolute values for cobalt and chromium have been shown to exist among laboratories owing to differences in calibration between assays.¹⁸

Only patients who completed their blood test were included in this study. Patient baseline characteristics and 1-year whole blood metal ion levels were retrospectively collected. We did not expect all patients to have had metal ion levels investigated at 1 year postoperative given that before 2010 metal ion testing was not routinely performed at our institution. The decision to measure metal ion levels was driven by patient symptomatology and radiographic findings. This practice changed following MHRA guidance issued in 2010. Patients who had their metal ion level tested at 1 year postoperative served to compare changes over the study period.

This study was approved by the local Conjoint Health Research Ethics Board.

Operative technique

All operations were carried out through a standard posterior surgical approach to obtain a 360° view of the acetabulum for optimal component positioning. Most patients received a spinal anesthetic at the time of the procedure, yet anesthetic type was left to the discretion of the anesthesiologist. Standard weight-based dose cefazolin was used for perioperative antibiotic prophylaxis.

All acetabular components were uncemented, relying on the porous, hydroxyapatite-coated surface for

Table 1. Characteristics of patients in whom blood metal ion levels were tested at long-term follow-up

Characteristic	Study cohort (n = 71 patients)		
	Total	Unilateral BHR	Bilateral BHR
Gender, n (%)	71 (100)	56 (79)	15 (21)
Male	54 (76)	43 (61)	11 (15)
Female	17 (24)	13 (18)	4 (6)
Age at surgery, mean ± SD (range), yr	49.4 ± 7.6 (24–68)	49.1 ± 8.6 (24–68)	50.0 ± 4.7 (39–55)
Male	50.9 ± 6.6 (36–68)	51.6 ± 6.9 (36–68)	48.7 ± 5.3 (39–54)
Female	44.1 ± 9.0 (24–55)	40.6 ± 8.7 (24–53)	52.1 ± 2.5 (49–55)
Body mass index at surgery, mean ± SD, kg/m ²	28.1 ± 6.0	27.2 ± 3.5	29.9 ± 9.0
Male	28.4 ± 5.2	27.8 ± 2.5	30.8 ± 10.9
Female	25.6 ± 5.1	24.6 ± 4.9	28.3 ± 5.4
Follow-up, mean ± SD (range), yr	12.7 ± 1.4 (10–15.1)	12.7 ± 1.3 (10–15.1)	12.4 ± 1.6 (10–15.1)

BHR = Birmingham Hip Resurfacing; SD = standard deviation.

long-term stability. The acetabula were underreamed to allow press-fit fixation. The acetabular components were then fully impacted with an intended 40°–45° of inclination and 15°–20° of anteversion.

The external diameter of the acetabular components ranged from 48 mm to 62 mm. The diameter of the acetabular component was either 6 mm or 8 mm larger than the corresponding femoral component. Osteophytes around the acetabulum were removed to avoid impingement.

Osteophytes on the femoral neck were removed to ensure an accurate measurement of the head:neck ratio. Implant sizing based on the femoral neck also ensured adequate head–neck offset. The McMinn alignment jig was used for intraoperative femoral orientation. All BHR femoral components were cemented using Simplex T bone cement (Stryker). The femoral components were placed in 5°–10° of valgus relative to the axis of the femoral neck.

All patients followed a standard postoperative hip arthroplasty care pathway. This included receiving dalteparin for 28 days postoperatively for venous thromboembolism prophylaxis and discharge from the acute care hospital 24–48 hours postoperatively. Patients were encouraged to mobilize early, with immediate weight bearing as tolerated. All patients had clinical follow-up at 2 weeks, 6 weeks, 3 months, and 1 year following surgery. Outpatient physiotherapy was instituted for all patients by 6 weeks postoperatively. A graduated return to sport was allowed without restrictions after 3 months.

Statistical analysis

All data were analyzed using Stata software (version 14). Baseline characteristics are presented as means with standard deviations (SD) or as a range. Mean metal ion levels are presented as means with SD, range and 95% confidence intervals (CI). Unpaired *t* tests were used to compare mean metal ion levels at 10 years between sexes. Paired *t* tests were used to compare changes in metal ion

levels during the follow-up period. We considered results to be significant at *p* < 0.05. All bilateral cases were considered as a single case for analysis.

RESULTS

Of the 113 patients scheduled for clinical follow-up in June 2019, 6 did not attend their appointment. Therefore, 107 patients were available for clinical follow-up.

Seventy-one patients (54 males and 17 females) completed their blood test following their appointment. Of these patients 56 (43 males and 13 females) had a unilateral BHR. These patients had a mean follow-up of 12.7 ± 1.3 (range 10–15.1) years and a mean age at index surgery of 49.1 ± 8.6 years. The mean body mass index (BMI) of these patients was 27.2 ± 3.5 kg/m². Fifteen patients (11 males and 4 females) had bilateral BHR. All 15 patients underwent staged BHR. These patients had a mean follow-up of 12.4 ± 1.6 (range 10–15.1) years and a mean age at index surgery of 50.0 ± 4.7 years. The mean BMI, measured at the time of the first procedure, of patients with bilateral BHR was 29.9 ± 9 kg/m². Characteristics of this cohort are presented in Table 1.

Thirty-five patients (49.3%) in this cohort were found to have had their metal ion levels tested 1 year postoperative. Characteristics of these 35 patients are presented in Table 2. All study participants had healthy renal function (serum creatinine was 87.3 ± 13.4 µmol/L in males and 75 ± 7.7 µmol/L in females).

Whole blood metal ion analysis

The mean long-term whole blood metal ion concentrations are presented in Table 3. The mean cobalt and chromium levels at long-term follow-up of the 56 patients with unilateral BHR were 3.12 ± 6.4 µg/L and 2.62 ± 2.7 µg/L, respectively. No significant difference was observed when cobalt and chromium levels were compared between sexes, although only 24% of patients in this group were female (cobalt: *p* = 0.21; chromium, *p* = 0.85).

Table 2. Characteristics of patients in whom blood metal ion levels were tested 1 year postoperative

Characteristic	Study cohort (n = 35 patients)		
	Total	Unilateral BHR	Bilateral BHR
Gender, n (%)	35 (100)	29 (83)	6 (17)
Male	27 (77)	22 (63)	5 (14)
Female	8 (23)	7 (20)	1 (3)
Age at surgery, mean ± SD (range), yr	46.8 ± 5.5 (34–55)	46.5 ± 6.1 (34–56)	48.9 ± 3.9 (43–53)
Male	47.6 ± 5.0 (36–56)	47.9 ± 5.4 (36–56)	48.7 ± 4.3 (43–53)
Female	44.2 ± 6.5 (33–53)	42.9 ± 6.6 (34–53)	23.4
Body mass index at surgery, mean ± SD, kg/m ²	27.3 ± 6.0	26.2 ± 3.3	33.1 ± 12.7
Male	28.5 ± 6.0	27.4 ± 2.2	35.5 ± 13.2
Female	22.8 ± 3.1	22.7 ± 3.4	23.4
Follow-up, mean ± SD (range), yr	13.4 ± 1.0 (10–15.1)	13.7 ± 0.8 (10.1–15)	13.1 ± 1.3 (10–15.1)

BHR = Birmingham Hip Resurfacing; SD = standard deviation.

Table 3. Metal ion levels tested at long-term follow-up

Metal ion	Study cohort (n = 71 patients)*			
	Mean ± SD	Range	95% CI	p value
Chromium, unilateral, µg/L (ppm)	2.62 ± 2.7	0.66–16.69	1.90 to 3.32	0.85
Male	2.42 ± 2.5	0.66–16.69	1.67 to 3.17	
Female	3.12 ± 3.2	0.88–10.43	1.36 to 4.88	
Cobalt, unilateral, µg/L (ppm)	3.12 ± 6.4	0.58–43.71	1.39 to 4.73	0.21
Male	2.47 ± 3.4	0.58–21.6	1.47 to 3.48	
Female	4.89 ± 11.7	0.91–43.65	–1.4 to 311.25	
Chromium, bilateral, µg/L (ppm)	1.83 ± 0.7	1.24–4.72	1.64 to 2.12	0.76
Male	2.48 ± 0.9	1.24–4.72	1.93 to 3.03	
Female	2.32 ± 0.8	1.64–3.49	1.58 to 3.05	
Cobalt, bilateral, µg/L (ppm)	2.78 ± 1.0	1.06–3.75	2.28 to 3.33	0.64
Male	2.08 ± 0.8	1.06–3.75	1.59 to 2.55	
Female	1.88 ± 0.3	1.52–2.23	1.62 to 2.18	

BHR = Birmingham Hip Resurfacing; CI = confidence interval; SD = standard deviation.
*Unilateral BHR, n = 56; bilateral BHR, n = 15.

The mean cobalt and chromium levels at long-term follow-up of the 15 patients with bilateral BHR were $2.78 \pm 1.0 \mu\text{g/L}$ and $1.83 \pm 0.7 \mu\text{g/L}$, respectively.

The 1-year mean whole blood metal ion levels of the 35 patients for whom these data were available are presented in Table 4. The mean cobalt and chromium levels at 1 year for the entire cohort were $1.73 \pm 1.8 \mu\text{g/L}$ and $2.46 \pm 2.1 \mu\text{g/L}$, respectively, and the mean long-term cobalt and chromium levels were $4.02 \pm 8.4 \mu\text{g/L}$ and $3.03 \pm 3.2 \mu\text{g/L}$. Neither changes in cobalt nor chromium levels were deemed significant (cobalt: $p = 0.09$; chromium: $p = 0.16$). The mean cobalt and chromium levels for unilateral cases at 1 year were $1.64 \pm 1.9 \mu\text{g/L}$ and $2.32 \pm 2 \mu\text{g/L}$, respectively, and the mean long-term cobalt and chromium levels were $4.32 \pm 9.3 \mu\text{g/L}$ and $3.04 \pm 3.5 \mu\text{g/L}$, respectively. Neither changes in cobalt nor chromium were deemed significant (cobalt: $p = 0.07$; chromium: $p = 0.08$). The mean cobalt and chromium levels for bilateral cases at 1 year were $2.08 \pm 0.9 \mu\text{g/L}$ and $3.14 \pm 2.0 \mu\text{g/L}$, respectively, and the mean long-term cobalt and chromium levels were $2.49 \pm 1.3 \mu\text{g/L}$, and $2.93 \pm 1.1 \mu\text{g/L}$, respectively. Ion level changes in this

group did not reach statistical significance (cobalt: $p = 0.06$; chromium: $p = 0.73$).

Four patients (5.6%) had metal ion levels above the MHRA's recommended threshold of $7 \mu\text{g/L}$ at the time of long-term follow-up. Two of these patients had elevated metal ion levels at long-term follow-up but normal levels at 1 year postoperative.

Patient 1

In a female patient who received unilateral BHR 14.1 years ago, cobalt and chromium levels 1 year postoperative were $5.73 \mu\text{g/L}$ and $2.55 \mu\text{g/L}$, respectively. At final follow-up she was found to have elevated cobalt and chromium levels: $43.65 \mu\text{g/L}$ and $10.17 \mu\text{g/L}$, respectively. Despite elevated metal ion levels, she was asymptomatic and voiced no concerns; however, at the latest follow-up she had a Harris Hip Score of 62 and a UCLA Activity Score of 5, suggesting unsatisfactory hip function and an inactive lifestyle. The femoral head size of her implant was 42 mm, and at latest follow-up this patient had an acetabular cup inclination (determined by the angle made by the acetabular cup and the horizontal axis)

Table 4. Secondary analysis comparing 1-year and long-term metal ion levels

Metal ion	Study cohort (n = 35 patients)*			p value
	Mean ± SD	Range	95% CI	
1-year chromium level, µg/L (ppm)	2.46 ± 2.1	0.78–11.06	1.76–3.16	0.16
Unilateral	2.32 ± 2.0	0.78–11.06	1.61–3.00	
Bilateral	3.14 ± 2.0	0.92–7.71	1.33–4.79	
Long-term chromium level, µg/L (ppm)	3.03 ± 3.2	0.66–16.64	1.97–4.09	0.08 (unilateral) 0.73 (bilateral)
Unilateral	3.04 ± 3.5	0.66–16.64	1.74–4.61	
Bilateral	2.93 ± 1.1	1.71–4.72	1.92–3.88	
1-year cobalt level, µg/L (ppm)	1.73 ± 1.8	0.33–9.09	1.13–2.33	0.09
Unilateral	1.64 ± 1.9	0.33–9.09	0.89–2.95	
Bilateral	2.08 ± 0.9	0.94–4.49	1.01–3.08	
Long-term cobalt level, µg/L (ppm)	4.02 ± 8.4	0.58–43.68	1.24–6.8	0.07 (unilateral) 0.06 (bilateral)
Unilateral	4.32 ± 9.3	0.58–43.68	1.18–7.69	
Bilateral	2.49 ± 1.3	1.51–3.77	1.65–3.25	

BHR = Birmingham Hip Resurfacing; CI = confidence interval; SD = standard deviation.
 *Unilateral BHR, n = 29; bilateral BHR, n = 6.

of 50°. Unfortunately, the patient was undergoing chemotherapy for metastatic gastric carcinoma, which could explain her inactivity. For this reason, the patient refused further investigation (metal artifact reduction sequence magnetic resonance imaging; MARS-MRI), as she had no interest in a possible revision surgery.

Patient 2

In a male patient who received bilateral BHR — the first performed 15.01 years ago and the second 9 years later — cobalt and chromium levels 1 year postoperative were 1.31 µg/L and 1.88 µg/L, respectively. At final follow-up he was found to have elevated cobalt levels (7.73 µg/L) but satisfactory chromium levels (5.63 µg/L). This patient did not present with any symptoms at follow-up and voiced no concerns. He had a Harris Hip Score of 97 and UCLA Activity Score of 7 at his latest follow-up, indicating a well-functioning prosthesis and a relatively active lifestyle. The femoral head size of his implants was 54 mm, and at latest follow-up this patient had an acetabular cup inclination of 42° for one hip and 50° for the other hip. The patient’s metal ion levels will continue to be monitored closely; however, revision surgery is not currently indicated.

Patient 3

In a male patient who received bilateral BHR — the first performed 14.1 years ago and the second 9.5 years before the last follow-up — long-term cobalt and chromium concentrations were elevated, at 21.65 µg/L and 16.69 µg/L, respectively. His cobalt and chromium levels at 1 year postoperative were also elevated, at 9.13 µg/L and 11.06 µg/L, respectively. This patient was asymptomatic. A MARS-MRI was obtained after a follow-up visit in clinic in 2019; it showed particle disease of the bilateral hips, with osteolysis and periarticular soft tissue collections. Just before the MARS-MRI the patient had a Harris

Hip Score of 100 and a UCLA Activity Score of 9, suggesting exceptional hip function and a very active lifestyle. The femoral head size of his implants was 54 mm, and at latest follow-up he had an acetabular cup inclination of 54°. The patient has not consented to revision surgery but is being monitored.

Patient 4

In a female patient who received bilateral BHR — the first performed 13.01 years ago and the second 9.7 years ago — the long-term cobalt level was normal (4.66 µg/L), but chromium was elevated (10.42 µg/L). She had not had metal ion levels determined at 1 year postoperative. The patient was asymptomatic. At the latest follow-up she had a Harris Hip Score of 99 and a UCLA Activity Score of 6, suggesting good hip function and a moderately active lifestyle. The femoral head size of her implants was 46 mm, and at latest follow-up she an acetabular cup inclination of 55°. The patient’s metal ion levels will continue to be monitored closely; however, revision surgery is not currently indicated.

DISCUSSION

While the screening of asymptomatic patients with BHR continues to be challenging, little evidence is available regarding the serial metal ion level changes that occur over time with these implants. In June 2017, the MHRA issued updated guidance for follow-up of patients with MoM hip replacements. They now recommend more intensive follow-up and screening. Unfortunately, some of the recommendations are not supported by scientific evidence and have not been found to be cost-effective.¹³

The premise of metal ion testing is that metal ion levels in the blood can serve as a surrogate marker of implant wear, thus potentially serving as a screening tool for identifying patients at risk of adverse reactions to metal debris.

These patients are at risk of irreversible soft tissue destruction and/or periprosthetic osteolysis.⁶ Importantly, it is recognized that such bone and soft tissue damage can occur without any noticeable symptoms.¹⁹ Timely assessment and treatment of these patients is paramount, as delays in diagnosis can risk jeopardizing the outcome of future revision surgery.

The MHRA has set a threshold of 7 µg/L or more of 1 or both metals to indicate the need for closer follow-up and cross-sectional imaging. This threshold has recently been shown to have a sensitivity and specificity of 52% and 89%, respectively, for predicting adverse reactions to metal debris.¹⁴ By reducing the threshold to 4.97 µg/L, specificity improved to 86%, but sensitivity was reduced to 63%. Consequently, Matharu and colleagues conducted a multicentre validation study of newly devised implant-specific blood metal ion thresholds to predict adverse reactions to metal debris in patients with MoM hip arthroplasty.²⁰ By using a threshold of 2.15 µg/L for cobalt in patients with a unilateral BHR and 5.5 µg/L for either cobalt or chromium in those with bilateral BHR, they improved the sensitivity and specificity to distinguish between patients with and without adverse reactions to metal debris to 78.9% and 86.7% for unilateral BHR and 70.6% and 86.8% for bilateral BHR. However, the blood metal ions were tested once at a mean of 6.9 years postoperative, which limits the applicability of the result beyond 10 years. Interestingly, Pahuta and colleagues undertook a meta-analysis and concluded that blood metal ion testing has no role in the diagnostic algorithm for adverse reactions to metal debris regardless of the threshold owing to the high rate of false positives.²¹

Several longitudinal studies have found little variation in metal ion levels in asymptomatic patients (including high-risk patients) in the short and long-term.^{22–24} Low and colleagues prospectively studied 152 asymptomatic patients with HRA patients who had serial ultrasounds.²⁵ They showed that asymptomatic patients with normal initial metal ion levels (< 2 µg/L) and normal initial ultrasound scans at a mean of 4 years from the index surgery had no risk of developing new pseudotumours within 5 years of the initial assessment, highlighting the value of comprehensive initial follow-up of patients. These findings are in keeping with those of earlier studies that showed that asymptomatic patients with normal cross-sectional imaging 2–8 years from the index surgery experience very few changes when imaging is repeated within 3 years.^{26,27} These findings suggest that asymptomatic patients may not require annual follow-up and metal ion testing, but that instead testing can be done at longer intervals.

How metal ion levels change over time remains unclear. Back and colleagues found that serum metal ion levels peaked between 6 and 9 months postoperatively and declined thereafter,²⁸ whereas Heisel and colleagues found that serum cobalt and chromium levels continu-

ously increased during the first 6 months and showed an insignificant decrease afterward.¹⁷ Therefore, it has become increasingly accepted that metal ion levels increase in the immediate postoperative period and then plateau and sometimes decline, raising the question of their use in routine screening during long-term follow-up. Daniel and colleagues prospectively followed 26 consecutive male patients with well-functioning unilateral BHR and determined blood ion levels at 1, 4 and 6 years.²⁹ Compared with levels at 1 year, they found a decreasing trend in the mean levels at 4 and 6 years.²⁹ The reduction observed in chromium levels was deemed significant, but this was not the case for cobalt.²⁹ This trend was corroborated in 80 unilateral BHRs with sequential ion measurements, however both cobalt and chromium levels were found to decrease significantly at 10 years.²² While our results did show an increase in metal ion levels between 1- and 10-year follow-up, the increase was not significant and well below the MHRA threshold, corroborating the belief that in asymptomatic patients with well-functioning BHRs, metal ion levels infrequently increase beyond 7 µg/L following the “run-in phase.” This may be partly explained by the film that is frequently produced on the articular surface of implants, which may act as a protective feature preventing further corrosion.³⁰

We do acknowledge that 2 of our patients (5.7%) had elevated metal ion levels at long-term follow-up despite their 1-year levels being normal. Numerous studies have attempted to define factors involved with increasing metal ion levels. Greater acetabular component inclination has been correlated with increasing metal ion levels, leading to greater edge loading and resulting in component wear.²² In addition, low contact patch to rim distance (< 10 mm) also places an articulation at risk for edge loading and independently predicts elevated metal ion levels.³¹ This parameter is defined as the distance between the centre of the area of contact between the femoral head and the acetabular component to the acetabular rim.³¹ In fact, this variable alone has a sensitivity and specificity of 83.3% and 83.5%, respectively, in predicting blood cobalt levels above 7 µg/L.³² In addition, smaller femoral head size (< 48 mm) and female sex have been associated with increased metal ion levels.³³ Of all these factors, femoral head size is responsible for the highest proportion of variance in blood metal ions.³³ Two of the 4 patients who had elevated metal ion levels at long-term follow-up had a femoral head size smaller than 48 mm. At latest follow-up all 4 patients had acetabular cup inclination greater than the intended 40°–45°. Therefore, this may suggest that patients should be subject to a comprehensive examination 1 year postoperative to ensure satisfactory metal ion levels, acetabular inclination, and patch to rim contact. Patients who satisfy these criteria may be able to have metal ions tested at longer

intervals than those currently recommended by the MHRA. Although the utility of metal ion screening remains a matter of debate, it is important to remain cognizant that increased metal ion levels can have systemic effects, therefore playing a role in the follow-up period.

Limitations

While the present study has introduced new information about long-term whole blood metal ion levels following BHR, it should be interpreted in light of its limitations. These include a small sample size and the lack of a control group, reducing the power of our results. Although only 5.7% of patients had elevated metal ion levels at long-term follow-up, the upper limit of the confidence interval was 19%, which limits the generalizability of our results. Many patients were excluded from the study as they did not follow through with the blood test requisitioned following their appointment. Of the 29 patients who received unilateral BHR and had 1-year and long-term ion levels determined, 7 patients had had a second BHR, but it was performed less than 10 years before latest clinical follow-up. This may help to explain the greater increase seen in the unilateral group than the bilateral group between the 2 time points. Despite these shortcomings, this study expands on current knowledge while allowing for introspection on the routine use of metal ion measurements during clinical follow-up of patients with a BHR. Further research is necessary to develop evidence-based guidelines.

CONCLUSION

Patients who have a well-functioning BHR beyond 10 years showed no significant increase in whole blood metal ion levels compared with levels at 1 year postoperative. Our results indicate that routine screening of metal ion levels, as per MHRA guidelines, may be unnecessary in asymptomatic patients with a well-functioning BHR. The clinical and radiographic outcomes for this patient cohort have been published previously.³⁴ We suggest that whole blood metal ion levels be routinely assessed at 1 year postoperative while testing thereafter be judicious and based on history and clinical findings. If a patient becomes symptomatic, metal ion levels should not serve as a standalone test, but rather done in addition to MARS-MRI or ultrasonography, as these imaging methods carry more weight in decision-making.

Affiliations: From the Cumming School of Medicine, University of Calgary; and Rockyview General Hospital & Alberta Hip and Knee Clinic, Calgary, Alta.

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References

- Hellman MD, Ford MC, Barrack RL. Is there evidence to support an indication for surface replacement arthroplasty? A systematic review. *Bone Joint J* 2019;101-B(Suppl A):32-40.
- Lieberman JR, Polkowski GG, Della Valle CJ. Practice management strategies among current members of the American Association of Hip and Knee Surgeons. *J Arthroplasty* 2016;31(Suppl):3-6.
- Holland JP, Langton DJ, Hashmi M. Ten-year clinical, radiological and metal ion analysis of the birmingham hip resurfacing: from a single, non-designer surgeon. *J Bone Joint Surg Br* 2012;94:471-6.
- Coulter G, Young DA, Dalziel RE, et al. Birmingham hip resurfacing at a mean of ten years: results from an independent centre. *J Bone Joint Surg Br* 2012;94:315-21.
- Murray DW, Grammatopoulos G, Pandit H, et al. The ten-year survival of the Birmingham hip resurfacing: an independent series. *J Bone Joint Surg Br* 2012;94:1180-6.
- Grammatopoulos G, Pandit H, Kwon YM, et al. Hip resurfacing revised for inflammatory pseudotumor have a poor outcome. *J Bone Joint Surg Br* 2009;91:1019-24.
- Crawford DA, Adams JB, Morris MJ, et al. Revision of failed metal-on-metal total hip arthroplasty: midterm outcomes of 203 consecutive cases. *J Arthroplasty* 2019;34:1755-60.
- Matharu GS, Pandit HG, Murray DW. Poor survivorship and frequent complications at a median of 10 years after metal-on-metal hip resurfacing revision. *Clin Orthop Relat Res* 2017;475:304-14.
- Catelas I, Lehoux EA, Hurda I, et al. Do patients with a failed metal-on-metal hip implant with a pseudotumor present differences in their peripheral blood lymphocyte subpopulations? *Clin Orthop Relat Res* 2015;473:3903-14.
- Gessner BD, Steck T, Woelber E, et al. A systematic review of systemic cobaltism after wear or corrosion of chrome-cobalt hip implants. *J Patient Saf* 2019;15:97-104.
- Prentice JR, Clark MJ, Hoggard N, et al. Metal-on-metal hip prostheses and systemic health: a cross-sectional association study 8 years after implantation. *PLoS One* 2013;8:e66186.
- Medical device alert: all metal-on-metal (MoM) hip replacements. London (UK): Medicines & Healthcare Products Regulatory Agency (MHRA); 2017. Available: https://assets.publishing.service.gov.uk/media/5954ca1ded915d0baa00009b/MDA-2017-018_Final.pdf (accessed 2020 May 27).
- Matharu GS, Mellon SJ, Murray DW, et al. Follow-up of metal-on-metal hip arthroplasty patients is currently not evidence based or cost effective. *J Arthroplasty* 2015;30:1317-23.
- Hart AJ, Sabah SA, Bandi AS, et al. Sensitivity and specificity of blood cobalt and chromium metal ions for predicting failure of metal-on-metal hip replacement. *J Bone Joint Surg Br* 2011;93:1308-13.
- Reito A, Puolakka T, Elo P, et al. Outcome of Birmingham Hip Resurfacing at ten years: role of routine whole blood metal ion measurements in screening for pseudotumours. *Int Orthop* 2014;38:2251-7.

16. De Smet K, De Haan R, Calistri A, et al. Metal ion measurement as a diagnostic tool to identify problems with metal-on-metal hip resurfacing. *J Bone Joint Surg Am* 2008;90(Suppl 4):202-8.
17. Heisel C, Streich N, Krachler M, et al. Characterization of the running-in period in total hip resurfacing arthroplasty: an in vivo and in vitro metal ion analysis. *J Bone Joint Surg Am* 2008;90(Suppl 3):125-33.
18. Saini R, Railton P, Boyd J, et al. Concordance between laboratories in metal ion testing in patients with metal-on-metal hip implants. *Can J Surg* 2019;62:9-13.
19. Almousa SA, Greidanus NV, Masri BA, et al. The natural history of inflammatory pseudotumors in asymptomatic patients after metal-on-metal hip arthroplasty. *Clin Orthop Relat Res* 2013;471:3814-21.
20. Matharu GS, Berryman F, Brash L, et al. The effectiveness of blood metal ions in identifying patients with unilateral Birmingham hip resurfacing and Corail-Pinnacle metal-on-metal hip implants at risk of adverse reactions to metal debris. *J Bone Joint Surg Am* 2016;98:617-26.
21. Pahuta M, Smolders JM, Sustante JL, et al. Blood metal ions are not a useful test for adverse reactions to metal debris: a systematic review and meta analysis. *Bone Joint Res* 2016;5:379-86.
22. van der Straeten C, Van Quickenborne D, De Roest B, et al. Metal ion levels from well-functioning Birmingham hip resurfacings decline significantly at ten years. *Bone Joint J* 2013;95-B:1332-8.
23. Reito A, Moilanen T, Puolakka T, et al. Repeated metal ion measurements in patients with high-risk metal-on-metal hip replacement. *Int Orthop* 2014;38:1353-61.
24. Reito A, Lainiala O, Nieminen J, et al. Repeated ion measurement in patients with bilateral metal on metal (ASRTM) hip replacements. *Orthop Traumatol Surg Res* 2016;102:167-73.
25. Low AK, Matharu GS, Ostlere SJ, et al. How should we follow-up asymptomatic metal-on-metal hip resurfacing patients? A prospective longitudinal cohort study. *J Arthroplasty* 2016;31:146-51.
26. van der Weegen W, Brakel K, Horn RJ. Asymptomatic pseudotumours after metal-on-metal hip resurfacing show little change within one year. *Bone Joint J* 2013;95-B:1626-31.
27. Reito A, Elo P, Puolakka T, et al. Repeated magnetic resonance imaging in 154 hips with large-diameter metal-on-metal hip replacement. *Acta Orthop* 2014;85:570-6.
28. Back DL, Young DA, Shimmin AJ. How do serum cobalt and chromium levels change after metal-on-metal hip resurfacing? *Clin Orthop Relat Res* 2005;438:177-81.
29. Daniel J, Ziaee H, Pradhan C, et al. Six-year results of a prospective study of metal ion levels in young patients with metal-on-metal hip resurfacings. *J Bone Joint Surg Br* 2009;91:176-9.
30. Mathew MT, Jacobs JJ, Wimmer MA. Wear-corrosion synergism in a CoCrMo hip bearing alloy is influenced by proteins. *Clin Orthop Relat Res* 2012;470:3109-17.
31. Amstutz HC, Le Duff MJ, Bhauria SK. Risk factors for wear-related failures after hip resurfacing in patients with a low contact patch to rim distance. *Bone Joint J* 2017;99-B:865-71.
32. Yoon JP, Le Duff MJ, Johnson AJ, et al. Contact patch to rim distance predicts metal ion levels in hip resurfacing. *Clin Orthop Relat Res* 2013;471:1615-21.
33. Matharu GS, Berryman F, Brash L, et al. Predicting high blood metal ion concentrations following hip resurfacing. *Hip Int* 2015;25:510-9.
34. Bourget-Murray J, Watt Kearns SJ, Lukenchuk J, et al. Birmingham Hip Resurfacing for osteoarthritis: a Canadian retrospective cohort study with a minimum 10-year follow-up. *Can J Surg* 2022;65:E296-302.