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Higher Blood Cobalt and Chromium Levels in Patients With Unilateral Metal-on-Metal Total Hip Arthroplasties Compared to Hip Resurfacings

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ABSTRACT

Background: Adverse soft tissue reactions in metal-on-metal (MoM) hip replacements are associated with cobalt (Co) and chromium (Cr) ions in blood. We report the prevalence and risk factors for elevated blood Co and Cr levels in patients with a unilateral MoM hip.
Methods: From a single institution, blood Co and Cr levels were analyzed in 1748 patients (692 hip resurfacings and 1056 total hip arthroplasties [THAs]). Concentrations exceeding 7 ppb were considered elevated, and the risk factors for elevated levels were calculated with binary logistic regression.
Results: Elevated blood metal ion levels were more common in MoM THA than in resurfacing patients (17.4% vs 5.9%, $P < .001$), and in 5 of the 7 THA brands, more than 20% of patients had elevated metal ion concentrations, whereas the proportion was less than 10% in all hip resurfacings. In resurfacings, small femoral head (odds ratio [OR] 1.30 per millimeter decrease [CI, 1.12-1.49]), high acetabular inclination (OR 1.15 per degree increase [CI 1.09-1.22]), and young age (OR 1.05 per year decrease [1.02-1.10]) were independent risk factors for elevated ions. In the THA group, female gender (OR 2.04 [CI 1.35-3.06]), longer time between surgery and ion measurement (OR 1.19 per year increase [CI 1.05-1.34]), and large headsize (OR 1.07 per millimeter increase [CI 1.01-1.13]) were risk factors for elevated ions.
Conclusion: Given the high percentage of elevated levels, the systematic surveillance of especially large diameter MoM THAs seems justified.

Higher than anticipated revision rates in metal-on-metal (MoM) hip arthroplasties have prompted medical device alerts by the authorities [1-4] and adverse reactions to metal debris (ARMDs) are thought to be the underlying reason for the increased failure rates of MoM hips [5]. Blood and serum cobalt (Co) and chromium (Cr) concentrations are widely used to depict increased wear of MoM bearing surfaces as increased concentrations are associated with increased volumetric wear [6] and component malpositioning [7].

Several guidelines have been presented for screening of MoM hips for ARMD [3,4,8-10]. These guidelines have been criticized to be out of date, some lacking proper risk stratification, and not being cost-effective [11]. The risk stratification is based on symptoms and implant type and size [3,9,10], as registry data have shown increased risk of failure especially for large-diameter (≥36 mm) THAs [1,2]. In addition, certain MoM brands are considered high-risk designs because of unacceptably high number of clinical failures [3,10,12]. Furthermore, in some guidelines, systematic blood Co and Cr measurements have been recommended for risk implants including large diameter stemmed MoM THAs [3], and small head size (<45 mm) resurfacings [9], although there are little published data to support this rationale. To our knowledge, blood Co and Cr ion concentrations and brand specific variance have only been reported in 1 large study involving MoM THAs [13]. Blood metal ion levels have been related to clinical failure, although the exact cutoff value for elevated blood metal ions is a debated issue [14].

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We sought to answer the following questions: (1) How common are blood metal ion levels exceeding United Kingdom Medicines and Healthcare products Regulatory Agency cutoff value of 7 parts per billion (ppb) [3], and, (2) what are the risk factors for elevated blood metal ion levels in patients with unilateral MoM hip replacement?

Patients and Methods

We identified 2398 patients (2868 hips) that had received a large diameter MoM hip replacement between 2001 and 2011 at our institution. All these patients were reviewed for potential inclusion in this retrospective comparative study (Fig. 1).

The inclusion criteria for the present study were (1) unilateral large diameter MoM resurfacing or stemmed THA and (2) at least 1 postoperative measurement of blood Co and Cr. Only patients with a unilateral MoM hip were included in this study as it is obviously impossible to evaluate the ion levels in bilateral MoM hips individually. A total of 470 patients were excluded because of having contralateral MoM hip arthroplasty. After exclusions, we ended up with a study population of 1928 patients with 751 hip resurfacings and 1177 large-diameter head (≥36 mm) THAs. Of patients with only 1 MoM hip, 304 patients had another hip arthroplasty with metal-on-polyethylene, ceramic-on-polyethylene, or ceramic-on-ceramic bearing surface on the contralateral side. There was no difference in blood Co (median 1.2 vs 1.2 ppb, $P = .506$ in resurfacings and 2.2 vs 2.4 ppb, $P = .939$ in THA) or Cr (median 1.4 vs 1.4 ppb, $P = .555$ in resurfacings and 1.6 vs 1.6 ppb, $P = .460$ in THA) concentrations between them and those patients with no contralateral hip arthroplasty, so the effect of contralateral non-MoM hip on blood metal ion levels was considered insignificant, and these patients were included in analyses as well.

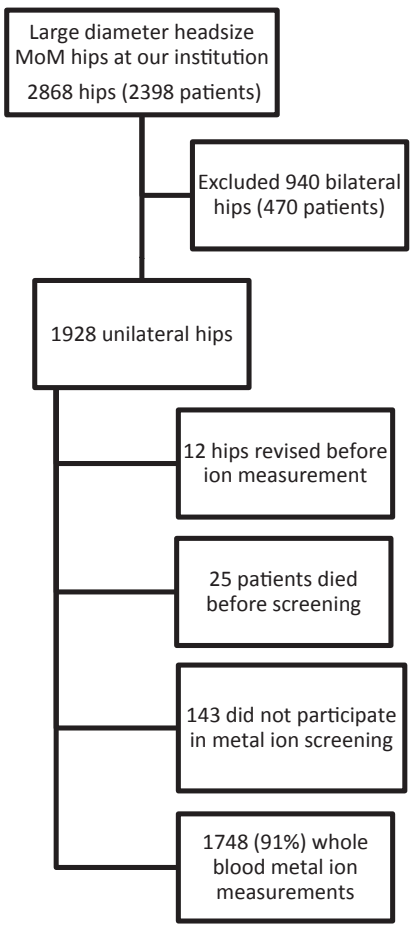

Fig. 1. Study flowsheet. MoM, metal-on-metal.

At our institution, resurfacing was used in young (89% of patients aged ≤65 years) and active patients with good bone quality. Contraindications for resurfacing were avascular necrosis of the femoral head, severe developmental dysplasia of the hip, insufficient bone quality, and renal dysfunction. Inflammatory arthritis was a relative contraindication. MoM THA was used in active patients who also were considered to benefit from large head size (eg, high dislocation risk) but had contraindications for resurfacing. Renal insufficiency was a contraindication for MoM THA. Surgeries were performed according to our standard protocol including posterior approach. Before the awareness of the risk for ARMD in MoM hip arthroplasties, patients were followed up according to our conventional follow-up program including clinical assessment by a physiotherapist at 1, 3, 5, and 8 years after surgery as well as anteroposterior and lateral plain radiographs at same intervals.

After the medical device alert by United Kingdom Medicines and Healthcare Products Regulatory Agency in September 2010 [3], we launched a systematic screening program of patients with Articular Surface Replacement (ASR; Depuy Orthopaedics, Warsaw, IN) resurfacing or ASR THA hips. Program included blood Co and Cr measurements and magnetic resonance imaging. At the beginning of 2012, the screening was extended to all patients with MoM hips. However, the screening of other MoM brands did not include systematic magnetic resonance imaging.

Blood samples were acquired from the antecubital vein using a 21-gauge needle connected to a Vacutainer system (Becton, Dickinson and Company, Franklin Lakes, NJ) and trace element tubes containing sodium EDTA. First 10 mL was disposed to avoid metal contamination from needle. Standard operating procedures were established for Co and Cr measurement using dynamic reaction cell inductively coupled plasma (quadripole) mass spectrometry (Agilent 7500 cx; Agilent Technologies, Santa Clara, CA). Blood Co or Cr levels over 7 ppb were considered elevated [3]. Measurements were made between January 2010 and September 2013. In patients with multiple measurements, only the first measurement was analyzed for this study.

Statistical Analysis

Medians and ranges are presented for Co and Cr because of skewed distributions. Mann–Whitney *U* test was used to test differences in Co and Cr levels between groups. Independent sample *T*-test was used for normally distributed variables. Binary logistic regression adjusted for implant brand, age, gender, time between index surgery and measurement, component head size, and cup inclination angle (measured from anteroposterior radiograph) was used to analyze potential risk factors for elevated blood metal ion levels. Range of motion (ROM) and body mass index (BMI) were not included in the final regression model because of substantial number of missing values, but they were fitted in the model before exclusion. Because ASR has been widely regarded as a high-risk brand, and was recalled by its manufacturer in 2010 [3,7,12], we compared the other brands against ASR in terms of risk for elevated blood metal ion levels. Age, component head size, inclination, and time between surgery and metal ion measurement were analyzed as continuous variables and for those we present odds ratios associated with 1-unit increase in exposure. Implant brands with less than 20 patients were combined to group "other" for regression analysis. Median Oxford Hip Scores with range are presented as background information for all implants. Two-sided $P < .05$ was considered statistically significant.