



Six-year results of a prospective study of metal ion levels in young patients with metal-on-metal hip resurfacings

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We describe the findings at six years in an ongoing prospective clinicoradiological and metal ion study in a cohort of 26 consecutive male patients with unilateral Birmingham Hip Resurfacing arthroplasties with one of two femoral head sizes (50 mm and 54 mm). Their mean age was 52.9 years (29 to 67). We have previously shown an early increase in the 24-hour urinary excretion of metal ions, reaching a peak at six months (cobalt) and one year (chromium) after operation. Subsequently there is a decreasing trend in excretion of both cobalt and chromium. The levels of cobalt and chromium in whole blood also show a significant increase at one year, followed by a decreasing trend until the sixth year.

The potential harmful effects of elevated systemic exposure to cobalt and chromium have been widely reported.¹⁻³ We have followed a consecutive cohort of 26 patients with unilateral Birmingham Hip Resurfacing (BHR) arthroplasties (Smith and Nephew, Warwick, United Kingdom) longitudinally in an ongoing clinicoradiological and metal ion study. We have previously published our observations at four years⁴ and now present a six-year update.

Materials and Methods

After informed consent, specimens of urine and whole blood were collected before and periodically after unilateral resurfacing with either a 50 mm or 54 mm femoral head in 26 consecutive male patients. Only two head sizes were included in order to reduce potential confounding from variable surface corrosion. Specimens were collected pre-operatively from all patients, who were templated and found likely to need 50 mm or 54 mm femoral components. Specimens from the patients who did not receive the stated head sizes were discarded after the operation. Those patients who lived abroad were excluded. None had a history of renal impairment. The mean age at operation was 52.9 years (29 to 67) and the mean height, weight and body mass index (BMI) prior to operation was 177 cm (165 to 187), 87 kg (59 to 119) and 27.9 (21.5 to 36.3), respectively.

The levels of metal ions in whole blood are recorded in concentrations expressed as $\mu\text{g/l}$. The daily output of metal ions in the urine is the total quantity excreted in 24 hours, expressed as $\mu\text{g}/24$ hours. Patient compliance

is better with a 12-hour rather than a 24-hour collection and, therefore, 12-hour collections were made and the daily output obtained by doubling the total 12-hour excretion.

Clinical and radiological review and the collection of 12-hour specimens of urine were undertaken before operation and after five days, two months, six months, one year and at two, four and six years. Specimens of whole blood were collected pre-operatively and at one, four and six years post-operatively. The review after one year was chosen as the first time point for combined whole blood and urine measurements because, based on a cross-sectional pilot study in patients with BHRs, we expected the run-in peak to occur at this time.⁵

Further details of patients, implants, specimen collection and instrumentation are described in earlier publications.^{4,6,7} Two of these patients have since undergone a contralateral hip resurfacing procedure and have been excluded. The results for the remaining 24 patients at six years are presented here. Non-parametric methods were used for the analysis of data relating to daily output of metal ions, as it was asymmetrically distributed, whereas parametric methods were considered appropriate for the levels of whole blood metal ions.

We used 95% confidence intervals and a value of $p < 0.05$ to indicate statistical significance.

Results

At six years all 24 patients had well-functioning pain-free resurfacings. None complained of pain or disability. The current Oxford hip

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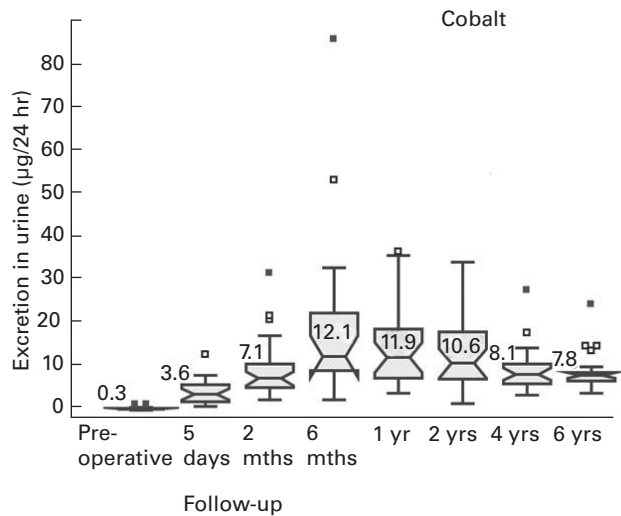


Fig. 1

Graph showing daily output (24-hour urinary excretion) of cobalt in patients with Birmingham hip resurfacings. Values shown are medians (horizontal lines), 95% confidence intervals of medians (notches) and interquartile ranges (boxes). The whiskers extend to the largest and smallest values that are within 1.5 times the corresponding box length. Outliers are shown as individual data points.

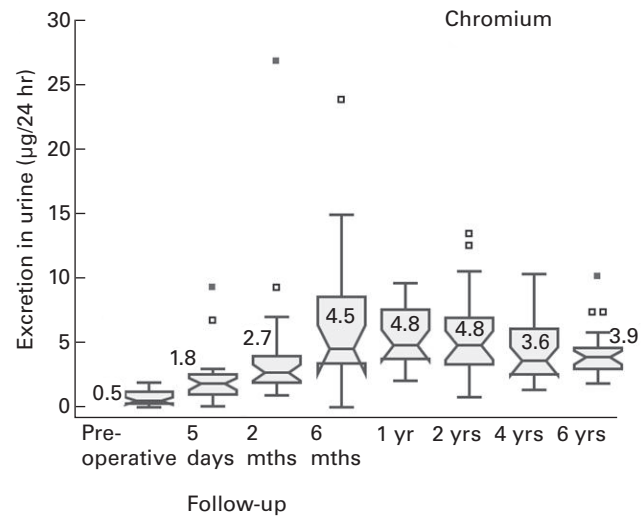


Fig. 2

Graph showing daily output of chromium in patients with Birmingham hip replacements. Box and whisker plots as in Figure 1.

score, in which the best possible score allowed is 12 and the worst is 60,⁸ ranged from 12 to 18 (mean 12.9 and median 12). The mean pre-operative Oxford scores before resurfacing was 35 (25 to 48). The mean Harris hip score⁹ obtained by postal questionnaire was 89/90 and the median 90/90 (78 to 90).

Monitoring of step activity revealed a mean activity rate of 2.0 million (1 to 3.2) cycles per year at six years, which was not significantly different from that at four years (2.1 million cycles (1 to 4.3, $p = 0.6$, Students *t*-test). The mean University of California Los Angeles (UCLA) activity level scale¹⁰ was 8.3 (6 to 10), similar to that at four years (mean 8; 6 to 10, $p = 0.3$, Students *t*-test). Activities included participating in moderately heavy occupational work and pursuing impact-loading leisure activities such as squash, mountain walking, hockey, five-a-side football, skiing and running.

We had earlier observed that the cobalt output in these patients showed an early peak at six months (median 12.1 $\mu\text{g}/\text{day}$), followed by a steady decline until four years. This declining trend continued at six years (7.8 $\mu\text{g}/\text{day}$), with the output significantly lower than that at six months ($p < 0.01$, Mann-Whitney test) (Fig. 1). The chromium output had also shown a similar but more delayed trend, increasing up to the one- and two-year reviews but decreasing by four years (Fig. 2). The median chromium output at six years (3.9 $\mu\text{g}/\text{day}$) was marginally greater, but the third quartile (4.5 $\mu\text{g}/\text{day}$) was lower than the corresponding values at four years (3.6 $\mu\text{g}/\text{day}$ and 5.8 $\mu\text{g}/\text{day}$ respectively) and the differences are not statistically significant ($p = 0.8$, Mann-Whitney test).

At six years the concentrations of cobalt and chromium in whole blood are significantly higher than before operation. Compared with the concentrations after one year, there is a reducing trend in the mean levels at four and six years. This reduction in cobalt levels was not statistically significant, but levels of chromium at four and six years were significantly lower than those after one year (Figs 3 and 4). There was no relationship between ion levels and the stature of the patient, their levels of activity or inclination of the acetabular component. However, the scatter of angles of inclination (35° to 49°) in this cohort was well controlled by a reproducible surgical technique without the need for navigation.

Discussion

The urinary output of metal ions based on timed excretion is a good measure of bearing wear and the total body burden of metal ions,¹¹ while the level of metal ions in the blood represents systemic exposure to metal. A review of the literature found only one report¹² of daily metal ion output in urine using HRICPMS (high resolution inductively coupled plasma mass spectrometry) analysis, in patients with M2a (Biomet, Warsaw, Indiana) 28 mm metal-on-metal total hip replacements (THR). The output of metal ions with that device was found to be excessive, leading to an early discontinuation of recruitment into the study.

Several factors lead to confounding variability in levels of metal ions from metal-on-metal bearings, which are sensitive to suboptimal implantation of both components, and to subtle differences in manufacture and metallurgy of the

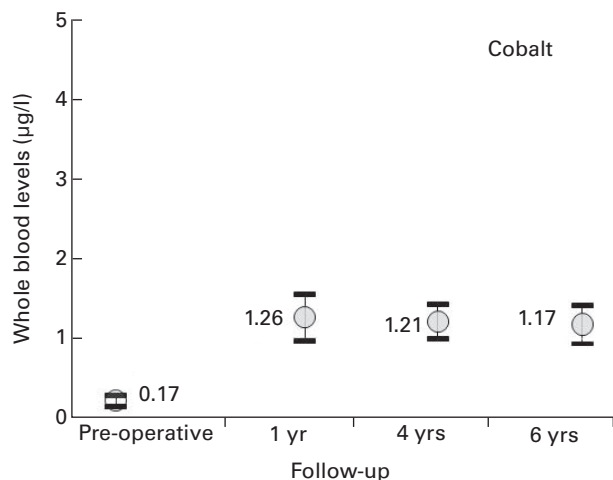


Fig. 3

Graph showing whole blood concentrations of cobalt in patients with Birmingham hip replacements before operation and after one, four and six years (mean \pm 95% confidence intervals).

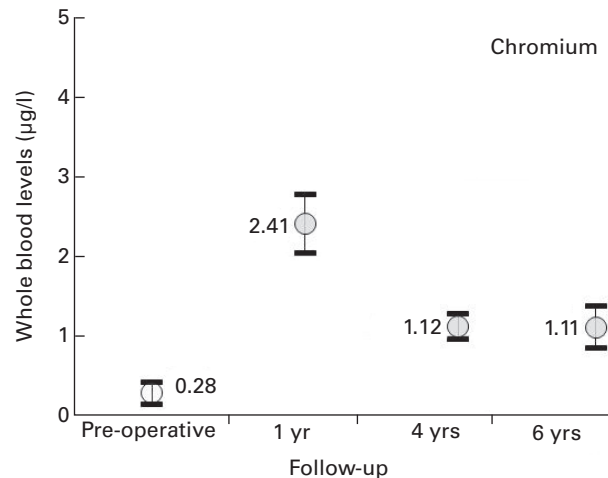


Fig. 4

Graph showing whole blood concentrations of chromium in patients with Birmingham hip replacements before operation and after one, four and six years (means \pm 95% confidence intervals).

implant. They are further influenced by the unknown variable of metal corrosion, which is related to the surface area of the component, a derivative of its diameter. In assessing metal release *in vivo* it is essential that all these variables are kept to a minimum. We were able to achieve a degree of uniformity in this study by using an alloy with an established clinical history, controlling the number of implant sizes to only 50 mm and 54 mm bearing diameters, and reducing variability in positioning of the components through a reproducible surgical technique.

Timed urine collection involves collecting all the urine during each voiding over a 12-hour period in a specimen container without spillage or contamination; men were considered more efficient at this task. The two sizes of bearing included represent 70% of the resurfacings in our centre. Young men with unilateral osteoarthritis of the hip are the most active resurfacing group, with 92% participating in sport and 62% participating in impact sport.¹³ We therefore assessed metal release in correctly implanted devices in this extremely active patient group, who are most likely to provoke active release of metal ions.

There are conflicting reports relating to levels of metal ions in metal-on-metal bearings of differing diameters. Two studies suggest higher blood levels in smaller-diameter articular surface replacement (DePuy International Ltd, Leeds, United Kingdom)¹⁴ and Durom (Zimmer, Winterthur, Switzerland)¹⁵ resurfacings than in those of larger diameter at a mean follow-up of around two years. Higher levels were reported in women than in men with the Durom resurfacings. However, these were retrospective observations in prospective studies of patients with unselected sizes, and with small numbers of patients in each size. Furthermore, the confounding effects of time from implantation and/or acetabular component inclination were not tightly controlled in these subgroups.

Antoniu et al¹⁶ recently described a prospective study comparing the blood levels of metal ions in ASR resurfacings with 28 mm (Metasul; Zimmer, Warsaw, Indiana) and 36 mm (Ultamet; DePuy Orthopaedics) diameter bearing metal-on-metal THRs, including larger numbers of patients in each subgroup compared with the previous reviews.^{14,15} They found that the 36 mm bearings produced significantly lower cobalt and chromium levels than the 28 mm THR and the resurfacing bearings at six months, but at one year there was no difference between the three groups. They also detected no differences in levels of metal ions between men and women. We have found no difference in the levels of metal ions, with respect to either the component size or gender in our own large volume of unpublished data on cross-sectional groups of unselected patients.

In vitro studies on metal-on-metal bearings demonstrate a period of increased wear during the early run-in, followed subsequently by very low wear. However, some clinical studies show an increasing trend in levels of metal ions in blood or its fractions over two,¹⁷ four¹⁸ and seven years.¹⁹ In one multi-centre study of resurfacings, the reason for this increasing trend was said to be the variability in acetabular component inclination achieved by different surgeons.¹⁷ In the other two,^{18,19} which were single-centre studies of 28 mm metal-on-metal THRs, the common denominator appears to be the use of low-carbon cobalt-chrome alloy in one or both bearing surfaces. In one of these studies, cobalt levels were continuing to increase in 42% of the patients at seven years.¹⁹

In this prospective longitudinal study both the daily output of metal ions and whole blood levels showed an early increase, but subsequently a progressively reducing trend. This trend has continued until six years, and patients remain active with well-functioning arthroplasties.

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