Effect of a Second Joint Arthroplasty on Metal Ion Levels After Primary Total Hip Arthroplasty

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Abstract

Serum metal ion levels increase after primary total hip arthroplasty (THA) regardless of bearing surface.

We conducted a study to determine the effect of a second joint arthroplasty on existing serum metal ion levels at long-term follow-up. Twelve patients underwent primary THA and then either another THA (8 patients) or total knee arthroplasty (TKA) (4 patients). The secondary procedures were performed a mean of 102.7 months (range, 36-144 months) after the index surgeries. The secondary THA group had significantly elevated levels of cobalt ion at 36 and 48 months, chromium ion at 12 and 24 months, and titanium ion at 48 and 72 months. The TKA group had no significant differences in cobalt, chromium, or titanium ion levels up to 72 months after surgery.

Overall, when metal-polyethylene THA was performed after primary THA, there was a trend toward elevated serum metal ion levels at all follow-up intervals. This trend should be investigated with larger clinical trials.

It has been established that serum metal ion levels increase after primary total hip arthroplasty (THA) regardless of type of head-liner articulation couple used.[1-5] With the recent focus on reported adverse responses to metal-on-metal THA, there is mounting concern regarding local soft-tissue reactions, systemic immune modulation, and end-organ deposition and damage with elevated serum metal ion concentrations. The metal components of joint replacements can undergo electrochemical corrosion resulting in formation of chemically active metal ion degradation products.[3] Tower[6] reported the cases of 2 patients who underwent metal-on-metal THA and developed systemic neurologic and cardiac complications associated with elevated serum cobalt levels. A cause-effect relationship was suggested by the improvement in systemic symptoms after revision surgery, which presumably lowered serum cobalt concentrations, though no postrevision serum measurements were reported, and case details were limited. Adverse systemic responses to metal ion debris from joint replacement are extremely rare. In addition, increased serum metal ion levels are not unique to metal-on-metal bearings, as use of other metal devices with damage accelerated by wear or corrosion can lead to elevated levels of metal in local and remote tissues.

As the United States population continues to age, the annual incidence of primary THA and total knee arthroplasty (TKA) continues to rise; in 2030, approximately 572,000 THAs and 3.48 million TKAs will be performed.[7] The question arises: Will adverse responses to increased serum metal ion concentrations from joint arthroplasty become more prevalent in the future, or will these cases remain rare occurrences? There is no generally accepted threshold above which serum concentrations of metal ions such as cobalt, chromium, and titanium are known to be toxic in patients with a joint replacement. However, cobalt and chromium have both been shown to be toxic in high concentrations in vivo, and titanium has been shown to be potentially carcinogenic at high levels in animal models.[8] Previous work has also shown that wear particles from THAs and TKAs can disseminate to the liver, spleen, and abdominal lymph nodes, causing as yet unknown long-term effects.[9]

Degenerative joint disease in a hip often affects the contralateral hip and knee, making a second total joint arthroplasty (TJA) necessary.[10] However, little is known about the effect of the secondary TJA on metal ion levels. In the study reported here, we sought to determine the effect of a secondary TJA on serum concentrations of cobalt, chromium, and titanium after a primary metal-on-polyethylene THA as well as the time course of concentration changes.

Materials and Methods

We prospectively enrolled a subset of 12 patients from

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a previous study[11] of metal ion data after primary THA, who were disqualified for having a second TJA. Research approval from our institutional review board and informed consent from the patients were obtained. Mean age was 63.4 years (range, 55-76 years). The 4 men and 8 women all underwent an initial primary metal-on-polyethylene THA for the treatment of osteoarthritis. All had a well-functioning prosthesis, as determined by their Harris Hip Scores, and none had radiographic evidence of loosening or osteolysis at interval follow-up or just before the second surgery. Eight patients had received cementless proximally porous-coated titanium-alloy femoral stems and titanium acetabular components. The Ti-6A1-4V femoral stem had a titanium fiber-metal porous-coated surface diffusion-bonded onto its proximal aspect. Of the 8 femoral components used, 6 were anatomic and 2 were Harris-Galante Multilock; both types were manufactured by Zimmer (Warsaw, Indiana). The acetabular component, inserted without cement, consisted of a titanium shell with a diffusion-bonded, titanium fiber-metal porous-coated surface (Harris-Galante II; Zimmer). Two titanium alloy self-tapping screws were used for fixation, and the bearing surface consisted of a modular cobalt-alloy femoral head and an ultra-high-molecular-weight polyethylene liner.

Two patients received cementless extensively porous-coated cobalt-alloy femoral stems with titanium-alloy acetabular components. Anatomical Medullary Locking (DePuy, Warsaw, Indiana) femoral components were inserted on the basis of preoperative templating and intraoperative bone quality. Also used were Duraloc (DePuy) acetabular sockets, titanium-alloy shells with a beaded titanium porous coating. The acetabular shells were secured to the pelvis with 3 porous-coated titanium-alloy spikes. A modular cobalt-alloy femoral head and an ultra-high-molecular-weight polyethylene liner were used for the articulation surface. The final 2 patients received a hybrid THA that consisted of a modular uncoated cobalt-alloy femoral stem inserted with cement along with a cobalt-alloy head. One Iowa femoral component and 1 Precoat femoral component (Zimmer) were used. The Harris-Galante II titanium acetabular component was inserted as described above and secured to the pelvis with 2 titanium alloy screws. A snap-fit ultra-high-molecular-weight polyethylene liner served as the bearing surface.

Of the secondary TJAs, 8 were THAs and 4 were TKAs. These procedures were performed a mean of 102.7 months (range, 36-144 months) after the index surgeries. All primary and secondary TJAs were performed between 1989 and 1998. The secondary THAs consisted of 3 cementless titanium-alloy femoral stem and titanium acetabular component reconstructions and 5 hybrid constructs following the descriptions above. The TKAs were cemented in place with a cobalt-chrome femur and a titanium tibial tray (Zimmer). Patients were excluded from the study if any metal implants other than the secondary TJAs were inserted during the follow-up intervals. Other exclusion criteria were component failure requiring revision surgery, medication use that would alter serum metal ion levels, and advanced systemic disease.

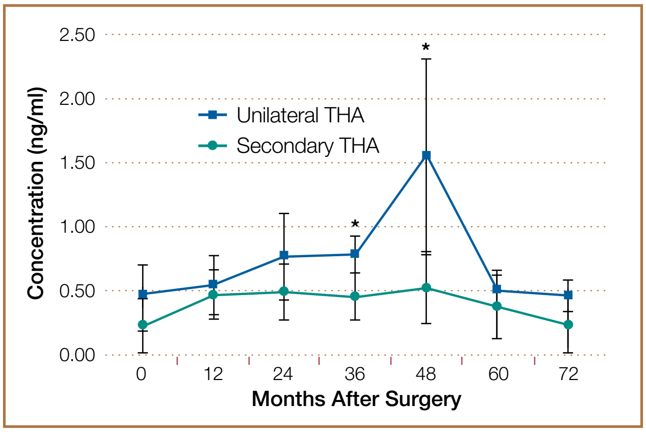

Figure 1. Cobalt ion levels after unilateral total hip arthroplasty (THA) and secondary THA from month 0 (baseline) to 72-month follow-up. Values are means with standard deviation bars. Asterisks indicate significant difference at P<.05.

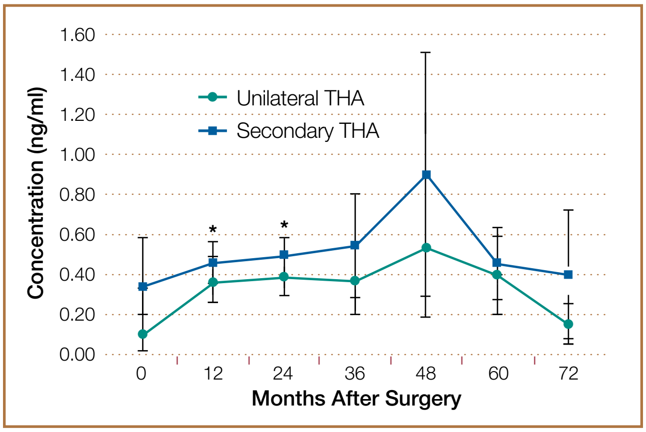

Figure 2. Chromium ion levels in unilateral total hip arthroplasty (THA) and secondary THA from month 0 (baseline) to 72-month follow-up. Values are means with standard deviation bars. Asterisk indicates significant difference at P<.05.

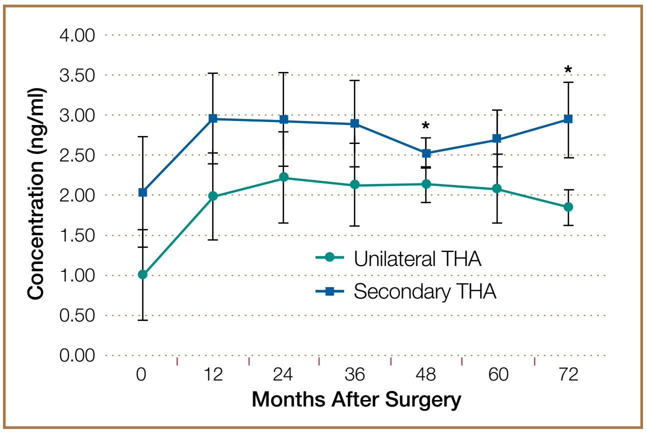

Figure 3. Titanium ion levels in unilateral total hip arthroplasty (THA) and secondary THA from month 0 (baseline) to 72-month follow-up. Values are means with standard deviation bars. Asterisks indicate significant difference at P<.05.

Blood samples for serum metal ion level analysis were collected before the secondary TJAs and at 3-, 6-, and 12-month intervals and annually thereafter. All vessels and utensils used for serum collection were verified—using previously described techniques—to be free of metal contamination.[3] Blood samples were obtained using siliconized butterfly needles in triplicate polypropylene syringes. The first syringe was used to rinse the system, and the contents of the second and third syringes were used for the metal-ion analysis. Immediately after being collected, the blood was separated and frozen at -80°C for long-term preservation as serum and clot fractions using a Class 100 biological safety hood. For contamination prevention, only ultrapure reagents were used, and processing vessels were acid-washed.

A high-resolution, sector-field, inductively coupled plasma mass spectrophotometer was used with the previously described method of additions (Element-2; Thermo Fisher Scientific Inc, Waltham, Massachusetts) to analyze the serum samples for cobalt, chromium, and titanium levels.[12] The technique for measuring serum metal ion levels was consistent and reproducible throughout the study. Detection limits were 0.04 ng/mL for cobalt, 0.015 ng/mL for chromium, and 0.2 ng/mL for titanium. Data reported are means with standard deviations (SDs) for each group at each time interval. SPSS statistics software (SPSS, IBM, Chicago, Illinois) was used to perform Friedman's tests to determine statistical significance, which was set at $P<.05$.

Results

Minimum 5-year data were available for all patients after second TJA. Mean follow-up was 96.4 months (range, 61-168 months). All concentrations of serum cobalt, chromium, and titanium were above the detection limits. Normal serum levels were previously reported to be 0.1 to 0.2 ng/mL (cobalt), 0.15 ng/mL (chromium), and less than 4.1 ng/mL (titanium).[3,13]

Patients who underwent TKA after primary THA had no significant differences in cobalt, chromium, or titanium ion levels from baseline up to 72 months after surgery. In addition, there were no significant differences in cobalt, chromium, or titanium levels at baseline between unilateral THA and secondary THA groups. Patients with a secondary THA had significantly elevated cobalt ion levels at 36-month follow-up, and these levels peaked at 48 months (**Figure 1**). Chromium levels in patients with a secondary THA were significantly elevated at 12-month follow-up, and increased concentration was sustained at 24 months (**Figure 2**). Patients with a secondary THA also had significantly elevated titanium levels at 48- and 72-month follow-up (**Figure 3**). Overall, when metal-polyethylene THA was performed after primary THA, there was a trend toward elevated serum metal ion levels at all follow-up intervals. This trend became significant only at the time points described.

Discussion

Elevated serum metal ion levels after primary THA is well described,[3,11,14-17] but the impact of a second TJA on these levels has not been well investigated. Commonly, patients with degenerative joint disease requiring hip arthroplasty often develop joint disease in an adjacent or contralateral joint necessitating another joint arthroplasty.[10] In the present study, cobalt ion levels after secondary THA were significantly increased 36 months after surgery and peaked at 48 months. Chromium levels were increased at both 12 and 48 months. Given our small sample size, the 48-month peak was driven largely by 1 patient with a significant increase in metal ion levels at that time interval. Titanium levels were significantly elevated at 48 months and continued increasing until the 72-month follow-up. The main finding in this study is that performing a secondary metal-polyethylene THA after a primary THA tended to result in higher levels of serum cobalt, chromium, and titanium at all follow-up intervals. However, these results are difficult to interpret, as only certain time periods were statistically significant. Another finding is that performing a secondary metal-polyethylene TKA after a primary THA had no significant effect on serum metal ion levels at any time period.

The 12 patients included in this study were recruited from the group disqualified for having a second TJA after a primary THA in our original study of metal ions.[11] The small sample size and the lack of power analysis in the present study are major limitations that may have prevented further trends and levels of significance from being detected. Small sample size likely also contributed to the larger standard deviations and to the variable significant differences in serum metal ion levels. Another limitation is that this study was not a randomized series, and there was a bias regarding implant type and fixation method, both of which were selected on the basis of surgeon preference. One of the general limitations regarding metal ion concentrations is that the wide variability in how measurements are gathered, analyzed, and reported in the literature makes comparisons between studies difficult.[18] In addition, detection of differences between groups has been difficult in previous studies because of variations among patients and among samples from the same patient with regard to the concentrations of serum metal ions.[18] Advantages of the present study are the long-term (72-month) follow-up and the prospective nature of the data collection.

Our previous prospective study described and quantified the rise in cobalt, chromium, and titanium ion levels after primary metal-on-polyethylene THA.[11] Patients with a well-functioning prosthesis containing titanium 36 months after surgery had a 3-fold increase in serum titanium levels, and patients with a cobalt-alloy prosthesis had a 5-fold increase in serum chromium levels. The predominant metal ion degradation products were found to result from fretting corrosion at the modular head-neck junction, because of the geometry of the coupling. Passive dissolution of extensively porous-coated cobalt-alloy stems was not found to be a significant mode of metal ion release into the body.

There are several modes of metal ion release, including passive dissolution, wear (mechanical), corrosion (electrochemical), and combined mechanical and electrochemical processes (eg, fretting corrosion).[19] Absence of a modular taper in knee replacements and lack of significant increases in any of the measured metal ion levels suggest that corrosion at the head-neck junction and possible fretting at the screw-cup interface may be responsible for the elevated metal ion levels observed after a secondary THA and not after a secondary TKA. Metal ion release from corrosion at the modular head-neck junction in the present study supports previous findings.[11,20] However, Sunderman and colleagues[21] reported increased levels of cobalt in the serum 6 to 120 weeks after TKA. In a prospective study of 10 patients who underwent TKA with cobalt-based-alloy components, Michel and colleagues[18] found a 2-fold increase in the level of cobalt in the serum 90 days after surgery. In 1999, we investigated the serum and urine concentrations of titanium, aluminum, and vanadium in patients with titanium alloy cementless primary TKA components.[17] Serum concentrations of titanium were 50 times higher in patients with failed patellar components than in control subjects and were 10 times higher in patients with carbon fiber-reinforced polyethylene bearing surfaces than in control subjects.

Increased serum metal ion concentrations derived from TJA may have yet unknown deleterious biological effects over the long-term. Accurate, longitudinal monitoring of serum metal concentrations is especially critical, given the dramatic increase over the past decade in the use of metal-on-metal bearings and increasing modularity of femoral prostheses. Even in the absence of increases in the concentrations of metal in the serum during workup, previous research has shown that deposition and accumulation of metal ions can occur locally and in remote organ stores in association with a well-functioning device.[4] In addition, the kinetics of metal ion production, transportation, and excretion is complex, which makes it difficult to interpret the significance of elevations in metal ions. The present study contributes to the growing body of literature investigating the bioreactivity and bioavailability of metal ion degradation products generated by the presence of joint replacements.

Patients with TJAs must be routinely monitored so that, should any complications arise, care can be expedited. Determining serum metal ion concentrations may be useful in the workup of TJA patients with unexplained local pain or systemic symptoms. Surgeons need to be aware of the rare systemic complications of metal devices undergoing accelerated wear and corrosion so that timely revision surgery can be considered. Future studies need larger sample sizes and longer follow-ups to determine the biomechanical and biochemical extent and impact of these elevated metal ion levels in local tissues and systemically. It will also be important to determine the impact of additional TJAs on this complex system and the factors that may potentiate any deleterious side effects of elevated circulating metal debris.

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This paper will be judged for the Resident Writer's Award.