The earliest recorded attempts at hip replacement date back to 1891 when Theodore Gluck of Germany used a prosthetic head made from ivory to replace the femoral head of an ailing patient. In 1940, the first successful metallic femoral head hip replacement was performed by Dr Austin T. Moore at Johns Hopkins Hospital. Since then, numerous modifications have been made to the various hip replacement systems, from changing materials to altering the method of fixation. Perhaps the most notable modification is the modern hip replacement developed by Sir John Charnley in 1962.

Another modification occurred when companies introduced metal-on-metal hip resurfacing and ultimately total hip arthroplasty (THA) systems using metal-on-metal bearing surfaces. Although these systems were initially designed to reduce wear and minimize dislocations, they are associated with significant problems. Systems using metal-on-metal bearing surfaces have ultimately had significantly higher revision rates when compared with metal-on-polyethylene surfaces. One cause of this high revision rate, which has generated significant academic interest and concern.

Effects of Cobalt and Chromium Levels Following Modular Hip Stem Total Hip Arthroplasty

Christopher R. Koziara, MD, MS; Daniel J. Lombardo, MD; Graysen R. Petersen-Fitts, MD; Toufic R. Jildeh, BS; Lawrence Morawa, MD

Due to the increased number of revision total hip arthroplasties (THAs) to correct pain secondary to fretting from modular hip stems, this study was conducted in an effort to correlate objective findings of serum cobalt (Co) levels, serum chromium (Cr) levels, and/or reactive tissue seen on metal artifact reduction sequence (MARS) magnetic resonance imaging (MRI) with a patient's need for revision THA. The study group comprised 66 patients, 18 of whom received MARS MRI. Serum Co levels, serum Cr levels, and standard numeric rating scale for pain were documented for all patients. Statistical analysis was then performed to determine whether there was a correlation between the aforementioned variables and the need for revision THA. Serum Cr levels were higher in patients with positive reactive tissue findings on MARS MRI, although this only approached significance (P=.083). Serum Co levels were higher in those undergoing revision THA, but this also only approached significance (P=.076). Pain scores were significantly different between those undergoing revision and those not (P<.001). It is the opinion of the authors that there is no objective finding in this study that can be used to identify patients who require revision THA secondary to fretting of a modular hip stem prosthesis. Only a patient's stated pain level can assist a surgeon in the decision-making process regarding the need for revision THA secondary to fretting. [Orthopedics. 2016; 39(5):288-292.]
Adverse local tissue reaction is characterized by periprosthetic soft tissue inflammation comprising a mixed inflammatory cell infiltrate and may show soft tissue necrosis and vascular changes. Adverse local tissue reaction is the result of various forms of metal corrosion resulting in the release of metal ions, metal oxides, and metallo-organophosphates into surrounding tissue. The effects of several such ions, including both cobalt (Co) and chromium (Cr), have been studied; Co(II) is cytotoxic, and both CR(VI) and Co(II) inhibit DNA repair. Thus, despite the initial promise of metal-on-metal bearing surfaces in hip implants, the problems caused by ALTR ultimately led to their falling out of favor.

In addition to innovations in bearing surfaces, modularity in THA has become a topic of great interest in the past 20 years. Following the success of modular femoral heads, systems with an additional modular junction between the neck and body of the stem became available. These dual-taper systems were designed to enhance the surgeon’s ability to re-create the patient’s anatomy via flexibility in stem size, length, and offset. Such biomechanically inspired stems sought to address 2 of the most common complications of THA: leg-length discrepancy and femoral offset leading to dislocation. One such system, the Rejuvenate Modular Hip System (Stryker, Kalamazoo, Michigan), includes the hydroxyapatite-coated modular stem and neck designed to provide surgeons with more options when adjusting leg length and offset.

Recently, poor outcomes from this particular modular hip stem THA became apparent when patients began to have numerous complications, including, but not limited to, pain and component loosening. Further investigation into the cause of these issues led to the discovery of ALTR, similar to that seen with metal-on-metal systems. Adverse local tissue reaction in these dual-taper systems is largely attributed to corrosion, in particular crevice and fretting corrosion. Fretting corrosion is caused by micromotion between the stem of the THA and the neck of the THA, resulting in physical damage to the chemically inert passivation layer that typically protects the implant. Crevice corrosion occurs when small sections of the implant surface are isolated from the surrounding aqueous environment by the surface of the adjacent metal component; then, if the oxide layer in the crevice environment is damaged, there may be insufficient oxygen or oxygen-containing species available to repassivate the surface, and the aqueous microenvironment in the crevice may become acidic, leading to further damage to the passivation layer and corrosion.

As of June 2012, Stryker issued a voluntary recall of the Rejuvenate modular hip implant because it has been associated with ALTR and early failure. Because many patients have received this implant and may require revision in the future, it is important to identify possible predictors of implant failure or revision necessity.

The purpose of this prospective study was to investigate the correlation between the effects of Co ions, Cr ions, reactive tissue seen on metal artifact reduction sequence (MARS) magnetic resonance imaging, and/or patients’ stated pain levels with the need for THA revision in patients who had received a primary THA with the Rejuvenate Modular Hip System. It was hypothesized that there would be a statistically significant correlation between the Co and Cr blood levels and the need for THA revision secondary to patients’ stated discomfort.

**Materials and Methods**

The study group comprised 156 patients who underwent modular hip stem THA with the Stryker Rejuvenate Modular Hip performed at the authors’ institution. Of the 156 patients, 66 had documented follow-up and were included in this study. Average follow-up was 55.22 months (range, 22-89 months). Eighteen of the 66 patients received MARS MRI. Chromium and Co blood levels were drawn from all 66 patients and placed in dark blue ethylenediaminetetraacetic acid (EDTA) tubes. Patients’ clinical signs and symptoms were noted and documented using standard progress notes in the electronic medical records. A total of 21 (31.8%) of the 66 patients elected to undergo revision THA revision at the time of most recent follow-up. Cobalt and Cr blood level studies, MARS MRI, and patients’ pain levels were all used in an effort to find statistically significant correlation between the aforementioned variables and the need for THA revision.

During analysis of patient satisfaction, a standard numeric rating scale of 0 to 10 was used to maintain consistency. In addition, all measurements of Co and Cr levels were made by the same 2 laboratories. Chromium levels were sent to Quest Diagnostics, Nichols Institute (Valencia, California). The reference value for a normal test used for Co was less than 1.0 µg/L as defined by the testing laboratory. Cobalt levels were sent to ARUP Laboratories (Salt Lake City, Utah). The reference value for a normal test used for Cr was less than 1.5 µg/L as defined by the testing laboratory.

Reactive tissue was documented as such for the 18 patients receiving MARS MRI (Figures 1-2). After charting all data obtained in spreadsheet format, averages were obtained for Co levels, Cr levels, and patient pain levels. The percentage of patients with local tissue reaction as noted by MARS MRI heterogeneity was also recorded. It was noted which patients received revision THA. Mean ion levels and pain scores were compared between groups using the Student’s t test. Additional analysis was subsequently performed to determine the correlation between cobalt and/or chromium levels, patients’ pain levels, and revision THA using univariate and multivariate linear regression modeling. The accuracy of these tests for predicting revision or positive findings on MRI were then assessed using receiver operating characteristic curves.

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ROC) analysis. This analysis plots the sensitivity and specificity of these tests using various cut-off values and can be interpreted by the area under the curve, where 0.5 to 0.7 represents a poor test, 0.7 to 0.9 represents a good test, and greater than 0.9 represents an excellent test. This type of analysis is commonly used with good outcomes in orthopedic research pertaining to the usefulness of various tests or screenings.23–26

Demographics were noted for each of the 66 patients in the study, such as age, height, weight, and body mass index, for which mean values were calculated, along with SDs and minimum and maximum values in the population.

RESULTS

Of 66 total patients with adequate follow-up, 46 (69.7%) were male, mean age was 63.9±14.5 years, and average duration of follow-up was 55.0±14.8 months (Table 1). A total of 21 (31.8%) of the 66 patients underwent revision surgery and 45 (68.2%) did not. Of the 18 patients with available MRI, 8 (44.4%) were positive for reactive tissue and 10 (55.6%) were negative. Mean ion levels for all patients were 3.98±3.17 µg/L for Co and 1.02±1.24 µg/L for Cr. Mean pain score for all patients was 3.31±2.62.

Cobalt and Cr levels were significantly correlated with each other (r=0.557; P<.001). However, there were no significant correlations between these levels and pain scores (Table 2). Although there were higher mean ion levels and pain scores in those who underwent revision THA, only the difference in pain scores was significant (Table 3). In addition, there was a trend toward increased ion levels and pain scores in those who had positive MRI imaging; however, this did not reach statistical significance (Table 4).

Cobalt and Cr levels were not accurate tests for predicting either revision or positive findings on MRI (Table 5), although Co levels approached significance for fairly predicting revision (P=.086). Pain was a good test for predicting revision THA (area under curve [AUC]=0.798; P<.001) (Figure 3); however, pain was not significantly useful for predicting positive findings on MRI (AUC=0.713; P=.131).

DISCUSSION

The purpose of this study was to investigate the correlation between the effects of Co ions, Cr ions, reactive tissue seen on MARS MRI, and/or patients’ stated pain

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DISCUSSION

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levels with the need for revision THA in patients who received primary THA with the Rejuvenate Modular Hip System.

The sample population in this study was largely male (69.7%), with an average age of 63.9 years at follow-up, which may not be representative of the general patient population undergoing THA. There were mean increases in ion levels for the cohort of patients requiring revision. Cobalt levels were higher than Cr levels on average, which is consistent with a previous case series for this implant. Unlike these previous reports, the current study compares ion levels in patients who underwent revision THA and those who were followed with observation. Differences in the serum Cr levels and patient pain levels between groups with and without evidence of reactive tissue on MRI approached significance (P=.083 and P=.060). Serum Co levels also differed between the group undergoing revision THA and the group followed with observation, but this also only approached significance (P=.076). The only analyzed variable, which was subjective, that showed statistical significance was the difference in pain scores between the group undergoing revision THA and the group not undergoing revision THA. Serum ion levels were not significantly correlated with pain.

These findings differ from previous studies of metal-on-metal bearing surfaces, where Co and Cr ion levels have shown to have better ROC characteristics while providing good specificity but poor sensitivity. This difference suggests that there is limited information and experience in managing patients with modular stems; therefore, further study is needed to develop meaningful and predictive algorithms in these cases.

Based on the current study’s results, there does not appear to be an objective finding with significance that can determine the need for patient revision due to fretting of modular hip stem systems. In the opinion of the authors, if an orthopedic surgeon is searching for an objective finding to assist with the decision-making process regarding revision THA, it is not serum Cr levels, serum Co levels, or MARS MRI reactive tissue findings.

This study has several limitations. First, this represents a single surgeon’s experience and may therefore differ based on varying indications for revision among surgeons. In addition, the number of patients included in this study (66) is relatively low and may have been underpowered for such an analysis. However, it is similar to the samples reported by other orthopedic surgeons studying Co and Cr levels in patients with modular hip stems. There were also limited follow-up MRI studies available for retrospective review. Lack of imaging studies may have prevented objective MRI results from reaching a level of significance. Also, because of the limited follow-up (less than 5 years), there may be crossover between groups because more patients develop symptoms and require the need for revision THA.

### Table 3

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean±SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No revision THA</td>
<td>3.48±2.99</td>
<td>.076</td>
</tr>
<tr>
<td>Revision THA</td>
<td>5.05±3.34</td>
<td>.083</td>
</tr>
<tr>
<td>Cr, µg/L</td>
<td>0.99±1.31</td>
<td>.756</td>
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<tr>
<td>No revision THA</td>
<td>1.09±1.06</td>
<td>.086</td>
</tr>
<tr>
<td>VAS pain score</td>
<td>2.4±2.45</td>
<td>&lt;.001</td>
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<tr>
<td>Revision THA</td>
<td>5.1±1.89</td>
<td>.076</td>
</tr>
</tbody>
</table>

**Abbreviations:** Co, cobalt; Cr, chromium; THA, total hip arthroplasty; VAS, visual analog scale.

#### Table 4

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean±SD</th>
<th>P</th>
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<tr>
<td>No revision THA</td>
<td>4.15±1.16</td>
<td>.635</td>
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<tr>
<td>Revision THA</td>
<td>5.01±3.40</td>
<td>.086</td>
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<tr>
<td>Cr, µg/L</td>
<td>0.46±0.43</td>
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<tr>
<td>No revision THA</td>
<td>1.32±1.41</td>
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<tr>
<td>VAS pain score</td>
<td>3.80±2.30</td>
<td>.060</td>
</tr>
<tr>
<td>Revision THA</td>
<td>5.63±1.51</td>
<td>.120</td>
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**Abbreviations:** AUC, area under curve; Co, cobalt; Cr, chromium; MARS, metal artifact reduction sequence; MRI, magnetic resonance imaging; VAS, visual analog scale.

#### Table 5

<table>
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<tr>
<th>Predictor</th>
<th>AUC</th>
<th>SE</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Revision</td>
<td>0.638</td>
<td>0.075</td>
<td>.086</td>
</tr>
<tr>
<td>Co</td>
<td>0.570</td>
<td>0.078</td>
<td>.373</td>
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<tr>
<td>Cr</td>
<td>0.588</td>
<td>0.149</td>
<td>.534</td>
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<tr>
<td>Positive MARS MRI</td>
<td>0.719</td>
<td>0.133</td>
<td>.120</td>
</tr>
</tbody>
</table>

**Abbreviations:** AUC, area under curve; Co, cobalt; Cr, chromium; MARS, metal artifact reduction sequence; MRI, magnetic resonance imaging; ROC, receiver operator characteristic; SE, standard error; THA, total hip arthroplasty.
revision surgery. Finally, the numeric rating scale of pain is a subjective measure, which may negatively affect these results. The inclusion of pain may confound results because increased pain would likely lead to an increased likelihood of undergoing revision THA.

**Conclusion**

Orthopedic surgeons must continue to search for improvements to assist with objective outcomes and patient satisfaction. Modular hip stem systems were one of these sought-after improvements that not only failed to provide improvement but also resulted in additional surgery and health care costs. Objective evidence is desired as a way to standardize the decision-making process regarding when to perform revision surgical intervention. Unfortunately, the current study shows no statistical significance with regard to objective variables when attempting to assist in the determination of whether a patient requires revision THA. Perhaps this provides additional confidence in the old adage: “Treat the patient and not the x-ray.”

**References**

29. Liow MH, Urish KL, Preffer FI, Nielson GR, Kwon YM. Metal ion levels are not correlated with histopathology of adverse local tissue reactions in taper corrosion of total hip arthroplasty [published online ahead of print February 4, 2016]. J Arthroplasty.